Patient Study ID: 201807 ____ ____ ____ ____ - ____ ____ ____ **Patient Initials** *(First, Mid, Last):* ____ ____ ____

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UNIVERSITY OF CALIFORNIA, IRVINE
RESEARCH SUBJECT INFORMATION, AUTHORIZATION AND CONSENT FORM

Randomized, Registry, and Roll-in Patients

TITLE:	Edwards PAS**C**A**L** Tr**A**n**S**catheter Valve Re**P**air System Pivotal Clinical Trial (**CLASP IID/IIF**): A prospective, multicenter, randomized, controlled pivotal trial to evaluate the safety and effectiveness of transcatheter mitral valve repair with the Edwards PASCAL Transcatheter Valve Repair System compared to Abbott MitraClip in patients with mitral regurgitation .
SHORT TITLE:	Edwards PASCAL CLASP IID/IIF Pivotal Clinical Trial
PROTOCOL NO.:	2018-07 WCG IRB Protocol #20182304 UCI IRB# 2411
SPONSOR:	Edwards Lifesciences, LLC
INVESTIGATOR:	Antonio Frangieh, MD, MPH, FACC 101 The City Drive South Orange, California 92868 United States
STUDY-RELATED PHONE NUMBER(S):	(714)-509-6280 (daytime) (714) 380-7735 (24-hours)
SUB-INVESTIGATORS:	Jin Kyung Kim, MD Jack Sun, MD Pranav Patel, MD Dawn Lombardo, DO

INTRODUCTION

You are being asked to participate in a research study. Participation is completely voluntary. Please read the information below and ask questions about anything that you do not understand. A researcher listed above will be available to answer your questions.

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Aug 02, 2023

BACKGROUND

Mitral regurgitation (MR) is a condition when your heart's mitral valve does not close tightly which causes blood to flow backwards in your heart. This condition increases the workload on the heart and if left untreated, it can increase the risk of worsening heart failure.

There are two major categories of mitral regurgitation:

1) Degenerative Mitral Regurgitation (DMR), also known as Primary MR occurs when there is a problem or injury involving the valve or leaflets themselves.
2) Functional Mitral Regurgitation (FMR), also known as Secondary MR occurs when the valve itself is normal, but problems with the heart muscle keep the valve leaflets from fully closing.

You have been asked to be a part of this study because despite medical therapy for your MR, you have been determined to have symptoms due to heart failure. In addition, your doctors have determined you are being considered for transcatheter mitral valve treatment.

For the DMR group (described later in this consent), the trial will compare the PASCAL System and MitraClip System for patients determined to be at prohibitive (high) risk for mitral valve surgery. This means that you have a high operative risk of death within 30 days after your open heart mitral valve surgery. For the DMR group, enrollment has been completed and the PASCAL Precision System has been approved by the FDA for use.

For the FMR group (described later in this consent), the trial will compare the PASCAL Precision System and MitraClip System with patients currently on optimal medical therapy who are deemed eligible for transcatheter mitral valve treatment. For the FMR group, trial enrollment is ongoing and the PASCAL Precision System is still considered to be investigational.

The standard medical treatments generally available to patients with mitral regurgitation, may only temporarily alleviate some of your symptoms. This treatment will not permanently alleviate your condition or cure your mitral regurgitation.

The PASCAL and MitraClip Systems are designed to reduce the amount of mitral regurgitation without the need for surgery; which is less invasive. It is unknown whether the amount of reduction in regurgitation that is achieved using the PASCAL implant system will benefit you.

The PASCAL Precision System was approved by the FDA for use in patients with DMR in September 2022 and is now available for commercial sale in the United States. This device is not yet approved by Health Canada.

Because enrollment in the FMR group is ongoing, the PASCAL Precision System is still considered to be investigational for use in patients with FMR. This means that the PASCAL Precision System has not yet been approved by the U.S. Food and Drug Administration (FDA) or Health Canada for commercial sale.

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Aug 02, 2023

The PASCAL Precision System has been approved since August 2022 for commercial sale in Europe for both DMR and FMR patients.

The MitraClip System is approved in the United States to treat patients with moderate to severe DMR who are determined to be at prohibitive risk for surgery as well as symptomatic heart failure patients with moderate to severe FMR.

The MitraClip device is a commercially approved device. However, according to the MitraClip device labelling, the safety and effectiveness of the device for patients with the following characteristics have not been established:

- patients with more than one significant leak in the valve,
- small mitral valve area of less than 4.0cm^2,
- patients with a lot of calcium deposits on their valve,
- deep indentations in the valve leaflets that lead to significant leakage,
- wide length of leaky leaflet area or gap between the leaflets (flail width >15mm and flail gap >10mm)

The use of the MitraClip device in these situations is at the discretion and clinical judgment of your physician. Your doctor can tell you if your valve characteristics have some of these characteristics. If it does and your physician, in consultation with the clinical trial case review and approval committee of the clinical trial, determines that you are an appropriate candidate for the MitraClip device, you will be randomized to receive the MitraClip device or the PASCAL device.

Edwards Lifesciences, LLC. is a medical device company. It is sponsoring (paying for and managing) this study. The Sponsor reimburses the institution for tests and procedures needed for this study.

STUDY PURPOSE

The goal of this study is to assess the safety and performance of the PASCAL Precision System compared to the MitraClip System in patients with symptomatic moderate to severe mitral regurgitation who may not be ideal candidates for mitral valve surgery and may be eligible for transcatheter mitral valve repair.

Up to 1195 patients will take part at up to 99 international study centers. This study is made up of 3 different groups described below: Randomized, Registry and Roll-in. If you have been selected as a roll-in or single-arm registry patient, you will not be randomized. Your study doctor or his/her staff will let you know which of these groups you are assigned. Your involvement in this study will be for approximately 5 years and your participation is voluntary.

Roll-in Cohort: The first few patients (up to 3) at your site, regardless of the type of mitral regurgitation who participate at this study center will be considered “roll-in” patients and will receive the experimental treatment, the Edwards PASCAL Precision System. The “roll-in” phase of this study is designed to provide experience and training for investigators and their staff at the centers participating in this study. As a roll-in patient, you will be given the same therapeutic treatment with the Edwards PASCAL Precision System and

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Aug 02, 2023

receive the same quality of medical care as any other person who is enrolled in this study. You will have the same follow-up procedures that are required for all study patients.

Randomized Groups:

Degenerative Mitral Regurgitation (DMR) Randomized Group:

If you agree to participate and your doctors have determined that you have **Degenerative MR (DMR)** and are at prohibitive (high) risk for surgery, you will be chosen at random to be in one of two groups in a 2:1 fashion. This means you will be twice as likely be treated with the PASCAL device as the MitraClip device.

1) DMR PASCAL Device Group (IID): Up to 200 patients will have a procedure to repair their mitral valve using the PASCAL System
2) DMR MitraClip Device Group (IID): Up to 100 patients will have a procedure to repair their mitral valve using the Abbott MitraClip Delivery System

Enrollment in the DMR Randomized Group has been completed and follow-up is ongoing. A total of 300 patients are participating in this DMR randomized CLASP IID study.

Functional Mitral Regurgitation (FMR) Randomized Group:

If your doctors have determined that you have **Functional MR (FMR)**, then the goal will be to compare the safety and performance of the PASCAL Precision System plus optimal medical therapy and the MitraClip System plus optimal medical therapy, for the reduction of FMR. If you agree to participate, you will have 50/50 chance of receiving being treated with the PASCAL device or the MitraClip device, to be in one of two groups:

1) FMR PASCAL Device Group (IIF): Up to 175 patients will have a procedure to repair their mitral valve using the PASCAL Precision System
2) FMR MitraClip Device Group (IIF): Up to 175 patients will have a procedure to repair their mitral valve using the Abbott MitraClip Delivery System.

Up to 350 patients will take part in the FMR randomized CLASP IIF study.

PASCAL Registry: Patients who are deemed eligible to receive the PASCAL procedure, but who are not deemed eligible to receive the MitraClip procedure will be given the option to enroll in this registry.

Enrollment in the DMR CLASP IID group has completed with 98 patients participating in the DMR single arm registry (non-randomized).

Enrollment in the FMR CLASP IIF group is ongoing and will have up to 150 eligible participants for the FMR single arm registry (non-randomized).

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AS MODIFIED
Aug 02, 2023

Non-randomized means patients will automatically be assigned to have a procedure to repair their mitral valve using the PASCAL Precision System. You will have the same follow-up procedures that are required for all study patients.

DEVICES

PASCAL Implant System

The PASCAL Precision System is an artificial device made of a spacer, paddles and metal clips covered with polyester fabric. The main components of the PASCAL Precision System are the PASCAL Precision Implant System, the Steerable Catheter, and the Implant Catheter. The PASCAL Precision Implant System is introduced to the femoral vein by a Loader through a Guide Sheath.

MitraClip Implant System

The MitraClip Device Implant is an artificial device made of a metal clip covered with polyester fabric. The main components of the MitraClip Clip Delivery system are the MitraClip Device Implant, the Delivery Catheter, and the Steerable Sleeve. The MitraClip Clip Delivery System is introduced to the femoral vein through a Steerable Guide Catheter, which includes a dilator.

The PASCAL and MitraClip implant devices are deployed and secured to the leaflets of the mitral valve, acting as a filler in the leaky area and providing repair to your diseased mitral heart valve to minimize the incorrect flow of blood in your heart. The implant systems do not require open-heart surgery and can be done using a minimally invasive technique.

The study physician performing the procedure has experience in transfemoral (through the vessels) and transseptal (through the wall between chambers of your heart) procedures and has received training by the manufacturer of the investigational (experimental) device.

STUDY PROCEDURES

Screening and Baseline Visit

Before any tests or procedures are performed, you will be asked to review and sign this approved consent form. A copy of this signed and dated consent form will be given to you. If you consent to participate in the study, research personnel will ask you questions and will perform tests and procedures to see if you qualify for entry into the study. Copies of your records may be placed in your research record as part of this study.

The following screening and baseline procedures and observations may be performed to determine if you qualify for entry into the study:

- Medical history. Your study doctor or his/her staff will ask you questions about your medical history and what medications you are taking.

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AS MODIFIED
Aug 02, 2023

- You will be given a targeted physical examination (includes vital signs, weight and height) and a clinical evaluation of your condition. Any findings will be written down in the study chart. You should ask the study doctor what you should expect during the examination. Your condition will be graded based on your ability to perform physical activities (NYHA class).
- Your risk of death before heart surgery will be calculated using the STS Risk Score and EuroSCORE II.
- You will be asked to do a six-minute walk test (6MWT) (a test to see how far you can walk in 6 minutes).
- You will undergo a neurological examination using the National Institutes of Health Stroke Scale (NIHSS).
    - All patients with a history of stroke will also undergo a Modified Rankin Scale (mRS) assessment.
- You will complete a set of Health Status Questionnaires that will help your study doctor assess your quality of life.
- You will answer a few questions regarding your functional status and ability to perform daily activities using the Canadian Study of Health and Aging Survey Clinical Frailty Scale.
- An ECG (a recording of the electrical activity of your heart) will be obtained.
- A transthoracic echocardiogram (TTE) and a transesophageal echocardiogram (TEE) will be performed.
    - A TTE is an ultrasound of the heart allowing assessment of the heart valves. A plastic probe is placed on the surface of the chest, over your heart, to provide a type of visualization of the study devices and your blood flow with pictures.
    - A TEE is when a specialized probe is passed into the esophagus (through your throat) allowing pictures to be taken from behind the heart. During this type of echo, you may be sedated or given a numbing agent in your throat to try and make you more comfortable during the procedure.
- Invasive Right Heart Pressure Monitoring may need to be performed if the research doctor needs to further evaluate the flow of blood in your heart, a small catheter (tube) will be placed in a vein leading to your heart.
- Blood will be collected for laboratory testing of your kidney and heart function.
    - A serum pregnancy test will also be performed for women of child-bearing potential.
    - The blood draw will consist of a needle being stuck into a vein in your arm (or other area where a vein can be accessed). Any remaining blood sample will be discarded according to hospital regulations.

If you do not meet these qualification requirements your participation in the study will be discontinued and you should talk to the study doctor about further treatment for your mitral regurgitation.

You may participate in this study if all criteria have been met and you have agreed to participate in this study by signing this consent. If enrolled, you will be scheduled for your implant procedure and may be given anticoagulation (blood thinning) medication (aspirin and clopidogrel), in preparation.

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AS MODIFIED
Aug 02, 2023

The following procedures and observations will be performed in association with the study implant procedure:

Study Implant Procedure

The following study procedures will occur before the implant procedure:

- Blood will be collected for laboratory testing.
    - A serum pregnancy test will also be performed for women of child-bearing potential.
- You will be asked if you have experienced any unusual symptoms or side effects since your last visit.

What happens during the Transcatheter PASCAL Precision System and MitraClip System Procedures?

The valve repair steps will be performed using a type of x-ray machine called fluoroscope (an x-ray that uses a special dye and camera to take pictures of the blood flow) so your doctor can visualize the device in your blood vessels and heart. The valve repair will be done using a minimally invasive technique. A catheter (small plastic tube) will be inserted through a small puncture in the groin via a vein leading directly to your heart. A needle will be inserted into the vessel and advanced into the heart to create a small puncture in the septum (heart wall between two heart chambers), which will provide access to the mitral valve. A flexible catheter will then be tracked through the vessel to deliver an implant to the mitral valve. Your mitral valve has two leaflets. The device implant will be carefully positioned to grasp each of these leaflets and bring them together to help reduce the leak in the valve. After the device implant is placed in the heart, the catheter used to deliver it will be removed. The vessel and incision will be closed.

You will be monitored in the operating room as needed with special attention to hemodynamic condition and cardiac rhythm. You will be subsequently monitored in the recovery room or ICU.

For patients receiving the PASCAL Precision System procedure, Edwards Representatives who have been trained on the device preparation will be in attendance during your implant procedure in person and/or remotely using secure broadcasting methods. The Edwards Representatives are responsible for the preparation of the Edwards PASCAL Repair System.

Both the PASCAL and MitraClip procedures will take place in a catheterization laboratory, operating room, or hybrid operating suite. The mitral valve repair procedures will be carried out under general anesthesia.

The following study procedures will occur during the implant procedure:

- Any unusual symptoms or side effects that are noted during your procedure will be collected, including any persistent ECG changes
- Transesophageal Echocardiogram (TEE)
- Procedural fluoroscopy
- Invasive Left Atrial Pressure Monitoring

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Aug 02, 2023

Post-Implant Visit

The following study procedures will be performed within 24 hours of your implant procedure:

- Changes to your medication will be recorded
- Blood will be collected for clinical laboratory testing
- You will be asked if you have experienced any unusual symptoms or side effects since the procedure

Discharge Visit

The following study procedures will be performed at discharge or at 7 days after your implant procedure, whichever comes first:

- You will be asked if you have experienced any unusual symptoms or side effects since the procedure
- Changes to your medication will be recorded
- Targeted Physical Exam
- Blood will be collected for clinical laboratory testing
- NIH Stroke Scale
- Modified Rankin Scale (if you experienced a stroke during the trial)
- Transthoracic Echocardiogram (TTE)
- ECG

Follow-up Visits after the Study Device is Implanted

An appointment will be scheduled for you to return to the study center approximately 1 month from your procedure date for your first follow up visit.

Post-procedure follow-up visits will be conducted at 1 month, 6 months, and annually for 5 years post-study implant. If you are not able to return to the site, the follow-up visit may be conducted by telephone contact, telemedicine visit or home visit. The following procedures will be conducted during each follow-up visits (unless otherwise noted):

- You will undergo a targeted physical examination and clinical evaluation at each visit
- Changes to your medication will be recorded at each visit
- You will be asked if you have experienced any unusual symptoms or side effects since the procedure at each visit
- A NIHSS assessment will be performed at each visit
- A mRS assessment will also be performed if you experienced a stroke during the trial
- Blood will be collected for clinical laboratory testing
    a. DMR CLASP IID Groups: through the one-year follow-up visit
    b. FMR CLASP IIF Groups: through the two-year follow-up visit
- An ECG will be obtained through 30 day visit
- A comprehensive TTE will be performed at each visit

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AS MODIFIED
Aug 02, 2023

- NYHA Class will be recorded at each visit
- Health Status Questionnaires through the two-year follow-up visit
- 6MWT
    a. DMR CLASP IID Groups: through the one-year follow-up visit
    b. FMR CLASP IIF Groups: through the two-year follow-up visit

Follow-Up Visit Windows

Post-procedure follow up visit window intervals are summarized in the below table.

Scheduled Follow-up Interval	Follow-up Window
1 month (30 days)	± 7 days
6 months (180 days)	± 30 days
1 year (365 days)	± 45 days
2 to 5 years	± 45 days

If during a follow-up visit, it is determined that you require a mitral valve reintervention, your physician will discuss the best treatment option for you.

Upon completing the 5 year visit, you will have completed the study, and the study doctor will discuss further treatment with you.

PARTICIPANT RESPONSIBILITIES

If you decide to take part in this clinical research study, following instructions and completing all study visits are important to make sure that the study results are complete and accurate. If you wish to stop participating in the study or if you find you have not followed instructions listed above, it is important that you notify the study doctor or study staff.

Your participation in this clinical research study is **entirely voluntary** and it is your right to refuse to participate or withdraw at any time without penalty or loss of benefits to which you are otherwise entitled. You are free to withdraw from the study at any time without giving any reason, even if you have confirmed in writing that you want to take part. Your decision to withdraw will not influence further treatment in our hospital.

Giving false, incomplete, or misleading information about your medical history, including past and present use of medications, could have a very serious effect on your health. It is very important that you give a true and complete medical history.

You may be exited from the study for any of the following reasons:

- You signed the consent, but your doctor deems you ineligible during the screening phase

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AS MODIFIED
Aug 02, 2023

- You undergo the study procedure but do not receive a study device. You will exit the study at the visits below or until resolution of any adverse events related to the procedure (whichever occurs later):
    a. All Randomized patients will be followed through their 5-year follow-up
    b. Roll-in and Registry Cohorts: at the 30 day follow-up visit
- You undergo study device explant or removal you will exit the study at the visits below:
    a. All Randomized patients will be followed through their 5-year follow-up
    b. Roll-in and Registry Cohorts: at the 30 day follow-up visit
- You choose to withdraw participation from the study or are withdrawn from the study by your doctor or the sponsor

POTENTIAL RISKS AND DISCOMFORTS

The potential risks that you may encounter by participating in this study are similar to the risk associated with standard cardiac catheterization, the use of anesthesia and the risks that could be caused by use of the PASCAL Precision System which could lead to the following: conversion to open surgery, urgent or non-urgent reoperation, explant, permanent disability or death. The implantation procedure and/or investigational device itself has the potential to cause some side effects or reactions. Currently, there is not enough information to predict the frequency and severity of these potential risks.

The implantation procedure also has the potential to cause some side effects or reactions. Complications with the PASCAL implant procedure you may experience may include, but are not necessarily limited to, the following:

Very common: more than 10%

- Bleeding
- Feeling sick to stomach and/or vomiting (Nausea and/or vomiting)

Common (7-10%)

- Heart muscle is not pumping as strong or as well as it should (heart failure)
- Infection

Less Common (4-6%)

- Abnormal blood test results (Abnormal laboratory values), which can indicate a variety of medical conditions or may have no clinical significance
- Abnormal or irregular heart rhythm in the top and bottom chamber of your heart (Arrhythmias)
- Bleeding in your digestive track (Gastrointestinal bleeding)
- Decreased blood pressure (Hypotension)
- Neurological symptoms, including dyskinesia, without diagnosis of TIA or Stroke (physical sign of a brain, spinal cord or nerve problem that is not caused by blood flow interruption to the brain)
- Kidneys do not work as they are supposed to or fail (renal insufficiency or failure)

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AS MODIFIED
Aug 02, 2023

Rare (less than 1-3%)

- Allergic reaction/hypersensitivity to contrast dye, medication, or device materials
- Anemia, a condition in which your blood does not have enough healthy red blood cells or decreased hemoglobin, (the cells that hold oxygen), and you may require transfusion
- Chest pain or discomfort (angina)
- An abnormal increase or decrease of minerals in your blood (electrolyte imbalance)
- A hole between the two upper chambers in your heart which may require procedure or surgery to close it (atrial septal injury requiring intervention)
  Fluid around the lungs (pleural effusion)
- Bulging of the walls of arteries or heart chambers due to weakening of the vessel wall or damage causing blood to leak between the layers of the vessel wall (aneurysm or pseudoaneurysm)
- Severe potentially life-threatening allergic reaction (Anaphylactic shock or toxic reaction)
- Abnormal communication between an artery and a vein (arterio-venous fistula)
- Heart stops beating suddenly (cardiac arrest)
- Fluid or blood around the heart, which may affect heart function (cardiac tamponade/pericardial effusion)
- Damage to your heart tissue or heart chambers (cardiovascular injury)
- Damage to the cord like strings that connect heart muscle to the heart valve (chord entanglement or rupture)
- A condition affecting the blood's ability to clot (coagulopathy, coagulation disorder, bleeding diathesis)
- Swelling caused by abnormal collection of fluid in certain body tissues (edema)
- Increase in body temperature higher than normal (Fever)
- High blood pressure (Hypertension)
- Bruising and collection of blood in the tissue (Hematoma)
- Heart arrhythmia that may require permanent pacemaker implantation which is a medical device that uses electrical pulses to create a normal heart rate (Permanent Pacemaker Implantation)
- Need to switch from a minimally invasive procedure to an open heart surgery, with the possibility of using a machine to circulate your blood outside of your body similar to the heart and lung machine (open heart surgery requiring cardio-pulmonary bypass machine).
- Shortness of breath or difficulty breathing (dyspnea)
- Death
- blood clots formed in the veins of the arms and/or legs (deep venous thrombosis)
- Damage to your heart valve from the device
- Inability or decreased ability to perform physical exercise and general weakness (Exercise intolerance or weakness)
- Inability to get the implant into proper place when placing it in the heart (Implant malposition or failure to deliver to intended site)
- Unintentional movement of the device from its intended position after implant (Implant migration)
- Air bubble, blood clot, or other material that can move in the vessels, block blood flow and cause tissue damage (emboli/embolization)
- An infection of the inner lining of your heart or one of your heart valves (endocarditis)

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AS MODIFIED
Aug 02, 2023

- Irritation, tear, narrowing, or injury to the tube that connects the throat to the stomach from one of the instruments that is used to look inside the heart (esophageal irritation or injury/ esophageal perforation or stricture)
- Inability to remove any part of the device that is not intended to stay inside after the implant procedure (device dislodgement)
- Death of tissue in your digestive tract due to lack of blood supply (gastrointestinal infarct)
- Low or unstable blood pressure which can mean your heart cannot pump enough blood to meet your body's needs (hemodynamic compromise)
- Red blood cells break or are destroyed (hemolysis)
- Bleeding (hemorrhage) requiring transfusion or intervention
- Break down or damage to the implant
- Blood clot formation on or near the device (device thrombosis)
- Redness, swelling, pain, heat, tenderness, loss of function of an area of the body as a reaction to injury) (inflammation)
- Blockage of blood flow in the heart due to the positioning of the device (LVOT obstruction)
- Inadequate blood supply to the lower section of the digestive tract (mesenteric ischemia)
- Damage to the native valve tissue (native valve injury)
- Narrowing of the native valve (native valve stenosis)
- Organs from more than one system do not function properly (multi-system organ failure)
- Heart attack (myocardial infarction)
- Pain
- Implant device becomes loose from where it was attached to the heart (single leaflet device attachment known as SLDA)
- Worsening of backward of flow of blood through the native valve (regurgitation)
- Damage to a nerve (nerve injury)
- Neurological event such as a stroke that could result in permanent symptoms that could be caused by a temporary blockage of blood flow to the brain in which symptoms fully resolve (stroke)
- Short term and temporary interruption of blood flow to the brain (TIA)
- Blood clot that blocks a blood vessel (thromboembolic event)
- Injury to the muscles in the lower chambers of the heart during procedure (papillary muscle damage)
- Impaired body movement, not being able to move portions of your body, or permanent disability (paralysis)
- Accidental movement of any piece or part of the implant device into a blood vessel (device embolization)
- Insufficient blood flow to the limbs (peripheral ischemia)
- Fluid buildup in the lungs (pulmonary edema)
- A blood clot that causes a sudden blockage in a lung artery, usually due to a blood clot that traveled from the leg (pulmonary embolism)
- Unexpected response to blood thinners
- Problem with breathing or the lungs which may require assistance with breathing for longer than expected (respiratory compromise and/or failure may require prolong intubation)
- Bleeding into a space in the abdomen (retroperitoneal bleed)

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AS MODIFIED
Aug 02, 2023

- Damage to the wall of the heart (ventricular wall damage or perforation/septal damage)
- Blood infection (septicemia /Sepsis)
- Painful, disfiguring and long-lasting skin damage due to exposure to energy released from x-ray (skin burn, injury or tissue changes)
- Loss of consciousness or dizziness (syncope)
- An infection or bleeding in any part of your urinary system — your kidneys, ureters, bladder and urethra (urinary tract infection and/or bleeding)
- Damage to a vessel including a blockage or tear (vascular injury or trauma)
- Sudden tightening up of the vessel (vessel spasm)
- The native valve does not close properly when the heart pumps out blood causing blood leakage around the device or through the valve (Worsening native valve regurgitation / valvular insufficiency
- Splitting open or failure of the surgical site to heal (wound dehiscence, delayed or incomplete healing)

With any investigational device and/or procedure there may be unforeseeable risks, which are not known at this time. Medical and/or surgical intervention may be required to correct clinical complications associated with the device and / or study procedure.

Randomization: You will be assigned to a study group by chance (like a coin flip) rather than by a medical decision made by the researchers. The treatment you receive may prove to be less effective or to have more side effects than the other study group(s), or than standard treatments available for your condition.

Pregnancy Risks

Women who are pregnant may not participate in this study. The effects of this treatment and follow-up requirements to an embryo or fetus are currently unknown. If you are a woman of child-bearing potential, and are not sterile, a small amount of blood will be collected, to confirm you are not pregnant, before the study procedure. If you become pregnant anytime during study participation, you will be exited from the study.

Please notify the study doctor or study staff if you experience any side effects or complications during the study. You will be monitored throughout the study in order to minimize risks.

Risks associated with anesthesia

While anesthesia is generally very safe there are some risks associated with anesthesia. The most common problems associated with anesthesia are feeling unwell or vomiting, bruising at the site of injections, sore throat or hoarse voice. Most patients do not have these problems. If these problems do happen, they usually get better very quickly. Damage to teeth may occur, but this is rare. The risk of brain damage or death due to anaesthesia is very rare.

The risk of problems from anesthesia increases for patients who are having more major surgery, those with medical problems and those that require difficult anaesthetic procedures. If you have any concerns about these issues, you should discuss them with the study team.

IRB APPROVED
AS MODIFIED
Aug 02, 2023

If during the research study the study doctor learns that you have a medical condition that was unknown, you will be made aware of the medical condition and offered the same treatment and care as if you were not in the research study. You and/or your study doctor can decide if you continue to participate in the research study.

Risks associated with exposure to radiation

This research study includes a fluoroscopy that will be exposing you to radiation from an x-ray machine. Although the amount of radiation you will be exposed to is higher than that of a usual x-ray, the risk of harmful effects from a single fluoroscopy is very small.

During the fluoroscopic procedure, the skin area exposed to the x-rays could react to produce an effect similar to sunburn. If a skin reaction occurs at all, it could show up from a few hours to a few days after the procedure, and usually goes away on its own. If you have a skin reaction, you should tell the study doctor immediately and you may be asked to return for a study visit.

All risks will be explained to you by your study doctor. Should any side effects occur, they will be fully assessed and you will be monitored closely.

In addition, it is important your primary care doctor is also notified of any significant changes to your health.

ANTICIPATED BENEFITS

We cannot guarantee or promise that you will receive any benefits from this research. Possible benefits may include: improvement in the symptoms related to your mitral regurgitation, the study procedure techniques include a less invasive procedure, shorter procedure time, and less anesthesia than in an open heart surgery for mitral valve repair or replacement.

Treatment with the study device may provide both short and long-term relief of your symptoms, provide improved mitral valve function, and an improvement of your cardiac function that could potentially increase your life expectancy and improve your quality of life.

It is possible that you will receive no direct benefit from this research study, but others may benefit in the future from your participation.

ALTERNATIVE TREATMENTS

You do not have to take part in this research study to receive treatment at this hospital. Other options may be available to you. Generally available options for patients with MR are as follows:

- Mitral valve surgery using another commercially available device to repair or replace your mitral valve

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AS MODIFIED
Aug 02, 2023

- Transcatheter mitral valve repair with another commercially available device
- Medical management (treatment with medication)

These options may temporarily alleviate some of your symptoms, but will not permanently alleviate your condition or cure your mitral regurgitation. Your study doctor will discuss these options with you before you decide whether or not to take part in this research study. You can also discuss the options with your local doctor.

However, you have been offered the opportunity to participate in this research study because your treating doctor and team have determined that your condition or valve anatomy may not be suitably treated by a surgical approach or other minimally invasive procedure.

The study doctor will explain the choices to you. **You do not have to participate in this study to receive treatment for your condition.** The study doctor will tell you more about the risks and benefits of participating in this study as compared to the risks and benefits of other treatments. Some of the study procedures might be done as part of your standard care even if you do not take part in this clinical research study. The study doctor or a member of the study staff can answer any questions you may have about the procedures that are not part of your standard care.

COMPENSATION

The Sponsor will provide a $50 stipend for each completed in-person follow-up visit (1 month, 6 month, 1, 2, 3, 4, and 5 year visits) required by the trial for up to $350.

With the exception of the stipend there will be no compensation for your participation in this trial.

COSTS

The Edwards Lifesciences, LLC will supply the device at no cost while you take part in this study. Any additional research-related tests, procedures or visits will also be provided at no cost while you take part in this study.

You and /or your health plan/insurance will be billed for the costs of any routine medical care you receive to diagnose and/or treat any medical condition(s) within the scope of this study. You and /or your health plan/insurance will need to pay for this routine care. You will also be responsible for any co-payments or deductibles required by your insurance. Some health plans/insurance companies will not pay the costs associated with these tests, procedures, and/or drugs. Financial counseling and itemized cost estimates are available upon request.

EMERGENCY CARE, LIABILITY, AND COMPENSATION FOR INJURY

It is important that you promptly tell the researchers if you believe that you have been injured because of taking part in this study. You can tell the researcher in person or call him/her at the number(s) listed above.

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If you feel you have been injured as a result of being in this study UCI will provide necessary medical treatment. The costs of the treatment may be covered by the University of California or the study sponsor Edwards Lifesciences, or billed to you or your insurer just like other medical costs, depending on a number of factors. The University and the study sponsor do not normally provide any other form of compensation for injury. For more information about this, you may call UCI Human Research Protections (949) 824-6068 or (949) 824-2125 or by e-mail at IRB@research.uci.edu

If the study sponsor covers these costs they will need to know some information about you like your name, date of birth, and Medicare Health Insurance Claim Number, or, if you do not have one, your Social Security Number. This information will be used to check to see if you receive Medicare, and, if you do, report the payment they make to Medicare. The study sponsor will not use this information for any other purpose.

CONFIDENTIALITY

Information from this study will be given to the sponsor. "Sponsor" includes any persons or companies which are contracted by the sponsor to have access to the research information during and after the study.

The information will also be given to the U.S. Food and Drug Administration (FDA). It may be given to governmental agencies in other countries where the study drug may be considered for approval.

Medical records which identify you and the consent form signed by you will be looked at and/or copied for research or regulatory purposes by:

- the research team
- authorized UCI personnel
- the sponsor

and may be looked at and/or copied for research or regulatory purposes by:

- the FDA
- Department of Health and Human Services (DHHS) agencies;
- governmental agencies in other countries;
- the University of California; and the Western Copernicus Group (WCG) IRB, Inc.

Absolute confidentiality cannot be guaranteed because of the need to give information to these parties. If the results of this study are made public at meetings or in scientific journal articles, information that identifies you will not be used.

Medical Care

If you agree to participate in this research study, a signed copy of this consent document and the privacy authorization form may be filed in your electronic medical record (EMR) and your study participation may be added to your EMR. This information will be used for your care and treatment and for healthcare operations, which may include billing and payment.

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Federal and state privacy laws give patients the right to access information about their care and treatment contained in their medical record. During this study, you may not be able to access certain information related to this study in your EMR until the study is complete to ensure that the study remains unbiased. By consenting to participate in this study, you are also consenting to this possible temporary withholding of your records. If necessary for your care, this information will be provided to you or your physician.

OTHER ISSUES TO CONSIDER WHEN DECIDING WHETHER TO PARTICIPATE IN THIS STUDY

Public Information about this Study:

ClinicalTrials.gov is a website that provides information about federally and privately supported clinical trials.

A description of this clinical trial will be available on http://www.ClinicalTrials.gov, as required by U.S. Law. This Web site will not include information that can identify you. At most, the Web site will include a summary of the results. You can search this Web site at any time.

Investigator Financial Conflict of Interest

The study doctor, Dr. Antonio Halais Frangieh, has financial interests in Edwards Lifesciences, the sponsor of the study. Antonio Halais Frangieh receives income and owns stock in the entity, which is in addition to their salary from the University of California, Irvine.

The nature of this financial interest and the design of the study have been reviewed by the UCI Conflict of Interest Oversight Committee (COIOC). The COIOC has determined that the researcher's financial interests are appropriately managed as to avoid compromising the quality or reliability of the study and furthermore, the UCI Institutional Review Board has determined that appropriate safeguards are in place to avoid adversely affecting your safety and welfare.

Use of Research Specimens

Any specimens (e.g., tissue, blood, urine) obtained for routine labs will be discarded or destroyed once they have been used for the purposes described in this consent.

PARTICIPATION AND WITHDRAWAL

You have the right to choose not to be in this study or to stop being a part of this study at any time without any consequences. This means that there will be no penalty or loss of medical benefits to which you are entitled.

If you choose to stop being a part of this study, you must first notify the study doctor immediately so that a plan can be provided for your continued medical care. At the time you stop taking part in the study, you will be asked to return for a final safety evaluation that will include gathering information about your current

medical condition and conducting any required procedures. For your own safety, you should go through the study exit procedures if you leave the study.

It is possible that your being part of this study may be stopped at any time without asking you. This might happen if you do not follow the instructions given by the study doctor or if the study doctor believes it to be in your best interest. The study may also be stopped for administrative, medical, or other reasons as determined by the study doctor, Edwards Lifesciences, LLC. or the regulatory authorities of your country.

Any significant new findings developed during the course of this research that might affect your safety will be provided to you and your study doctor.

While participating in this study, you should not take part in any other study. This is to protect you from possible injury that may arise.

QUESTIONS / INFORMATION

Contact the research team listed at the top of this form during office hours for any of the following reasons:

- if you have any questions about your participation in this study,
- if you feel you have had a research-related injury or a reaction to the study drug, or
- if you have questions, concerns or complaints about the research

Call the 24-hour number also listed on the top of this form at any time to report a research-related injury or a health concern possibly related to the study drug.

If you have questions about your rights as a research subject or if you have questions, concerns, input, or complaints about the research, you may contact:

WCG IRB
1019 39th Avenue SE, Suite 120
Puyallup, Washington 98374-2115
Telephone: 1-855-818-2289
E-mail: researchquestions@wcgirb.com

WCG IRB is a group of people who perform independent review of research. WCG IRB will not be able to answer some study-specific questions, such as questions about appointment times. However, you may contact WCG IRB if the research staff cannot be reached or if you wish to talk to someone other than the research staff.

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Aug 02, 2023

CONSENT SIGNATURE

You should not sign and date this consent form until all of your questions about this study have been answered by a member of the research team listed at the top of this form. You will be given a copy of this signed and dated consent form and the "Research Subject's Bill of Rights" to keep.

Participation in this study is voluntary. You may refuse to answer any question or discontinue your involvement at any time without penalty or loss of benefits to which you might otherwise be entitled. Your decision will not affect your future relationship with UCI or your quality of care at the UCI Medical Center.

If, during the course of this study, significant new information becomes available that may relate to your willingness to continue to participate, this information will be provided to you by the research team listed at the top of the form.

Your signature below indicates you have read the information in this consent form and have had a chance to ask any questions you have about this study.

If the research described in this form involves your protected health information (PHI), you will be asked to sign a UC HIPAA Research Authorization form authorizing the access, use, creation, and/or disclosure of your health information which is appended at the end of this form.

I agree to participate in the study.

_____ _____
Subject Signature **Date**

_____
Printed Name of Subject

_____ _____
Signature of Person Obtaining Informed Consent **Date**
(Individual must be listed on Page 1 of this consent)

_____
Printed Name of Person Obtaining Informed Consent

Patient Study ID: 201807 ____ ____ ____ ____ - ____ ____ ____ **Patient Initials** *(First, Mid, Last):* ____ ____ ____

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Aug 02, 2023

A witness signature is required on this consent form only if: (Researchers: check which one applies)

☐ Consent is obtained from the subject via the Short Form process, as approved by the IRB.
☐ The subject has decision-making capacity, but cannot read, write, talk or is blind.
☐ The subject's guardian/legally authorized representative (LAR) cannot read, write, talk or is blind.
☐ The IRB specifically mandated a witness signature for this study (e.g., high risk and/or invasive research procedures).

Note: The witness must be impartial (i.e. not a member of the subject's family, not a member of the study team).

For the witness:
I confirm that the information in this consent form was accurately explained to and understood by the subject or legally authorized representative and that informed consent was given freely.

_____ _____
Witness Signature **Date**
(If no witness signature is required, this witness signature section of the consent form may be left blank).

_____
Printed Name of Witness

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Aug 02, 2023

UNIVERSITY OF CALIFORNIA, IRVINE
Research Subject's Bill of Rights

The rights listed below are the right of every individual asked to participate in a research study. You have the right:

1. To be told about the nature and purpose of the study.
2. To be told about the procedures to be followed in the research study, and whether any of the drugs, devices, or procedures is different from what would be used in standard practice.
3. To receive a description of any side effects, discomforts, or risks that you can reasonably expect to occur during the study.
4. To be told of any benefits that you may reasonably expect from the participation in the study, if applicable.
5. To receive a description of any alternative procedures, drugs, or devices that might be helpful, and their risks and benefits compared to the proposed procedures, drugs or devices.
6. To be told of what sort of medical treatment, if any, will be available if any complications should arise.
7. To be given a chance to ask any questions concerning the research study both before agreeing to participate and at any time during the course of the study.
8. To refuse to participate in the research study. Participation is voluntary. You may refuse to answer any question or discontinue your involvement at any time without penalty or loss of benefits to which you might otherwise be entitled. Your decision will not affect your right to receive the care you would receive if you were not in the experiment.
9. To receive a copy of the signed and dated written consent form and a copy of this form.
10. To be given the opportunity to freely decide whether or not to consent to the research study without any force, coercion, or undue influence.

If you have any concerns or questions regarding the research study you should contact the study team listed at the top of the consent form.

I can also contact the WCG IRB, Inc. which helps protect research study participants. I can reach the WCG IRB, Inc by calling 855-818-2289 from 8:00 AM to 5:00 PM, Monday to Friday. If I call this office and do not speak English or Spanish, I should have someone available who can interpret for me. I may also write to WCG IRB, Inc., 1019 39th Avenue SE Suite 120, Puyallup, WA 98374-2115. To get a copy of the bill of rights I may contact the research team or go to **https://research.uci.edu/wp-content/uploads/experimental-subjects-b-o-r.docx**

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Aug 02, 2023

UCI IRB # 2411

UNIVERSITY OF CALIFORNIA IRVINE HEALTH
PERMISSION TO USE PERSONAL HEALTH INFORMATION FOR RESEARCH

Study Title (or IRB Approval Number if study title may breach subject's privacy): Edwards PAS**C**A**L** Tr**A**n**S**catheter Valve Re**P**air System Pivotal Clinical Trial (**CLASP IID/IIF**): A prospective, multicenter, randomized, controlled pivotal trial to evaluate the safety and effectiveness of transcatheter mitral valve repair with the Edwards PASCAL Transcatheter Valve Repair System compared to Abbott MitraClip in patients with mitral regurgitation

Principal Investigator Name: Antonio Frangieh, MD

Sponsor/Funding Agency (if funded): Edwards Lifesciences, LLC

A. What is the purpose of this form?

State and federal privacy laws protect the use and release of your health information. Under these laws, the University of California or your health care provider cannot release your health information for research purposes unless you give your permission. Your information will be released to the research team which includes the researchers, people hired by the University or the sponsor to do the research and people with authority to oversee the research. If you decide to give your permission and to participate in the study, you must sign this form as well as the Consent Form. This form describes the different ways that health care providers can share your information with the researcher, research team, sponsor and people with oversight responsibility. The research team will use and protect your information as described in the attached Consent Form. However, once your health information is released by UC Irvine Health it may not be protected by the privacy laws and might be shared with others. If you have questions, ask a member of the research team.

B. What Personal Health Information will be released?

If you give your permission and sign this form, you are allowing your health care provider to release the following medical records containing your Personal Health

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Aug 02, 2023

Information. Your Personal Health Information includes health information in your medical records, financial records and other information that can identify you.

☒ Entire Medical Record
☐ Ambulatory Clinic Records
☐ Progress Notes
☐ Other Test Reports
☐ Other (describe): Type Here (Description of Other Health Information)
☐ Lab & Pathology Reports
☐ Dental Records
☐ Operative Reports
☐ Discharge Summary
☐ Consultations
☐ Emergency Department Records
☐ Financial Records
☐ Imaging Reports
☐ History & Physical Exams
☐ Psychological Tests

C. Do I have to give my permission for certain specific uses?

Yes. The following information will only be released if you give your specific permission by putting your initials on the line(s).

_____I agree to the release of information pertaining to drug and alcohol abuse, diagnosis or treatment.

_____I agree to the release of HIV/AIDS testing information.

_____I agree to the release of genetic testing information.

_____I agree to the release of information pertaining to mental health diagnosis or treatment.

D. Who will disclose and/or receive my Personal Health Information?

Your Personal Health Information may be shared with these people for the following purposes:

1. To the research team for the research described in the attached Consent Form;
2. To others at UC with authority to oversee the research
3. To others who are required by law to review the quality and safety of the research, including: U.S. government agencies, such as the Food and Drug Administration or the Office of Human Research Protections, the research sponsor or the sponsor's representatives, or government agencies in other countries.

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AS MODIFIED
Aug 02, 2023

E. How will my Personal Health Information be shared for the research?

If you agree to be in this study, the research team may share your Personal Health Information in the following ways:

1. To perform the research
2. Share it with researchers in the U.S. or other countries;
3. Use it to improve the design of future studies;
4. Share it with business partners of the sponsor; or
5. File applications with U.S. or foreign government agencies to get approval for new drugs or health care products.

F. Am I required to sign this document?

No, you are not required to sign this document. You will receive the same clinical care if you do not sign this document. However, if you do not sign the document, you will not be able to participate in this research study.

G. Optional research activity

If the research I am agreeing to participate in has additional optional research activity such as the creation of a database, a tissue repository or other activities, as explained to me in the informed consent process, I understand I can choose to agree to have my information shared for those activities or not.

☐ I agree to allow my information to be disclosed for the additional optional research activities explained in the informed consent process.

H. Does my permission expire?

This permission to release your Personal Health Information expires when the research ends and all required study monitoring is over.

I. Can I cancel my permission?

You can cancel your permission at any time. You can do this in two ways. You can write to the researcher or you can ask someone on the research team to give you a form to fill out to cancel your permission. If you cancel your permission, you may no longer be in the research study. You may want to ask someone on the research team if canceling will affect your medical treatment. If you cancel, information that was already collected and disclosed about you may continue to be used for limited

purposes. Also, if the law requires it, the sponsor and government agencies may continue to look at your medical records to review the quality or safety of the study.

J. Signature

Subject

If you agree to the use and release of your Personal Health Information, please print your name and sign below. You will be given a signed copy of this form.

_____

Subject's Name (print)—*required*

_____

Subject's Signature

_____

Date

Witness

If this form is being read to the subject because s/he cannot read the form, a witness must be present and is required to print his/her name and sign here:

_____

Witness' Name (print)

_____

Witness' Signature

_____

Date