Late-Breaking Clinical Trials I

Room 305, Moscone South

Thursday, May 08, 2014

1:30 – 3 p.m.
LB01-01

SHOCKLESS IMPLANT EVALUATION (SIMPLE): A RANDOMIZED TRIAL OF ROUTINE DEFIBRILLATION TESTING, COMPARED TO NO TESTING, AT TIME OF DEFIBRILLATOR IMPLANTATION

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Introduction: Defibrillation testing (DT) is conducted to evaluate the efficacy of the implanted cardioverter defibrillator (ICD) to detect and terminate ventricular fibrillation (VF). Although DT has been a part of the ICD implant procedure in all randomized ICD trials, it has never been shown to independently improve outcomes. Cohort studies suggest rare but serious complications due to DT and secondary analyses from randomized trials suggest a possible harm from ICD shocks. As a result, recent registries have shown that DT is in decline. The SIMPLE trial was designed to provide a definitive answer to the question of whether routine DT is safe and whether it is required.

Methods: Patients (N=2500) undergoing their initial ICD implant for standard primary or secondary prevention indications were randomly assigned (1:1) to have DT done at the time of implant or not. In the DT arm, the protocol required at least one successful termination of VF at 17J or two successes at 21J; with system revision for failure to meet criteria. The first shock energy in all zones was programmed to 31J in both treatment arms. The primary outcome is a composite of failed appropriate shock or arrhythmic death. The trial was designed primarily to establish the non-inferiority of ICD implantation without DT compared to implantation with DT. The most important secondary outcome is all-cause mortality. The safety of intra-operative DT is evaluated for the 30 days following ICD implantation, using a composite of death, myocardial infarction, stroke, anoxic brain injury, systemic or pulmonary embolism, heart failure, need for chest compressions or aortic balloon pump, need for intra-operative vasoconstrictors of > 15 minutes, non-elective intubation, pneumothorax, cardiac perforation, ICD infection, arterial line complication, aspiration pneumonia or unplanned ICU stay. All shocks, deaths and safety outcomes were centrally adjudicated by blinded committee.

Application: There were 2500 patients randomized to the two treatment approaches in 18 countries. The average length of follow-up was 3.1 (P25-75: 2.7-3.7) years and only 1.7% of patients were lost to follow-up. The SIMPLE database was frozen on March 10th and analyses will be completed by April 4th. The efficacy and safety results will be available for presentation in full by May 2014.

Next Steps: It is our hope to present the main results (efficacy and safety) at the Heart Rhythm Society Scientific Sessions in 2014. SIMPLE is the only large randomized trial designed to examine clinical outcomes, and will help determine if DT should routinely be performed at the time of ICD implant.

LB01-02

ADENOSINE-GUIDED PULMONARY VEIN ISOLATION FOR THE TREATMENT OF ATRIAL FIBRILLATION: RESULTS OF THE PROSPECTIVE MULTICENTER RANDOMIZED ADVICE TRIAL

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LB01-03

ABLATION OF CLINICAL STABLE VENTRICULAR TACHYCARDIA VERSUS SUBSTRATE BASE ABLATION ON LONG TERM FREEDOM FROM ANY VT: RESULTS FROM A RANDOMIZED MULTICENTER STUDY VISTA

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Introduction: Catheter ablation of stable monomorphic ventricular tachycardia (VT) represents a therapeutic option to reduce ICDs shocks in patients with VT and ischemic cardiomyopathy (IC). Whether only ablation of the clinical VT or more extensive substrate based ablation is better remain unclear. We sought to investigate whether a substrate based ablation approach improves the outcome at follow up, when compared to conventional ablation of the clinical VT in a randomized prospective trial.

Methods: This was an open-label, randomized, multicenter study comparing the effectiveness of two ablation approaches for the treatment of VT in patients (pts) with IC presenting with stable VT. Eligible subjects were randomly assigned (1:1 ratio) to undergo ablation only of the presenting clinical VT at the site of the critical isthmus (group 1) versus a substrate-based ablation approach (group 2). Substrate ablation was empirically extended throughout the entire scar to target all “abnormal” electrograms. Primary endpoint was recurrence of any sustained VTs, ICD shocks and ATP therapy at device interrogation. Using log-rank test, the study was designed to detect at least 25% difference in success rate (50% to 75%) at 12 month follow-up (hazard ratio (h1/h0)=0.415, null hazard 0.057) at one-sided Type I error (alpha) of 0.025, and 80% power. Pts were followed-up for at least 12 months. Kaplan-Meier test was used to compare success rate between groups, multivariate Cox model was used for identifying significant risk factors.
predictors of success.

**Application:** The final study population was composed by 118 pts (60 pts assigned to group 1, and 58 assigned to group 2). The clinical baseline characteristics were not different between groups. The mean left ventricular ejection fraction was 32.6±14.1% vs. 32.0±9.9% (P=0.8) in group 1 and 2 respectively. Group 1 and group 2, patients failed 1.5±0.7 and 1.4±0.7 antiarrhythmic drugs (AADs) (p=0.9).

In all pts the clinical VT was not inducible at the end of the procedure. Follow-up data was available for all pts. At the 12 month follow-up, 31(51.7%) in group 1 and 49 (84.5%) pts in group 2 were free from any clinical VA (log-rank p <0.001). After adjusting for age, gender, LVEF in Cox multivariate analysis, ablation of the clinical VT alone was associated with significantly higher recurrence (hazard ratio (HR) 3.09; p = 0.014). One arterio-venosus fistula occurred in group 1 while 1 pericardial effusions in group 1 and 2 in group 2 (p=0.62) were reported.

**Next Steps/Future:** This is the first randomized trial showing that a substrate based ablation approach is superior to the ablation of the clinical VT in pts with ischemic cardiomyopathy presenting with stable ventricular tachycardia.

**LB01-04**

PROPHYLACTIC PULMONARY VEIN ISOLATION DURING ISTHMUS ABLATION FOR ATRIAL FLUTTER. THE PREVENT AF STUDY I

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Although catheter ablation of isthmus-dependent atrial flutter (AFL) is successful at eliminating the target arrhythmia, many patients subsequently experience new onset atrial fibrillation (AF). This trial was a prospective single-blind longitudinal parallel-controlled randomized clinical trial in patients whose sole detected clinical arrhythmia was AFL with no known AF. Patients were randomized to either cavo-tricuspid isthmus (CTI) ablation alone or CTI with concomitant pulmonary vein isolation (PVI). All patients received an implantable loop recorder (ILR). Fifty patients completed the trial and patients in each group were well-matched. CTI was successful in all patients; PVI was successful in the 25 randomized patients to CTI + PVI. Procedure (p < 0.0001) and fluoroscopy (p < 0.0001) times were longer in the CTI + PVI group. More patients in the CTI only group experienced new onset AF, 52% vs 12%, during follow-up for minimum of one year (p = 0.005) (Figure 1). No patient experienced recurrent AFL. The one-year AF burden on ILR also favored the CTI + PVI group compared to the CTI only group: 8.3% vs 4.0% (p = 0.034) (Figure 2). In the CTI only group, 32% patients subsequently required another ablation for AF. The performance of PVI and male gender were independent predictors of freedom from AF.

Conclusion: In the PREVENT-AF Study I randomized clinical trial of patients in whom only typical AFL had been observed clinically, the addition of PVI to CTI ablation resulted in a marked reduction of new onset AF during clinical follow-up as assessed by continuous ILR.
**LB01-05**

**INCREASED ADHERENCE TO REMOTE MONITORING IS ASSOCIATED WITH REDUCED MORTALITY IN BOTH PACEMAKER AND DEFIBRILLATOR PATIENTS**

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**Introduction:** Remote monitoring (RM) is associated with reduced mortality in implantable cardioverter-defibrillator (ICD) and cardiac resynchronization therapy defibrillator (CRT-D) patients. However, it is unknown whether this association applies to pacemaker (PM) patients. Additionally, the relationship between the extent of adherence to RM and survival has not been explored for any device type.

**Methods:** Patients implanted with a St. Jude Medical™ PM, CRT-P, ICD, or CRT-D device (2008-2011; >90 days) and not enrolled in a clinical trial were included. Age, gender, device type, and surveillance duration were ascertained using device tracking data. Weekly RM service utilization (RMSU) was determined from Merlin.net™. All-cause survival was prospectively compared for each device type among patients with high (≥75%), low (0%<RMSU<75%), or no (0%) RMSU using multivariable Cox proportional hazards modeling with gender as a covariate and stratification on age.

**Application:** We evaluated 348,742 patients (73 ± 14 years, 61% male) with a PM (n=191,756, 55%), ICD (n=87,628, 25%), CRT-D (n=61,348, 18%) or CRT-P (n=8,010, 2%). Patients with RMS had significantly greater survival than patients without (adjusted HR: 1.81 [CI: 1.77−1.86], p< 0.001). This relationship was preserved for all device types, including PMs (Figure). Furthermore, patients with high RMSU had significantly greater survival than patients with low RMSU (adjusted HR: 2.23 [CI: 2.16-2.31], p< 0.001).

**Next Steps/Future:** Utilization of RM is associated with improved survival. For the first time, improved survival is observed in PM patients and patients with the highest adherence to RM (irrespective of device type). The reasons for these associations require further investigation as they may have important implications for individual patient care and best-practice. Zip-code level demographics data, including four-year college degree, income, poverty level, phone service, food stamps, race, employment, health care insurance, and urban/rural location will be assessed as potential explanatory variables and incorporated onto the final survival analysis.

**LB01-06**

**DUAL-TARGETED THORACIC SPINAL CORD STIMULATION FOR HEART FAILURE AS A RESTORATIVE TREATMENT (SCS HEART): FIRST-IN MAN EXPERIENCE**

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**Introduction:** Dysregulation of the autonomic nervous system plays an important role in the pathophysiology and progression of heart failure (HF). Prior pre-clinical studies suggested that neuromodulation with thoracic spinal cord stimulation (SCS) improves left ventricular (LV) function and remodeling in systolic HF.

**Methods:** In this prospective, multicenter pilot trial, we evaluated the safety and efficacy of an SCS system implant (St. Jude Medical) for treatment of HF, employing dual thoracic SCS leads targeted along the midline and the left side at T1-3 levels. Patients (pts) were NYHA Class III, LV ejection fraction (LVEF) 20-35%, all had implantable defibrillators and were on stable optimal medical therapy. Devices were programmed to provide SCS for 24hrs/day (50Hz at pulse width 200μs). Pts were followed for safety and efficacy endpoints (changes in NYHA Class; QoL; Minnesota Living with HF Questionnaire [MLHFe10points]; peak maximum oxygen consumption [VO2max ≥1mL/kg/min]; NT-proBNP ≥300pg/ml or 35%; and LVEF ≥5%; and LV end-systolic volume [LVESV ≥35%]).
≥20mL or 10%) at baseline vs. 6 mths). The efficacy endpoint results were grouped to determine the composite score. [ClinicalTrials.gov Identifier: NCT01362725]

**Application:** All 17 consented pts (all male, 63±10yrs) had successful SCS implant without major complication. There were no treatment related serious adverse events, including proarrhythmia and device-device interaction, but 1 pt died of progressive HF at 7.5 mths. Among the 15 pts who completed the efficacy endpoint assessments, the composite score improved by 4.2±1.3, and 11/15 pts (73%) showed improvement ≥4/6 efficacy parameters; Individual parameters: NYHA (3.0 vs. 2.1, P=0.002; 13/17 improved); MLHFQ (42±26 vs. 27±22, P=0.026; 12/17 improved); VO2max (14.6±3.3 vs. 16.5±3.9ml/min/kg, P=0.013; 10/15 improved); LVEF (25±6 vs. 37±8%, P<0.001; 14/16 improved); and LVESV (174±57 vs. 140±37ml, P=0.002; 11/16 improved) were also significantly improved after 6 mths of SCS, except NT-proBNP (2363±2303 vs. 2816±4494pg/mL, P=0.52).

**Next Steps/Future:** This first-in-man trial shows that dual-targeted thoracic SCS was safe and improved symptoms, functional status and LV function and remodeling in pts with severe, symptomatic systolic HF.