Heart Rhythm 2013

34th Annual Scientific Sessions

Late-Breaking Clinical Trials II

Four Seasons Ballroom 1

Friday, May 10, 2013

1:30 - 3 p.m.

SP22 Special Session: Late-Breaking Clinical Trials II

CHAIRS:

Andrea M. Russo, MD, FHRS, *Cooper University Hospital, Camden, NJ*

Gordon F. Tomaselli, MD, FHRS, *Johns Hopkins University - Div. of Cardiology, Baltimore, MD*

LB02-01

Percutaneous *In Vivo* Placement Of A Novel Intracardiac Leadless Pacemaker: Results From The First-in-man Leadless Study

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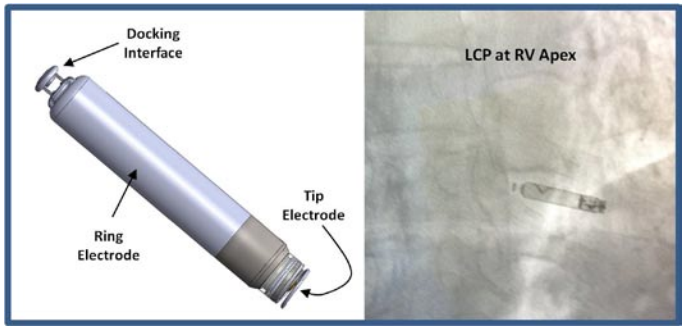
Introduction: While overall safe and effective, conventional pacemakers are limited by complications related to the pacing leads and generator pocket. A novel percutaneously-delivered leadless cardiac pacemaker (LCP) was developed to be implanted in the RV and function in a VVIR capacity with a battery life ~8 yrs. This multicenter trial evaluated the *in vivo* implantation of the LCP in patients requiring a permanent VVI(R) pacemaker.

Methods: In the prospective, non-randomized, single-arm LEADLESS study, non-pacemaker dependent patients requiring a VVI(R) pacemaker were enrolled. The study evaluated safety of the device as a primary end-point and assessed device performance including: RV pacing function, battery longevity, rate response, implant success rate and implant times as secondary endpoints. A single-turn helix affixes the LCP (Nanostim, Inc) to the endocardium. The LCP's proximal end has a docking feature for repositioning and retrieval capability. The pacemaker senses RV blood temperature to provide an increase in pacing rate with increased metabolic demand. The LCP was implanted in the RV via femoral venous access using a deflectable delivery catheter under x-ray guidance through an 18Fr sheath. Pacing/sensing thresholds were determined at baseline prior to device release; if sub-optimal, the device was repositioned. The LCP performance was evaluated post-implant at 2 d, 2 wks, 6 wks and 3 mos. After release, a retrieval catheter could be used to remove the LCP using the docking interface (see Figure).

Application: Results demonstrating safety, performance and ease of use in this study can help provide an alternative to conventional pacemaker therapy eliminating the need for leads and the surgical pocket. (Results will be available in May 2013.)

Next Steps/Future: This first-in-man study demonstrates the feasibility, safety and efficacy of a leadless cardiac pacemaker for right ventricular pacing. Pre-clinical studies with implanted defibrillator leads have also demonstrated the capability for the technology to evolve to include: dual chamber, CRT and bi-ventricular pacing. Long-term follow-up will offer comparison to conventional pacemakers.



LB02-02

Eighteen Month Results From The Prospective Registry And Follow-up Of Patients Using The Lifevest Wearable Defibrillator (WEARIT-II Registry)

Ilan Goldenberg, MD, Helmut Klein, MD, Wojciech Zareba, Steve Szymkiewicz, MD, Chingping Wan, MD and Arthur Moss. University of Rochester Medical Center - Heart Research Follow-up Program, Rochester, NY, Zoll, Pittsburg, PA

Introduction: Many patients potentially eligible for an implantable cardioverter defibrillator (ICD) present with a transient or undefined arrhythmic risk. In this patient subset the Wearable Carioverter Defibrillator (WCD) provides continuous arrhythmia monitoring and automatic defibrillation within a minute of detection of a potentially fatal ventricular tachyarrhythmia. The WEARIT-II Registry was designed to provide prospective data on the safety and efficacy of this bridging strategy.

Methods: WEARIT-II is an ongoing prospective follow-up Registry of patients prescribed the WCD in the US. Outcomes measures included clinical and arrhythmic events, appropriate and inappropriate WCD discharge, and the need for an ICD following termination of WCD usage. The study was approved by the Institutional Review Board and all patients gave written informed consent for participation.

Application: Between August 2011 and March 8 2013, 758 patients who were prescribed a WCD in the US were enrolled into the Registry. Mean age was 60 ±12 yrs and 32% were women. Dilated cardiomyopathy was present in 520 (69%) of patients (61% ischemic and 39% nonischemic), with a mean left ventricular ejection fraction (LVEF) of 25% (±11%). A WCD

was prescribed for inherited arrhythmias in 95 (13%) of patients. The average WCD wearing days was 80 ± 51 days with an average daily use of 21 ± 3 hours. Arrhythmia data from WCD interrogations by indication are presented in the Table below. A total number of 67 sustained ventricular tachyarrhythmic events occurred in 16 patients, corresponding to a rate of 40 sustained episodes per 100 person-years, whereas the rates of inappropriate WCD therapy and death were low (0.4% and 0.5%, respectively). Upon termination of WCD use (n=594) 251patients (42%) received an ICD. The most frequent reason for a decision not to implant an ICD following WCD usage was improvement in LVEF (39%).

Next Steps/Future: Our findings from the WEARIT-II Registry suggest that in a real world setting a management strategy that incorporates the WCD can be safely used to bridge a decision for appropriate ICD therapy. The ongoing WEARIT-II US Registry is currently extending to Europe and Israel.

Summary of arrhythmia data detected by the WCD

Arrhythmia type	Total number of events	Event rate (per 100 patient years)	
		Patients with Cardiomyopathy	Patients with Inherited Arrhythmias
Appropriate WCD therapy for fast VT/VF	15	9	42
Sustained VT spontaneously terminated without WCD therapy (use of device response button)	52	42	120
NSVT	92	65	60
Atrial fibrillation /SVT	106	72	133

LB02-03

Ablation Of Symptomatic Paroxysmal Atrial Fibrillation Using Novel Contact Force Catheter: SMART-AF Trial

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Introduction: Catheter ablation is important for treatment of paroxysmal atrial fibrillation (PAF) Animal studies suggest a correlation between electrode-tissue contact and radiofrequency (RF) lesion generation Theoretical benefits of contact force (CF) sensing technology include feedback to user of adequate tissue contact to guide safe and effective lesions On behalf of the SMART-AF investigators, we report on outcomes of PAF ablation using the THERMOCOOL® SMARTTOUCH™ catheter

Methods: Prospective, multicenter, non-randomized study Enrollment criteria included > 3 symptomatic episodes of PAF within 6 months of enrollment and failure of ≥ 1 AAD (Class I - IV) Patients with AF > 30 days in duration, age < 18, or ejection fraction < 40% were excluded Ablation included pulmonary vein isolation with confirmed entrance block as procedural endpoint Primary effectiveness endpoint was freedom from documented symptomatic AF, atrial tachycardia (AT), or atrial flutter (AFL) episodes through 12-month follow-up, without AAD change or repeat ablation after 3-month blanking period

Results: A total of 172 subjects were enrolled at 21 sites (mean age = 59 ±11 0 years, 72 1% male, 95 9% Caucasian), where 161 subjects had study catheter inserted and 160 subjects underwent RF application Excluding 38 roll-in subjects, 122 subjects were evaluated for effectiveness Medical history included hypertension (59%), structural heart disease (19%), and diabetes (12%) Mean left atrial diameter=38 6 ± 6 1 mm AFL history was present in 31% Mean number of symptomatic AF episodes in the 6 months prior to enrollment=42 ± 90 (median=15, range 3-800) Procedure-related serious adverse events (AEs) occurring within 7 days of the procedure, as adjudicated by an independent safety committee, included tamponade (4), chest pain (1), pericarditis (2), heart block (1, prior to RF application), and vascular access complications (3) By Kaplan-Meier analyses,12-month freedom from AF/AFL/AT recurrence=71 9%, with protocol adjudicated success=69 4% due to AAD changes in 3 subjects The average CF/procedure=17 9± 9 4g, and average percent of time CF was within investigators' selected ranges=73 5±18 2% Freedom from AF/AFL/AT recurrence (84 4% vs 65 1%, p=0 025) and protocol adjudicated success (83 7% vs 60 7%, p=0 011) were higher in procedures where CF was within investigator-selected range >82% of the time

Conclusion: Preliminary analysis showed that primary effectiveness and safety endpoints were met, with no unanticipated device-related AEs Increased percent of time within investigator-targeted CF ranges correlates with

increased freedom from arrhythmia recurrence and protocol-adjudicated success

LB02-04

Progression of atrial Fibrillation After A Failed Initial Ablation Procedure In Patients With Paroxysmal Atrial Fibrillation: A Randomized Comparison Of Antiarrhythmic Drug Therapy Vs Re-ablation

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Introduction: Antiarrhythmic drugs (AAD) are generally used as first-line therapy to treat patients with atrial fibrillation (AF), but effectiveness remains inconsistent. Catheter ablation has become an alternative therapy for patients with paroxysmal (P)AF, but patients may recur and receive AAD. The aim of this prospective, randomized study was to assess if an early re-ablation is superior to AAD therapy (control) in patients with previous failed pulmonary vein isolation (PVI) PAF, by means of the diagnostic data stored in a subcutaneous AF monitor.

Methods: Patients with a history of symptomatic PAF eligible for AAD therapy or re-ablation after a previous failed initial ablation procedure involving only PVI were eligible for this study. Patients were randomized to AAD therapy or re-ablation procedure using a coded envelope system and were followed for 3 year to assess rhythm by means of an implanted cardiac monitor.

Results: 154 patients had symptomatic AF recurrences after the blanking period post-ablation and were randomized to AAD therapy (propafenone, flecainide and/or sotalol; N = 77) and to re-ablation (N = 77). At the end follow-up, 61 (79%) patients in AAD group and 19 (25%) patients in re-ablation group demonstrated AF% progression (increasing AF burden >30% from before randomization; p<0.01). In AAD group AF% significantly increased compared with patients of re-ablation group: at 36 months AF% was 18.8±11.4% vs 5.6±9.5%, respectively (p<0.01). In addition, 18 (23%) patients in AAD group and 3 (4%) patients in re-ablation group progressed to persistent AF (p<0.01). Moreover, 45 (58%) of the 77 re-ablation group patients became AF/AT-free on no antiarrhythmic drugs; in contrast, in the AAD group, only 9 (12%) of the 77 patients were AF/AT-free (p<0.01).

Conclusions: In this prospective randomized controlled clinical trial, redo AF ablation was substantially more effective than AAD in reducing the progression and prevalence of AF after the failure of an initial ablation based on information derived from an implanted monitoring device.

LB02-05

Clinical Significance Of Short AT/AF Episodes: Results From The Registry Of Atrial Tachycardia And Atrial Fibrillation Episodes In The Cardiac Rhythm Management Device Population (RATE)

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Introduction: The clinical implications of atrial tachycardia and fibrillation (AT/AF) < 5 min in duration remain uncertain. The “RATE Registry” was designed to follow 5,000 patients (pts), with no history of AT/AF over the prior 3 months, for 2 years after implant of a pacemaker (PM) or ICD. Device-reported data are less reliable when episodes of AT/AF last <5 minutes. It is only possible to make reliable conclusions about short episodes when detailed adjudication of electrograms (EGMs) is done. We have, therefore, adjudicated more than 35,000 EGMs. Hypotheses tested: 1) short AT/AF episodes are associated with adverse clinical outcomes; 2) short AT/AF episodes confer a high risk of subsequent longer episodes.

Methods: All EGMs were evaluated in 600 randomly selected pts (300 PM and 300 ICD) by teams of 2 adjudicators, documenting all rhythms and AT/AF characteristics (duration, rate, regularity and morphology) to provide 95% confidence of defining the true AT/AF incidence. All EGMs from pts with a pre-specified clinical event or death during follow up (f/u) as well as from a 2:1 case-control match of these pts were also adjudicated. Short episodes of AT/AF were categorized by their length: 20 beats, but with onset and offset within the same EGM. Long AT/AF episodes were defined when the onset and/or offset of AT/AF was not present in the same EGM.

Application: Between 2007 and 2012, 5,379 pts were enrolled (3,141 with PMs and 2,238 with ICDs), 61.7% male; age 70 ± 13 years and CHADS2 score of 2 ± 1. Median f/u was 23 months. Interobserver agreement ranged from 95.2% for AT/AF presence, to 84.1% for AT/AF morphology. From the random sample, 49.8% of pts (49% of PM, 51% of ICD) had at least one EGM demonstrating AT/AF. Only short AT/AF episodes were documented in 12% of pts. There were 359 deaths and 478 hospitalizations (333 pts) for predefined clinical events, including AT/AF (78 pts), heart failure (183 pts), stroke or TIA (45 pts), cardiac syncope (11 pts), and ventricular

arrhythmia (42 pts). Detailed characterization of short AT/AF episodes was undertaken based on manual adjudication of EGMs, and correlation with adjudicated clinical events.

Next Steps/Future: In this study with more pts, longer f/u, and more events by far than prior studies, we will report whether short episodes of AT/AF in PM/ICD pts predicted clinical events as well as transition to longer AT/AF episodes. In contrast to prior studies, we will characterize these short AT/AF episodes based on visual adjudication, and describe their morphological types and clinical associations. Our conclusions will have considerable importance for clinical practice, as no current guidelines specify how to manage these pts with short AT/AF episodes.

LB02-06

Putting Evidence Into Practice: Shock Reduction Results From 4,131 Patients In The Prospective Shock-less Study

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Background: ICD shocks are associated with increased anxiety, healthcare utilization, and mortality. However, published programming strategies to safely avoid unnecessary shocks are often not used in clinical practice. Shock-Less showed that giving clinicians a site-specific report displaying their ICD programming improved usage of evidence-based recommendations by up to 20%. Our objective was to determine if this behavior change is associated with a reduction in shocked episodes in a real-world setting.

Methods: Primary (PP) and secondary prevention ICD patients (pts) were enrolled between 2009 and 2012 at 118 sites. Clinicians received reports starting 9 months after their first enrollment. The reports displayed their parameter settings in relation to evidence-based targets: number of intervals to detect VF, longest treatment interval, SVT discriminators, Lead Integrity Alert, and anti-tachycardia pacing. Clinicians programmed ICDs at their discretion. An independent committee adjudicated shocked episodes as appropriate or inappropriate. The primary outcome was time to first all-cause shock. Pts enrolled AFTER the first report were compared to pts enrolled BEFORE (censored at 1st visit after report to avoid bias) using Kaplan-Meier and Cox models adjusting for factors shown to be associated with shocks.

Application: There were 2693 pts implanted BEFORE the first report and 1438 AFTER. Pts were 85% PP with a median follow-up of 1 year. At least 1 shocked episode occurred for 265 pts (10%) in the BEFORE cohort and 116 pts (8%) in the AFTER cohort. Pts implanted after a site received its first report had a 27% relative risk reduction in shocked episodes (HR=0.73, 95% CI: 0.58-0.91, p=0.005). The reduction remained significant when adjusted for covariates (HR=0.71, p=0.003). Hazard ratios for appropriate and inappropriate shocks were both 0.73.

Next Steps/Future: In real-world practice, providing clinicians with reports that improved adherence to evidence-based shock reduction programming was associated with reduced risk of ICD shocks. Establishing methods that improve clinician adherence to evidence-based programming is crucial to reducing ICD patient morbidity and potentially mortality.