Information sheet

Study Name: **Rationale and design of Dabigatran for Mitral Stenosis Atrial Fibrillation Trial**
Version no.: v.1.2 (18/Nov/2019)

Protocol no.: DAMS-01
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Study site: Queen Mary Hospital
Study Principal Investigator: Prof. SIU Chung Wah David

You are being invited to take part in a research study. Before you decide, it is important to understand why the research is being done and what it will involve. Please take time to read the following information carefully. Ask the study doctor or research staff any questions you may have before signing the attached consent form.

About This Study
The purpose of our study is to find out the efficacy and safety of non-vitamin K oral anticoagulants (NOACs), the drugs used to prevent ischemic stroke for atrial fibrillation (AF) patients.

Why have I been chosen?
You are suffering from atrial fibrillation, a heart disease associated with 5-fold increase in ischemic stroke risk. Currently, NOAC is one of the most effective drug groups in preventing ischemic stroke under this condition. Among these AF patients, some have underlying valvular heart diseases with particularly high risk for stroke for those with mitral stenosis (MS) and the annual stroke rate ranges from 4% to 17% if left un-anticoagulated.

However, there's lack of research-based evidence to indicate the efficacy and safety of NOACs for patients with both AF and MS. As a result, there're still no standard guidelines for stroke prevention management regarding to NOACs for AF patients with underlying moderate to severe MS. On the other hand, there's recent foreign study suggesting the potential role of NOACs amongst AF patients with underlying MS in stroke prevention.

Concerning the very high risk for stroke for AF patients with underlying MS, also higher baseline risk of intracranial haemorrhage and higher ischemic stroke risk in Asian populations, we launch this study aiming at comparing the efficacy and safety of one of the NOACs – Dabigatran (150mg or 110mg according to subjects' renal function) – with normal warfarin

therapy in AF patients with moderate or severe MS. We plan to recruit a total of 686 subjects randomizing into 2 groups of investigational Dabigatran and warfarin in a 1:1 ratio. Since you have carried both heart problems, you are invited into our study.

What will happen to me if I take part?

If you meet the criteria of this study and are being enrolled, our investigator(s) shall have a short interview with you (less than 10 minutes) to explain the benefits and potential side effects of NOACs. Enough time will be given for understanding and solving any queries raised, and written consent has to be signed for agreement of study participation. You will then be randomized into either Dabigatran or warfarin group, which is open to your notice.

Study period of individual participants will be around 1 year. We will obtain medical history directly from you, hospital record as well as electronic medical record under Hospital Authority. Within the study time frame, you will have the first follow-up at 2-week interval after randomization. After that, we will arrange regular follow-ups of every 4 months for you to monitor the effect and safety of the drug prescribed until the study ends. We will perform certain investigations during study visits, including physical examination, echocardiography (during the first visit only) and blood sampling via venipuncture. You will be responsible to comply with the scheduled study visits, study procedures and prescription plan, and report to us as soon as possible for any adverse effects appear.

There are no extra expenses anticipated for participating in the clinical trial. You simply need to pay for the regular specialty follow-up fee and the regular medication fee under Hospital Authority policy as usual for each time scheduled or unscheduled follow-ups. On the other hand, there will not have reimbursement in any forms from the study.

What are the benefits of participating?

NOAC is currently a self-financing item under Hospital Authority. That means patients need to purchase the drug themselves or only patients meet certain medical criteria will the item be free. In this study, according to randomization, you will be given free-of-charged NOAC for stroke prevention secondary to AF, which is significantly safe and efficacious over the traditional warfarin therapy. Close monitoring by experienced medical staff will be held to ensure your safety.

Besides, your contribution is important to provide valuable information for stroke prevention strategy for patients with mitral stenosis and that may be immediately translatable to real clinical practice. It may also provide necessary evidence for establishing relevant universal guidelines.

What if something goes wrong?

Both dabigatran and warfarin are registered medications under the Pharmacy and Poisons Ordinance (Cap. 138) in Hong Kong Special Administrative Region. They have been overseen for their safety, efficacy and quality. Being randomized into either group (a 50/50 chance like flipping a coin) in this study, you will be prescribed corresponding anticoagulant with dosage adjustment based on your coagulation or renal blood-check result, according to standard medical guidelines.

As with all other researches regarding to clinical trial, there may involve harms and risks that are already known or currently unknown and unforeseen with the drug treatment. You are free to raise queries and concerns to our investigators prior to consenting and at any time during the study. Our medical staff will closely monitor your condition throughout the whole study period and you are responsible to tell our research staff as soon as possible for any changes in medical condition. Below are listed known side effects of the two anticoagulants.

Side effects of Dabigatran:

Common – nausea / diarrhea / indigestion / stomach upset / stomach pain / stomach burn / unexpected bruising / minor bleeding

Less common or rare – allergy / skin rash / itchiness / headache / dizziness / weakness / unexpected or uncontrollable bleeding / coffee-ground vomiting / brown urine / black stool / swelling / pain

Side effects of Warfarin:

Common – unexpected bruising / minor bleeding / bloating / nausea / vomiting / diarrhea / loss of appetite

Less common or rare – allergy / skin rash / itchiness / headache / dizziness / weakness / unexpected or uncontrollable bleeding / coffee-ground vomiting / brown urine / black stool / swelling / pain

Facts between Dabigatran and Warfarin:

Dabigatran	Warfarin
No need for regular blood-check	Regular blood-check
Fixed dosage	Regular dosage adjustment based on blood result
Not much food avoidance	A number of food that can affect drug efficacy has to be avoided

We indeed do not expect significant harms related to your participation to the study. In the

unlikely event of harm resulting directly from your participation in this study, medical treatment will be provided. Discontinuation of study treatment depends on discretion of investigator based on your medical condition, subsequent management and alternative medication use. Your willingness will be taken into consideration and prioritize. We are open to discussion to your concern and you definitely have the rights at any time to informedly withdraw from the study.
There are no special compensation arrangements provided to you in this study. If you are harmed due to someone's negligence, you may have grounds for a legal action but you may have to pay for it. Regardless of this, if you wish to complain about any aspects of the way you have been approached or treated during the course of this study, the normal health service complaint mechanisms will be available to you.

If you have any queries related to the insurance coverage from your own insurer(s) for your participation in the study, please discuss with your insurance consultant(s).

What are the alternatives for treatment?
Your participation in this study is absolutely voluntary. You may choose not to participate in this study by simply telling our research staff. If you decline this study, your medical appointments and medications will remain unchanged, or you may have to take alternative medical advice from doctor(s). You also have the rights at any time to withdraw from the study. In this case, we may arrange a final study visit for assessing and monitoring your health status. Your future follow-up appointments will be scheduled and conducted as directed by your physician. Your decision will not in any way affect your medical care or treatments.

What if new information becomes available?
During the course of the study, if any new information becomes available that may affect investigators' medical decision and/or relate to your willingness to continue to participate in this study, your research doctor will tell you about it in a timely manner and discuss with you. You would have the rights of access to personal data and known study results, if and when needed.

There are no foreseeable circumstances that the study will be ended unintentionally. Unless there is safety concern of the investigational drug from relative studies or from drug manufacturers, the study will be held according to protocol. In case of official mid-way termination of study, participants will be arranged similarly as of study discontinuation, with additional medical assessment and treatments as required to ensure patient safety.

Will my participation in this study be kept confidential?
As a subject in this research study, all your information will be kept confidential. Your name or your personal identity will not be used for any public purposes, publications, or transmitted

outside of the medical centre. Under the laws of the Hong Kong Special Administrative Region and, in particular, the Personal Data (Privacy) Ordinance (Cap. 486), you enjoy or may enjoy rights for the protection of the confidentiality of your personal data, such as those regarding to the collection, custody, retention, management, control, use (including analysis or comparison), transfer in or out of Hong Kong, non-disclosure, erasure and/or in any way dealing with or disposing of any of your personal data in or for this study.

By consenting to participate in this study, you expressly authorize the access to, the use of, and the retention of your personal data by the investigator(s) and members of his research team, representatives of the sponsor, and Institutional Review Board of the University of Hong Kong / Hospital Authority Hong Kong West Cluster (HKU/HA HKW IRB) for the purposes and in the manner described in this informed consent process.

By consenting to participate in this study, you also expressly authorize relevant government agencies (e.g. Hong Kong Department of Health) to get access to your personal data for the purpose of checking and verifying the integrity of study data and assessing compliance with the study protocol and other relevant requirements.

For any queries, you should consult the Privacy Commissioner for Personal Data or his office (tel no.: 852-2827-2827) as to the proper monitoring or supervision of your personal data protection so that your full awareness and understanding of the significance of compliance with the law governing privacy data is assured.

Who should I contact if have questions?

If you have any questions regarding to this study, you may contact Dr. Siu Chung Wah at 852-2255-3597. If you have any queries regarding to your rights in the study, you may contact the Secretary of HKU/HA HKU IRB at 852-2255-4086.

Consent Form

Study Name: **Rationale and design of Dabigatran for Mitral Stenosis Atrial Fibrillation Trial**

Study Principal Investigator: Prof. SIU Chung Wah David

By signing below, I agree that:

1. I confirm that I have read and understood the information sheet for the above study and have had the opportunity to ask questions.
2. I understand that my participation is voluntary and that I am free to withdraw at any time, without giving any reasons, without my medical care or legal rights being affected.
3. I understand that sections of any of my medical notes may be looked at by responsible individuals or from regulatory authorities where it is relevant to my taking part in research. I give permission for these individuals to have access to my records.
4. I agree to take part in the above study.

_____	_____	_____
Participant's signature	Participant's name	Date
_____	_____	_____
Witness's signature	Witness's name	Date
_____	_____	_____
Investigator's signature	Investigator's name	Date