

COVER PAGE

Title of Study:

A Prospective Comparative Study of Rivaroxaban versus Warfarin in Patients with Mechanical Heart Valves

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CONSENT FORM

PART I [INFORMATION SHEET]

Invitation to be Part of a Research Study

You are invited to participate in a research study entitled **Rivaroxaban versus Warfarin in Patients with Mechanical Heart Valves** as a research participant. The purpose of this information sheet (Part I of consent form) is to provide you with sufficient information regarding the study that you may decide whether or not you would like to participate. If you have any question regarding the study or this form you are welcome to ask the project team. Please note you will only be included in the study if you consent to participate and sign the consent certificate (Part II of consent form).

Who is conducting this Research?

This study is being conducted by Dr Musfireh Siddiqeh(cardiac surgeon) Executive director of Rawalpindi institute of Cardiology

This study is funded by no one.

What is the purpose of this study?

The purpose of this study is to Determine use of Rivoroxaban in metallic heart valves. Currently tablet warfarin is used as standard practice in patients of metallic heart valves to keep valve functioning and preventing thrombus formation on metallic heart valves. However it requires a lot of frequent monitoring in form of blood tests to monitor INR which is to be kept in a certain range .Also tablet warfarin has a lot of drug and food interactions all which may affect its efficacy sometimes leading to suboptimal levels and sometimes causing excessive thinning of blood which may lead to bleeding at times life threatening .This is quite difficult for patients who live in far flung areas and have limited access to tertiary care hospitals leading to frequent complications. On other hand Tablet Rivaroxaban has proven role and is being used as in other diseases such as pulmonary embolism DVT for purpose to keep blood from clotting and is preferred over warfarin in such scenario reason being it does not require frequent monitoring nor does it have such significant drug interactions with food and other drugs as warfarin does.

Our aim is to use tablet rivaroxaban in place of warfarin in patients with metallic heart valves with strict monitoring initially. If rivaroxaban can be used with same efficacy as warfarin we will make it a standard practice in our institute this will greatly help patients especially those who lack facility of frequent INR monitoring by blood samples and those who are unable to maintain optimal INR due to food and drug interactions

Why am I selected/invited to participate in this study?

You have been invited to participate in the study as you meet the eligibility criteria *i.e have a metallic heart valve and find it difficult to maintain optimal INR in range .*

However, you should not participate in this study if you can strictly monitor INR .

What will I have to do as a research participant?

If you consent to participate in the study, you will be asked to get echocardiogram done every 10 days initially for a month then monthly for six months.

If at any point there is increased pressure gradient (according to echo criteria) observed on echo patient will be immediately admitted and started on injection heparin /thrombolysis .

How long will I be the part of study?

Your participation in this study will last for total one year .

You will be admitted initially to start drug and will be kept admitted for 5 to 7 days with daily echocardiogram (done by classified cardiologist) after discharge you will be followed up frequently . you will have an echocardiogram at each follow up which will be free of cost.

FOLLOW UPS being

Every 10 days for 1 month

monthly for 12 months

if at any point patient becomes symptomatic he should immediately come for follow up can telephone principal investigator or come directly to ER of RIC

Does the study involve any EXPERIMENTAL drug or procedure?

This study involves use of Tablet Rivoroxaban as a blood thinner(anticoagulant) in place of tablet warfarin in patients with metallic heart valves who are unable to maintain optimal INR(blood thinning ratio) or those who have experienced a stuck valve despite being on warfarin.

Tablet rivoroxaban is currently being used as an anticoagulant as standard practice in patients with DVT (deep venous thrombosis) and in patients with pulmonary embolism(clot in pulmonary artery) with very good results . However its role in metallic heart valves is yet to be proven . Recent trial RIWA role of rivoroxaban 15mg twice daily was randomized with dose adjusted tab warfarin in two groups .Results revealed comparable results in-terms of bleeding and thromboembolic events in both groups .

Tab rivoroxaban does not require frequent INR monitoring (by blood sampling) and doze is adjusted according to weight of patient unlike tablet warfarin its doze needs to be titrated according to INR suboptimal INR will result in complications such as stuck valve and high INR may lead to bleeding complications . Also tablet warfarin has frequent interactions with drugs and food thus acquiring an optimal INR is often a very difficult task especially in our population who lack facility to get INR checked frequently .

In such patients if we are able to use Tablet rivoroxaban which only requires intensive monitoring initially will prove to be greatly beneficial as they will remain stable and would not need frequent blood sampling and can avoid complications of suboptimal INR or excessive bleeding.

What are the possible harms, risks or discomforts I may experience during the study?

While participating in this study you may experience the following risks or discomforts:

1. Stuck valve (thrombus formation on valve) to avoid this complication you will be frequently monitored in initial period by echocardiogram done by our experienced cardiologists.
2. Bleeding diathesis : Although risk of bleeding complications is low as compared to warfarin yet if you experience any such complication it can be managed by blood transfusion if massive.

If you are or become pregnant during this study, there may be risks to the embryo or fetus that are currently unforeseeable. You are advised to inform us and u will be started on injection heparin in first trimester tab warfarin in second trimester and again inj heparin after 36 weeks.

How will I be managed if I experience any harm due to the study?

In case you experience any harm/discomfort we will provide you with immediate echocardiogram to see extent of thrombus on echo and according to severity index you will be shifted initially to injection heparin/clexane and then thrombolysis if required. Redo surgery is rarely required.

What are the benefits of my participation in the study?

The results of this study will benefit society if rivoroxaban can be used with same efficacy as warfarin we will make it a standard practice in our institute this will greatly help patients especially those who lack facility of frequent INR monitoring by blood samples and those who are unable to maintain optimal INR due to food and drug interactions

Tablet rivoroxaban which only requires intensive monitoring initially will prove to be greatly beneficial as they will remain stable and would not need frequent blood sampling and can avoid complications of suboptimal INR or excessive bleeding.

We may learn information about your health as part of the research. We will share this information with you .

Is there any cost associated with my participation in the study and will I be compensated?

You will not have to bear any costs as a research participant

Who will have access to my information collected during the study?

Your identity in this study will be treated as confidential. However, it is possible that other people and offices such as DRAP responsible for making sure research is done safely and responsibly will see your information.

To protect confidentiality of the study records and data, the following measures will be taken: All data will be kept on electronic medical record.

Will my information or my bio-specimens be used for anything other than the current study?

Information about you, will not be used for any purpose other than as described above

What if I do not wish to participate in the research?

There will be no penalty or loss of benefits to which you are otherwise entitled if you choose not to participate.

What are my rights as a research participant?

You are free to choose whether or not to participate in this study.

You may withdraw to participate in the study for any reason by just informing treating consultant i.e principal investigator . Also you will be provided with any significant new findings developed during the course of this study that may relate to or influence your willingness to continue participation. In the event you decide to discontinue your participation in the study. ,

In addition, your participation in the study may be terminated by the investigator without your consent under the following circumstances if you are noncompliant to medication or develop any complications,

Whom should I contact for any query regarding the study?

You are encouraged to ask questions at any time during this study. For further information *about the study*, contact principal investigator Dr Musfireh Siddiqeh phone numb 03345548005

CONSENT FORM

PART II [CERTIFICATE OF CONSENT]

I *certify that the* information provided in the Consent Form Part I [Information Sheet] of the study entitled Use of rivoroxaban in metallic heart valves has been read [by/to] me. I have had the opportunity to ask questions about it and any questions that I have asked have been answered to my satisfaction. I consent voluntarily to participate as a participant in this research.

Participant's Name (printed) _____

Participant's Signature

Date

CERTIFICATE BY WITNESS

In case where the research participant is illiterate, a literate witness must sign (if possible, this person should be selected by the participant and should have no connection to the research team).

I have witnessed the accurate reading of the consent form to the potential participant, and the individual has had the opportunity to ask questions. I confirm that the individual has given consent freely.

Print name of witness _____

AND

Thumb print of participant

Signature of witness _____

Date _____



STATEMENT BY THE RESEARCHER/PERSON TAKING CONSENT

I have accurately read out the information sheet to the potential participant, and to the best of my ability made sure that the participant understands the provided information.

I also confirm that the participant was given an opportunity to ask questions about the study, and all the questions asked by the participant have been answered correctly and to the best of my ability. I confirm that the individual has not been coerced into giving consent, and the consent has been given freely and voluntarily.

A copy of this ICF has been provided to the participant.

Name of Researcher/person taking the consent_____