Screening

1. **How is a drug naïve patient defined?**

   A patient that does not have more than a 7-day history of therapeutic AAD use (Class I or III), or ≥ 24 hours amiodarone, for the treatment of persistent AF, except for pill-in-the-pocket AAD use, which is permitted (per exclusion criteria #1).

2. **Are patients treated with betablockers eligible for the study?**

   Yes, only patients that are treated with AAD Class I or III for more than 7 days, or amiodarone for more than 24 hours will be excluded from the study.

3. **For a patient to qualify to AVANT GUARD, he/she will require documentation of AF by two ECGs with continuous AF taken at least 7 days apart. Why 7 days apart?**

   The population targeted AVANT GUARD are persistent AF Patients. Persistent AF is currently defined as lasting for greater than 7 days: we will need documented proof of either a 24 hour continuous ECG or two ECGs with continuous AF separated 7 days or more.

4. **The patient has an operational ICM other than a LUX-Dx ICM. Can we remove a ICM that was implanted >6 months ago to allow patient to qualify for the study and then have a LUX re implanted per study requirements?**

   If a subject already has an ICM >6months and is allowed to receive a new LUX-Dx to be eligible for study participation. Please consult first CTM and medical director before enrollment in the study.

5. **When can patients in the trial have WATCHMAN/LAAC implanted and is it considered "cardiac surgery"?**

   In coordination with medical directors, LAAC/Watchman is not considered cardiac surgery. Patients can have a LAAC at any time within the trial.

6. **If a patient had an ablation in the right atrium for atrial tachycardia, can he/she be included in the trial?**

   Per exclusion criteria #2b, a patient with a right atrial ablation for atrial tachycardia could be enrolled in the study: 2.b. Any prior atrial endocardial, epicardial or surgical ablation procedure for arrhythmia, other than right sided cavotricuspid isthmus ablation or for right sided SVT

7. **Is co-enrolment with another study allowed?**

   If a subject is enrolled in another investigational study or registry that would directly interfere with AVANT GUARD he/she could not participate in the trial, except when the subject is participating in a mandatory governmental registry, or a purely observational registry with no associated treatments. In this case, it should be brought to the attention of the Clinical Trial Manager at Boston Scientific to determine eligibility.

Enrolment and randomization

1. **When would a patient know if he will be in the AAD or the PFA arm?**

   Once a subject is consented to the study and the verification of all inclusion and exclusion criteria is being performed, he/she will be randomized to either the PFA or the AAD arm. This will happen within a maximum of 30 days from the enrolment date.

2. **Why will AVANT GUARD enrollments be randomized in a 2:1 ratio and not 1-1?**

   Patients in the AVANT GUARD study are randomized 2:1 to provide enough sample size to power for the primary safety endpoint, which is only assessed in randomized PFA subjects, while minimizing the overall sample size.

PFA arm

1. **Should the FARAPULSE PFA system be used for redo procedures?**

   The FARAPULSE PFA System should always be used until the last subject in the study completes their last 12-month follow-up visit, which is when the primary endpoint is reached. This means a commercial system cannot be used before we have all the data needed to file our PMA report to the FDA and we have all the data for our primary endpoint for all subjects.

2. **Repeat PFA during blanking period recommended if arrhythmia recurrence occurs 6 weeks post Index procedure. Why the 6 weeks?**

   Repeat PFA during blanking period recommended if arrhythmia recurrence occurs 6 weeks post Index procedure. After 6 weeks, all the recurrence from inflammation should be gone. One repeat PFA ablation procedure is permitted during blanking period.

AAD arm

1. **Can patients randomized to AAD treatment receive PFA ablation if AAD fails?**

   Subjects randomized to AAD are eligible to receive an ablation after the blanking period: if there is a detectable occurrence of atrial tachyarrhythmia (AF, AFL or AT) lasting ≥ 1 hour (if asymptomatic) or ≥ 30 seconds (if symptomatic) outside of the blanking period (e.g., primary endpoint event); and if the recurrence occurred despite the use of maximally tolerated therapeutic dose antiarrhythmic drug therapy; and if the recurrence was of sufficient clinical severity to warrant a change in therapy at the discretion of the Investigator.

2. **What if a subject in the AAD arm is medically required to receive an ablation during the blanking period?**

   PFA ablation during the blanking is not recommended, AAD dose should be titrated up to the maximum tolerated dose. If it is medically required to perform an ablation, this will be an endpoint failure and a protocol deviation must be reported.

LUX-Dx ICM

1. **How will we compare the outcome of the study with other studies if we use an ICM, which will detect more arrhythmias than traditional arrhythmia monitors?**

   Comparing outcomes across studies is always difficult due to differences in baseline risk factors, endpoint definitions, arrythmia monitoring compliance, etc.. AVANT GUARD is a randomized study designed to compare outcomes across randomized arms within this study (1st line PFA ablation vs. AAD with possibility of delayed PFA ablation), as opposed to comparing outcomes from AVANT GUARD to those from other studies.

2. **Why is it recommended to have LUX-Dx inserted at baseline?**

   It is recommended to have LUX-Dx inserted at baseline to start capturing baseline data for all subject prior to the therapy initiation.

Follow-up

1. **Why is AF recurrence defined as 1 hour asymptomatic or 30 seconds symptomatic? How can this be compared with other studies?**

   A publication of data on healthcare utilization revealed that AF recurrence after ablation for PAF in durations of <1 hour, had hospitalization rates similar to those of patients free of recurrence. Significant differences in hospitalization rates, with longer durations (> 1 hour) were most pronounced for durations >24 hours. Considering these findings, a 1-hour recurrence duration, & a duration cutoff of 30 seconds has been considered for the detection of symptomatic episodes was considered clinically meaningful by the study Steering Committee.

2. **What if a patient gets an AF recurrence intervention in an emergency at a different hospital. How do we ensure that emergency cardioversions/AAD taken are captured in case patient goes to an HCP/emergency room outside of the study facilities?**

   Source documentation related to the AF recurrence intervention will need to be requested from that other site as a reference. Patients should be educated that if any visits/procedures outside the study site occurs, they must report it to the study team as per their patient card.

3. **Where would the patients enrolled in the study be followed? Would they be followed in the referral site or in the study site?**

   Patients enrolled in the AVANT GUARD study are required to be followed at the study site.

4. **Is pill in the pocket amiodarone considered a treatment failure after the initiation of the randomized therapy?**

   The use of amiodarone is prohibited during the entire study. If used, this is considered as a treatment failure.