# B-LBCT02
# Late-Breaking Updates from Clinical Trials and Registries

**Friday, May 11, 2018**
**8 - 9:30 a.m.**

**CHAIRS:**

Andrew D. Krahn, MD, FHRS. *Sauder Family and Heart & Stroke Foundation of BC, Vancouver, BC, Canada*

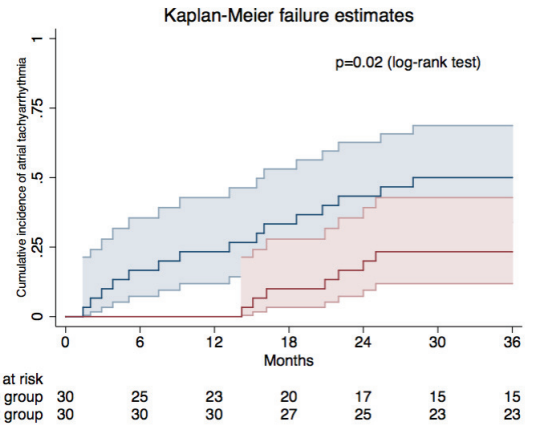
Andrea M. Russo, MD, FHRS. *Cooper University Hospital, Moorestown, NJ*

## B-LBCT02-01

### THREE-YEAR OUTCOMES AFTER BOTULINUM TOXIN INJECTIONS INTO EPICARDIAL FAT PADS FOR ATRIAL FIBRILLATION PREVENTION IN PATIENTS UNDERGOING CORONARY ARTERY BYPASS GRAFTING

Alexander B. Romanov, MD, PhD, Evgeny Pokushalov, MD, PhD, Dmitry Ponomarev, MD, Sevda Bayramova, MD, Vitaly Shabanov, MD, Artem Strelnikov, MD, David Sergeevichev, MD, Denis Losik, MD, Boris Kozlov, MD, Sunny S. Po, MD, PhD and Jonathan S. Steinberg, MD, FHRS. E. Meshalkin National Medical Research Center of the Ministry of Health of the R, Novosibirsk, Russian Federation, Institute of Cardiology, Siberian Division of Russian Academy of Medical Sciences, Tomsk, Russian Federation, University of Oklahoma, Heart Rhythm Institute, Oklahoma City, OK, Summit Medical Group, Short Hills, NJ

**Introduction:** Botulinum toxin injections into epicardial fat pads in patients undergoing coronary artery bypass grafting (CABG) has resulted in substantial atrial fibrillation (AF) suppression during early postoperative period and 1-year follow up without serious adverse events in a pilot program. To assess the 3-year clinical outcomes and AF prevention by botulinum toxin injections into epicardial fat pads in patients undergoing CABG.
**Methods:** Sixty patients with history of paroxysmal AF and indications for CABG were randomized to either botulinum toxin (50U/1ml at each fat pad; botox group; n=30) or placebo (0.9% normal saline, 1ml at each fat pad; placebo group n=30) injections into 4 posterior epicardial fat pads. All patients received an ICM with regular follow-up. The primary endpoint of the extended follow up was incidence of any atrial tachyarrhythmia including AF and atrial tachycardia after 30 days of procedure until 36 months on no antiarrhythmic drugs. The secondary endpoints included clinical events and AF burden.
**Applications:** At the end of 36 months, the incidence of any atrial tachyarrhythmia was 23.3% in the botox group as compared to 50% in the placebo group (hazard ratio 0.36, 95% confidence interval 0.14-0.88, p= 0.026) (**Figure**). The three-year AF burden was significantly lower in the botox group compared to the placebo group: 1.4% vs 6.9% (p < 0.001). In botox group, 2 (7%) patients were hospitalized during follow-up compared to 10 (33%) in placebo group (p=0.02); and there were no major clinical adverse events in botox group versus 4 patients (13%) in placebo group who developed stroke or died (p=0.1).
**Next Steps/Future:** Injections of botulinum toxin into epicardial fat pads in patients undergoing coronary artery bypass grafting resulted in a sustained substantial reduction of atrial tachyarrhythmia incidence and AF burden during 3-year follow-up, accompanied by reduction in hospitalizations and major clinical adverse events. A large-scale multicenter randomized trial is needed to focus on hard clinical outcomes to more comprehensively test the value of botulinum toxin injections during cardiac surgery.




## B-LBCT02-02

### MYOCARDITIS IS AN UNDERRECOGNIZED ETIOLOGY OF SYMPTOMATIC PREMATURE VENTRICULAR CONTRACTIONS - INSIGHTS FROM THE MYOCARDITIS AND VENTRICULAR ARRHYTHMIA (MAVERIC) REGISTRY

Dhanunjaya R. Lakkireddy, MD, FHRS, Bharath Yarlagadda, MD, Mohit K. Turagam, MD, Tawseef A. Dar, Valay K. Parikh, MD, Sneha Kola, MBBS, Mark Hamblin, MD, Megan Krause, MD, Tom Rosamond, MD, Sudharani Bommana, MS, Melissa Jaeger, Heidi M. Carroll, Cherie Nydegger, Donita Atkins, BSN, Courtney C. Jeffery, NP and Rakesh Gopinathannair, MA, MD, FHRS. Kansas City Heart Rhythm Institute, Overland Park, KS, Cardiovascular Research Institute, Kansas City, KS, Mount Sinai Medical Center - Ichan School of Medicine, New York, NY, Kansas University Medical Center, Overland Park, KS, University of Kansas Medical Center, Kansas City, KS, Kansas City Heart Rhythm Institute, Overland Park, MO, University Of Kansas Hospital, Kansas City, MO, University of Louisville School of Medicine, Cardiology/EP, Louisville, KY

**Introduction:** Symptomatic premature ventricular contractions (PVCs) are common in clinical practice. Myocarditis often goes unrecognized with a potential for continued disease progression & cardiomyopathy. PVCs may be marker of underlying myocarditis; identification and Rx of myocarditis may improve outcomes.
**Methods:** 107 patients with symptomatic PVCs and no underlying ischemic heart disease (IHD) prospectively had viral & autonomic serology,18F-Fluorodeoxyglucose Posi-

tron Emission Tomography (FDG-PET), cardiac magnetic resonance imaging (CMR) & myocardial biopsy. Pts with focally positive PET scans were labelled as Myocarditis & were treated with immunosuppressive therapy (IST) as first line therapy followed by ablation as needed. Response to Rx was assessed by repeat PET scan & holter monitor at 3-monthly intervals. Optimal clinical response was defined as greater than 80% decline in PVC burden + resolution of uptake on PET scans. Suboptimal response was defined as <80% decrease in VA burden on cardiac monitoring with lack of PET resolution.

**Applications:** The cohort were 41% males with 57±15 years & 47±11.8% LVEF. +ve PET s/o myocarditis was seen in 51% (55/107); CMR was correlative of PET in 27.4%. In 47% of patients PVC site of origin correlated with site of inflammation (maximal intensity). IST was started in 83.6% (46/55) of PET positive patients. 32 patients (69.5%) received IST alone and 14(30.5%) underwent IST and catheter ablation. Optimal response was seen in 76% (29/38) and suboptimal response was seen in 24% (9/38) over a mean follow up of 6±3 months. 37% who had LV dysfunction EF improved (Δ13 ± 6%). Lymphocytic infiltrative myocarditis was the most common pathologic finding (46%,13/28) , biological markers were not diagnostic. 67% (4/6) untreated patients had worsening EF (Δ10 ± 4%) over 6 months F/U.

**Next Steps/Future:** A significant number of patients with symptomatic PVCs have underlying myocarditis identified by FDG-PET& IST may significantly impact outcomes. A randomized control trial assessing the impact of IST in pts with PVCs & myocarditis should be done to better understand the etiopathogenesis & Rx strategies.

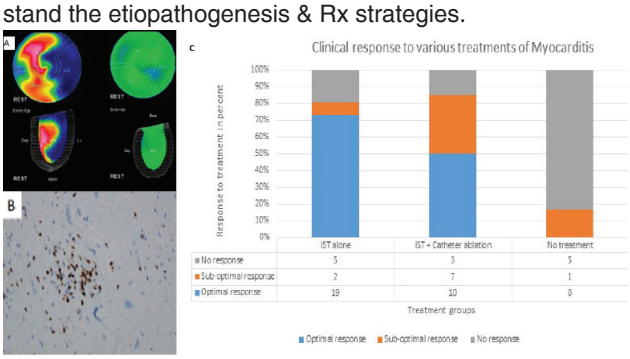



**Figure:**
**A - Shows FDG PET scan with focal involvment of the septal aspect of the LV which completely resolved after combination IST with steroids and methotrexate for 6 months.**
**B - is the biopsy result showing lymphocytic infiltrative suggestive of possible chronic viral myocarditis.**
**C- shows response to IST and IST+ Catheter ablation.**

## B-LBCT02-03

### LOWER ADHERENCE DIRECT ORAL ANTICOAGULANTS USE IS ASSOCIATED WITH INCREASED RISK OF THROMBOEMBOLIC EVENTS THAN WARFARIN - UNDERSTANDING THE REAL-WORLD PERFORMANCE OF SYSTEMIC ANTICOAGULATION IN ATRIAL FIBRILLATION

Dhanunjaya R. Lakkireddy, MD, FHRS, Edward Karst, CCDS, Srijoy Mahapatra, MD, FHRS, Jeffrey R. Winterfield, MD, FHRS and Moussa Mansour, MD, FHRS. Kansas City Heart Rhythm Institute, Overland Park, KS, Abbott, Los Angeles, CA, Abbott, Edina, MN, Medical University of South Carolina, Mount Pleasant, SC, Massachusetts General Hospital, Cardiac Arrhythmia Unit, Boston, MA

**Introduction:** Anticoagulation (AC) mitigates risk of thromboembolic events (TE) in patients with non-valvular AF. Warfarin for decades & recently direct oral anticoagulants (DOACs) have been effective. Real-world data have pointed to inconsistent adherence to (AC), but it is not clear if event risk is elevated during gaps or if events occur even during periods of adherence.

**Methods:** This observational cohort study evaluated administrative claims for pts in the IBM Watson Health Market Scan databases receiving a prescription of warfarin or a DOAC for NVAF from 1-2015 to 6-2016. Exclusions were-$CHA_2DS_2$-VASc 0-1, transient AF, other requirement for AC, thrombocytopenia & anemia; the remaining patients were stratified based on index prescription (warfarin or DOAC). Outcomes, through Dec. 2016, were hospitalization for TE (ischemic stroke or systemic embolism), hemorrhagic stroke & major bleeding. Event rates are reported for warfarin and DOACs at higher adherence (dosage covering >80% of days)& lower adherence (covering 40-80% of days). A Cox proportional-hazards model will incorporate basic characteristics, comorbidities & a time-dependent covariate for anticoagulation based on prescription dosage to associate adherence to outcomes.

**Applications:** The cohort included 52,365 patients prescribed warfarin & 67,686 prescribed any of the four DOACs. Lower adherence occurred in 47% of pts using warfarin & 31% on DOACs. Compared to higher-adherence warfarin, thromboembolic events were 14% less likely for higher-adherence DOAC (P<0.001), 48% more likely for lower-adherence warfarin (P<0.001) & 69% more likely for lower-adherence DOAC (P<0.001).

**Next Steps/Future:** Nearly half of pts prescribed warfarin & just under one third of those using DOACs do not maintain adherence above 80%. We plan to update the abstract with 2017 data & use the time-dependent Cox model to determine if event risk is higher during medication usage or gaps in adherence. Pts with lower adherence may be candidates for device therapies that obviate the need for chronic AC.

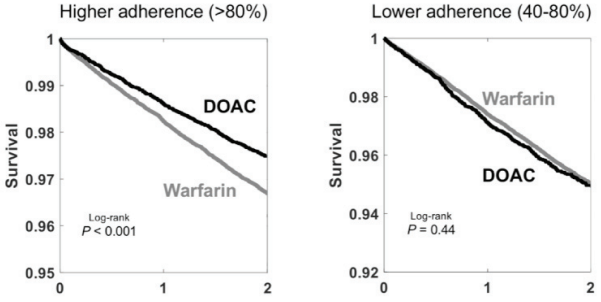



**Figure**: Freedom from thromboembolic events for patients prescribed warfarin or DOACs with higher and lower adherence.