B-LBCT01
Late-Breaking Clinical Trials

Thursday, May 10, 2018
8 - 9:30 a.m.

CHAIRS:

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B-LBCT01-01

PREVENTION OF ARRHYTHMIA DEVICE INFECTION TRIAL (PADIT)

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Introduction: Cardiac implantable electronic device (CIED) implantation is typically performed in specialized centers using standardized protocols. Device infection is a major complication, usually requiring device removal. A single pre-operative dose of cefazolin is currently recommended to prevent device infections, but this regimen does not provide coverage against up to 30% of microorganisms causing infection. We sought to determine whether the use of an incremental perioperative antibiotics strategy would be superior to a single preoperative dose of cefazolin to prevent device infection, using a cluster randomized cross-over trial.
Methods: Over 4 six-month periods, 28 centers used either conventional or incremental antibiotic treatment in all patients at the time of device implant, crossing between treatments in random sequence. Conventional treatment was pre-surgical cefazolin infusion, with vancomycin for penicillin allergic patients. Incremental treatment was a combination of pre-surgical cefazolin and vancomycin, bacitracin pocket wash, and post-operative oral cephalexin for two days. Cefazolin was omitted in penicillin allergic patients. The primary outcome was hospitalization for device infection within one year in high risk patients (generator replacement, system revision or cardiac resynchronization), with additional analysis of high and low risk patients (new ICD and pacemaker implant were enrolled in 6 of the 28 sites).
Applications: Device procedures were performed in 19,603 patients, of which 12,842 were high risk. The mean age for the overall population was 72.0±13.1 years, 40% of patients had a history of heart failure, and 33.9% were female. The majority of high-risk patients underwent CIED generator change (N=7916, 61.6%). Hospitalization for infection rates will be reported for high risk and all patients, along with sensitivity analyses. Subgroup analyses will be presented to identify any relevant patient or site characteristics that influence the impact of incremental therapy. Antibiotic related adverse events were rare (0.3%).
Next Steps/Future: This cluster randomized cross-over trial is the largest comparative device trial performed to date, that will provide novel insights into best practices to prevent device infection.

B-LBCT01-02

RANDOMIZED CONTROLLED TRIAL OF CARDIAC CONTRACTILITY MODULATION IN HEART FAILURE: THE FIX-HF-5C STUDY

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Introduction: Cardiac contractility modulation (CCM) therapy for patients with persistent symptomatic heart failure (NYHA III and IV) consists of nonexcitatory electrical signals delivered to the heart during the absolute refractory period. The objective of this prospective FIX-HF-5C study was to confirm a subgroup analysis of a prior study (FIX-HF-5) showing that CCM significantly improved exercise tolerance (ET) and quality of life (QoL) in patients with ejection fractions (EF) between 25 and 45%.
Methods: 160 patients with NYHA III or IV symptoms despite guideline recommended therapy, QRS duration <130ms and LVEF 25% to 45% were randomized to continued medical therapy alone (Control) or to continued medical therapy plus CCM delivered by the Optimizer system (Treatment) for 24 weeks. Peak VO_2 (pVO_2, primary endpoint), Minnesota Living with Heart Failure Questionnaire (MLWHFQ), NYHA and 6-minute hall walk (6MHW) test were measured at baseline, 12 and 24 weeks. Bayesian repeated measures linear modeling was used for the primary endpoint analysis with 30% borrowing from the FIX-HF-5 subgroup. Safety was assessed by the percentage of patients free of device-related adverse events with a prespecified lower bound of 70%.
Applications: The difference in pVO_2 between Treatment and Control was 0.836 mlO_2/kg/min with a 95% Bayesian credible interval of (0.123, 1.552 mlO_2/kg/min), satisfying the primary endpoint. MLWHFQ ($p<0.001$), NYHA ($p<0.001$) and 6MHW ($p=0.01$) were all better in Treatment vs Control. There were 7 device-related events, yielding a lower bound of 80% of patients free of events.
Next Steps/Future: The FIX-HF-5C study met its pre-specified objectives, confirming the safety and efficacy of CCM in the target population of heart failure patients. Specifically, CCM was safe and improved ET and QoL by multiple measures in the specified group of HF patients. CCM represents a promising new therapy for such patients.

B-LBCT01-03

TARGETED LEFT VENTRICULAR LEAD IMPLANTATION IN NON-LEFT BUNDLE BRANCH BLOCK PATIENTS: PRIMARY RESULTS OF THE ENHANCE CRT PILOT STUDY

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Introduction: Data on the effectiveness of cardiac resynchronization therapy (CRT) in patients with non-left bundle branch block (non-LBBB) is limited and when available has been shown to be suboptimal compared to LBBB patients. CRT is usually delivered through an anatomical implant approach placing the left ventricular (LV) lead in the mid-lateral or posterolateral wall. Since the left ventricular activation sequence in non-LBBB patients is different from that in LBBB, it was postulated that targeting the region of increased electrical delay (QLV approach), may serve as a more individualized strategy in this cohort of patients.
Objective: This study compared the effects of a QLV-based LV lead location implant strategy to a standard of care (SOC) anatomical implant approach in non-LBBB patients on the Clinical Composite Score (CCS) after 12 months of follow-up.
Methods: A total of 248 patients were enrolled at 29 U.S. centers. Following enrollment, patients were randomized in a 2:1 ratio between a QLV-based implant (QLV arm) and SOC anatomical implant approach (SOC arm) and implanted with a St. Jude Medical quadripolar CRT-D system per the 2013 ACCF/AHA/HRS guidelines. The primary endpoint was the CCS (NYHA class, Patient Global Assessment, heart failure events and cardiovascular death) after 12 months of follow-up.
Applications: A total of 190 subjects were available for data analysis at 12 months of follow-up (128 QLV arm; 62 SOC arm). Of these, 39 subjects had worsening heart failure events (8 cardiac deaths and 31 heart failure hospitalizations), 26 in the QLV arm and 13 in the SOC arm. There were no differences in baseline characteristics between the QLV and SOC arms. The CCS responder rate at 12 months of follow-up was 63.7% in the QLV arm and 71.4% in the SOC arm ($p=0.388$). Subjects demonstrated a statistically significant improvement in MLWHF score from baseline to 6 months and to 12 months in the SOC arm (18.4 ± 23.3 and 15.1 ± 20.9) and in the QLV arm (17.6 ± 27.6 and 17.0 ± 26.0) (all $p<0.001$). There were statistically significant increases in LVEF from baseline to 6 and to 12 months for the SOC arm ($5.0 \pm 8.4\%$ and $5.5 \pm 11.0\%$) and for the QLV arm ($5.5 \pm 11.0\%$ and $5.8 \pm 9.6\%$) (all $p<0.001$). There were no significant differences between the two interventional arms in quality of life or LVEF.
Next Steps/Future: CRT in non-LBBB patients was associated with a marked clinical improvement as evidenced by the CCS and favorable reverse remodeling. However, there was no difference in the outcome of patients between the QLV arm vs. the SOC anatomical left ventricular lead implantation arm. Further analysis pertinent to the interactions between the QLV strategy and final anatomical lead locations along with updated results will be presented at the HRS meeting.

B-LBCT01-04

A RANDOMIZED PRAGMATIC TRIAL OF STRATEGIES OF PERMANENT PACEMAKER VERSUS IMPLANTABLE CARDIAC MONITOR IN OLDER PATIENTS WITH SYNCOPE AND BIFASCICULAR BLOCK