PATIENT INFORMATION AND INFORMED CONSENT

Study Title	Left Atrial Appendage (LAA) Occlusion with The Amplatzer™ Amulet™ Device: The Southeast Asia Observational Study
Study Name	SEA Amulet™ Study
Principal Investigator	Dr. Koh Keng Tat (Sarawak Heart Centre)
Sub-Investigators	Dr. Oon Yen Yee (Sarawak Heart Centre) Dr. Alan Fong Yean Yip (Sarawak Heart Centre) Dr. Ong Tiong Kiam (Sarawak Heart Centre)
Site Name	Sarawak Heart Centre
Sponsor	Sarawak Heart Centre
Funder	St. Jude Abbott Medical

Dear Patient,

You are being invited to take part in a research study: the SEA Amulet™ Study. Before you decide, it is important for you to understand why the research is being carried out and what it will involve.

Please take time to read the following information carefully. This patient information form describes the nature, advantages, risks and discomforts of this study.

Ask your study doctor if there is anything that is not clear or if you would like more information. Take your time to decide whether or not you wish to take part. You should not sign this document until you understand all of the information presented in the following pages and until all of your questions about the research have been answered to your satisfaction.

Description and relevance of this study to you

100 patients who are indicated for Left Atrial Appendage Occluder (LAAO) with the Amplatzer™ Amulet™ will participate in this study. The device is intended to prevent blood clots formed in the left atrial appendage (LAA), which is a pouch-like part of the

heart extending off the side of your left heart chamber which acts as a decompression chamber when the chamber pressure is high, from entering the bloodstream and potentially causing a stroke.

This is a prospective and retrospective, multicenter observational study where the study is being performed to explore on the short-term and long-term safety and efficacy of LAA occlusion with Amplatzer™ Amulet™ Device in Southeast Asia Population on a real-world basis. The study is considered research. You may or may not benefit personally from participation in the study, but your participation may provide knowledge that will benefit others.

Why am I being asked to take part?

Your doctor has determined you have non-valvular atrial fibrillation. Non-valvular atrial fibrillation is an irregular and often very rapid heart rhythm that can lead to blood clots in the heart.

When the heart pumps in an irregular, uncoordinated way, there is a decreased flow of blood to the body, which is typically slow moving and likely to cause a blood clot. In the majority of cases, the clots form in the LAA. Left atrial appendage occlusion (LAAO), is a treatment strategy to reduce the risk of the blood clots from entering the bloodstream and causing a stroke.

Your doctor will determine whether it is required for you to undergo the treatment. After the treatment, follow-up sessions will be conducted to observe on your condition. This is an observational study, where the data obtained will be used for research study. The intention of this inform consent is for data collection only.

What is the purpose of the study?

This scientific study is intended to explore on the short-term and long term (1 year) safety and efficacy of LAA occlusion with the Amplatzer™ Amulet™ Device in Southeast Asia population on a real-world basis.

The safety and efficacy of LAAO with Amplatzer™ Amulet™ occluder device has been well studied in the European population and showed a favorable efficacy and safety outcomes, however, there is no data from the Asia population. It is therefore imperative to have a regional study on the safety and efficacy of LAAO with Amplatzer™ Amulet™ in the Southeast Asia region.

How long will I be involved in this study?

Your participation will last approximately 1 year, including the follow-up for outcomes.

What will happen if you take part?

If you agree and give consent to take part in this study, the study data, including your medical information, may be used and shared for legitimate study and scientific purposes, or for future use in research. Your suitability for receiving the treatment will be reviewed (called Screening).

A. Screening

Prior to the procedures, you will undergo baseline evaluation for:

a. demographics and concomitant medications;

b. indication for LAAO;

c. medical history such as mRS*, CHA2DS2-VASc score**, HAS-BLED score***,

d. 12-lead ECG (a medical test that detects heart beat abnormalities by measuring electrical activity);

e. echocardiogram (a scan to look at the heart and nearby blood vessels), and

f. pre-procedural imaging with CT scan or TOE.

*mRS: Modified Rankin Scale (mRS) assess disability in patients who have suffered a stroke and is compared over time to check for recovery and degree of continued disability. A score of 0 is no disability, 5 is a disability constant care for all needs; 6 is death.

**CHA2DS2-VASc score: A validated tool to predict the risk of stroke and blockage of blood flow in patients with irregular heartbeats.

***HAS-BLED score: A risk score to estimate the 1-year risk for major bleeding in patients with irregular heartbeats.

B. Treatment

You will be given Amplatzer™ Amulet™ LAAO implant treatment if your treating doctor thinks that it is necessary for you to be implanted after Screening period. The device has a distal lobe and a proximal disc, connected by an articulated waist. The device lobe has six to 10 pairs of stabilizing wires and is meant to be implanted in the proximal 10-15mm of the LAA, whereas the device disc is intended to cover the ostium (opening of right coronary artery, a blood vessel in heart) at the left heart chamber.

During the treatment, transesophageal echocardiography (TOE) or intracardiac echocardiography (ICE) will be performed only when combined with the pre-procedural imaging. TOE is done by inserting a probe with a transducer down the gullet and this provides a clearer image of the heart using high-frequency sound waves (ultrasound). ICE on the other hand is a catheter-based form of echocardiography that gathers images from within the heart, rather than by gathering images of the heart by sending sound waves through the chest wall, like what TOE does. Both TOE and ICE are used to examine the structures of the heart. Adverse event assessment will also be performed to observe for any possible side effects.

C. Visits and tests

After your procedure, you will be evaluated to determine the duration of hospital stay. Your study doctor will observe for any potential side effects and undesirable events. Medication use will also be discussed with you.

You will return to the hospital for at least 3 follow-up visits after:

a. 1 month to 3 months;

b. 6 months (+/- 2 weeks) and

c. 12 months (+/- 6 weeks)

During all the visits, your study doctor will discuss with you again for your medication use based on your condition. The condition is judged based on some safety and efficacy outcomes such as:

- All-cause and cardiovascular mortality (death attributable to some heart diseases or problems)
- Bleeding events
- Build up of fluid in the double-layered, saclike structure around the heart
- Device dislocation
- Device related blood clots formation in blood vessels
- Access site complications
- Stroke
- Blockage of blood vessels.

TOE or CT scan will only be conducted for first two follow-up visits (1M to 3M and 6M). Interim and unscheduled visit might be needed if your study doctor/site staff thinks they are needed.

Patient shall attend the clinical site as and when required per the standard of care at the site. Required data shall be collected as they become available.

What will happen at the end of the treatment?

Your participation in the treatment stops when:

- You have completed all the visits (including the follow-up visits)
- You choose to stop
- The study doctor considers it best for you to stop

Following the end of the treatment if you have withdrawn from the study before its conclusion, your study doctor (or appointed delegate) may seek to establish your long-term health status for a period of not more than 6 months (from Day 1 of study period), by accessing your hospital records, or publicly available sources such as national registries, newspaper obituaries and social networking websites. Attempts may also be made to contact you or your relatives to ascertain this information. If you do not want this information about you to be collected, you may record your objection with your study doctor at any time.

This study is concluded once all the participants have completed the study.

What is expected from you?

This is an observational study, the purpose of this inform consent is for data collection only. Your consent to participate in this study indicates that you agree to have the medical data collected to be used in this study. In order to carry out the study properly, it is important that you follow the study instructions. Your doctor and nurse will support you as best they can. As a participant in this study, you will be asked to:

- Not participate in another medical study in which the active treatment arm may confound the results of this study;
- Follow the recommendations of your study doctor and adhere to the study plan and scheduled follow-up contacts;
- Take standard medications as instructed by your doctor.

It is important that you contact the study doctor if:

- You are admitted to hospital or are going for treatment there;
- You suddenly develop any new health problems, or an existing health problem becomes worse;
- There are any changes to your medication, either prescribed by your family doctor or those you buy at a pharmacy, including herbal or alternative therapies or remedies;
- Your contact details change;
- You have any questions or concerns.

What are the potential risks and discomforts?

All medications and treatments may cause certain side effects and can have temporary and permanent side effects and can cause unforeseen side effects. Side effects can vary from mild to very serious, even causing death.

The potential risk and undesirable effects resulting from the use of Amplatzer™ Amulet™ occluder device are the same as for other occluders. These include (but not limited to):

- Air embolism (Bubble(s) enter a blood vessel and blocks it)
- Allergic reaction
- Anaesthesia reactions
- Abnormal heartbeats
- Bleeding
- Stop beating of heart
- Fluid accumulation around heart muscle causing excessive pressure on the heart
- Death
- Movement of device to an unintended location within the body with resulting obstruction of an organ or vessel
- Device migration
- Embolic event (Blockage of blood vessel)
- Fever
- Blockage of blood vessel due to foreign substance lodged in the bloodstream
- High blood pressure/low blood pressure
- Infection
- Multi-organ failure
- Heart attack
- Perforation
- Build up of extra fluid in the space around the heart
- Kidney failure/dysfunction
- Seizure
- Significant residual flow
- Stroke
- Blood clot formation
- Transient ischemic attack (Temporary period of symptoms like those of a stroke)
- Vascular access site (an opening made in your skin and blood vessel during a short operation) injury
- Blood vessel injury

Serious adverse events (Serious side effects related to the study) occurring during the Follow Up Period will be reported and followed up. Concomitant medications relevant to serious adverse events i.e. serious side effects that are related to study treatment occurring during the Follow-Up Period will be reported and followed up. All the

medications and treatments used during the study, including medications that are taken before procedure, after procedure and follow-ups will be recorded.

What are the possible advantages and disadvantages of taking part?

Your participation may not benefit you directly, your participation in the study may, however, help patients in the future by improving the knowledge of diseases and improving medical care.

Disadvantages of participation in the study may be:

- The additional time it will take for you to complete study follow-up visits (hospital visits or telephone contacts);
- Instructions you need to follow

Is there any alternative treatment?

You may receive the standard treatment(s) to treat your disease. You have the option to discuss with your doctor to receive treatment or to choose other therapy (including commercially available medicines such as blood thinners, heart rate medicines, and heart rhythm medicines or other devices according to the hospital's standard of care).

Your study doctor will discuss with you all the risks and potential benefits of available alternative treatments.

Will I be informed if new information become available during the study?

Your study doctor will inform you or your legal representative in a timely manner of any new information learned during the study that may affect your willingness to continue your participation. If you decide not to continue in the study, your study doctor will make arrangements for your care to continue. If you decide to continue in the study, your study doctor will ask you to sign and date an updated consent form.

What will happen if I don't want to carry on with the study?

Participation is voluntary. It is up to you to decide whether you take part.

If you decide not to participate, you do not need to do anything further. You do not need to sign anything. You do not need to state why you do not wish to participate. If you are a patient, you will receive the treatment you would otherwise also receive. If you do participate, you can always change your mind and withdraw during this study.

You may withdraw from the study at any time without this negatively affecting you and without the loss of benefits you would otherwise be entitled to. If you do withdraw from the study after the procedure, the occluder will not and cannot be removed.

Should you participate in the study and withdraw from the study at a later date, we will not make any new information about you available for the study. However, information collected before you withdraw from the study remains part of the study. If you do not object, you will be contacted by phone to inquire about your health status at the end of the study.

If there is any new information about the study that is important for you, the study doctor will let you know. You will then be asked whether you still want to continue your participation.

Will the study be suspended or terminated before it is concluded?

Not applicable. This is an observational study and not an interventional study, where patients are consented for the purpose of data collection.

Will my records/ data be kept confidential?

For this study it is necessary to collect your medical and personal data. Each study subject will receive a code that will be marked on the data. Your name will be deleted. All the documents in the study will be filed and kept in a locked room with limited access. All electronic data will be stored in a password-protected database. The study data and documents will be kept up to 7 years after the completion of study. Study data is destroyed after period of storage.

Your doctor and the study sponsor will handle your participation confidentially. You will not be referred to by name, address, telephone number or other direct identifying data in the study files. All of your personal data will be replaced with a number that cannot be linked directly to you, except by the study team.

Who will have access to my medical records and research data?

- Study monitors and auditors or its authorized representatives, who check that the study is being performed correctly and that the information collected about you is accurate;
- Ethical committee that approved this study and ensures that your rights and well-being are safeguarded;
- Regulatory authorities involved in keeping research safe for participants.

Study data with your personal and research data will not be shared with any unauthorized third parties, this includes the company/funder providing the study grant or funding.

What will happen to your data?

This study may only be performed by collecting and using your medical information. Therefore, by signing this form you specifically authorize your information to be checked, transferred, and processed as follows:

- The authorized representatives of the Ethics Committee (EC), and regulatory authorities' inspectors may review your medical information by direct access to your medical records.
- Study data may be used and shared for legitimate study and scientific purposes, including if you do not object, for future use in research.
- The study results might be published or presented. If the results of this study are presented in a medical journal or at a symposium, none of your personal information will be revealed.
- All information pertaining to the study will be stored for 7 years after the completion of the study and may be forwarded for analysis. Your data will only be sent in encoded form.

Who funds this study?

This is an investigator-initiated research where the investigator or the study site, Sarawak Heart Centre serves as the Sponsor. The study was supported by an educational research grant from St. Jude Abbott Medical (the funder). The funds supported by the funder is mainly used to manage the data management and to support the purpose of this study, which is to collect the data both retrospectively and prospectively. The LAA occluders that were implanted are funded by pensioner Tabung Bantuan Perubatan, Ministry of Health (MoH) or self-paying. The purpose of this study is to collect study data only.

Will I receive compensation for participating in this study?

Your participation in the study will not entail any additional costs for you. You will not be paid for your participation.

Who should I contact if I have additional questions/problems during the course of the study?

If you have questions about the study, or about your rights in the study, please contact your study doctor. You are encouraged to ask any and as many questions as you would like so that you can decide if you wish to take part or not.

All the relevant details can be found in Appendix A: Contact details.

Your doctor has the right to terminate this study or your individual participation in it if he/she is of the opinion that continuation of the study may lead to undesirable events. You must inform your doctor if you suffer disease or injury during the course of the study or are admitted to a hospital for any reason.

It is recommended that you keep a copy of this document so that you may review it later if necessary. Thank you for your attention.

Appendix A: Contact details

Further information and who to contact

The person you may need to contact will depend on the nature of your query.

If you want any further information concerning this study or if you have any medical problems which may be related to your involvement in the project (for example, any side effects), you can contact the following people:

Clinical contact person

Name	Dr. Koh Keng Tat
Position	Consultant Cardiologist
Telephone	+6082 668111
Email	keng_tat@hotmail.com

If you have any questions, feedback or complaints about any aspect of the research study, the way it is being conducted or any questions about being a research participant in general, then you may contact:

Reviewing EC approving this research and contact details

Reviewing EC name	Medical Research and Ethics Committee
EC contact person	Secretariat
Telephone	+603-3362 8205
Email	mrecsec@moh.gov.my

CONSENT FORM

Study Title: Left Atrial Appendage (LAA) Occlusion with The Amplatzer™ Amulet™ Device: The Southeast Asia Observational Study

Study Name: SEA Amulet™ Study

I voluntarily consent to participate in this study as described in this patient information sheet.

- I confirm that I have read the information about the SEA Amulet™ Study, that I have had the opportunity to ask questions and have had sufficient time to think about it.
- I understand that hospital visits or phone call follow-up are required for the study that will take place 1-3 month(s), 6 months and 1 year after occluder implantation.
- I know that the ethics committee/internal assessment committee has evaluated and approved this study.
- I understand that all documents that are part of my medical dossier will be handled with strict confidentiality. I also understand that my medical dossier may be reviewed by the responsible person of the sponsor (Sarawak Heart Centre) or a representative, the ethics committee/internal assessment committee and/or regulatory authorities.
- I give all of these persons permission to review my dossiers.
- I understand that my participation is voluntary and that I may withdraw at any time, without having to give a reason and without this having any consequences for my medical care or legal rights.
- I can request additional information at any time.
- I consent to my GP and/or treating physician being informed about my participation in this study.
- I consent to my medical information pertaining to the study being stored for 7 years after the completion of this study and being sent for analysis.
- I will receive a copy of the patient information and consent form signed by the doctor.

Patient or legal representative:

Name:	Identity Card Number:
Signature:	Date (dd/mm/yyyy):
Relationship to patient*:	

*Relationship to patient is only required if you sign as legal representative

Doctor:

I hereby declare that I have informed the patient about the goal, the potential risks and consequences of the above-named study.

Name:	Identity Card Number:
Signature:	Date (dd/mm/yyyy):

Impartial Witness (if applicable):

I confirm that the information in the consent form and any other written information was accurately explained to, and apparently understood by the patient, and that verbal informed consent was freely given by the patient.

Name:	Identity Card Number:
Signature:	Date (dd/mm/yyyy):
Relationship to patient:	Relationship to study or doctor: