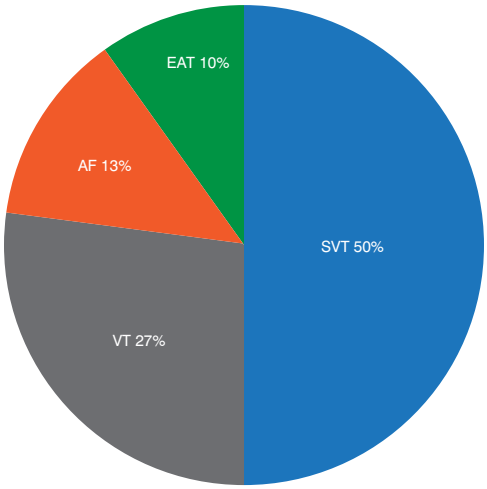
Dr. Nguyen and colleagues are conducting a prospective trial throughout a 1-year period to investigate the usefulness of ECG tracings generated by the AliveCor device in pediatric patients, and to evaluate user satisfaction.

To be included in the trial, patients were required to be aged ≤21 years, have documented paroxysmal arrhythmia, and own an iPhone 4 or 5. Users were instructed to email ECG tracings of concern directly from the application for review by pediatric cardiac electrophysiologists. Following interpretation, patients were contacted with results and further care instructions. They were also required to complete online surveys regarding their experience and satisfaction with the device and cardiac care team.

In total, 30 patients (aged 2 months to 18 years; median age 12.5 years) were enrolled in the study. To date, 144 ECG tracings have been received from 20 patients, and the highest number of tracings received from a single patient during a 1-month period was 15. Users deemed ECGs as concerning 45% of the time. Signal quality allowed unequivocal rhythm diagnosis in 141 of 144 (98%) tracings; motion artifact prevented evaluation of the remaining three tracings. The most frequent diagnosis was supraventricular tachycardia (n=15; 50%), followed by ventricular tachycardia (n=8; 27%), atrial fibrillation (n=4; 13%), and ectopic atrial tachycardia (n=3; 10%; Figure 1).

Figure 1. Rhythm Diagnosis From Smartphone ECG Tracings



AF=atrial fibrillation; EAT=ectopic atrial tachycardia; SVT=supraventricular tachycardia; VT=ventricular tachycardia.

Reproduced with permission from HH Nguyen, MD.

Forty-four surveys have also been received to date, 68% of which are from parents. The results of the user survey thus far have been positive, with 98% of users indicating that the device is very easy to use and 93% indicating the ease at which it transmits tracings. Of users, 98% expressed a high level of comfort in using the device for arrhythmia management, and 99% indicated continued interest in using it after the study ends.

The parents of younger patients also provided feedback noting that the device can record their child's heart rhythm for prompt diagnosis without the need to visit the emergency room (ER) or pediatrician's office. They did, however, indicate the difficulty of device placement on small children. In addition, some noted that because the device was on the parental phone, it was not with the child at all times.

These preliminary data demonstrate that smartphone-enabled ECG devices can produce diagnostic tracings in children, with high use and user satisfaction. Such devices can help pediatric electrophysiologists better manage chronic arrhythmia by optimizing pediatric outpatient care, limiting ER use, and thereby reducing health care costs, concluded Dr. Nguyen.

Ranolazine and Dronedarone in Combination Show Synergistic Effects on AF Suppression

Written by Nicola Parry

Peter R. Kowey, MD, Lankenau Medical Center, Wynnewood, Philadelphia, Pennsylvania, USA, presented results from the Phase 2 Study to Evaluate the Effect of Ranolazine and Dronedarone When Given Alone and in Combination in Patients With Paroxysmal Atrial Fibrillation trial [HARMONY; NCT01522651]. This randomized, double-blind, placebo-controlled trial demonstrated that a combination of ranolazine and low-dose dronedarone reduced the burden of paroxysmal atrial fibrillation (PAF) when compared with either drug alone.

Both ranolazine and dronedarone are drugs that block multiple ion channels. Dronedarone is approved for management of patients with PAF. Ranolazine not only is approved for chronic angina but also has been shown to have antiarrhythmic effects [Mason PK, DiMarco JP. *Circ Arrhythm Electrophysiol* 2009]. Neither of these drugs, however, has proved very effective for the treatment of PAF when used as monotherapy.

Dr. Kowey and colleagues conducted a study to determine if the combination of ranolazine and low-dose dronedarone is superior to individual drug therapy in reducing the burden of atrial fibrillation (AF) in patients with PAF.

To be included in the trial, patients were required to be aged ≥18 years, with a history of PAF documented within the prior 12 months, and a dual-chamber programmable pacemaker with AF detection capabilities (implanted at least 3 months prior to screening).

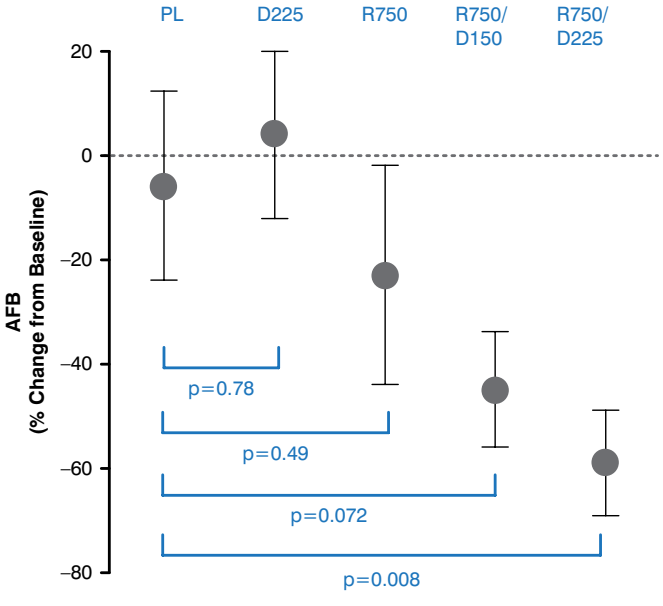
Exclusion criteria included persistent or permanent AF, a history of atrial flutter or atrial tachycardia without successful ablation, other acutely reversible causes of AF, a prior heart transplant, or a history of stroke 3 months prior to screening.

In total, 134 patients were enrolled and randomly assigned to five groups: placebo (n=26), ranolazine 750 mg twice daily (BID) (n=26), dronedarone 225 mg BID (n=26), ranolazine 750 mg and dronedarone 225 mg BID (n=27), or ranolazine 750 mg and dronedarone 150 mg BID (n=26).

The primary end points were the relative and absolute changes from baseline in AF burden (AFB) at 12 weeks. Secondary end points included the change in AFB at each study visit, the percentage of patients with a 50% reduction of AFB, and the safety and tolerability of dronedarone and ranolazine when used as monotherapy and/or in combination.

Compared with placebo, the patient group treated with ranolazine 750 mg and dronedarone 225 mg BID had a statistically significant reduction in AFB from baseline to 12 weeks (p=0.008; Figure 1). The reduction in AFB for those in the ranolazine group and in the dronedarone 150 mg BID and ranolazine 750 mg daily group was not statistically significant (p=0.072 and p=0.49, respectively). In addition, the patient group treated with dronedarone 225 mg BID showed no difference in percentage change in AFB when compared to placebo (p=0.78).

Figure 1. Percentage Change in AFB From Baseline to 12 Weeks



AFB=atrial fibrillation burden; D225=dronedarone 225 mg BID; R750=ranolazine 750 mg BID; R750/D150=ranolazine 750 mg and dronedarone 150 mg BID; R750/D225=ranolazine 750 mg and dronedarone 225 mg; PL=placebo.

Reproduced with permission from PR Kowey, MD.

From baseline to 12 weeks, a ≥70% reduction of AFB occurred in 45% and 27% of patients in the ranolazine 750 mg–dronedarone 225 mg BID and ranolazine 750 mg–dronedarone 150 mg BID groups, respectively, compared to an 11% reduction in the placebo group. Neither ranolazine nor dronedarone 225 mg BID alone reduced AFB when compared with placebo (only 17% and 9%, respectively).

There were very few serious adverse events (AEs) reported in the treatment groups, and there was no dose relationship with respect to either serious AEs or those leading to treatment discontinuation. Dizziness and constipation were some of the most frequent serious AEs reported.

In summary, the HARMONY trial showed that ranolazine and dronedarone lowered AFB as compared to placebo or either agent when used as monotherapy. In addition, there was a dose–response relationship seen with the effects of dronedarone when used in combination with ranolazine.

Dr. Kowey concluded by noting that plans are now underway to further study these agents with 2 large Phase 3 trials. One trial plans to study the effects of dronedarone and ranolazine on the time to recurrent atrial fibrillation. The other trial will study the effects of dronedarone and ranolazine on cardiovascular death or hospitalization.

Favorable Phase 2 Data for Ranolazine in AF

Written by Nicola Parry

Gaetano De Ferrari, MD, Policlinico S Matteo and University of Pavia, Pavia, Italy, presented results of the Ranolazine in Atrial Fibrillation Following an Electrical Cardioversion randomized trial [RAFFAELLO; NCT01534962], an international, double-blind, parallel, Phase 2, dose-ranging study testing three oral ranolazine doses. The results demonstrated safety and provided favorable findings with regard to efficacy for patients with atrial fibrillation (AF).

Although antiarrhythmic medications are widely used in managing patients with AF, with the aim of reducing mortality and hospitalizations, their use has been limited by a combination of toxicity and only modest efficacy. Ranolazine is a relatively new drug approved for the management of chronic angina that blocks late sodium currents, and although it also reduces supraventricular