

SWOG Cancer Research is a network of more than 5,000 cancer physician-researchers at more than 650 institutions working to improve the practice of medicine in preventing, detecting, and treating cancer. Since the 1950s, more than 200,000 participants have enrolled in SWOG-led clinical trials. The advances in treatment and prevention that have come from those trials have improved the lives and health of millions more.

NRG Oncology, also part of the NCI's National Clinical Trials Network, is directing the related S1207-E01 study.

Where is this trial open?

Hundreds of hospitals and medical centers all across the United States and Canada are opening the trial, and centers in several other countries may as well. You can find a list of sites where the e3 study is open at swog.org/patients/e3.

Who can I talk to if I have questions?

Your study doctor can answer questions and give you an informed consent document with more information about the e3 trial. You can learn more from the online sources below, available from the NCI:

- About clinical trials: 1.usa.gov/RygYOz
- Clinical trials & insurance coverage: 1.usa.gov/RyhhJp
- Should I take part in a clinical trial? 1.usa.gov/Pr5LkN
- Adjuvant therapy for breast cancer: 1.usa.gov/QmpIrU

This brochure is meant as a patient's introduction to the e3 (S1207) breast cancer clinical trial. It does not replace the study's detailed informed consent form or information from your study doctor.
protocol rev 11/13/14



THANK YOU for your interest in the e3 clinical trial.

Patients whose breast cancer growth is driven by hormones usually get several years of hormone therapy. This is also known as *endocrine therapy*.

Hormone therapy reduces the amount of estrogen available to your body's cells.

Some research suggests that the drug everolimus (Afinitor®) may make hormone therapy even more effective. But doctors don't know for sure.

The e3 study should tell us whether this is true. It should tell us whether adding a year of everolimus to hormone therapy helps patients with high-risk breast cancer delay or prevent cancer's return.



e³ Breast Cancer Study

evaluating everolimus with endocrine therapy (s1207)

Information for Patients

Can everolimus make hormone therapy more effective for patients with high-risk breast cancer?



swog.org/patients/e3

National Cancer Institute NCT01674140 SWOG-S1207

What is a clinical trial?

A clinical trial is one of the final stages of a long and careful research process. Clinical trials are research studies done with patients or healthy volunteers to learn whether promising approaches to cancer prevention, diagnosis, and treatment are safe and effective, and to answer questions that will improve care.

Who can take part in the e3 trial?

You may be eligible to take part in e3 if items 1 - 5 below are true for you:

- 1) you are a woman or man with invasive breast cancer
- 2) your breast cancer is hormone receptor-positive
- 3) your breast cancer is HER2-negative
- 4) you have completed surgery and chemotherapy and, if your doctor has recommended it, radiation therapy
- 5) your breast cancer is considered high-risk because you fall into category A, B, or C below:
 - A) You had a tumor with a diameter of at least 2 cm *and* your Recurrence Score (RS) on the OncotypeDX genetic test is 25 or higher, OR
 - B) Your cancer spread to 1, 2, or 3 of your lymph nodes *and* either your OncotypeDX Recurrence Score is 25 or higher or you have Grade III disease (without a Recurrence Score), OR
 - C) Your cancer spread to 4 or more of your lymph nodes (regardless of your Oncotype DX Recurrence Score).

What will I do in the study?

If you choose to participate and are eligible, you will have a physical exam and a set of blood tests done and will be given a supply of pills. These will be either the study drug (everolimus) or a placebo (an inactive pill) that looks the same as the study drug. You will take two pills each morning for up to one year.

more inside →

You will also get a study calendar. Each day you will write down how many pills you took that day and any side effects you may have.

Tissue samples that were removed during your surgery will be sent to a central lab for analysis to learn more about your cancer.

Everyone on the study will also get standard hormone therapy designed to reduce the amount of estrogen available to tumor cells. There are several different forms of hormone therapy you and your doctor may choose among.

You may also be invited to join the related Behavior and Health Outcomes study (S1207-EO1), which uses questionnaires to help assess what impact everolimus might have on how quickly you recover from the effects of your earlier surgery, chemotherapy, and/or radiation therapy.

How will this differ from the care I will get if I don't join this study?

The daily pills you would take on this study (everolimus or placebo) are not standard treatment for this cancer. But most of the blood tests and physical exams needed for the study are part of the standard treatment you will probably get whether or not you join the study. Hormone therapy is standard treatment for people with your type of cancer.

Will I get everolimus or will I get a placebo? Who will decide?

You will be assigned to one of two study groups – the everolimus group or the placebo group – at random. A computer program will make the assignment. You have a fair and equal chance – a 50/50 chance – of being placed into either of the study groups.

Why will I be assigned to a study group at random?

Doctors don't yet know whether adding everolimus to hormone therapy will benefit patients

with your type of cancer. This study should answer that question by comparing outcomes in patients who get everolimus to outcomes in patients who do not (patients who get a placebo).

These two study groups should be as similar as possible overall. Assigning patients randomly helps ensure human choice doesn't subtly skew the characteristics of the groups in some way that may make results less definitive.

This type of randomized, controlled trial is considered the most reliable and impartial method of learning which medical treatments work best.

Will I know which study group I am in?

Neither you nor your doctor will know which study arm you are in. After you've completed the trial you can learn whether you received everolimus or a placebo.

Why is this drug being tested?

Earlier research showed that everolimus may increase the effectiveness of hormone therapy for some breast cancer patients.

Has this drug been used for treating breast cancer before?

Everolimus is approved for treating advanced kidney cancer and for treating metastatic breast cancer (breast cancer that has spread to other parts of the body). Its use in this trial is investigational, to determine whether it helps in treating earlier stages of breast cancer as well.

What side effects might I see from everolimus?

Your doctor can tell you about possible side effects, which may include fatigue; bruising or bleeding; increased risk of infection; raised cholesterol, triglycerides, and/or blood sugar levels; mouth sores; skin rash; diarrhea; and nausea.

During your first six weeks on the trial, your study team will call you once a week (or talk to

you at your office visits) to ask you about possible side effects. Let them know of any you are experiencing, as prompt treatment can often help reduce the severity of these effects. If side effects do become severe, your doctor may prescribe a lower dose of the study drug or may ask you to stop taking the drug temporarily or permanently.

My cancer is gone. Why should I risk another drug and its side effects?

Although you may be cancer free after surgery and the other treatments you have had, you are still at risk that the cancer will return at some time in the future. This trial tests whether everolimus can reduce that risk and help delay or prevent recurrence of the cancer.

What benefits will I see by joining the trial?

You may or may not see any direct benefits from joining this study. While doctors hope that adding everolimus will make endocrine therapy more effective, there is no proof of this yet. We do know that the information from this study will help doctors learn more about using everolimus as a treatment for cancer. This knowledge could help future cancer patients.

What precautions do I need to take when using the study drug?

Take two pills together each day with a glass of water, preferably in the morning with a light, low-fat meal. Do not chew or crush the study pills, and don't remove them from the sealed "blister-pack" until you are ready to take them.

You should avoid grapefruit and grapefruit juice while taking everolimus, as they can cause the drug to build up in your bloodstream. You should also not take St. John's Wort while on the drug.

Because everolimus suppresses the immune system, while you are taking it you should not get any vaccine that's made from a live bacteria

or virus. The FluMist nasal spray flu vaccine is one example of a vaccine made from a live virus (but a flu *shot* would be okay).

You should not become pregnant or father a child while taking part in this trial because the drugs used can affect an unborn baby. If pregnancy is a possibility, you should use a highly effective, non-hormonal form of birth control while on this study and for at least two months after you complete treatment.

Can I leave the study if I want to?

Yes. Your study team would like to track your health status for 10 years after you enroll, but you have the right to leave the study at any time. If you decide to stop participating, please tell your doctor so you can stop taking the drugs in a safe manner.

How would taking part affect the cost of my health care?

The study drug for e3 (everolimus or placebo) is being provided at no cost by the manufacturer.

The other treatments and routine tests are considered part of standard care for your condition, and you or your insurance company will be billed (just as if you were not in a clinical trial).

Will my insurance cover the trial costs?

Insurance companies and Medicare generally cover the routine costs of care required in clinical trials, but coverage varies from plan to plan. Check with your insurance provider.

The website of the National Cancer Institute (NCI) has more information on clinical trials and insurance coverage at 1.usa.gov/RyhhJp.

Who is conducting the e3 clinical trial?

The e3 study is being conducted by the SWOG Cancer Research cooperative group within the National Cancer Institute's National Clinical Trials Network.