There were no device migration or dislodgements, no infections, no mechanical failure or early battery depletion, and no pro-arrhythmias detected after 1 year.

A completely self-contained, single-chamber, leadless cardiac pacemaker is stable and highly reliable over a 1-year time frame, with few safety issues. This small study suggests the leadless pacemaker could represent a paradigm shift in cardiac pacing. Future studies include a USA multicenter, prospective, single-arm FDA study of ~667 patients indicated for ventricular pacing and rate-adaptive therapy, as well as a European observational study (both studies are in progress). Also in development is an atrial LCP that will perform dual- or multi-chamber pacing.

Evidence of Added Benefit With Edoxaban in Patients With Paroxysmal AF

Written by Maria Vinall

Among patients with atrial fibrillation (AF) treated with anticoagulants, differences in baseline characteristics only partially account for the differences in outcome by AF subtype. Robert P. Giugliano, MD, SM, Brigham and Women's Hospital, Boston, Massachusetts, USA, presented results of a secondary data analysis from the Effective Anticoagulation with Factor Xa Next Generation in Atrial Fibrillation–Thrombolysis in Myocardial Infarction 48 trial [ENGAGE AF-TIMI 48; NCT00781391]. These results showed that therapies that reduce bleeding while maintaining efficacy in the prevention of stroke (as compared with warfarin) may be especially beneficial in patients with paroxysmal AF.

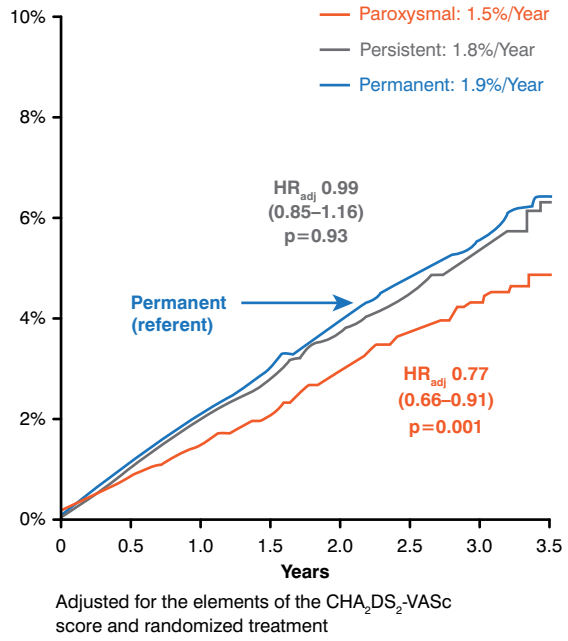
Edoxaban is a direct, oral, once-daily Factor Xa inhibitor. In the ENGAGE AF-TIMI 48 trial, both high and low doses of edoxaban were at least as effective as warfarin in preventing stroke and systemic embolic events (SEE) in patients with AF at moderate to high risk of stroke and caused less bleeding [Giugliano RP et al. *N Engl J Med* 2013].

The objective of the secondary analysis was to compare the baseline characteristics by AF subtype at presentation and compare the efficacy and safety of edoxaban by subtype during the 2.8 years median follow-up using the primary efficacy and safety outcomes from the main trial (efficacy=stroke or SEE; safety=ISTH major bleeding). Additional key secondary trial end points were also considered. For the ENGAGE AF-TIMI 48 trial, 21,105 patients with documented AF of any duration during the prior 12 months and a $CHADS_2$ score of greater than or equal to 2 were enrolled. For this secondary analysis, patients were categorized as having paroxysmal (n=5366 patients), persistent (n=4868), or permanent (n=10,865) AF based on the randomization ECG.

Patients with paroxysmal AF were more likely to be younger and female, to have a higher rate of diabetes, a lower $CHADS_2$ score, to have a history of coronary artery disease or dyslipidemia, and to be receiving antiarrhythmic therapy. Patients with permanent AF were slightly older and more were likely to have a higher $CHADS_2$ score and heart failure, as well as a higher incidence of prior stroke. They were also less likely to be vitamin K antagonist therapy-naïve.

The rate of stroke or SEE adjusted for elements of the CHA_2DS_2-VASc score, the group with paroxysmal AF was 23% lower in patients with paroxysmal AF as compared to permanent AF (adjusted HR, 0.77; 95% CI, 0.66–0.91; p=0.001); there was no difference in the rate of stroke or SEE between the permanent and persistent groups (Figure 1). Regarding the primary safety outcome, the adjusted rates for major bleeding were similar across all three groups.

Figure 1. Primary Efficacy Outcome by AF Subtype



SEE=systemic embolic events.

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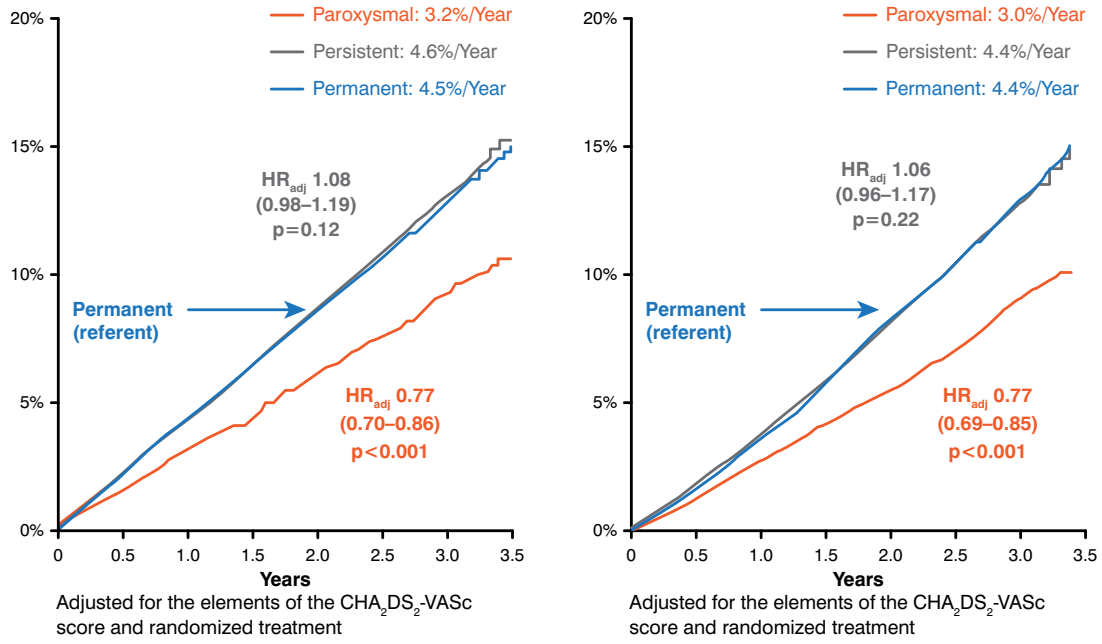
Compared with subjects with permanent AF, subjects in the paroxysmal group had a lower risk for the key combined secondary outcome of stroke plus SEE plus cardiovascular death after adjusting for the CHA_2DS_2-VASc score (adjusted HR, 0.77; 95% CI, 0.70–0.86; p<0.001).

There was no difference between the permanent and persistent groups (Figure 2). The outcome was similar for mortality, with patients in the paroxysmal group having a 23% reduction in the adjusted HR for death and no difference between patients with permanent versus persistent AF (Figure 2).

The risk for cardiovascular death was approximately 25% lower and the risk for the primary net outcome (stroke, SEE, major bleeding, or death) was approximately 13% lower in the paroxysmal group versus the permanent group after adjustment. There was no difference in the outcomes for intracranial hemorrhage. The results described for subjects with persistent AF were not different from those described for patients with permanent AF (Table 1).

Efficacy outcomes (stroke or SEE; combined stroke, SEE and cardiovascular death; all-cause mortality; or cardiovascular death) were similar between patients treated with edoxaban and those treated with warfarin regardless of the edoxaban dose (high versus low dose) or AF subtype. With respect to safety, there was a reduction in the proportion of patients who had major bleeding, those who had a combination of stroke, SEE, major bleeding and death, and, in particular, those patients who had intracranial hemorrhage with both doses of edoxaban for all AF subtypes.

Figure 2. Key Secondary Outcomes by AF Subtype



CV=cardiovascular; SEE=systemic embolic events.

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Table 1. Other Outcomes by AF Subtype

	Paroxysmal AF			Persistent AF		
	Adj HR	95% CI	p Value	Adj HR	95% CI	p Value
Cardiovascular death[1]	0.75	0.66–0.85	<0.001	1.10	0.98–1.23	0.10
Intracranial hemorrhage[2]	0.90	0.66–1.23	0.51	0.89	0.63–1.24	0.48
Primary net outcome[3]	0.87	0.80–0.94	<0.001	1.04	0.96–1.12	0.32

AF=atrial fibrillation.

Referent group=permanent AF; Net Primary Outcome=stroke, systemic embolic events, major bleeding, or death.

1. Adjusted for the elements of the CHA_2D_2-VASc score and randomized treatment; 2. Adjusted for elements of the HAS-BLED score and randomized treatment; 3. Adjusted for CHA_2D_2-VASc, HAS-BLED, and randomized treatment.

In conclusion, patients with paroxsymal AF were at a lower risk for stroke or SEE but had a similar risk of bleeding as patients with more sustained AF. Compared with patients with well-managed warfarin dosages (time in therapeutic range of 68.4%), edoxaban was associated with a reduced incidence of stroke or SEE, cardiovascular death, and bleeding, as well as more favorable net outcomes across all AF subtypes.

Defibrillators Programmed With Longer Detection Intervals Safe for Secondary Prevention Patients

Written by Nicola Parry

Laurence D. Sterns, MD, Royal Jubilee Hospital, Victoria, British Columbia, Canada, presented results of the secondary prevention substudy of the Study to Evaluate System Safety and Clinical Performance of the Protecta Implantable Cardioverter Defibrillator (ICD) Plus Cardiac Resynchronization Therapy Defibrillator (CRT-D) trial [PainFree SST; NCT00982397]. This prospective, randomized, multicenter study demonstrated that defibrillators programmed with longer detection intervals are safe for secondary prevention in patients with ICDs.

Although previous studies have shown that extended ICD detection times for ventricular tachycardia or ventricular fibrillation (VF) reduce inappropriate therapies and mortality in primary prevention patients [Gasparini M et al. *JAMA* 2013; Moss AJ et al. *N Engl J Med* 2012; Wilkoff BL et al. *J Am Coll Cardiol* 2008], the effect of prolonged ICD detection in secondary prevention patients who have already experienced episodes of sudden cardiac arrest and are at increased risk for a deadly irregular heart rhythm had not been evaluated.

Prof. Sterns and colleagues conducted the PainFree SST trial to investigate the safety of prolonged detection for ventricular tachycardia or VF in secondary prevention patients. To be included in the study, patients were required to have secondary prevention indications for ICD.

Patients with mechanical tricuspid valves, those enrolled in concurrent drug or medical device studies, and those who were unwilling to provide written informed consent to participate in the study or who anticipated being unable to complete it were excluded from the trial.

The PainFree SST trial enrolled a total of 2790 patients receiving ICDs programmed with technology that enables the devices to discern whether an abnormal heart rhythm is life threatening. Of these participants, 705 were included in this substudy and were randomly assigned 1:1 to either standard interval detection (VF number of intervals to detect, 18 of 24; n=353) or extended interval detection (VF number of intervals to detect, 30 of 40; n=352) of ventricular tachycardia or VF ≥188 beats/minute.

The primary end point was freedom from arrhythmic syncope at 1 year. Secondary end points included time to first arrhythmic and all-cause syncope, appropriate therapy or inappropriate shock, and mortality.

At baseline, 35% of patients had atrial arrhythmias, and 33% had histories of syncope. At 1 year, 7 patients in the standard group and 11 in the prolonged group had arrhythmic syncope. The arrhythmic syncope–free rate was similar between the standard and prolonged groups (98.0% vs 96.9%; p=0.012 for noninferiority). There was no statistically significant increase in the time to first arrhythmic syncope (HR 1.52; 95% CI 0.66–3.52; p=0.32), incidence of all-cause syncope (HR, 1.17; 95% CI, 0.59–2.32; p=0.66), appropriate VF zone therapies (HR, 0.98; 95% CI, 0.67–1.43; p=0.91), time to first appropriate shock (HR, 1.04; 95% CI, 0.70–1.53; p=0.85), or incidence of inappropriate shocks (1.0% vs 1.3%, p=0.74). However, in the prolonged group, the VF therapy rate (1.5 vs 0.4, p=0.0001), VF shock rate (0.9 vs 0.27, p=0.0026), and VF antitachycardia pacing rate (0.57 vs 0.16; p=0.0019) were significantly lower.

The results of this substudy demonstrated that extended interval detections did not result in statistically increased risk for syncope in secondary prevention patients. Prof. Sterns concluded that the prolonged detection programming strategy may be considered as a strategy to reduce inappropriate shocks in patients with ICDs.

Smartphone-Enabled ECG Devices Produce Diagnostic Tracings in Children

Written by Nicola Parry

Hoang H. Nguyen, MD, Washington University School of Medicine, St. Louis, Missouri, USA, presented results of the prospective, single-center Smartphone Pediatric Electrocardiogram trial [SPEAR] demonstrating that smartphone-enabled electrocardiogram (ECG) devices can produce accurate tracings of diagnostic and therapeutic quality in children in the remote setting.

Smartphone-enabled ECG recorders have the ability to enhance physician reach and patient care by facilitating ECG assessment in patients in remote areas. One such example is the AliveCor 1-lead ECG device, which consists of 2 exposed electrodes on the back of a smartphone case. This device generates an ECG when a finger of each hand is placed on each of the electrodes, and the electrical signal is processed and transmitted to the phone's AliveCor application.