Late-Breaking Clinical Trials I

Ballroom West

Thursday, May 14, 2015

1:30 - 3 p.m.
LBCT01-01
IMPACT OF REMOTE MONITORING ON CLINICAL EVENTS & HEALTHCARE UTILIZATION: A NATIONWIDE ASSESSMENT

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Introduction: Randomized and observational data indicate remote monitoring (RM) improves patient survival. However, it is unknown whether RM reduces healthcare utilization (HCU).

Methods: We investigated whether RM was associated with reduced all-cause clinical events and HCU costs, using a large real-world cohort from MarketScan® Commercial and Medicare Supplemental (MS) claims databases. Patients (pts) ≥21 years implanted with a pacemaker (PPM), ICD, or CRT, between 4/2008-3/2013, with ≥12 months MS enrollment before and after implant were included. Patients without follow-up (FU, clinic or RM), within 120 days after implant were excluded. Cohort was dichotomized on RM use. Device FU regimens and HCU (hospitalization events and costs) were determined from claims after implant. The hazards of these events were compared in RM+clinic vs clinic-only FU methods using negative binomial regression accounting for demographics and comorbidities.

Application: We evaluated 61,717 pts (72 ± 13 yrs, 63% male) with PPM (n=36,497, 60%), ICD (n=18,991, 31%), or CRT (n=6,229, 10%). Only 46% of patients used RM, these had less frequent clinic FU (but more frequent FU when inclusive of RM) than pts without RM, measured as mean time interval between FU (MIBF, months, Table.) Patients with RM had lower all-cause hospitalization (hosp) costs ($/pt-yr) and fewer hosp (events/pt-yr) for every device type (Table.) For all types, the adjusted hosp hazard ratio [HR] is 0.84, p<0.001. Reduced risks of hosp were prominent in those with heart failure (n=13,662, adjusted HR 0.79, p<0.001) and atrial fibrillation (n=27,207, adjusted HR 0.85, p<0.001). RM was also associated with fewer hosp days compared to clinic only follow-up (195 vs 266 per 100 pt years, p<0.001.)
Next Steps/Future: For pts on a regular FU regimen RM is associated with reduced HCU, irrespective of device type. On average, utilization of RM avoids 8.9 hospitalizations, 70.6 hospital days and saves $196,800 per 100 pt-year. Since fewer than half of patients routinely utilize RM, this represents a major opportunity for quality improvement. Determinants of RM adoption (patient and physician factors) and mediators between RM use and HCU require further elucidation.

**LBCT01-02**

**VENTURE-AF: A RANDOMIZED GLOBAL TRIAL EVALUATING UNINTERRUPTED RIVAROXABAN AND VITAMIN K ANTAGONISTS IN PATIENTS UNDERGOING CATHETER ABLATION FOR NONVALVULAR ATRIAL FIBRILLATION**

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**Introduction:** The uninterrupted vitamin K antagonist (VKA) strategy for catheter ablation (CA) of atrial fibrillation (AF) has been shown to be safe and continues to gain acceptance globally as a preferred approach. Although several observational studies suggest the practicality of using a novel oral anticoagulant (NOAC) periprocedurally, there is a general consensus that the need exists for a more rigorous evaluation of the use of uninterrupted NOACs in this setting. This is the first randomized study to evaluate the safety and efficacy of uninterrupted rivaroxaban and uninterrupted VKA therapy in patients with nonvalvular (NV) AF undergoing CA.

**Methods:** This was a global-multicenter, phase 3b, randomized (1:1), open-label, active-controlled study in AF patients undergoing CA with uninterrupted rivaroxaban or uninterrupted VKA. Up to 5 weeks prior to CA, patients with NVAF were assigned to either uninterrupted rivaroxaban 20 mg once-daily or to uninterrupted VKA and study drugs were continued for 30 days after CA. The primary endpoint was major bleeding events up to 30 days after CA. Secondary endpoints included the occurrence of thromboembolic events (myocardial infarction, stroke, systemic embolization, or vascular death), other bleeding events and other adverse events (AEs). Endpoints were adjudicated by an independent blinded CEC using GUSTO, ISTH, and TIMI bleeding criteria.

**Application:** A total of 248 patients were randomized at 46 sites in 5 countries. A total of 221 patients underwent CA. No patients were lost to follow-up. The average age was 59.5 ± 10 (SD) years, the estimated mean CHA2DS2-VASc was 1.6 and the diagnosis of paroxysmal AF was present at baseline in 73.4% of the patient population. For the period during and following CA, there was 1 ISTH major bleeding event in the VKA treatment group and no GUSTO severe/life threatening or TIMI major bleeding events. There was 1 ischemic stroke and 1 vascular death event in the VKA treatment group. The numbers of any-bleeding and procedure-attributable events were similar for rivaroxaban and VKA (17 vs. 18; and 17 vs. 19, respectively). The majority of bleeding events were mild or insignificant. For patients taking ≥ 1 dose of study drug, the numbers of patients with a serious AE were comparable (17[13.8%] for rivaroxaban vs. 20[16.5%] for VKA).

**Next Steps/Future:** Uninterrupted rivaroxaban appears to be a safe alternative to VKA in patients undergoing CA for NVAF.

**LBCT01-03**

**CRYOBALLOON VERSUS OPEN IRRIGATED RADIOFREQUENCY ABLATION IN PATIENTS WITH PAROXYSMAL ATRIAL FIBRILLATION: THE PROSPECTIVE, RANDOMIZED CONTROLLED, NON-INFERIORITY FREEZEAF STUDY**

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**Background:** There are only a few studies comparing pulmonary vein isolation (PVI) using open irrigated radiofrequency energy ablation (RF) versus the cryoballoon ablation (Cryo) for patients with paroxysmal atrial fibrillation (PAF).

This is the first large prospective, randomized controlled, non-inferiority study comparing the effectiveness and safety of the Cryo versus RF energy for PVI in patients with PAF. The study
design was published in the American Heart Journal, 2010; 159(4), 555-560. ClinicalTrials.gov Identifier: NCT00774566

**Methods:** 322 P receiving PVI were randomized to either Cryo (n=156) or RF (n=159) ablation. Inclusion criteria were documented symptomatic PAF and at least one failed antiarrhythmic drug therapy (incl. β-blocker) (AAD). Primary endpoint was freedom of PAF without AADs and without persistent complications at 6 and 12 months. Clinical follow-ups were at 3,6,9 and 12 months, Holter ECG and event recordings for at least 7-14 days were performed at 6 and 12 months. All PAF episodes > 30sec were considered as a failure. Redo-procedures were only allowed after the 6 months follow-up using the same energy source. Secondary endpoints include the mid- and long-term clinical success, procedural data and safety parameters. MRI/CT scans were performed before and after 3 months to scan for PV stenosis in all patients.

**Results:** 315 P with PAF were analyzed (59.8 ± 8.6 years, 191 female). Baseline characteristics were similar in both groups. Follow-up was completed at 6 months in 98.4% and at 12 months in 92.4%. Redo-procedures were performed in 19.9% in the Cryo and 19.5% in the RF group. Procedure success rates for the intention to treat population at 6 months and 12 months were 63% and 68% for Cryo and 64% and 65% for the RF group, respectively. P-values for the non-inferiority margin were at 6 months p=0.011 and at 12 months p=0.001. P-values for the per protocol analysis at 6 months and 12 months are p=0.009 and p=0.002 respectively. Complications: No cardiovascular death and no stroke/TIA occurred; Phrenic nerve palsy occurred in 5.1% and 0% and PV stenosis 0% and 1.9% for Cryo and RF, respectively.

**Conclusion:** This large prospective, randomized controlled study demonstrates the non-inferiority of the Cryo ablation versus RF ablation in Ps with PAF.

**LBCT01-04**

**BOTULINUM TOXIN INJECTION IN EPICARDIAL FAT PADS FOR PREVENTION OF ATRIAL FIBRILLATION AFTER CARDIAC SURGERY: ONE YEAR FOLLOW UP OF RANDOMIZED PILOT STUDY**

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**Background:** Animal models suggest that the neurotransmitter inhibitor, botulinum toxin, when injected into the epicardial fat pads can suppress 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 (P) AF undergoing coronary artery bypass graft (CABG) surgery.

**Methods and Results:** Patients with history of PAF and indication for CABG were randomized to botulinum toxin (Xeomin, Merz, Germany; 50 U/1 mL at each fat pad; n=30) or placebo (0.9% normal saline, 1 mL at each fat pad; n=30) injection into epicardial fat pads during surgery. Patients were followed for 1-year to assess maintenance of sinus rhythm using an implantable loop recorder (ILR). Patients were well matched for clinical and surgical characteristics. All patients in both groups had successful epicardial fat pad injections without complications. The additional time during CABG for injection was 11 ± 6 mins. The incidence of early postoperative AF within 30 days after CABG was 2 of 30 patients (7%) in the botulinum toxin group and 9 of 30 patients (30%) in the placebo group (P=0.024). Between 30 days and up to the 12-month follow-up examination, 7 of the 30 patients in the placebo group (27%) and none of the 30 patients in the botulinum toxin group (0%) had recurrent AF (P=0.002). During 12-month follow-up, the mean AF burden on the ILR was significantly reduced by botulinum toxin compared to placebo, 0.07±0.1% vs 1.5±0.6%, respectively (p<0.001). There were no complications observed during the 1-year follow-up.

**Conclusion:** Botulinum toxin injection into epicardial fat pads during CABG provided substantial atrial tachyarrhythmia suppression both early as well as during 1-year of follow-up, without any serious adverse events. Clinical Trial Registration URL: http://www.clinicaltrials.gov. Unique identifier: NCT01842529
LBCT01-05

WIRELESS LV ENDOCARDIAL STIMULATION FOR CRT: PRIMARY RESULTS OF THE SAFETY AND PERFORMANCE OF ELECTRODES IMPLANTED IN THE LEFT VENTRICLE (SELECT-LV) STUDY

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Introduction: Indicated patients do not benefit from conventional CRT (ConCRT) because of lead issues such as an inability to place the CS lead or lack of clinical improvement with CRT. LV endocardial pacing has been proposed as a potential solution. We assessed the safety and performance of the novel Wireless Cardiac Stimulation System, WiCS-LV, to provide endocardial LV stimulation.

Methods: SELECT-LV is a non-randomized, 6 EU-center study of CRT-indicated pts with either a failure of ConCRT, or requiring an upgrade but unsuitable for ConCRT. The WiCS-LV includes a 9mm leadless pacing electrode implanted at the endocardial mid-lateral LV free wall, using a retrograde aortic approach with a steerable 12Fr sheath; fluoroscopy and TTE/ICE helped assess LV wall thickness at potential implant locations. The electrode is activated by a submuscular ultrasonic transmitter (Tx) synchronized to RV pacing pulse of a standard ICD / pacemaker. The Tx is connected to a battery implanted subcutaneously in the left mid-axillary line. The primary efficacy endpoint was successful CRT by 12 lead EKG at 1 mo post-implant. Primary safety events included device / procedure complications within 24 h and at 1 mo.

Application: Of 39 enrolled pts, 3 did not have an adequate acoustic window and 1 withdrew pre-implant. Implant was attempted in 35 (90%): age 65±8 yrs, 30 male, 15 ischemic CM (43%), EF 25.6±6.4%, NYHA 2.7±0.5 and baseline QRS 174±29 ms. Implantation was successful in 34 (97%); one pt had intra-operative VF precluding continuation. The most common indication for WiCS was the inability to perform CS pacing (24, 69%). Of the 27 pts followed for 1 mo, 96% achieved the primary endpoint, consistent CRT. At 1 month, the mean QRS reductions were 36.8ms and 52.7ms as compared with intrinsic and RV pacing, respectively; this was maintained in pts at 6 mo (n=19). Complications were separated into procedure-related (5, 15%), procedure and device related (1, 3%), unrelated (1, 3%), and as yet un-adjudicated (3 including 1 death 4 days after aborted implant, 9%).

Next steps / Future: This multicenter experience has demonstrated the feasibility of direct, wireless endocardial LV pacing to achieve CRT.

LBCT01-06

THE EVERA MRI STUDY

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Introduction: Magnetic resonance imaging (MRI) of conventional implantable cardioverter-defibrillators (ICD) is contraindicated due to potential patient (pt) risks of MRI. We evaluated the safety and efficacy of an ICD system specially designed for full body MRI without restrictions on heart rate or pacing dependency.

Methods: The Evera MRI Study was a multicenter, randomized evaluation of pts with de novo eligibility for an ICD. Pts received an Evera MRI single or dual chamber ICD connected to pre-specified leads. Pts were assigned 2:1 to undergo MR imaging at 1.5 T of the cardiac, thoracic, cervical and head regions to maximize radiofrequency exposure up to 2W/kg specific absorption rate (SAR) and gradient field exposure to 200 T/m/s (MRI group, n=175) or a 1-hour waiting period without MRI (control, n=88). The composite primary safety objective was >90% freedom from MRI-related complication within 30 days post-MRI and sustained tachyarrhythmia occurring during MRI. The co-primary efficacy endpoints compared changes from the pre-MRI/waiting period to 1 month later between groups for ventricular pacing capture threshold (VPCT) (non-inferiority test, 10% margin) and
ventricular sensed amplitude (8% margin). A subset of MRI group pts underwent ventricular fibrillation (VF) induction testing post-MRI to characterize arrhythmia sensing, detection and therapy.

**Results:** In 42 centers, 275 pts were enrolled (76% male, age 60.4±13.8 yrs, 74% primary prevention indication). The safety endpoint was met with 100% freedom from the composite endpoint (p<0.0001). Both efficacy endpoints were also met with minimal differences in the proportion of MRI and control pts who demonstrated a ≤0.5 V increase in VPCT (100% MRI vs 98.2% control, non-inferiority p<0.0001, Figure) or a ≤50% decrease in R-wave amplitude (99.3% MRI vs 98.8% control, non-inferiority p=0.0001). Thirty-four VT/VF episodes (20 induced; 14 spontaneous) occurred in 24 subjects post-MRI, with no impact to sensing, detection or treatment observed.

**Conclusion:** This is the first in human randomized study of an ICD system designed for full body MRI at 1.5 T. This system is safe and the MRI scan does not adversely affect the electrical performance or treatment of ventricular arrhythmias of the ICD system.