Official Title: A Phase 3 Randomized Placebo Controlled Clinical Trial of Donepezil in Chemotherapy Exposed Breast Cancer Survivors With Cognitive Impairment
NCT02822573
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Study Title for Study Participants: DONEPEZIL FOR COGNITIVE IMPAIRMENT

OFFICIAL STUDY TITLE FOR INTERNET SEARCH ON HTTP://WWW.CLINICALTRIALS.GOV: WFU 97116 – A PHASE 3 PLACEBO CONTROLLED CLINICAL TRIAL OF DONEPEZIL IN CHEMOTHERAPY EXPOSED BREAST CANCER SURVIVORS WITH COGNITIVE IMPAIRMENT

Informed Consent Form to Participate in Research

Stephen Rapp, PhD, Principal Investigator

What is the usual approach to my memory function as related to my breast cancer treatment?

You are being asked to take part in this research study because you have memory problems following chemotherapy for breast cancer. There is no standard of care for memory loss associated with breast cancer and chemotherapy. Many patients may undergo formal memory testing. Patients are encouraged to "stay mentally active" by reading, using word games, puzzles and other brain stimulating activities. Other interventions may include memory training programs, or use of other medications that may help memory loss.

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,
- or you may choose to do nothing.

WHY IS THIS STUDY BEING DONE?

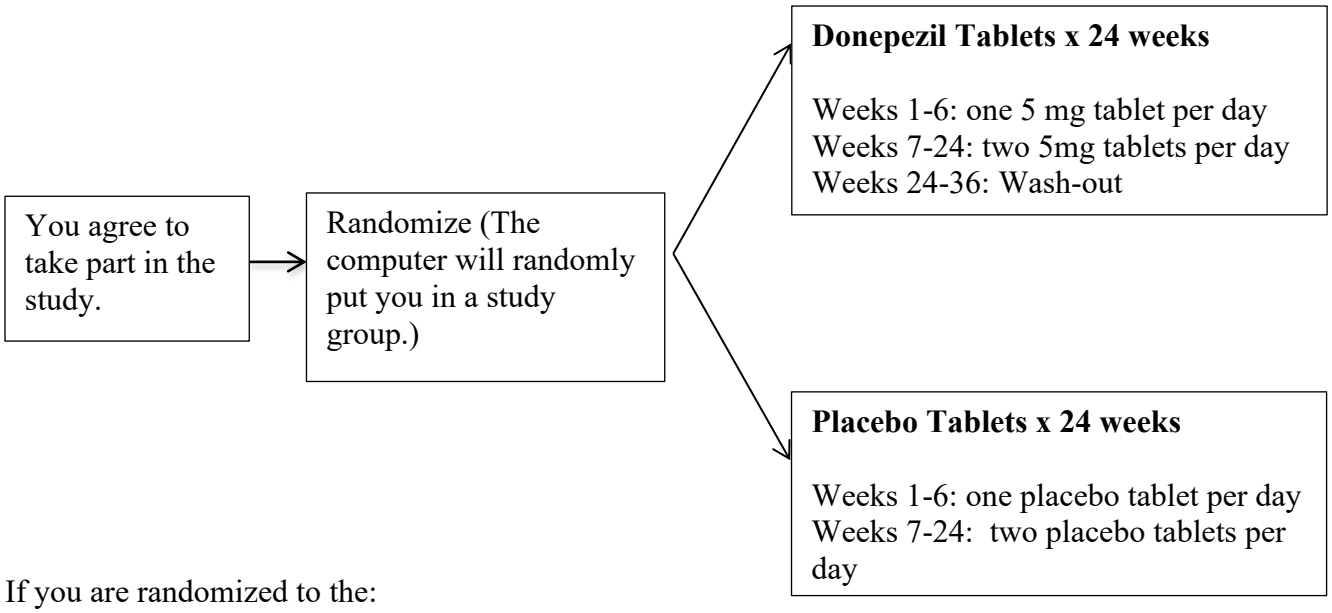
Donepezil is currently FDA approved for the treatment of mild to moderate dementia of the Alzheimer's type, but not for its use in this study evaluating cancer-related cognitive dysfunction in breast cancer survivors. There will be about 276 people taking part in this study.

The purpose of this study is to compare the safety and effects of donepezil (Aricept) or placebo on people and their risk of memory problems after receiving chemotherapy for breast cancer.

WHAT ARE THE STUDY GROUPS?

This study has two study groups. Group 1 will receive the study drug donepezil and Group 2 will receive a placebo, a pill that looks like the study drug but contains no medication.

A computer will by chance assign you to one of the treatment groups in the study. This is done because no one knows if one study group is better, the same, or worse than the other group. Once you are put in a group, you cannot switch to the other group. Neither you nor your doctor will know if you are receiving the study drug or placebo. Your doctor cannot choose which group you will be in.



If you are randomized to the:

- **Donepezil Group:** You will be asked to take one 5 mg donepezil tablet by mouth each day for 6 weeks. Then, you will be asked to take two 5 mg donepezil tablets by mouth each day until the end of the study (18 weeks). This will be a total of 24 weeks.

If you are randomized to the:

- **Placebo Group:** You will be asked to take one placebo tablet by mouth each day for 6 weeks. Then, you will be asked to take two placebo tablets by mouth each day until the end of the study (18 weeks). This will be a total of 24 weeks.

Both Groups will fill in a drug diary and mail it back to the study nurse at 6 weeks. You will be asked to bring your completed drug diaries to the 12 and 24 week study visits.
Three and six weeks after starting your pills the study nurse will call to ask you about any side effects you may be having while taking the donepezil or placebo.

During weeks 24 – 36 you will not take study pills. This is called a "Wash-Out" period. At the end of this wash-out period, you will have a nurse visit to complete study questionnaires.

HOW LONG WILL I BE IN THE STUDY?

You will be in this study for 36 weeks. You will receive the study medication for 24 weeks. Even if you do not finish the study, your doctor will continue to watch you for side effects and follow your condition for 24 - 36 weeks.

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 condition. However, there are some extra lab tests and questionnaires that you will need to have if you take part in this study.

Before you begin the study:

You will need to have the following extra tests to find out if you can be in the study:

- Pregnancy test if you are able to have children
- Memory Questions:

  If the Memory Questions show that you can take part in the study, and you choose to take part, then you will need the following extra lab tests, memory tests and Quality of Life questions. These tests and questions are not part of the usual approach for your condition.

At the beginning of the study, you will have the following:

- Blood draw for APOE genotyping:

  APOE genotyping is an important part of the study. This blood sample is required for you to take part in this study and you must be willing to allow this sample to be stored for future research. This sample may be used to learn more about other diseases.

- Nurse assessment to evaluate current medications, family history or problems you may be experiencing, additional memory questions and complete questionnaires about things like your mood and well-being, language, and how you organize your thoughts.

- Study drug or placebo will be given at your baseline visit.

- You will be given one 5 mg tablet of donepezil to take by mouth once a day or one placebo tablet to take by mouth once a day at weeks 1-6. These tablets should be swallowed whole. You should take the tablets at the same time every day. This may be in the morning or evening; with or without food.

- You will be given a drug diary to complete and send to the study team by mail at six weeks.

You will have approximately two teaspoons of blood withdrawn from a vein or currently placed central line (port-a-cath) at the beginning of the study. If you are a woman of child-bearing potential, you will have an additional 1teaspoon of blood withdrawn to verify your pregnancy status for study eligibility. The total amount of blood withdrawn during the study will be about 2- 3 teaspoons.

Your privacy is very important and the researchers will make every effort to protect it. Your test results will be identified by a unique code and the list that links the code to your name will be kept separate from your sample and health information. However, study results will not be made available to you or your study doctor.

Neither you nor your health care plan/insurance carrier will be billed for the collection of the blood sample that will be used for this study.

During the study:

- At 3 weeks and 6 weeks after starting your study medication, the nurse will call you to make sure you are not having problems taking your study medication. If you are not having any problems at 6 weeks, the drug dose will increase to two 5 mg tablets of donepezil once a day or two placebo tablets once a day starting at week 7.

- You will come for a visit with the study nurse at12 weeks and 24 weeks. The study nurse will ask what medications you are taking, problems you may be experiencing, ask memory questions and complete questionnaires about things like your mood and well-being memory, language, and how you organize your thoughts. You will be asked to bring your completed drug diaries when coming for these visits. At 24 weeks you will stop taking your study medication.

- At 36 weeks, you will return for a visit with the study nurse. You will be asked about medications you are taking, problems you may be experiencing, asked memory questions and complete questionnaires about things like your mood and well-being memory, language, and how you organize your thoughts. This is called the wash-out period. This will help us to determine if there is a worsening of cognitive symptoms and test performance following withdrawal of treatment

The memory questions will be given to you by a trained study staff who will explain how to do them. It will take about 30-45 minutes to complete during each nurse visit.

BLOOD COLLECTION FOR DNA APOE GENOTYPING

As part of this study, a blood sample will be obtained so that DNA from your blood sample will be purified. DNA, or deoxyribonucleic acid, stores and transmits inherited traits, such as eye color or blood type. APOE genotyping works with DNA to help express these traits. As part of this research project, your DNA and APOE genotyping will be studied in an effort to find out if there are genes that contribute to medical conditions that are part of this study. Because we do not know how the results of this DNA/APOE genotyping study relate to your individual health, the

results of the research will not be given to you or your doctor. These results will also not be placed in your medical records.

Your blood sample will be stored with a unique identifier. The unique identifier will be a randomly assigned number and only the principal investigator or select study personnel identified by him will have access to the code that links the unique identifier to you. Your name, address, social security number, etc., will never be disclosed to future researchers and neither will the code that links your identifiers to the sample.

Your sample will be processed in the Center for Genomics and Personalized Medicine Research (CGPMR) at Wake Forest University Baptist Medical Center. The sample will be stored in the CGPMR and it will be given only to researchers approved by Dr. Rapp. An Institutional Review Board (IRB) must also approve any future research study using your blood sample.

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

If you choose to take part in this study, there is a risk that:

- You may lose time at work or home and spend more time in the hospital or doctor's office than usual.
- You may be asked sensitive or private questions which you normally do not discuss. There is a risk someone could get access to the personal information in your medical records or other information researchers have kept about you. Someone might be able to trace this information back to you. The researchers believe the chance that someone will identify you is very small, but the risk may change in the future as people come up with new ways of tracing information. In some cases, this information could be used to make it harder for you to get or keep a job. There are laws against misuse of genetic information, but they may not give full protection. The researchers believe the chance these things will happen is very small, but cannot promise that they will not occur.
- There can also be a risk in finding out new genetic information about you. New health information about inherited traits that might affect you or your blood relatives could be found during a study.
- Risks associated with blood draws: You may experience discomfort, bruising and/or bleeding where the needle is inserted for the blood test. Occasionally some people become dizzy lightheaded or feel faint. Infection may occur on rare occasions.

There is also a risk that you could have side effects from donepezil.

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 soon, some may last a long time, or some may never go away.
- Some side effects may interfere with your ability to have children.
- 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 see 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 drugs to try to reduce side effects.

The bullets below show the most common and the most serious side effects that researchers know about. There might be other side effects that researchers do not yet know about. If important new side effects are found, the study doctor will discuss these with you.

COMMON, SOME MAY BE SERIOUS (≥20% CHANCE)
• Diarrhea 5-15 % dose related • Loss of Appetite 2-8 % dose related • Muscle Cramps 3-8 % • Nausea 3-19 % dose related • Trouble in sleeping 2-14% • Unusual tiredness or weakness 1-8 % • Vomiting 3-9 % dose related

OCCASIONAL, SOME MAY BE SERIOUS (<20% CHANCE)
• Headache 3-10 % • Dizziness 2-8 % • Weight loss 3-5 % dose related

RARE, SOME MAY BE SERIOUS
• High blood pressure 3% • Risk of seizures <1% • Slow heart beat > 1% • Neuroleptic malignant syndrome (NMS) (fever, severe muscle cramps, confusion, unusual heartbeat) <1%

Let your study doctor know of any questions you have about possible side effects. You can ask the study doctor questions about side effects at any time.

Reproductive risks:
You should not get pregnant, breastfeed, while in this study. The donepezil used in this study could be very damaging to an unborn baby. Check with the study doctor about what types of birth control, or pregnancy prevention, to use while in this study.

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

This study may or may not help you because we do not know how the study drugs will compare to the usual approach for your condition. This study may help us learn things that could help people in the future.

The research that may be performed with your blood sample is not designed to help you specifically. There is no personal benefit to you from taking part in this aspect of the research study. It might help people who have diseases at some point in the future, but it is not known if this will happen. The results of the research performed with your blood will not be given to you or your doctor. The results will not be put in your medical record. The research using your blood sample will not affect your care.

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 research staff know as soon as possible. If you stop, you can decide whether or not to talk to the investigators or study staff to provide your medical information to the organization running the study.

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
- If 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.

For questions about your rights while in this study, call the ***(insert name of institution)*** Institutional Review Board at ***(insert phone number)***

WHAT ARE THE COSTS OF TAKING PART IN THIS STUDY?

The donepezil will be supplied at no charge while you take part in this study. The cost of getting the donepezil ready and giving it to you is also provided at no charge. The memory questions, pregnancy testing, and DNA/genotype testing will also be performed at no charge. It is possible that the donepezil may not continue to be supplied while you are on the study. Although not likely, if this occurs, your study doctor will talk to you about your options.

You and/or your health plan/insurance company will need to pay for all of the other costs of 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 feel you have been injured or hurt as a result of taking part in the study, it is important that you tell the study doctor immediately. You will get medical treatment if you are injured or hurt as a result of taking part in this study.

The study sponsors will not offer to pay for medical treatment for injury. Your insurance company may not be willing to pay for study-related injury. If you have no insurance coverage, you would be responsible for any costs. Even though you are in a study, you keep all of your legal rights to receive payment for injury caused by medical errors.

If you feel this injury was a result of medical error, you keep all your legal rights to receive payment for this even though you are in a study.

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 like 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, and/or information about your specimen, from this study 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:

- Wake Forest Center for Genomics.
- Personalized Medicine Research Lab.
- The study investigator and his/her staff.
- The Institutional Review Board, IRB, is a group of people who review the research with the goal of protecting the people who take part in the study.
- The Food and Drug Administration and the National Cancer Institute in the U.S., and similar ones if other countries are involved in the study.

WHERE CAN I GET MORE INFORMATION?

You may visit the NCI Web site at http://cancer.gov/ for more information about studies or general information about cancer. You may also call the NCI Cancer Information Service to get the same information at: 1-800-4-CANCER (1-800-422-6237).

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

WHO CAN ANSWER MY QUESTIONS ABOUT THIS STUDY?

You can talk to the study doctor about any questions or concerns you have about this study or to report side effects or injuries. Contact the study investigator, *(insert name of study doctor at* _____ *(insert telephone number.*

MY SIGNATURE AGREEING TO TAKE PART IN THE STUDY

I have read this consent form or had it read to me. I have discussed it with the research staff and my questions have been answered. I will be given a signed copy of this form. I agree to take part in this study.

Participant's Signature (Printed):_____

Participant's Signature: _____ Date: _____Time:_____ am pm

Signature of person(s) conducting Informed Consent Discussion:

_____ Date:_____ Time:_____ am pm