

Good morning members of the Advisory Panel. My name is Burke Barrett and I am the Vice President of Regulatory and Clinical Affairs for CardioFocus. I would like to thank the FDA, both for the initiative made earlier this year to seek alternative clinical study designs for the evaluation of percutaneous AF devices, and for the opportunity to speak briefly this morning.

CardioFocus is a small 24-person medical device company developing a balloon-based catheter system intended to isolate the pulmonary veins in the treatment of AF. We have no sales and only this one product and so the clinical and regulatory environment for the evaluation of this product is the key factor we face as a company. Let me describe our experiences to date.

After a very straightforward FDA review, our IDE was approved and we initiated our first clinical site in February of this year. Our study is an RCT with anti-arrhythmic drug therapy as the control arm. Our experiences with patient recruitment to date have been

very challenging for a number of reasons and details have been provided confidentially to the FDA for the panel package.

Enrollment in clinical studies can, in general, be challenging and so we looked at several factors in order to assess our enrollment experience. We have recently made some protocol changes that may improve enrollment, but in general, we believe our enrollment criteria are similar to most AF IDE studies ongoing as all companies are working from the same FDA Guidance as currently being implemented by the FDA. We have a large number of study sites, currently 16, and plan to expand to add more sites. Our technology is investigational and that may cause some initial reluctance, but it seems to be interesting enough to the EP community and our clinical sites in particular, to undertake the study. Our clinical study sites are all very active in AF ablation and have reasonably large AF ablation case volumes. Our clinical study sites report that patient reluctance to be randomized to drug after already having failed a drug

and being referred to the ablation center is a primary reason for screen failures, even with the enticement of possible early cross-over to ablation once a drug failure occurs.

To date, our study sites have screened more than 60 candidates to enroll each patient. The average of three ongoing studies, based on data provided to AdvaMed, shows that about 55 candidates need to be screened to enroll one study patient. So, in order to complete enrollment of a typically sized study of 200-250 patients may mean screening more than 10 thousand candidates. This is a daunting task for the clinical study sites. If you extrapolate the screening experience onto a total of four to six ongoing plus soon to be launched percutaneous AF studies, the enormity of the patient screening effort in this field becomes obvious.

One company recently reported completing enrollment in an AF ablation study that we believe took about three

years for the enrollment phase. Based again on data from three companies that have ongoing AF studies and provided information to AdvaMed, we project similar three-year enrollment periods. When the study initiation process of around a year is added to one-year patient follow-up and one-year post-study to gather data and prepare regulatory submissions, the current pivotal or Phase III clinical and regulatory process for percutaneous AF products is around 6 years. This is for an acute procedure that typically lasts 4-8 hours, not an implantable device and we question if this meets the spirit of a least burdensome approach.

We evaluated the alternative clinical study design presented by Dr. Brockman of the FDA in January of this year. We are very encouraged by this FDA effort to seek alternative regulatory paths to the current randomization to drug route. However, given the unknowns of the design details that would ultimately be acceptable and the potential issues regarding powering

the study, we decided to keep working on our ongoing trial as opposed to changing designs and restarting.

When we first designed our study, we sought input from a significant number of EPs. We were told by many of them that a study comparing AF ablation to medication did not make for strong clinical science because patients that failed a drug are being randomized to additional drug therapy as the control. Additionally, the complications are not directly comparable between ablation and drug.

The publication of the HRS consensus statement on AF in May of this year was a significant event. It establishes, among other things, (1) that ablation strategies which target the PV's are the cornerstone of most AF ablation procedures, (2) definitions for follow-up and monitoring guidelines and (3) Standards for Reporting Outcomes in Clinical Trials in Section 12 of the Statement. We believe that using the HRS Consensus statement as a basis, reasonable objective performance criteria or OPC's can be established for the evaluation

of safety and effectiveness of percutaneous AF ablation devices. Single-procedure success rates using a 90-day blanking period and a strict criterion for failure over a 1-year post-ablation follow-up could be established. Likewise, ablation-related complication rate OPC's could be established based on the literature and expert clinical opinion. We hope that you will consider this alternative OPC approach today.

Again, thank you for the opportunity to share the experiences of conducting our study with the Panel.