

**INFORMED CONSENT DOCUMENT FOR PARTICIPATION
OF A SUBJECT IN A RESEARCH STUDY**

**A Single Arm Phase II Pilot Study of Euthyroid Hypothyroxinemia in
Metastatic Breast Carcinoma**

Aultman Health Foundation

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INTRODUCTION

This is a clinical trial, a type of research study. Your study doctor will explain the clinical trial to you. Clinical trials include only people who choose to take part voluntarily. Please take your time to make your decisions about taking part. You may discuss and consult with friends, family and your health care team. If you have any questions, you can ask your study doctor for more explanation.

You are being asked to take part in a research study. The following information is being given to you to explain the purpose of the study, what you will be asked to do as a participant, and the potential risk and benefits. It will also explain that you do not have to participate in this study to receive medical care. You are encouraged to ask questions before deciding whether you wish to participate, or at any time during the course of the study. You will be told of any new findings that may influence your decision to continue to participate.

We understand that information about you and your health is personal. We are committed to protecting the privacy of that information. Because of this commitment, we must obtain your authorization before we may use or disclose your protected health information for the purposes of this clinical trial. Another form called the "*Authorization to Use and/or Disclose (Release) Individually Identifiable Health Information for Research Purposes*" provides that authorization and helps us make sure that you are properly informed of how this information will be used or disclosed.

In order to participate in this study, you will be required to sign both this consent document and the authorization document.

WHO IS CONDUCTING THIS STUDY?

This study is being carried out under the sponsorship of Aultman Health Foundation.

WHAT IS THE USUAL TREATMENT OF HYPOTHYROIDISM IN METASTATIC BREAST CANCER PATIENTS?

You are being asked to participate in this study because you have metastatic breast cancer. Approximately 20 out of every 100 patients with metastatic breast cancer will also have hypothyroidism, or low thyroid function, which is most commonly treated with levothyroxine or T4 (SYNTHROID TM), an oral thyroid replacement therapy.

WHAT ARE MY OTHER CHOICES IF I DO NOT TAKE PART IN THIS STUDY?

If you decide not to take part in this study, you have other choices. For example:

- You may choose to have the usual approach described above.
- You may choose to take part in a different study, if one is available.

WHY IS THIS STUDY BEING DONE?

The purpose of this study is to compare any good and bad effects of using triiodothyronine or T3 to levothyroxine in patients who are undergoing treatment for metastatic breast cancer and have hypothyroidism or low thyroid function. This study will allow researchers to test whether this new approach is better, the same, or worse than the usual approach of using levothyroxine. The study will also look at what percentage of women who are undergoing treatment for metastatic breast cancer have underactive thyroid function or hypothyroidism.

Triiodothyronine has been approved by the Food and Drug Administration (FDA) of the United States for the treatment of hypothyroidism. Triiodothyronine and levothyroxine both work by providing replacement thyroid hormone but are felt to have different effects on cancer cells which is why the study is being conducted.

The study researchers would also like to learn more about fatigue and quality of life. All study participants will be asked to complete a standardized questionnaire, commonly referred to as FACT-B.

WHAT ARE THE STUDY GROUPS?

This is a Phase II trial so all the study participants will be in one group. All participants will be prescribed triiodothyronine (CYTOMEL/liothyronine sodium).

Approximately 30 subjects will be enrolled in this study.

STUDY PROCEDURES

Initial thyroid screening tests will determine if you qualify for the study. The study will also require an electrocardiogram (often called ECG or EKG, a heart tracing device) at baseline.

Once the baseline screening tests are completed you will meet with the study team and you will be switched from levothyroxine (T4) to triiodothyronine (T3) (CYTOMEL/liothyronine sodium). You will be asked to stop taking your levothyroxine (T4) and wait four (4) days before you start taking the study medication triiodothyronine (T3).

You will take your prescribed dose of triiodothyronine (CYTOMEL/liothyronine sodium) tablet(s) every day. Your study doctor will prescribe whether you should take the study medication once per day, or twice per day. It is suggested that you take the study drug each day at the same time. The tablets should NOT be crushed.

You will be asked to take the study drug, triiodothyronine, for 9 months. At the end of this period it will be up to you and your physician whether you stay on triiodothyronine or switch back to levothyroxine. There is a follow up visit at 12 months.

There are prescriptions, over the counter medications and dietary supplements (sometimes known as alternative or complementary) which may interact with the study drugs and cause side effects. You should provide a complete list of all your medications and supplements at the time of enrollment to the study.

Tell your doctor about all other medicines you use, especially:

- antidepressants;
- birth control pills or hormone replacement therapy;
- blood thinner such as warfarin (Coumadin, Jantoven);
- digoxin (digitalis, Lanoxin);
- epinephrine (EpiPen) or norepinephrine (Levophed);
- insulin or oral diabetes medication;
- medications that contain iodine (such as I-131);
- salicylates such as aspirin, Nuprin Backache Caplet, Kaopectate, Pamprin Cramp Formula, Pepto-Bismol; or
- steroid medication such as prednisone.

This list is not complete and other drugs may interact with Cytomel/liothyronine sodium. Tell your doctor about all medications you use. This includes prescription, over-the-counter, vitamin, and herbal products. Do not start a new medication without telling your doctor.

You will undergo periodic blood testing to determine and adjust your dose as needed to maintain a satisfactory thyroid level. Your oncologist will continue your cancer treatment such as chemotherapy or hormonal therapy.

You will also have blood work and scans per treating physician's discretion to monitor the status of your cancer.

You will complete the quality of life survey at time of enrollment and then every 12 weeks for the duration of the study. The questionnaire will take approximately 10-15 minutes to complete.

HOW LONG WILL I BE IN THIS STUDY?

You will be followed for approximately 1 year. The clinical trial team will work closely with you and your other health care providers.

WHAT EXTRA TESTS AND PROCEDURES WILL I HAVE IF I TAKE PART IN THIS STUDY?

Most of the exams, tests, and procedures you will have are part of the usual approach for your cancer care. However, there are some extra tests and procedures that will need to be completed. Baseline blood work and electrocardiogram (heart tracing) will be completed. In the beginning of the study you will see the clinical trial team every 4 weeks for the first 12 weeks. At these visits you will have blood work drawn to monitor your thyroid status. After 12 weeks, blood work will be ordered every 12 weeks, or more often if the study doctor feels it is necessary. You will be required to attend clinic visits with the study doctor every 12 weeks throughout the duration of the study. Scans will be ordered by your treating oncologist. You will be requested to complete a questionnaire at the time of enrollment and at each clinic visit.

WHAT POSSIBLE RISKS CAN I EXPECT FROM TAKING PART IN THIS STUDY?

If you choose to take part in this study, the following is a list risks that you may experience:

- Lose time at work or home and spend more time in the hospital or doctor's office than usual.
- Be asked sensitive or private questions which you normally do not discuss. You have the right not to answer any questions you are not comfortable with.
- The drug used in this study may affect how different parts of your body work, especially your thyroid levels. The study doctor will be testing your blood and will let you know if changes occur that may affect your health.
- There is also a risk that you may have side effects from the study drug.

Here are important points about side effects:

- The study doctors do not know who will or will not have side effects.
- Some side effects may go away, some may last a long time, or some may never go away.
- Some side effects may be serious and may even result in death.

Here are important points about how you and the study doctor can make side effects less of a problem:

- Tell the study doctor if you notice or feel anything different, so they can determine if you are having a side effect.
- The study doctor may be able to treat some side effects.
- The study doctor may adjust the study drug to try and reduce side effects.

Possible side effects of Triiodothyronine/liothyronine sodium

Per product labeling adverse reactions, other than those indicative of hyperthyroidism because of overdose are rare. In rare instances, allergic skin reactions have been reported.

Signs and symptoms of overdose include: Headache, irritability, nervousness, sweating, arrhythmia (including tachycardia), increased bowel motility and menstrual irregularities. Chest pain or heart failure may be induced or aggravated. Shock may also develop. Massive overdosage may result in symptoms resembling thyroid storm.

Other side effects include:

- Fatigue
- Temporary hair loss/thinning of hair

Unanticipated side effects may occur which have not been reported. If you have any unusual symptoms, report them immediately to your doctor.

WHAT POSSIBLE BENEFITS CAN I EXPECT FROM TAKING PART IN THIS STUDY?

It is not possible to know at this time if the study drug, triiodothyronine is better than the usual approach, so this study may or may not help you. This study will help researchers learn things that will help people in the future.

CAN I STOP TAKING PART IN THIS STUDY?

Yes. You can decide to stop at any time. If you decide to stop for any reason, it is important to let the study doctor know as soon as possible so that you can stop safely. If you stop, you can decide whether or not to let the study doctor continue to provide your medical information to the research team.

The study doctor will tell you about new information or changes in the study that may affect your health or your willingness to continue in the study.

The study doctor may take you out of the study:

- If your health changes and the study is no longer in your best interest
- If new information becomes available
- If you do not follow the study rules
- If the study is stopped by the sponsor, IRB or FDA.

WHAT ARE MY RIGHTS IN THIS STUDY?

Taking part in this study is your choice. No matter what decision you make, and even if your decision changes, there will be no penalty to you. You will not lose medical care or any legal rights.

If you have any questions about **YOUR RIGHTS AS A RESEARCH SUBJECT**, contact the Aultman Health Foundation Human Research Review Board in the Office of Research, 2600 Sixth Street SW, Canton, Ohio 44710 (330-323-6793) (email HumanResearch.ReviewBoard@aultman.com) You may contact them if you feel under any pressure to enroll or continue to participate in this study.

WHAT ARE THE COSTS OF TAKING PART IN THIS STUDY?

The triiodothyronine/liothyronine sodium will be prescribed by the study doctor. You have the option to have the prescription filled at Aultman Hospital, or you may have it filled at a pharmacy of your choice. The cost of the medication will be charged to you or your insurance company. The cost of triiodothyronine/liothyronine sodium may be higher depending upon your prescription coverage plan. There is limited funding available to help cover the medication costs for patients that qualify for Aultman's financial assistance programs (application for eligibility required). The blood work and electrocardiogram required as part of this study will be provided to you free of charge. Costs of clinic visits and disease monitoring are considered routine care and therefore will be billed to you or your insurance company.

You and/or your health plan/insurance company will need to pay for all the other costs of treating your cancer while in this study, including the cost of tests, procedures, or medicines to manage any side effects, unless you are told that certain tests are supplied at no charge. Before you decide to be in the study, you should check with your health plan or insurance company to find out exactly what they will pay for.

You will not be paid for taking part in this study.

WHAT HAPPENS IF I AM INJURED OR HURT BECAUSE I TOOK PART IN THIS STUDY?

If you are injured or hurt as a result of taking part in this study and need medical treatment, please tell your study doctor.

Aultman will provide necessary medical treatment but they have not arranged to provide compensation for any injury you may suffer as a direct consequence of the non-negligent performance of the

procedures described above. However, by signing this form, you do not give up your right to seek payment for harm you receive while participating in this study. The costs for treatment will be billed to your insurance company. If you have no insurance, you would be responsible for any costs. You should check with your insurance company to see what they will cover.

WHO WILL SEE MY MEDICAL INFORMATION?

Your privacy is very important to us and the researchers will make every effort to protect it. Your information may be given out if required by law. For example, certain states require doctors to report to health boards if they find a disease such as tuberculosis. However, the researchers will do their best to make sure that any information that is released will not identify you. Some of your health information will be kept in a central database for research. Your name or contact information will not be put in the database.

There are organizations that may inspect your records. These organizations are required to make sure your information is kept private, unless required by law to provide information. Some of these organizations are:

- Aultman Health Foundation Human Research Review Board, a group of people who review research with the goal of protecting those who take part in the study.
- Aultman Cancer Center
- The Food and Drug Administration
- National Cancer Institute in the United States of America.

WHERE CAN I GET MORE INFORMATION?

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

WHO CAN ANSWER QUESTIONS ABOUT THIS STUDY?

You can talk to your study doctor or your research coordinator about any questions or concerns you have about this study or to report side effects or injuries. Contact your study doctor or your research coordinator at the telephone number and address listed on the first page.

If you have any questions about COMPENSATION OR MEDICAL TREATMENT FOR RESEARCH-RELATED INJURIES contact the Aultman Health Foundation Human Research Review Board in the Office of Research, 2600 Sixth St SW, Canton, Ohio 44710 (330-363-6793) (email: HumanResearch.ReviewBoard@aultman.com)

If you have any question about YOUR RIGHTS AS A RESEARCH SUBJECT, contact the Aultman Health Foundation Human Research Review Board in the Office of Research, 2600 Sixth St SW, Canton Ohio 44710 (330-363-6793) (email: HumanResearch.ReviewBoard@aultman.com)

You may also contact them if you feel under any pressure to enroll or continue to participate in this study.

OPTIONAL SUBSTUDY: RECORDS FOLLOW-UP FOR PARTICIPANTS WHO DO NOT MEET ELIGIBILITY FOR TREATMENT STUDY

If you do not meet eligibility for participation in the treatment portion of this study, the investigators of this study would like to follow your health through medical records review. Your treatment plan and monitoring are at the discretion of your treating physician, not this study plan. We are only asking to collect information on the care that you receive as part of standard practice. Please indicate your willingness to participate in this optional follow-up sub-study.

I agree to medical records follow-up if I do not qualify for the treatment portion of this study.

I DO NOT agree to medical records follow-up if I do not qualify for the treatment portion of this study.

CONSENT TO PARTICIPATION IN STUDY

By signing my name below, I confirm the following:

- I have read (or had read to me) this entire consent document. All of my questions have been answered to my satisfaction.
- The study's purpose, procedures, risks and possible benefits have been explained to me.
- I agree to let the study team use and share the health information and other information gathered for this study.
- I voluntarily agree to participate in this research study. I agree to follow the study procedures as directed. I have been told that I can stop at any time.

IMPORTANT: You will be given a copy of this signed document for your records. A second copy will be kept together with the Investigator's research records on this study. A third copy will be placed in your Aultman Hospital medical record.

Please keep it where you can find it easily. It will help you remember what we discussed today.

Research Participant's Name [PRINT]:

Research Participant's Signature:

Date/Time

INVESTIGATORS CONFIRMING STATEMENT

I have given this research subject information on the study, which in my opinion is accurate and sufficient for the subject to understand fully the nature, risks and benefits of the study, and the rights of a research subject. There has been no coercion or undue influence.

INVESTIGATOR/INDIVIDUAL OBTAINING CONSENT

Date

I have explained the purpose of the research, the study procedures, identifying those that are investigational, the possible risks and discomforts and potential benefits. I have answered any questions regarding the research study to the best of my ability.

SIGNATURE OF TREATING PHYSICIAN

Date

My signature certifies I am the physician medically responsible for the subject enrolled in this research study.