A NON-RANDOMIZED, CONSECUTIVE ENROLLMENT EVALUATION OF THE DESolve® NOVOLIMUS ELUTING BIORESORBABLE CORONARY SCAFFOLD SYSTEM IN THE TREATMENT OF PATIENTS WITH *DE NOVO* NATIVE CORONARY ARTERY LESIONS

Elixir Medical Clinical Evaluation of the DESolve® Novolimus Eluting Bioresorbable Coronary Scaffold System

"DESolve Nx Trial – DESolve CX Arm"

Informed Consent, Revision A, 23 October 2015

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PATIENT INFORMED CONSENT

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Elixir Medical Clinical Evaluation of the DESolve® Cx Eluting Bioresorbable Coronary Scaffold System

"DESolve Nx Trial"

ELX-CL-1003

Introduction

You are being invited to take part in a research study that will include up to 30 patients a study arm of the DESolve Nx Clinical Trial.

It is important that you read and understand several general principles that apply to <u>all</u> participants in this clinical study:

(a) taking part in the study is entirely voluntary;
(b) personal benefits to you may or may not result from taking part in the study, but knowledge may be gained from your participation that will benefit others;
(c) you may withdraw from the study at any time without penalty or loss of any benefits to which you are otherwise entitled. If you withdraw from the study, the scaffold will not and cannot be removed.

The nature of the study, the benefits, risks, discomforts and other information about the study are detailed in this informed consent. Changes to the study or significant new findings discovered during the course of this study, which may affect your willingness to continue participating in the study, will be provided to you. You are urged to discuss any questions you have about this study with the staff member(s) who explain it to you.

This study was approved by an independent medical ethics committee, which is connected to this hospital, and will be conducted in collaboration with other ethics committees, in accordance with the Guidelines for Good Clinical Practice (ICH / GCP) and the Declaration of Helsinki for the protection of participants in clinical Studies (as amended in 2000).

Background

Your physician has determined that one of your coronary arteries has a significant narrowing that is causing decreased blood flow to your heart muscle. There are two methods commonly used to correct this problem. The first is balloon angioplasty which is usually followed by the placement of a stent. Balloon angioplasty does not leave a permanent device in the artery after the balloon catheter is removed. Stent placement means that a small metal scaffold (stent) is left behind after the balloon is removed and the stent becomes a permanent part of your artery. Metal stents have

been used successfully for many years to treat narrowings in both coronary arteries and bypass grafts (saphenous vein grafts).

One issue with balloon angioplasty or with stent implantation is restenosis or renarrowing of the artery after treatment. Recently, there have been several breakthrough studies demonstrating that by coating a stent with a small amount of drug, the occurrence of restenosis can be reduced. The amount of drug placed on the stent is many times less than the amount taken either in a pill form or given by injection. This is possible because there is localized delivery of the drug only to the treated area in the artery.

A potential issue associated with metal stents, with or without drugs, is the permanent nature of the device. It is possible that in the event of a surgical procedure becoming necessary such as coronary artery bypass grafting (CABG), the permanent stent can limit the ability of the surgeon to place a bypass graft. Therefore, Elixir Medical, sponsor of this study, as well as other companies are looking at scaffolds that will be completely absorbed by the body over a period of time, similar to bioabsorbable stitches. In this way, the narrowing in your artery can be opened, the local delivery of drug will help prevent any renarrowing of the treated area, and finally, the scaffold itself will bioabsorb over a period of time essentially leaving behind a normal vessel.

The CE Mark approved (approved for sale) DESolve Cx Novolimus Eluting Bioresorbable Coronary Scaffold System has two main components, the drug Novolimus and the scaffold. Novolimus is from the same family of drugs which are approved around the world as immunosuppressant drugs given to patients following organ transplantation. The drug has both anti-inflammatory and immunosuppressant properties and is similar to sirolimus, and zotarolimus, which are currently approved for use on metallic drug eluting stents. The dose of the drug on the scaffold is approximately 5 mcg of Novolimus per mm of scaffold length (65 mcg for a 14 mm scaffold, 85 mcg for an 18 mm scaffold and 125 on a 28 mm scaffold) and is many times less than the typical oral or IV dose (e.g. sirolimus at 2 mg which equals 2000 mcg) of similar drugs taken by a patient on a daily basis following organ transplantation. One of the advantages of this scaffold is that the dose on the scaffold is lower than the average dose found on other drug eluting stent systems (e.g. 111 – 144 mcg for a similar size stent).

The drug Novolimus has been tested is three clinical studies, enrolling over 400 patients. These studies have shown that the drug is safe and has very good effectiveness in reducing the amount of renarrowing as compared to both metal stents without a drug coating and as compared to stents with a drug coating. While there were small differences in the devices used in these studies, each used a metal stent coated with a polymer (either durable meaning it does not bioabsorb or a bioabsorbable polymer) and the same dose of the drug Novolimus. The results of these studies were quite good which indicates the initial safety and effectiveness of the drug and stent system. If you would like more information on these studies, your physician will provide it to you.

The drug is applied to the scaffold using a thin biodegradable coating called a polymer that allows the release of the drug over a set period of time. The majority of the drug on the DESolve Cx Scaffold will be released over approximately 4 weeks and the remaining polymer will erode in approximately 6-9 months essentially leaving behind only the scaffold. In addition to the studies conducted by Elixir, this polymer coating is similar to polymer coatings that have been used on vascular implants and has a good safety record.

The next component is the scaffold. The scaffold is made from a bioabsorbable polymer, and is similar to the polymer used to hold the drug, although the scaffold itself does not contain any of the drug Novolimus. The scaffold is designed to bioabsorb over a period of approximately 1 – 2 years leaving nothing behind in the treated vessel. Extensive testing of this device has been completed in the laboratory setting and has demonstrated the safety of the DESolve Cx Novolimus Eluting Bioresorbable Coronary Scaffold System.

In this arm of the study, approximately 30 subjects will be enrolled and all will receive the DESolve Cx scaffold coated with Novolimus. The DESolve scaffold comes in two thicknesses: 120 µm and 150 µm. The 150 µm device was already evaluated in the first arm of this study which enrolled 126 subjects and showed excellent results and has subsequently received CE Mark approval also. In this study arm the 120 µm device will be evaluated.

The research staff will be able to answer any questions you have concerning the study design or about the scaffold system itself.

Purpose and Procedures

The purpose of this study is to evaluate long-term safety, effectiveness and performance of the DESolve Cx Novolimus Eluting Bioresorbable Coronary Scaffold System. Patients deemed by their physician to be eligible for this new treatment will be enrolled in this study. Prior to beginning all study procedures, you will have a physical exam, an ECG (a measurement of your heart's rhythm) and approximately 1 tablespoon (15 cc) of blood drawn. These exams are all standard and are not unique to this study. The narrowing in your artery will first be opened with an angioplasty balloon which will be guided to the narrowed portion of the artery. When the balloon is in the right position, it is inflated to stretch open the narrowed blood vessel. During the balloon inflation, your blood vessel is blocked for a short time, and you could experience some pain. Normally this pain subsides as soon as the balloon is deflated. The balloon may be inflated more than once to ensure the artery is open for scaffold placement.

The scaffold implantation is done in the exactly same manner as the balloon procedure described above. The scaffold which is mounted on a balloon is guided to the narrowing in the blood vessel. The balloon is inflated to expand the scaffold so that it lines the wall of the blood vessel. To ensure that the scaffold is fully expanded, a different balloon may be used in the same manner as described above to ensure optimal expansion of the scaffold. After satisfactory results are obtained, the balloon is removed, leaving behind the expanded scaffold to provide support to the artery.

After the scaffold has been implanted and the desired result obtained, the scaffold will be checked, using intravascular imaging. Intravascular ultrasound (IVUS) imaging uses sound waves (ultrasound) to create a picture inside of the vessel. A tiny catheter that sends and receives the ultrasound waves is threaded into the treated artery immediately after scaffold placement.

In addition, optical coherence tomography (OCT) will also be completed in a subset of patients. This imaging catheter uses an infrared light source to create images. The advantage of OCT is that it provides very detailed visualization of the scaffold, even better than the visualization using either using angiography or IVUS.

Following the procedure you will be required to take routine medications, which will include Clopidogrel (or other similar drug such as Prasugrel or Ticagrelor) for a period of one year and aspirin for at least five years. **It is very important that you take these medicines everyday** as they are intended to help prevent your blood from clotting. Please do not stop taking the medications without first getting approval from your doctor. Both clopidogrel and aspirin are medications that are routinely given following stent or scaffold implantation and are not specific to the goals of this study.

Medical staff will closely observe you until hospital discharge. After discharge, you will undergo several follow-up sessions, either via telephone or a visit to your physician's office at 1, 6, and 12 months and then annually for a total of 2 years. The office visits may or may not include blood tests. For all patients, angiographic follow-up will be completed at 6 months and during this exam IVUS and OCT will also be performed. The staff will inform you when to return for your clinical, and angiographic examinations. It is only with these examinations, will we be able to evaluate the effectiveness and performance of the DESolve Cx Eluting Bioresorbable Coronary Scaffold System.

Potential Risks

The use of stenting for the treatment of atherosclerotic, *de novo* lesions in native coronary arteries has been shown to be a safe and effective treatment with minimal risks. These risks are not specific to this study device and are similar to any angioplasty or drug eluting stent implantation procedure.

There is extensive clinical experience with coronary catheterization procedures, balloon angioplasty, stenting, IVUS and OCT. However, even with the successful implantation of the scaffold, there is a still a chance of the treated area re-narrowing. The re-narrowing of the coronary artery may cause the return of your chest pain. If re-narrowing occurs, it may require further treatment, including bypass surgery, additional angioplasty or stent placement. The risks associated with angiography have been explained to you by your doctor. The potential complications of IVUS and OCT are similar to those of the angiography procedure but also include the potential for coronary artery spasm which can result in chest pain or discomfort and is immediately treatable with medication. Serious complications are rare with ultrasound or OCT.

The additional angiogram, IVUS and OCT procedures carry a risk of exposure to radiation. The patients in the study will receive an additional effective dose of approximately 10 millsieverts during the angiogram, IVUS and OCT procedure (if in the OCT sub-set). As a perspective, the effective dose received by persons each year from natural background radiation is about 2 millisieverts.

The drug used on the scaffold is in such a low dose there is little potential to cause side effects. However, if you experience any signs of an allergic reaction such as rash, itching or swelling, inform your physician immediately. Previous stent studies involving the use of clopidogrel have shown a 1 to 2 % chance of a blood clot forming within the stent. As with any balloon or stent procedure, if clotting of the stent does occur, it may lead to repeat catheterization, angioplasty, myocardial infarction (heart attack), urgent bypass surgery, or death. Other risks may include bleeding into the stomach, bleeding at the puncture site used for your procedure (upper thigh or

arm), stroke and reduced white blood cell count. These risks are not specific to this study device and are similar to any angioplasty or drug eluting stent implantation procedure.

Finally, this treatment may involve some additional risks to you, the nature of which is unknown or may involve unforeseeable risks to you or your embryo or fetus if you become pregnant.

Potential Benefits
The use of drug eluting coronary stents has been shown to reduce the incidence of re-narrowing in the artery at the treated site. The additional benefit is the bioerodable property of this scaffold which over time is intended to completely biorebsorb leaving nothing behind in the vessel.

Confidentiality
Your physician and the study sponsor will maintain your participation in this study confidential. You will not be identified by name, social security number or tax identification number, address, telephone number, or any other direct personal identifier in the study records. However, copies of your angiography, and as applicable, IVUS, OCT and MSCT images, which may contain your full name, will be sent to a core lab for analysis of results.

When results of a study such as this are reported in medical journals or symposia, the identification of patients is withheld. Medical records of participants are maintained according to current legal requirements and will be made available for review to the appropriate Regulatory Authorities, the study sponsor or its representatives.

Policy Regarding Research-Related Injuries
In the event of injury resulting in your participation in this research there will be no monetary compensation or subsidized medical treatment for this injury provided to you by the study sponsor, (Name of the Institution) or any person involved in this research project.

Insurance
The Sponsor will ensure that appropriate insurance will be maintained during the course of the study as required by the law.

The risk that results from this study is covered, by Article 29 of the Belgian Law of 7 May 2004 which deals with human studies. In accordance with this law, the sponsor is liable for damages suffered by the participant or his successor through direct or indirect connection with the study. For this study, the sponsor has secured a contract of insurance, in accordance with Article 29 of the Act of 7 May 2004, through Newline Underwriting Management Ltd., Suite 5/4 The London Underwriting Centre, 3 Minster Court, Mincing Lane, London EC3R 7DD, United Kingdom. The insurance number is 59001710A254. Tell your doctor if your condition deteriorates. If you suffer physical damage because of your participation in this research study, you will receive the necessary treatment without incurring any additional costs. All types of injuries shall be covered by this insurance.

Payment (or additional cost to patients)
Patients will not incur additional charges for participation in this clinical study nor will patients receive any payment for participation in this study.

Pregnancy (risk to fetus)
Pregnant or nursing women are excluded from this study as well as women of childbearing potential as there is inadequate information about the long-term effect of this drug in pregnant women. There is no evidence of effect on fertility in males, however the effect of the drug on human sperm is not known.

Alternative Treatment(s)
There are alternative methods available to treat the narrowing in your coronary artery all of which carry similar risks and benefits as with the investigational device and include: conventional balloon angioplasty, stent implantation with an approved stent including approved drug eluting stents described earlier in this consent form; atherectomy, whereby a cutting device is used to remove the material causing the narrowing. Coronary Artery Bypass Graft (CABG surgery) can be used to bypass the narrowed section of the artery thereby improving flow to the artery. The risks associated with CABG are similar to angioplasty but may also include risks associated with the surgery or anesthesia. The research team can answer any questions you may have concerning alternative treatments. .

Problems or Questions
The Sponsor has the right to suspend or terminate the Study at any time; reasons may include manufacturing supply or important safety information. Additionally, your doctor has the right to terminate this study or your individual participation at any point if it is believed that important adverse events might result from its continuation. Your doctor has the right to terminate this study or your individual participation at any point if he/she believes that important adverse events might result from its continuation. Should any problems or questions arise with regard to this study, with regard to your rights as a participant in clinical research or with regard to any research-related injury, you may contact the Principal Investigator,

Physician Name:_____

Telephone number:_____

Your family physician will be advised of your participation in this trial.

You should inform your physician if you sustain any injury during the course of this study or are admitted to a hospital.

It is suggested that you retain a copy of this document for your later reference and personal records.

CONSENT FORM

A Study of a Drug Eluting Biorebsorbable Scaffold for the Treatment of Coronary Artery Disease

Elixir Medical Clinical Evaluation of the DESolve® Cx Novolimus Eluting Bioresorbable Coronary Scaffold System - "DESolve Nx Trial"

ELX-CL-1003

Principal Investigator:_____

Clinical Investigation Site: _____

Please check each box.

☐ I have heard and understood an explanation of the research project I have been invited to take part in, my questions have been answered, and I have been given a copy of the participant information sheet.

☐ I understand that my participation in this study is voluntary and that refusal to participate will result in no penalty or loss of benefits to which I am entitled.

☐ I understand that if I refuse to participate or withdraw from the project my medical care will not be affected in any way. If I do withdraw from the study, the scaffold will not and cannot be removed.

☐ I understand the compensation provisions for this study as outlined in the Participant Information section.

☐ I agree representatives appointed by the sponsoring company or regulatory authorities and hospital Ethics Committee representatives reviewing my medical file for the sole purpose of checking the accuracy of the information recorded for the study.

I agree to my general practitioner (GP) being informed. Yes ☐ No ☐

I agree to allow the data collected and my relevant personal information to be used in the clinical study: Yes ☐ No ☐

By signing below, I voluntarily agree to participate in the clinical study and will comply with the clinical study directions provided by the research staff.

Signed (Participant):_____ **Date and Time**_____
(dd/mmm/yyyy) (HH:MM)

Printed Name of Participant:_____

Consent Obtained By:

_____ _____
Name **Signature and Date**

Witness:

_____ _____
Name **Signature and Date**