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| **5.1** | **Study Title** | Comparison of pulsed field ablation versus radiofrequency thermal ablation in atrial fibrillation | |
| **PI** | Rajeev Pathak | |
| **Ref** | 2023.ETH.00191 | |
| **Reviewer** | Robert Schmidli | |
| **What is your recommendation for this item?** | | | |
| Approve without changes Approve out of session with changes Not Approve and resubmit  *There are too many issues to be addressed to allow this protocol to be approved out of session* | | | |
| **Review** | | | |
| * 1. **Research Merit and Integrity (NS1.1):** | | | |
| **Does the research proposal ask a relevant/worthwhile research question?** | | | **Yes/~~No~~** |
| Pulmonary vein isolation (PVI) by radiofrequency ablation (RFA) is currently used for catheter ablation in AF but risks oesophageal or phrenic nerve injury. Pulsed field ablation (PFA) may produce less collateral damage by use of a high electric field gradient, as it does not cause thermal injury. Cardiac cell membranes undergo increased permeability when exposed to high electric field gradients, leading to cell death. Pulmonary vein is main source of triggers for AF. | | | |
| **Has the researcher justified the need for this research?** | | | **Yes/~~No~~** |
| Justified on grounds that PFA may be superior to RFA, and comparative data are limited | | | |
| **Will the proposed methodology answer the research question(s)?** | | | **~~Yes~~/No** |
| 40 patients will be assigned treatment in an alternate 1:1 fashion. Suitable patients will have paroxysmal or persistent AF, resistant or intolerant to anti-arrhythmic drugs. Follow-up in 3, 6, 12/12 ECG, 6- & 12-month holter. Efficacy assessed with recurrence of arrhythmia or need for escalation of anti-arrhythmic drugs. Recurrent arrhythmias can be managed by whatever means during first 90 days blanking period after initial procedure, without penalty to effectiveness endpoint. Primary endpoints: (1) freedom from atrial arrhythmia of ≥30s outside of 90-day blanking period, without or with use of AAD at or below historic maximum dose, (2) freedom from serious procedure/device-related adverse events.  *There is no stratification of patients (eg. paroxysmal vs persistent AF)*  *See comments on statistics* | | | |
| **Is the protocol following good clinical practice?** | | | **~~Yes~~/No** |
| Study staff consist of cardiologists with experience in AF ablation and clinical trial coordination, and a higher degree research fellow. Procedure will be performed at TNCPH. Device is not currently on the Australian Register of Therapeutic Goods and is not licenced for this indication. Has been used in a multicentre clinical study in the USA with FDA investigational device exemption. TGA approval expected by the time of trial completion. Benefits are considered to outweigh risks.  *Is there evidence that benefits of PFA outweigh risks, when compared to RFA?*  *Will the nature of the procedure be revealed to patients on request?*  *Provide details of data security at Canberra Heart Rhythm*  *Costs for procedures and hospital stay are not outlined in PICF or elsewhere. What is the estimated cost?*  *What are Jenish Shroff’s qualifications?*  *Will subjects be given a choice of treatment, or will treatment be assigned after enrolment?*  *There is no independent monitoring* | | | |
| **Are the power calculations, indicating the number of recruits required, accurate?** | | | **~~Yes~~/No** |
| 20 patients in each arm  *There are no power calculations* | | | |
| **Is the proposed statistical analysis robust and accurate enough to deal with the data generated?** | | | **Yes/~~No~~** |
| Yes – probably (insufficient expertise) | | | |
| **Are the drug safety issues fully addressed?** | | | **Yes/No** |
| Detailed explanation of risks. See below | | | |
| **Are the risks to recruits detailed in the proposal listed fully and completely in the PICF?** | | | **~~Yes~~/No** |
| *Explain “thermal energy”, “electroporation”, “percutaneously”, “indifferent electrode” (PICF p2)*  *A diagram or video would be useful to describe PFA technique*  *Explain: “The cardiac procedure to be undertaken will be identical to that performed as standard care at the National Capital Private Hospital and it does not involve any investigational therapy.” – PFA is not an established procedure*  *Overall, PICF contains too much jargon*  *Complaints, compensation procedures need to be explained*  *PICF does not state that PFA is not TGA approved* | | | |
| **Suggested Comments to the Researcher from HREC** | | | |
| **RMI (NS1.1)** | | | |
| **Do you have comments for the HREC to consider against any of the other NS criteria?** | | | **Yes/No** |
| **Justice (NS1.4)** | | | |
| **Beneficence (NS1.6)** | | | |
| **Respect (NS1.10)** | | | |
| **General Comments on Risks and Benefits** | | | |