INFORMED CONSENT FORM (ICF)

I. RESEARCH PARTICIPANT OR LEGAL RESPONSIBLE IDENTIFICATION DATA

1.NAME:.....
IDENTITY DOCUMENT NUMBER: ..... SEX: M F
BIRTH DATE: ...../...../.....
ADRESS: ..... Nº..... APT: .....
DISTRICT:.....CITY:.....ZIP:
.....PHONE:(.....).....

2.LEGAL RESPONSIBLE:.....
NATURE (kinship, guardian, healer, etc.): .....
IDENTITY DOCUMENT NUMBER: ..... SEX: M F
BIRTH DATE: ...../...../.....
ADRESS: ..... Nº..... APT: .....
DISTRICT:.....CITY:.....ZIP:
.....PHONE:(.....).....

You are being invited to participate in a study.

Please read this term carefully as it tells you what you need to know about the objectives of this study. If you agree to take part in this study, you must sign and date this term. Your subscription means you have received the necessary information and wish to participate in this study.

II. DATA ON SCIENTIFIC RESEARCH:

TITLE OF THE RESEARCH PROTOCOL: Efficacy of adding trastuzumab to standard chemotherapy in patients with HER2-negative advanced gastric cancer and HER2-positive expression in circulating tumor cells.

RESPONSIBLE RESEARCHERS:

Dr. Rachel Simões Pimenta Riechelmann - Director, Clinical Oncology Department, A.C. Camargo Cancer Center - Brazil.
Dr. Mauro Daniel Spina Donadio - Clinical Oncologist at A.C. Camargo Cancer Center - Brazil.

STUDY DESIGN AND OBJECTIVE:

You are being invited to participate in this clinical study to be conducted at the AC Camargo Cancer Center - Brazil.

You are diagnosed with inoperable advanced / metastatic gastric cancer. At this time, standard treatment is performed with fluorpyrimidine and platinum-containing chemotherapy (FOLFOX), and only when tumor tissue biopsy shows strong expression of a protein called HER2 is the addition of an anti-HER2 antibody called trastuzumab standardized. It is already known that it is possible to identify circulating tumor cells called circulating tumor cells (CTC) in which expression of tumor proteins such as HER2 can be found. Some studies show that there may be disagreement in HER2 expression between CTCs and tumor biopsy, either CTC expressing HER2 when biopsy is not expressed or vice versa. The present study aims to evaluate the expression of HER2 in patients with relapsed or metastatic gastric cancer and what would be the efficacy of adding trastuzumab to chemotherapy when the biopsy is negative for HER2, but there is expression of this protein in CTCs. Therefore, it is not an experimental drug or regimen other than the current standard treatment, but using this trastuzumab treatment when the therapeutic target, HER2, is present only in CTCs.

In this study you are being asked to participate on a voluntary basis, treatment will continue as long as the tumor is controlled and you feel well. If neither the biopsy nor CTC express HER2, there is no target for trastuzumab drug activity and its treatment will be performed only with standard chemotherapy, under the supervision of the Clinical Oncology team, without prejudice to their care.

PROCEDURES TO BE PERFORMED AND THEIR PURPOSES

All patients who agree to participate in the study may be submitted to the collection of 10 ml of blood for CTC analysis in two moments. Initially all will have CTC collected prior to chemotherapy treatment and HER2-positive cases will receive standard treatment of fluoropyrimidine-based platinum chemotherapy and we will associate trastuzumab at the standard dose for how long the treatment works and you feel well. The company Libbs, which produces the biosimilar trastuzumab used in AC Camargo, will donate the drug to you. The second CTC collection will be performed when the tumor grows after chemotherapy and trastuzumab only for participants who were HER2-positive at the first collection and receiving trastuzumab treatment.

You will be accompanied by the study team through consultation within 3 weeks after starting treatment, when we will evaluate symptoms related to the disease and any side effects, routine physical and laboratory tests; Every 12 weeks

(or 3 months) you will perform imaging examinations (chest, abdomen and pelvis tomography, or abdomen and pelvis resonance) to evaluate treatment efficacy. An echocardiogram will also be performed to evaluate heart function that can rarely be altered with trastuzumab, also at no cost to you as this is a routine test for HER2 positive gastric cancer patients because the trastuzumab label in Brazil describes that this medication is indicated in first-line advanced HER2 positive gastric cancer, without specifying by which diagnostic test the HER2 result was obtained.

After a one-year period in the study, lab and imaging exams will be held every 12 weeks for as long as you feel well and the disease does not grow on imaging.

Except for the circulating tumor cell screening test, blood and imaging tests are already part of the AC Camargo Cancer Center's treatment routine and you will not have more tests than you would if you did not participate in this research.

DESCRIPTION OF DISORDERS AND EXPECTED RISKS IN STUDY PROCEDURES

Trastuzumab: Trastuzumab is an antibody used to treat stomach and breast cancer and has been used by thousands of people. Below are the expected side effects:

Common (≥10%):

- Gastrointestinal: nausea (6-14%); vomiting (4-28%)
- Cardiac: Reduction of left ventricular ejection fraction (decreased ability of the heart to pump blood to the body) (4-10%)
- Infusional: infusion-related reaction (allergic reactions and nonspecific symptoms such as malaise during medication application) (21-40%)
- Neurological: headache (10%)

Uncommon or rare (<10%):

- Cardiac: arrhythmia / palpitation (3%); heart failure (2% -severe <1%)
- Hematologic: anemia (4%), neutropenia (3%)
- Gastrointestinal: abdominal pain / constipation / dyspepsia / stomatitis (2%)
- Non-specific disorders: fatigue (8%); fever (6%); asthenia / chills / peripheral edema (5%); noncardiac chest pain (3%)
- Immunological: allergic reaction (3%)
- Infectious: nasopharyngitis (8%); influenza (4%); upper airway infections (3%); urinary tract infections (2-5%)
- Musculoskeletal: Arthralgia (8%); low back pain (5%); myalgia / limb pain (4%); bone pain / muscle spasms (3%)
- Neurological: dizziness (4%); tingling / dizziness (2%)
- Psychiatric: insomnia (4%); depression (3%); anxiety (2%)
- Respiratory: cough (5%); dyspnea (3%); sore throat / rhinitis (2%); epistaxis (1%)
- Skin: rash (4%); nail disorders (3%); pruritus (2%); erythema (1%)
- Vascular: hot flushes (6%); hypertension (4%); lymphedema (3%)

BLOOD COLLECTIONS FOR CURRENT TUMOR CELL RESEARCH

The risks to which you will be subject are the risks inherent in any venipuncture such as: local pain at the time of the puncture, some local bleeding, bruising and rarely phlebitis (puncture vein infection), but this will be avoided by proper cleaning of the puncture site. puncture and procedure by qualified professional. Although rare, bruise may occur (when blood comes out of the skin, resulting in a blue or purple, round, uneven or irregular spot) after blood collection. If this happens to you, there is nothing to do but wait until it disappears (disappears within 7 days).

RISKS RELATED TO PREGNANCY

There is evidence of human fetal risk with the use of trastuzumab in pregnant women. Impaired fetal growth and renal function, intrauterine growth retardation, and skeletal abnormalities associated with oligodrams (decreased amniotic fluid) during the second and third trimesters have been reported. The use of standard chemotherapies for your tumor type (5-Fluoruracil, Oxaliplatin, Capecitabine) is also not advisable during pregnancy. Therefore, as part of the follow-up routine and regardless of participation in this study, women of childbearing potential are advised to use effective contraception during treatment and for at least 7 months thereafter. Breastfeeding is not recommended due to potential secretion in breast milk. If you become pregnant while participating in the study, you should notify the study doctor immediately.

BENEFITS FOR PARTICIPANT

The hypothesis of the study is that trastuzumab exerts antitumor action in patients with advanced gastric cancer who express HER2 on CTCs but not on biopsy and that it is a safe treatment without the addition of serious adverse effects that can shrink the tumor and control the disease. longer than chemotherapy alone. Therefore, we expect trastuzumab to treat your illness and to preserve your quality of life. However, only at the end of the study can we conclude about the presence of any benefit. If this proves, it is possible that in the future, larger studies will need to be performed before the proposed scheme can be used on a larger scale. Other patients in the future may benefit from the information obtained from this study.

ALTERNATIVE TREATMENTS

If you do not accept (or cannot) participate in this study, your oncologist will discuss standardized therapies in this setting and there will be no harm to your treatment or care. The alternative in this case is chemotherapy alone without trastuzumab.

PAYMENT TO RESEARCH PARTICIPANT

Participating in this study will not incur any additional costs to you and no payment will be made if you agree to participate in this study. You are entitled to compensation if you incur damages associated with the study. Any damage resulting from your participation in the study will be assessed and treated according to the benefits and care to which you are entitled. By signing this consent form you are not waiving any of your legal rights.

VOLUNTARY PARTICIPATION / STUDY DISCONTINUATION

Participation in this study is entirely voluntary (you decide whether to join or not). Even if you decide to participate in the study, you can leave it at any time without explanation and may even refuse to publish data collected about you. If this happens doctors will no longer collect data about you, but may post non-personal information collected prior to cancellation. This decision will not affect your future medical treatment in any way.

The study doctor may also withdraw you from this study if you think this is best for you, or if the study is stopped earlier than planned because it is considered unsafe.

CONFIDENTIALITY

If you choose to participate in this study, your health information and record of your participation will be kept confidential and confidential. Researchers will identify you with a unique number and initials of your name (not using your full name). A copy of this informed consent will be filed in your AC Camargo Cancer Center medical record. However, there is a risk of loss of confidentiality; We will take all possible steps to ensure that this does not occur.

GUARANTEE OF ACCESS

Questions about the procedures should be directed to the researchers listed at the end of this consent form.

Subscriptions

I confirm that I have read the Informed Consent Form and had the opportunity to clarify all my doubts regarding this study. I understand that if I have any further questions regarding the study or my participation in the future, I may contact you at +55 11- 2189-5000 extension 2779.

Through my signature, I agree to participate in this study as a volunteer. I have received a copy of this Informed Consent.

Participant Name (Capital) Date ____/____/_____

Participant Signature

Investigator's name (capital) Date ____/____/_____

Investigador Signature

In case a witness or legal representative is required:

Name of witness / legal representative (capital) Date ____/____/_____

Signature of Witness / Legal Representative

Contact with investigators:

Dr. Rachel Riechelmann and Dr. Mauro DS Donadio - Department of Clinical Oncology - A.C. Camargo Cancer Center - Professor Antonio Prudente Street, 211. São Paulo- SP. Brazil; Phone: +55 (11) 2189-5000 extension 2779 (8am to 5pm) or +55 (11) 98565-9911 (24h)

Research Ethics Committee of the A.C. Camargo Cancer Center - Professor Antonio Prudente Street, 211. São Paulo-SP. Brazil; Phone: +55 (11) 2189-5000 extension 5020 (8am - 5pm)