Late-Breaking Clinical Trials II

Room 305, Moscone South

Friday, May 09, 2014

8 – 9:30 a.m.
LBCT02 Session: Late-Breaking Clinical Trials II

Friday, May 9, 2014
8-9:30 a.m.

CHAIRS:
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LB02-01

CHRONIC PERFORMANCE OF LEADLESS CARDIAC PACING: ONE YEAR FOLLOW-UP TO THE LEADLESS TRIAL

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Introduction: While highly reliable, conventional cardiac pacemakers are limited by potential short and long-term complications related to either the transvenous lead (the weakest link of the pacing system) or the subcutaneous pulse generator. The leadless cardiac pacemaker (LCP) eliminates the transvenous lead, subcutaneous pocket and intra-system connections, since the pulse generator and sensing/pacing electrodes are fully contained within a single unit. In a prospective, multicenter, non-randomized study, we reported the feasibility of LCP implantation, and short-term (3 months) stability of measures of pacing performance. However, the chronic stability and performance of leadless pacemakers is unknown.

Methods: Thirty-three patients with an indication for single-chamber (ventricular) pacing were enrolled. Patients were implanted between December 2012 and April 2013. The Nanostim LCP (St. Jude Medical, St. Paul MN) was delivered to the right ventricle using a deflectable delivery catheter and affixed to the myocardium using a distal single-turn (screw-in) steroid-eluting helix. The nominal pacing amplitude and sensing thresholds were 2.5 V and 2.0 mV, respectively. The implant success rate was 97% (n = 32/33), the mean procedure duration was 28 ± 17 minutes, the average time to hospital discharge was 31 ± 20 hours and the overall complication-free rate was 94% (n = 31/33). All successfully implanted patients will be followed for one-year.

Application: The investigators will report the performance results of leadless cardiac pacemaker for all patients at one year of follow-up. Measures of lead performance will include sensing (R-wave amplitude), pacing threshold and impedance, as compared to the original implant. Additional data to be reported will include burden of pacing, rate-responsiveness operation, estimated battery longevity and any changes in clinical condition.

Next Steps/Future: The one-year results of the LEADLESS trial will shed light on the chronic safety and feasibility of leadless cardiac pacing. Leadless cardiac pacemakers represent a paradigm shift in cardiac pacing, but their widespread adoption is dependent on their chronic performance and reliability.

LB02-02

BOTULINUM TOXIN INJECTION IN EPICARDIAL FAT PADS CAN PREVENT RECURRENTS OF ATRIAL FIBRILLATION AFTER CARDIAC SURGERY: RESULTS OF A RANDOMIZED PILOT STUDY

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Introduction: Animal models suggest that botulinum toxin injection into the epicardial fat pads suppressed atrial fibrillation (AF) inducibility. The aim of this prospective randomized double-blind study was to compare the efficacy and safety of botulinum toxin injection into epicardial fat pads for preventing atrial tachyarrhythmias in patients with paroxysmal atrial fibrillation undergoing CABG surgery.

Methods: Patients were randomized to botulinum toxin (Xeomin, Germany; n=30) or 0.9% normal saline (control; n=30) injection into epicardial fat pads. Patients were followed for 30 days to assess maintenance of sinus rhythm.

Application: There were no significant differences between the groups in the median time until extubation, or intervals from end of surgery to eligibility for and to actual discharge from the ICU (all P > 0.05). There were no significant differences in CK-MB levels in the postoperative period. Postoperative AF occurred in 2 (7%) of 30 patients in the botulinum toxin group and in 9 (30%) of 30 patients in the placebo group (log-rank test P=0.024). There was no significant difference in the postoperative hospital length of stay between groups (P=0.12), with a median (25th-75th percentile) length of stay of 6 (5-8) days in the botulinum toxin group versus 6 (4-8) days in the placebo group. Other postoperative complications, including death, were similar between groups (all P > 0.05).

Next Steps/Future: Botulinum toxin injection in epicardial fat pads provided atrial tachyarrhythmia suppression after cardiac surgery without any serious adverse events.

ATRIAL FIBRILLATION PATIENTS WITH CONTRAINDICATIONS TO ORAL ANTICOAGULATION THERAPY TREATED WITH LAA LIGATION: INITIAL LONG-TERM CLINICAL OUTCOMES

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Introduction: LAA ligation with the LARIAT suture delivery device has been used to prevent thrombus formation within the LAA in atrial fibrillation (AF) patients at high risk of thromboembolic events that have contraindications to oral anticoagulation (OAC) therapy. We report the initial clinical follow up in patients with contraindications to OAC therapy who underwent LAA ligation and post-ligation who were treated with only aspirin or aspirin and clopidogrel post-procedure.

Methods: 140 consecutive AF patients with contraindications/intolerances to OAC therapy underwent attempted LAA ligation between December of 2010 and February 2012. LAA closure was verified by LA angiography and TEE. Patients had a follow up TEE between 30-45 days. Post-LAA ligation, patients were treated with only ASA, ASA plus clopidogrel or no anti-thrombotic drugs. No patients were threatened with OAC therapy post-LAA ligation. Patients have been followed prospectively for LAA closure, adverse events, stroke, cardiovascular death and total mortality. 136 of 140 patients with an average CHADs2 score of 2.8 underwent LAA ligation. All four of the unsuccessful LAA ligation patients had pericardial adhesions. 135 of 136 patients had 100% acute LAA closure. The unsuccessful patient had a multi-lobed LAA in which one lobe was not fully closed. There were no device complications. Procedural complications included 2 patients who required surgery due to RV puncture/laceration. There was one peri-procedural death occurring at post-op day 2 due to a pulmonary embolus. Pericarditis occurred in 8 patients. At the 30-45 day follow up TEE, 112 of 122 (92%) patients had complete closure (< 1 mm leak), 9 of 122 patients (7%) had between a 2 mm leak to 4 mm leak. 14 patients refused follow up TEE. There was one patient who had an embolic stroke after 3 months. This occurred in the patient in which one lobe was not closed. Another patient had a presumed embolic stroke at 18 months. There were 2 additional non-embolic strokes occurring at 1 month and after 6 months. There were 3 non-device/procedure related deaths occurring after 6 months. Average follow-up was 22 months.

Application: LAA ligation effectively excludes the LAA in the majority of patients with acceptable procedural adverse events. The low incidence of embolic events in this high-risk AF population following LAA ligation suggests that LAA ligation may be a protective option in preventing thromboembolic events in patients who have contraindications to oral anticoagulation therapy.

Next Steps/Future: The results of the study provide the rationale, efficacy rates and safety profile to help develop a prospective, multi-center randomized stroke study in AF patients with contraindications/intolerances to OAC therapy.

BASELINE CHARACTERISTICS, OUTCOMES, AND COMPARISON OF EDOXABAN VS WARFARIN BY AF SUBTYPE IN 21,105 PATIENTS ENROLLED IN THE ENGAGE AF-TIMI 48 TRIAL

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Introduction: Prior studies suggest the risk of stroke is similar across patterns of AF (paroxysmal, persistent, permanent), while less data are available on the risk of bleeding by AF subtype. The ENGAGE AF-TIMI 48 trial showed that both high and low doses of the once-daily oral Factor Xa inhibitor edoxaban were non-inferior to warfarin to prevent stroke and
systemic embolic events (SEE) and caused less bleeding, but detailed analyses by AF subtype have not been reported.

**Methods:** We categorized 21,105 patients enrolled in ENGAGE AF-TIMI 48 as having paroxysmal (<7 days duration), persistent (≥ 7 days but < 1 year), or permanent (≥ 1 year or failed cardioversion) AF based on the randomization ECG. All patients had AF recorded in the prior 12 months and CHADS2 score ≥ 2+. We evaluated clinical efficacy and safety outcomes during the 2.8 years median follow-up and compared results by AF subtype. We explored treatment interactions by AF subtype for the primary (efficacy = stroke/SEE; safety = ISTH major bleeding) and key secondary trial endpoints.

**Application:** Patients with paroxysmal AF were more likely women, had fewer risk factors for stroke, and were more likely on concomitant aspirin and amiodarone (Table). The individual rates of stroke/SEE, ischemic stroke, CV death, and all-cause mortality were lower with paroxysmal AF. There were no differences in hemorrhagic stroke by AF subtype. Rates of major bleeding were similar across AF subtypes, but less severe bleeding endpoints (clinically relevant non-major [CRNM], all bleeding) were increased in patients with paroxysmal AF. The efficacy and superior safety profile of edoxaban as compared to warfarin was preserved across the subtypes of AF.

**Next Steps/Future:** In a large RCT of patients with AF treated with anticoagulation, differences in baseline characteristics only partially explain why outcomes vary by AF subtype. Therapies such as edoxaban that reduce bleeding compared to warfarin, while maintaining efficacy to prevent stroke (as seen in ENGAGE AF-TIMI 48), may be especially attractive in patients with paroxysmal AF, as these patients appear to be at higher risk of non-major bleeding and lower risk of ischemic stroke and death.

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**LB02-05**

SAFETY AND EFFICACY OF LEFT VENTRICULAR ENDOCARDIAL LEAD PACING FOR CARDIAC RESYNCHRONIZATION THERAPY: PRIMARY RESULTS OF THE ALTERNATE SITE CARDIAC RESYNCHRONIZATION (ALSYNC) STUDY

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**Introduction:** Cardiac resynchronisation therapy (CRT) reduces mortality/heart failure decompensation and improves quality of life in indicated patients. However, many do not benefit due to failure to deliver the left ventricular lead (LV) (5%–10%) via coronary sinus or lack of symptomatic improvement (~30%). We investigated the safety and efficacy of LV endocardial (LVE) pacing using a Model 3830 lead delivered using a novel atrial transeptal system.

**Method:** ALSYNC is a non-comparative, non-randomised, prospective clinical study with a minimum of 12 months follow up in 16 European and 2 Canadian centers. Patients enrolled were indicated for CRT but had failed a conventional implant attempt or were non-responders at least six months post-implant. The ALSYNC system comprises a deflectable catheter, a pre-shaped inner catheter, an RF-powered transseptal puncture guidewire, and dilator. The system enables a subclavian approach and targeted LVE lead delivery. Post implant, patients receive long term warfarin therapy (target INR 3). The primary study objective is safety assessment of the system at 6 months follow-up defined as a complication rate < 30% related to the lead delivery system, implant procedure and the 3830 lead.

**Application:** ALSYNC enrolled 138 patients (78% male, 68 years, 40% ischemic, 50% prior AF), 78% due to failed prior implant and 22% due to non-response. Successful LVE pacing was achieved in 118 out of 133 (89%) attempts. With 75% patients having completed 6 month follow-up, ALSYNC lead delivery system, implant procedure and LV lead-related complication rate is 17%. At 6 months, 57% of patients improved in NYHA class and 56% improved in LVESV≥15%. Of the patients enrolled due to conventional system non-response, 48% improved in NYHA class and 53% improved in LVESV≥15% at 6 months follow-up. Ischemic stroke (1 patient with suboptimal anticoagulation) and transient ischemic attacks were observed (table) but none led to a persisting neurological deficit.

**Next Steps/Future:** Our preliminary findings show a high
proportion of patients receiving CRT benefit from LVE pacing who otherwise have limited heart failure therapy options.

LB02-06

POINT BY POINT RADIOFREQUENCY ABLATION VERSUS THE CRYOBALLOON OR A NOVEL COMBINED APPROACH: A RANDOMIZED TRIAL COMPARING THREE METHODS OF PULMONARY VEIN ISOLATION FOR PAROXYSMAL ATRIAL FIBRILLATION (THE CRYO VERSUS RF TRIAL).

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Introduction: Catheter ablation of paroxysmal AF using the Cryoballoon (CRYO) has yielded similar success rates to conventional wide encirclement using radiofrequency ablation (RF), but randomised data are lacking. Pilot data suggested a higher success rate with a combined approach (COMBINED) than with either modality alone. We compared the success rate with these 3 strategies in a randomized controlled trial.

Methods: Patients undergoing first time paroxysmal AF ablation were randomised to RF, CRYO or COMBINED. Pulmonary vein (PV) electrical isolation confirmed using a circular mapping catheter was the procedural end-point for all cases. The RF group underwent wide encirclement of the PVs using an irrigated radiofrequency ablation catheter guided by a 3D mapping system. Contact force sensing catheters were not used. The CRYO group underwent ostial PV ablation using the Arctic Front cryoballoon. If PV isolation could not be achieved using the cryoballoon alone then further point by point lesions were added. The COMBINED group underwent wide encirclement of the PVs to achieve PV isolation, followed by 2 empirical applications of the cryoballoon to each PV ostia. Patients were followed up at 3, 6 and 12 months with 7 days of ambulatory ECG monitoring. The primary end point was the 1 year success rate, defined as freedom from arrhythmia following the 3 month blanking period off antiarrhythmic drugs after a single procedure.

Application: 237 patients were randomised. Success at 1 year was achieved in 47% in the RF group, 67% in the CRYO group, and 76% in the COMBINED group at 1 year (p = 0.015 for RF versus CRYO, p < 0.001 for RF versus COMBINED, and p = 0.166 for CRYO versus COMBINED). Procedure time was 211 (IQR 174-256) minutes for RF compared to 167 (136 - 202) minutes for CRYO and 278 (243 - 327) minutes for COMBINED (p < 0.001 for RF versus COMBINED, RF versus CRYO, and CRYO versus COMBINED groups). In the Cryo group, 69% of patients had all PVs isolated with the Cryoballoon alone, the remainder required point by point ablation to achieve PV isolation. There were 4 complications in the CRYO group (all phrenic nerve palsies), 4 in the RF group, and 3 in the COMBINED group. All 6 phrenic nerve palsies across the CRYO and COMBINED groups recovered (median recovery time 8.5 months, range 3-17).

Next Steps/Future: PV isolation for paroxysmal AF is faster with CRYO and results in a higher single procedure success rate than wide encirclement using conventional point by point RF ablation. The COMBINED approach was not superior to CRYO alone. Multicenter trials are needed to confirm whether CRYO is superior to RF.

Clinical Trials Registration: NCT01038115