PATIENT INFORMATION SHEET

Study title: "Multi-center, open-labeled, non-randomized study to evaluate the technical performance and safety profile of the VORTX Rx® for ablation of primary and metastatic liver tumors (Theresa Study)".

Protocol code: 03. CP.0.3

Version: 2.0, 26 September 2018.

Sponsor: HistoSonics, Inc.

Principal investigator: _____

Site: _____

Introduction

We are writing you to inform you about a research study which we are inviting you to participate in. The study has been approved by the Medicinal Products Clinical Research Ethics Committee and the Spanish Agency of Medicines and Medical Devices (AEMPS) in accordance with current legislation, Royal Decree 1090/2015, of 4 December, and European Regulation 536/2014, of 16 April, regulating clinical trials with medicinal products, and applicable regulatory requirements for investigation with medical devices, in particular the Circular 7/2004 of the AEMPS regulating clinical investigations with medical devices.

Our intention is only for you to receive correct and sufficient information so that you can decide whether you wish to participate or not in the study. Please read this information sheet carefully and we will answer any questions you may have.

You can also consult with the people you consider appropriate.

Voluntary participation

We are inviting you to participate in this study because you have inoperable hepatocellular carcinoma (the most common type of primary liver cancer in adults) or unresectable (unable to be removed with surgery) liver metastases or you have not responded or relapsed to conventional therapies. You should know that your participation in the study is entirely voluntary and you can decide NOT to participate. There is no disadvantage to you for not participating. If you decide to participate, you can change your decision and withdraw your consent at any time, without it affecting your relationship with your doctor and without any detriment to your health care.

Purpose of the study

Surgery is currently the best initial treatment available for patients with liver cancer or metastasis in the liver. However, surgery can be performed in few patients, because it is

limited by the patient's liver function (whether it is adequate or impaired) and by characteristics related to the tumor (size of tumor, number of tumors, etc.), among other factors. Furthermore, chemotherapy and radiotherapy are ineffective for this type of cancer because they often cause toxicity or collateral damage.

Percutaneous (access via needle-puncture of the skin) "Ablation" techniques (they destroy the tumor without removing it) represent a noninvasive alternative for these patients in whom surgery cannot be performed. "Ablation" techniques for treatment of liver tumors are mainly thermal, that is, heat is used by applying different types of energy that produce deep heating (radiofrequency, microwave energy, or high-intensity ultrasound) to destroy the tumor or part of the tumor. However, thermal ablation techniques are chiefly limited by the heat that is dissipated by the numerous blood vessels in the liver, which reduces the efficacy of this type of treatment and makes several sessions necessary to try to eliminate the tumor or metastases. Furthermore, the deep heat that is applied with these techniques can damage tissues adjacent to the liver or parts of the liver itself. Taking into account the noninvasive principle of ablation techniques and attempting to overcome these limitations arising from the application of thermal energy, a potentially promising ablation technique called "histotripsy" has been developed. This non-invasive, non-thermal ablation technique uses high-intensity acoustic energy (energy transmitted or transported by sound waves) to destroy tumor tissues. The mechanism results in cellular destruction. This procedure, in contrast to thermal ablation methods, does not require insertion of probes or needles electrodes into the tumor through the skin. Histotripsy ultrasound energy is externally applied from the outside of the body through the intact skin using a "therapy transducer" (a bowl shaped device that sends out the sound waves). This bowl shaped device is placed into a water bath on the patient's abdomen and is moved inside the water bath above the skin surface. The sound waves pass through the water and through the skin and reach the organs underneath. The histotripsy procedure is image-guided using an ultrasound scan, which allows the surgeon to easily monitor treatment as it progresses, with the intent of achieving great precision. This ablation technique causes the destruction of the tumor tissue on which it is applied by transforming the tumor into a liquified mass without cells that can be naturally eliminated by the body, leaving little scarring or fibrous remnant which may be replaced with liver tissue over time. Due to the characteristics of histotripsy, this technique may be an optimal alternative for the treatment of liver tumors with fewer complications than conventional ablation techniques.

The VORTX Rx® intended purpose is for the ablation of soft tissue, including liver tumors, and is the medical device that makes it possible to use the histotripsy technique in clinical practice. This medical device allows the delivery of histotripsy ultrasound waves from the

outside of the body to destroy tumors while the surgeon can visualize and direct the process through the real-time image from the computer screen of the ultrasound. The VORTX Rx® device, in a different configuration, was first used in a clinical application for the treatment of benign prostatic hyperplasia (a noncancerous enlargement of the prostate), and has been adapted for use in malignant tumors, including liver tumors.

The purpose of this study is to evaluate the technical performance of the VORTX RX (ability of this device to destroy the targeted tissue on which the technique is applied) and the safety of this medical device for the treatment of patients with hepatocellular carcinoma or metastasis in the liver from breast, lung, pancreas, and/or colorectal cancers.

Description of the study

Approximately 10 adult patients with inoperable hepatocellular carcinoma or unresectable metastases of the liver are planned to be included in this study. The study aims to evaluate the technical performance and the safety of histotripsy using the VORTX Rx® performed in these patients.

The safety of histotripsy using VORTX Rx® will be evaluated based on the occurrence of adverse events, that is, any unexpected medical complications that may occur during the study and may or may not be related to the histotripsy procedure or use of the medical device (VORTX Rx®). All adverse events occurring during the study will be considered.

If you meet the screening criteria for this study, and you decide to volunteer to be part of the study, you will undergo the histotripsy ablation using the VORTX Rx® medical device. You will be required to come to the hospital for the histotripsy procedure that will be performed in a surgery room of the centre. You will undergo the histotripsy procedure under general anesthesia to ensure the surgeon´s complete control, reduce your discomfort, and provide control over your breathing and motion during the procedure. After the histotripsy procedure you will be hospitalized for up to 24 hours. You will be discharged within 24 hours whenever you have not experienced any complication requiring extended hospitalization.

You may undergo up to three separate histotripsy ablation procedures during the study when clinically indicated and at the discretion of your doctor. At least one-month period is required to have elapsed between the last ablation performed and the next ablation session. Each histotripsy procedure will consist in the ablation of a single tumor or multiple tumor lesions. More than one tumor can be treated in the same session whenever these tumors are close enough and meet the criteria defined for a targeted tumor to be treated with histotripsy. Additionally, a tumor that has been treated with histotripsy can be retreated upon investigator discretion (i.e. in case that residual tumor is detected). Retreatment of a tumor will be performed 1 month after the prior ablation of the tumor.

After each histotripsy procedure, you will be required to follow your doctor's instructions and come to the clinic for your doctor to evaluate your clinical course 1 day (during hospitalization), 1 week, 1 month and 2 months after this procedure.

Study activities

Study duration

It is estimated that each patient will remain in the study for a minimum of 2 months (if one histotripsy is performed) with a maximum follow up period to be determined by the number of histotripsy procedures performed and what is medically appropriate..However, it is anticipated that no more than 9 months should be required for patient follow up.

Number and frequency of visits

The study consists of a screening period that will be performed for a maximum of 2 months prior to histotripsy, (hospitalization), and 4 follow-up visits that will be performed 1 day (during the hospitalization), 1 week, 1 month and 2 months after each histotripsy procedure. This schedule of follow-up visits will apply after each histotripsy procedure (in case of multiple histotripsy sessions). These visits may coincide considering that a one-month period should elapse between histotripsy sessions and taking into account the monthly periodicity of the post-histotripsy follow-up.

Evaluations at the screening period

Before starting the study, you will be provided with a detailed explanation of the study, you will be given this document, and you will be asked if you agree to participate by signing a paper called informed consent that will be provided to you along with this information document.

Once you have given your consent to participate in the study, information will be collected from your medical history, the evaluations needed to determine your current health status and the status of your disease and to confirm that you meet all the criteria to be included in the study will be performed.

The tests and procedures that will be performed to confirm whether you can participate in the study and to have an assessment of your status at the start of the study are described below. Some of these tests and procedures may be part of your usual medical care and will be performed even if you do not participate in the study. If a test or procedure has been performed recently, it may not be necessary to repeat it.

- Recording of your demographic data, such as date of birth, sex and race.

- Review of your medical history, including other diseases you suffer from or have suffered from (in the last 5 years), and the medication you are taking.
- Collection of a urine sample to perform a pregnancy test (if you are a women) within 2 weeks prior to histotripsy ablation, since for safety issues, the participation of pregnant women or women of childbearing age not using adequate contraceptive methods is not permitted.
- Recording of data about your current health status through a complete physical examination, including:
    - Evaluation of your body measurements (weight, height, body mass index [measure of association between weight and height]).
    - Determination of your vital signs (temperature, blood pressure, heart rate and respiratory rate).
    - Evaluation of your performance status (your ability to perform daily activities, self-care, etc.).
- Performance of an electrocardiogram.
- Performance of a blood and urine test.
- Recording of data related to the tumor or metastasis in the liver, such as date of diagnosis, tumor disease stage (according to a method for classifying tumors based on their size, lymph node involvement and metastasis), characteristics of the tumor or metastases (number, size, location in liver, etc.), previous therapies (surgery, chemotherapy, other ablation techniques, etc.), among others.
- Performance of imaging techniques: magnetic resonance imaging (MRI) and other imaging techniques that are necessary such as computed tomography (CT), based on medical judgment, to characterize and assess the tumor or the metastases in the liver.
- Quality of life assessment: you will be asked to fill out a questionnaire (called QLQ-C30) to evaluate your quality of life, including questions about how your disease has affected your life in the previous week.
- Procedure simulation: within 7-14 days prior to the procedure day, MRI of the targeted tumor will be conducted to identify the location and dimensions of the targeted tumor. In addition, VORTX Rx® system will be used to assess the targeted tumor to ensure adequate and clear visualization using ultrasound-image guidance.

<u>Evaluations on day of the histotripsy ablation</u>

- Performance of a blood test.

- Data on the ablation procedure by histotripsy that was performed on you: the duration, and the location of the tumor(s) treated.
- Recording of adverse events that may have occurred during the histotripsy procedure and complications occurring immediately after the procedure.
- Recording of the medication administered after the histotripsy procedure.
- Recording of requirement of blood transfusion after the procedure (yes/no).

Evaluations in the follow-up visits after histotripsy (after 1 day, 1 week, 1 month and 2 months)

- Performance of a blood and urine test.
- Physical examination, including vital signs.
- Handing out of a quality of life questionnaire that you will be asked to complete.
- Self-evaluation of your pain on a scale from 0 to 100, where 0 is “no pain” and 100 is “the worst possible pain”. This evaluation of you pain will only be performed on the visits after 1 day and 1 week of the histotripsy procedure.
- Recording of new adverse events since the last visit and follow-up of those you have suffered previously.
- Recording of medication administered: the use of new treatments, discontinuation of others, etc. will be recorded.
- Performance of imaging techniques (MRI and optionally CT in case that MRI cannot be performed or based on the investigator´s judgment):
    - Visit 1 day after histotripsy: the success of the procedure in destroying the tumor on which the technique was applied will be evaluated (technical success).
    - Follow-up visits at 1 week, 1 and 2 months after histotripsy: the course of the lesions remaining after performing histotripsy will be evaluated.

  The follow-up visits at 1 and 2 months after histotripsy may coincide in case of multiple histotripsy sessions considering that a one-month period should be elapsed between histotripsy procesures and taking into account the monthly periodicity of the post-histotripsy follow-up. Therefore, in case of coincident post-histotripsy visits, if a laboratory test has been performed within the last week as a part of the post-histotripsy follow-up, it will not be necessary to repeat this assessment. Similarly, the imaging assessment (MRI or CT) will be performed once in case of coincident post-ablation visits.

The study visits and procedures are shown in the following table:

Procedures and data collection	Screening (day -60 to 0)	Visit on day of each histotripsy procedure (if applicable) (baseline)	Follow-up visits after each histotripsy procedure (if applicable):			
			1 day after	1 week after	1 month after	2 months after
Informed consent	X					
Demographic data	X					
Medical history	X					
Pregnancy test	X					
Data related to tumor disease	X					
Imaging techniques	X	X	X	X	X	X
Blood test	X	X	X	X	X	X
Urine test	X		X	X	X	X
Quality of life questionnaire	X				X	X
Pain evaluation scale		X	X	X		
Data related to histotripsy		X				
Recording of medication received		X	X	X	X	X
Recording of adverse events		X	X	X	X	X

Risks and discomforts from participation in the study

You may experience side effects as a result of the procedures used in this study. Side effects may be mild to very severe and may vary from one person to the next. All persons participating in the study will be closely followed to detect any side effect. However, the sponsor, the study doctor, and the other doctors do not know all the effects that could occur. The study doctors could give you drugs to help reduce the side effects and will monitor your course.

You should inform the study doctor of any adverse event you experience while participating in the study and of any change in your medication. You should not modify the medication you are taking or take other medicines or “medicinal plants” without previously consulting with the study doctor, and you should comply with the study visits and activities.

Side effects or risk of the study medical device

The potential risks associated with the VORTX Rx® used for liver tumors will include the typical potential risks of ablation methods, the risks related to the ultrasound energy, the complications related to the patient position, and the risks related to contact of the skin with the ultrasound coupling device on the patient. In addition, since you will undergo the histotripsy procedure under general anesthesia, there is a potential risk for complications related to the anesthesia.

Potential risks typically associated with ablation methods

It is expected that the potential risks associated with the study device when used for ablation of tumors in the liver are similar to those typically associated with current ablation procedures and liver surgery. The more serious complications described include, but not limited to, hemorrhage requiring transfusion, visceral perforation (bowel or stomach), rupture of the blood vessels or the bile duct, liver failure, myocardial infarction, lung damage, or embolism. Other complications may be abscess, soft tissue or skin lesions and burns, damage to vascular system, thrombosis, ascites (accumulation of fluid, usually serous fluid which is a pale yellow and clear fluid, that accumulates in the abdominal cavity), subcapsular hematoma (one in the subcapsular space of the kidney), cryo-shock (syndrome of multiorgan failure experienced by few patients after hepatic cryotherapy), post-ablation syndrome (low-grade fever, malaise, chills, myalgia delayed pain, and nausea and vomiting), pleural effusion (a condition in which excess fluid builds around the lung), asymptomatic pleural effusions and minimal asymptomatic perihepatic (or renal) flood or blood collections seen at imaging.

Clinical risks related to the use of ultrasound

The study medical device supplies ultrasound energy for the destruction of tumors, and ultrasound images are also used to provide image-guided guidance for the surgeon. This introduces a clinical risk that is typical of other liver ablation methods. Also, the tissues through which ultrasound energy passes may be at risk of physical effects associated with the application of ultrasound.

Patient position

You will remain under general anesthesia lying face up on a bed throughout the procedure with your chest/abdomen in contact with the study medical device (VORTX Rx®), so you may have a typical clinical risk for remaining in this position.

Contact with skin during the procedure

There is a clinical risk due to potential sensitivity or reaction of the skin from being in contact with the study device. However, these risks have been minimized by limiting exposure to contact with the skin by the use of known contact materials.

General anesthesia

Since you will undergo histotripsy ablation under general anesthesia, the risks associated with general anesthesia also have to be considered.

Several measures will be taken to ensure that the potential benefits outweigh the potential risks for patients participating in this study. Measures include: 1) careful selection of patients; 2) a detailed pre-procedure assessment; 3) complete training and qualification of investigators; 4) close monitoring of the study device and rigorous post-ablation follow-up.

Possible benefits

There are no guaranteed benefits from participating in the study. However, patients like you with liver cancer or metastases in the liver who are included in this study may benefit from partial elimination of the tumor tissue using the study medical device. Therefore, the possibility exists that you will reduce your overall tumor burden, which may result in a favorable impact on your prognosis and quality of life. In addition, the probable benefits to health for this palliative patient population from use of the study device, for its intended uses, and conditions of use, when accompanied by adequate directions and warnings against unsafe use, outweigh the probable risks.

Pregnancy and lactation

There are no data on the use of histotripsy in pregnant women and the studies in animals are insufficient to determine the effects on pregnancy, embryonic/fetal development, and postnatal development. Based on this, you will not be able to participate in the study if you are pregnant. If you suspect that you have become pregnant while participating in the study, please inform the study doctor immediately. The study doctor or his/her staff will inform you about the possible risks for the foetus and the options you may have available to you. The doctor will also follow up your pregnancy and may therefore ask you for information at specific times during your pregnancy and up to 30 days after delivery.

Processing of personal data required in this study will be in accordance with the Regulation (EU) 2016/679 of the European Parliament and of the Council of 27 April 2016 on personal data protection.

Alternative treatments

If you decide not to participate in the study, your treatment and care will not be affected in any way. Please talk to your doctor about the options you have before deciding whether to participate or not in the study.

Insurance

The study sponsor has an insurance policy that complies with current legislation (Royal Decree 1090/2015) and will provide compensation and indemnity in case of harm to your health or injuries that could occur in relation to your participation in the study, provided they are not a consequence of the disease being studied or of the progression of your disease as a consequence of the ineffectiveness of the treatment.

If you would like more information about this section, consult the principal investigator of the study at your site.

We inform you that it is possible that your participation in this clinical trial may modify the general and particular conditions (coverage) of your insurance policies (life, health, accident, etc). Therefore, we recommend that you contact your insurer to determine whether your participation in this study will affect your current insurance policy.

Personal data protection

In accordance with the provisions of Regulation (EU) 2016/679 of the European Parliament and of the Council, of 27 April 2016, on the protection of natural persons with regard to the processing of personal data and on the free movement of such data; this is to inform you that your personal data will be managed as specified below:

- **Data controller:** HistoSonics, Inc
- **Data processor:** Dynamic Science S.L.
- **Purpose:** To conduct clinical research in the area of oncology.
- **Legal basis for processing of the data:** Consent of the interested party to participate in the THERESA study with code: 03.CP.0.3.
- **What recipients will your data be passed on to?**
  Your personal information will always be processed using a code (pseudonymized) so that only the doctor will know your real identify. Your pseudonymized (coded) data may be transferred to third parties for research purpose similar to those described in this document.
- **Your rights:** you may exercise your rights to access, rectification, erasure, restriction of processing, data portability and to object, provided that the exercise of these rights does not affect the research purposes for which the data were collected.

For further information, please consult the ADDITIONAL INFORMATION.

Expenses and economic compensation

The study sponsor is responsible for managing study funding. For the conduct of the study, the sponsor of the study has signed a contract with the study doctor and the site where it will be performed.

You will not have to pay for drugs or the specific tests of the study. Your participation in the study will have no additional cost for you to routine clinical practice and you will be reimbursed for extra expenses (for example meals, trips) generated by your participation in the study up to 50 euros. Expenses above that amount may be approved by sponsor if fair and customary is exceeded. Presentation of the corresponding tickets or invoices will be required.

Other relevant information

A description of this clinical trial will be available at http://reec.aemps.es, as required by Spanish legislation.

Any new information regarding the device used in the study found during your participation that may affect your willingness to participate in the study, will be notified to you by your doctor as soon as possible.

You should also understand that you may be withdrawn from the study if the sponsor or study investigators deem it appropriate for safety reasons, for any adverse event due to the study device, or because they think that you are not complying with the established procedures. In any of these cases, you will receive an adequate explanation of the reason that caused your withdrawal from the study. By signing the attached consent form, you agree to comply with the study procedures explained to you.

You should know that it is possible that your primary care doctor may be aware of your participation in this study.

What treatment will I receive when the clinical trial is ended?

Your participation in the clinical trial does not imply changes in the subsequent treatments you may receive after its completion. When your participation ends, you will receive the best available treatment that your doctor considers most appropriate for your disease. Please talk to your doctor about the options you have.

Collection and use of biological samples for research purposes

During the study it is intended to collect an extra amount of blood at each study visit when blood samples are taken for hematology and biochemistry evaluation as part of the study procedures. These additional blood samples will be sent, processed and stored at a central laboratory (Echevarne Laboratory, Barcelona) to be available for additional, originally unforeseen studies and or new scientific evidence arises in this field of research.

Once the clinical trial is completed, all blood samples obtained during the study will be stored in the Echevarne Laboratory where these samples will be preserved for up to 3 years for future investigation. The storage of biological samples will meet the ethical and legal requirements provided in the RD 1716/2011.

The biological samples will be handled, stored, and treated according to the Law 14/2007 of biomedical research, which regulates the use of biological samples for such purposes.

You should know that the following conditions will apply at all times:

A) The donation of the samples is totally voluntary. You should know that you can give your consent to participate in the study without authorizing the collection and storage of additional samples for future investigation as explained above. If you decide not to give your consent for the sending and subsequent analysis of the samples, this will not be detrimental to you.

B) You will be informed of the purpose of the analysis for which the samples will be used.

C) Samples will be identified using numeric codes (no data that identify you will appear), maintaining confidentiality at all times in accordance with current legislation and regulations.

D) The persons responsible for the custody of the samples will guarantee that the identity of the patient (donor) is not accessible to the researchers who handle and analyze said samples. Your anonymity will be preserved at all times as indicated above.

E) If after you have given consent to obtain and analyze the sample for this study you would like to withdraw your consent (revocation of consent), you may do so freely without having to specify the reason. I addition, if deemed appropriate, you can request the destruction of the samples stored, as well as the elimination of the data obtained from the analysis of the samples, communicating it to the principal investigator of your centre.

F) The results obtained from the analysis of the samples may be published maintaining confidentiality at all times.

G) You will not receive any economic or other compensation for the donation of the sample.

H) Under no circumstances and at any time, the samples will be a direct profit motive, either for the sale of the material or the rights to study them.

I) The current legislation on the protection of personal data will be applied (Regulation (EU) 2016/679 on Data Protection).

Obtaining and publishing the video recording of the procedure for research purposes

A video recording of the ablation procedure (histotripsy) is intended to be performed for all patients participating in this study for research purposes.

The recording (the entire recording or a part of it) could be presented together with the results of the study in congresses/scientific meetings, published in scientific journals, and for feedback for engineering improvements, preserving their personal identity at all times. Your consent is therefore requested to record the procedure that you will undergo if you agree to participate in this study.

The video recording will be performed by the investigator and his collaborators during the histotripsy procedure at the surgery room of the centre. Only the areas restricted to the liver area will be recorded, avoiding, as far as possible, areas of their body by which they can be identified (for example tattoos, scars or recognizable birthmarks).

You should know that the following conditions will apply at all times:

A) The video recording of the procedure is totally voluntary. You could give your consent to participate in the study without authorizing the recording of the procedure. If you decide not to give your consent for the recording, this will not be detrimental to you.

B) The recording will be identified using numeric codes (no data that identify you will appear), maintaining confidentiality at all times in accordance with current legislation and regulations.

C) The recording will be stored in electronic format, maintaining anonymity at all times.

D) If after you have given consent to obtain and publish the video recording you would like to withdraw your consent (revocation of consent), you may do so freely without having to specify the reason. I addition, if deemed appropriate, you can request the destruction of the video recording stored, communicating it to the principal investigator of your centre.

E) The video recording may be published maintaining confidentiality at all times.

G) You will not receive any economic or other compensation for the recording.

H) Under no circumstances and at any time, the recording will be a direct profit motive, either for the sale of the material or the rights to study them.

I) The current legislation on the protection of personal data will be applied (Regulation (EU) 2016/679 on Data Protection).

Contact in case of questions

If during your participation you have any questions or need to obtain more information, please contact _____,
of the Department of _____ and telephone number _____

ADDITIONAL INFORMATION ON THE PROCESSING OF PERSONAL DATA

Data controller and data processor:

The THERESA study (hereinafter called the "Study") was developed by HistoSonics and the data collected through your participation will be processed directly by Dynamic Science S.L., with Tax ID number: B63286280, and registered office at Av. de Josep Tarradellas, 8-10, Planta 5ª, Puerta 4, 08029 – Barcelona, Spain.

Dynamic puts at your disposal our Data Protection Officer, Nairoby Guzmán, who may be contacted at the email address comunica@dynasolutions.com or by sending a letter to her attention to Av. de Josep Tarradellas, 8-10, Planta 5ª, Puerta 4 08029 – Barcelona, Spain.

Purpose of processing of the information collected in the Study

Analysis of the information you share with us will allow us to further knowledge in Oncology. The conclusions from the analysis of these data will benefit the community in general, so your contribution will help all the affected population.

The planned research purposes cannot be carried out without the processing of the data described in the Patient Information Sheet/Informed Consent Form of the Study.

Possible benefits of transfer of your data in the Study

This consent for processing your data in no case substitutes for the consent that must be signed prior to inclusion in the Study or the successive modifications to which it may be subjected.

Legal basis

The processing of your data is based on the explicit, affirmative and unambiguous consent expressed directly by you and documented by the signing of this document.

The research linked to this Study has been evaluated and approved by Ethics Committee of Clinical Research of Mútua Terrassa University Hospital, as described in the Patient Information Sheet.

Also, we strictly comply with Regulation (EU) 2016/679 of the European Parliament and of the Council, of 27 April 2016, on the protection of natural persons with regard to the processing of personal data and on the free movement of such data.

Data assignments and/or transfers

The information collected during the research may be transferred to third parties provided the data are pseudonymized (coded). Although not all future recipients of the data collected for research purposes can be foreseen, it will be ensured that such transfers will always be

between countries that guarantee the protection and safeguarding of the data under conditions equivalent to those required in Spain and Europe, and always in the context of scientific research.

Exercise of your rights

Your participation in this research is entirely voluntary and you may exercise your rights to access, rectification, erasure, restriction of processing, data portability and to object, provided that the exercise of these rights does not affect the research purposes for which the data were collected. To request changes in the data of which you are the owner, you can send an email to comunica@dynasolutions.com or request it by sending a letter to the attention of Data Protection Officer to Av. de Josep Tarradellas, 8-10, Planta 5ª, Puerta 4 08029 – Barcelona, Spain. You should attach a copy of your National ID card/Resident Alien ID number in order to confirm the ownership of the data.

You are also informed that you have the right to withdraw your consent whenever you wish and to file a complaint before the Spanish Data Protection Agency if you consider that the data controller and/or data processor of your data has unjustifiably restricted or prevented the exercise of your rights.

If you do not wish for your personal information be collected, do not participate in this Study.

Information source

All the information collected in the Study comes from you as the data owner, from consultation of your medical records and other official medical records, and from information sources directly linked to the Study. No searches in social networks, requests for information from third parties not linked to the Study or from other alternative information sources, will be made.

Security measures

All data collected in the Study are pseudonymized (coded) for subsequent processing. The information recorded is encrypted for its transfer to the study database. In addition, daily, weekly and monthly backup copies are made of all internal, external and cloud servers. All servers have anti-virus protection, firewalls, controlled accesses, continuous surveillance, alarms, and other pertinent security measures, to ensure your information is protected against attacks and accidental losses.

In the event of serious security breaches, you will receive a notification from the Data Protection Officer of Dynamic within not more than 72 hours.

Duration of your data in the Study Record

The data collected for research purposes must be retained for at least 25 years in accordance with applicable legislation. Therefore, these data cannot be eliminated before the established period once they have been included in the Study File.

INFORMED CONSENT OF PARTICIPANT

Study title: "Multi-center, open-labeled, non-randomized study to evaluate the technical performance and safety profile of the VORTX Rx® for ablation of primary and metastatic liver tumors (Theresa Study)".

Protocol code: 03. CP.0.3; **Version:** 2.0, 26 September 2018.

I, _____ (full name of participant):

- ☐ I have read the information given to me about the study.
- ☐ I have been able to ask questions about the study.
- ☐ I have received enough information about the study.
- ☐ I have talked with _____ (name of investigator).
- ☐ I understand that my participation is voluntary.
- ☐ I understand that I can withdraw from the study:
  - At any time.
  - Without having to give any explanations.
  - Without any consequence to my medical care.
- ☐ I understand that with my participation in the study, I consent to the processing and communication of the data that is collected for the study in the terms established in the patient information sheet that has been given to me.
- ☐ I will receive a signed and dated copy of this informed consent document.

Taking this into consideration, I freely GRANT my CONSENT to participate in the study and give my consent for the transfer and processing of my personal data in accordance with the provisions of this document.

Signature of participant — Signature of investigator

Date: ____/____/____ — Date: ____/____/____

(Name, signature and date in handwriting by patient)

I would like to be informed of any information arising from this research that may be relevant to my health:

- ☐ YES
- ☐ NO

Signature of participant — Signature of investigator

Date: ____/____/____ Date: ____/____/____

(Name, signature and date in handwriting by patient)

Collection and use of biological samples

- ☐ Yes, I agree to the collection of an additional amount of my blood during the study for future research purposes and the use of blood samples as indicated.
- ☐ NO, I do not want that an additional amount of my blood is collected for future research purposes during the study.

Obtaining and publishing the video recording of the procedure for research purposes

- ☐ YES, I agree with the video recording of the ablation procedure I will undergo and the use of the recording as indicated.
- ☐ NO, I do not want that the ablation procedure I will undergo is recorded.

WITNESSED INFORMED CONSENT OF PARTICIPANT

Study title: "Multi-center, open-labeled, non-randomized study to evaluate the technical performance and safety profile of the VORTX Rx® for ablation of primary and metastatic liver tumors (Theresa Study)".

Protocol code: 03. CP.0.3; **Version:** 2.0, 26 September 20182.0, 26 September 2018.

I, _____(full name of witness), as a witness, I affirm that in my presence Mr/Ms _____ (full name of participant) has been informed and has read the information sheet which was given to him/her about the study, and that:

- ☐ He/she has been able to ask questions about the study.
- ☐ He/she has received enough information about the study.
- ☐ He/she has talked with_____ (name of investigator).
- ☐ He/she understands that his/her participation is voluntary.
- ☐ He/she understands that he/she can withdraw from the study:
  - At any time.
  - Without having to give any explanations.
  - Without any consequence to his/her medical care.
- ☐ He/she understands that with his/her participation in the study, he/she consents to the processing and communication of the data that is collected for the study in the terms established in the patient information sheet that has been given to him/her.
- ☐ He/she will receive a signed and dated copy of this consent form.

Taking this into consideration, he/she freely GRANTS his/her CONSENT to participate in the study and give his/her consent for the transfer and processing of his/her personal data in accordance with the provisions of this document.

Signature of witness — Signature of investigator

Date: ____/____/____ — Date: ____/____/____

(Name, signature and date in handwriting by witness)

The participant would like to be informed of any information arising from this research that may be relevant to his/her health:

- ☐ YES
- ☐ NO

Signature of witness | Signature of investigator

Date: ____/____/____ | Date: ____/____/____

(Name, signature and date in handwriting by witness)

The study participant has indicated that he/she cannot read/write.

A member of the study staff has read the consent document, reviewed and discussed it with the participant, and the participant was given the opportunity to ask questions or consult with other people.

The witness must be an impartial person, unrelated to the study.

Collection and use of biological samples

- ☐ Yes, he/she freely agree to the collection of an additional amount of his/her blood during the study for future research purposes and the use of blood samples as indicated.
- ☐ NO, he/she does not want that an additional amount of his/her blood is collected for future research purposes during the study.

Obtaining and publishing the video recording of the procedure for research purposes

- ☐ YES, he/she freely agree with the video recording of the ablation procedure he/she will undergo and the use of the recording as indicated.
- ☐ NO, he/she does not want that the ablation procedure he/she will undergo is recorded.