February 23, 2026

Amendment 3

NCI Protocol #: NRG-GY033
Local Protocol #: NRG-GY033

NCI Version Date: February 23, 2026

The following changes have been made:

Section	Comment
Footer	• Version date has been updated to February 23, 2026

Research Study Informed Consent Document

Study Title for Participants: Study to test the drug darolutamide along with the drugs leuprolide acetate and exemestane in patients with recurrent ovarian granulosa cell tumors

Official Study Title for Internet Search on http://www.ClinicalTrials.gov: Protocol NRG-GY033, "A Phase II Study of Androgen Receptor (AR) Inhibition by Darolutamide in Combination with Leuprolide Acetate and Exemestane in Recurrent Adult-Type Ovarian Granulosa Cell Tumor" (NCT# 06169124)

Overview and Key Information

What am I being asked to do?

We are asking you to take part in a research study. This study has public funding from the National Cancer Institute (NCI), part of the National Institutes of Health (NIH) in the United States Department of Health and Human Services. We do research studies to try to answer questions about how to prevent, diagnose, and treat diseases like cancer.

We are asking you to take part in this research study because you have a recurrent androgen receptor (AR) positive adult-type ovarian granulosa cell tumor.

Taking part in this study is your choice.

You can choose to take part or you can choose not to take part in this study. You also can change your mind at any time. Whatever choice you make, you will not lose access to your medical care or give up any legal rights or benefits.

This document has important information to help you make your choice. Take time to read it. Talk to your doctor, family, or friends about the risks and benefits of taking part in the study. It's important that you have as much information as you need and that all your questions are answered. See the "Where can I get more information?" section for resources for more clinical trials and general cancer information.

Why is this study being done?

This study is being done to answer the following question:

How well does the drug combination of darolutamide, leuprolide acetate, and exemestane work in treating your type of recurrent cancer?

We are doing this study because we want to find out if this approach is helpful in treating your type of ovarian tumor. This study will not directly compare this drug combination to the usual approach to treatment and therefore the study will not determine if this drug combination is better or worse than the usual approach. The usual approach is defined as care most people get for recurrent adult-type granulosa cell tumors of the ovary.

What is the usual approach to my adult-type ovarian granulosa cell tumor?
The usual approach for patients who are not in a study is treatment with FDA approved chemotherapy drugs. Carboplatin and paclitaxel is the preferred treatment regimen. Sometimes other combinations are used.

What are my choices if I decide not to take part in this study?
- You may choose to have the usual approach described above.
- You may choose to take part in a different research study if one is available.
- You may choose not to be treated for cancer.
- You may choose to only get comfort care to help relieve your symptoms and not get treated for your cancer.

What will happen if I decide to take part in this study?
If you decide to take part in this study, you will get the drugs darolutamide, leuprolide acetate, and exemestane until your cancer gets worse or your study doctor determines that continuing in the study is not in your best interest.

After you finish your treatment, your doctor and study team will watch you for side effects. They will check you every 3 months for 2 years after treatment. After that, they will check you every 6 months for 3 years. This means you will keep seeing your doctor for 5 years after treatment.

What are the risks and benefits of taking part in this study?
There are both risks and benefits to taking part in this study. It is important for you to think carefully about these as you make your decision.

Risks
We want to make sure you know about a few key risks right now. We give you more information in the "What risks can I expect from taking part in this study?" section.

If you choose to take part in this study, there is a risk that the combination of darolutamide, leuprolide acetate, and exemestane may not be as good as the usual approach at shrinking or stabilizing your cancer or preventing your cancer from coming back.

There is also a risk that you could have side effects from the study drugs. These side effects may be worse and may be different than you would get with the usual approach for your cancer.

Some of the most common side effects that the study doctors know about are:
- Anemia (which may require blood transfusion)
- Pain
- Constipation
- Tiredness
- Dizziness
- Hot Flashes

There may be some risks that the study doctors do not yet know about.

Benefits
There is evidence that darolutamide, leuprolide acetate, and exemestane can shrink or stabilize your type of cancer. It is not possible to know now if the study drugs will extend your time without disease compared to the usual approach. This study will help the study doctors learn things that will help people in the future.

If I decide to take part in this study, can I stop later?

Yes, you can decide to stop taking part in the study at any time.

If you decide to stop, let your study doctor know as soon as possible. It's important that you stop safely. If you stop, you can decide if you want to keep letting the study doctor know how you are doing.

There are two options of stopping treatment:

1. The first option is that you stop treatment with darolutamide, leuprolide acetate, and exemestane, but you would continue follow up visits (no treatment) to see how you are doing. If you agree to let your study doctor continue to follow you, you will continue to be part of the study so that we can follow you to see how you are doing and if your cancer comes back. We would continue to collect information about how you and your cancer are doing and to see how the treatment affected you and your cancer. This is considered that you go "off treatment" but not "off study" and you would not withdraw consent.

2. The second option is to stop treatment and not allow your study doctor to collect any information on how you and your cancer are doing and how the treatment affected you and your cancer. This is considered "withdrawal of consent" and you would go "off treatment" and "off study".

Your 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.

Are there other reasons why I might stop being in the study?

Yes. The study doctor may take you off the study if:

- Your health changes and the study is no longer in your best interest.
- New information becomes available and the study is no longer in your best interest.
- You do not follow the study rules.
- The study is stopped by the Institutional Review Board (IRB), Food and Drug Administration (FDA), or study sponsor (the National Cancer Institute (NCI). The study sponsor is the organization who oversees the study.

It is important that you understand the information in the informed consent before making your decision. Please read, or have someone read to you, the rest of this document. If there is anything you don't understand, be sure to ask your study doctor or nurse.

What is the purpose of this study?

The purpose of this study is to test the good and bad effects of the drug darolutamide in combination with leuprolide acetate and exemestane. Darolutamide in combination with leuprolide acetate and exemestane could shrink your cancer, but it could also cause side effects, which are described in the risks section below. The study doctors hope to learn if the study drugs will shrink your cancer.

Darolutamide, leuprolide acetate, and exemestane have already been approved individually by the FDA to treat other cancers. This combination of drugs is not approved by the FDA for the treatment of this type of ovarian cancer.

There will be about 37 people taking part in this study.

What are the study groups?

This study has only one group. All participants will receive the same treatment. In this study, you will get darolutamide along with leuprolide acetate and exemestane.

Treatment schedule: For each treatment cycle you will take darolutamide by mouth twice a day, you will receive a leuprolide acetate injection on Day 1, and you will take exemestane by mouth once a day. Each cycle lasts 28 days.

These drugs are not approved by the FDA for treatment of your disease.

What exams, tests, and procedures are involved in this study?

Before you begin the study, your doctor will review the results of your exams, tests, and procedures. This helps your doctor decide if it is safe for you to take part in the study. If you join the study, you will have more exams, tests, and procedures to closely monitor your safety and health. Most of these are included in the usual care you would get even if you were not in a study.

Some exams, tests, and procedures are a necessary part of the research study, but would not be included in usual care. Listed below are procedures that will be done for research purposes only:

Your study doctor will need to use some of the tissue left over from your biopsy or surgery when you were diagnosed with cancer. This sample is a required part of the study. The tissue sample will be used to identify changes in the tumor that may help doctors in the future predict if patients will respond to the drugs being used in this study. You or your study doctor will not get the results of this testing.

What risks can I expect from taking part in this study?

General Risks
If you choose to take part in this study, there is a risk that darolutamide along with the combination of leuprolide acetate and exemestane may not be as good at shrinking or stabilizing your cancer.

You also may have the following discomforts:

- Spend more time in the hospital or office.
- Be asked sensitive or private questions about things you normally do not discuss.
- May not be able to take part in future studies.

The study drugs used in this study could be very harmful to an unborn or newborn baby. There may be some risks that doctors do not yet know about. If applicable, it is very important that you check with your study doctor about what types of birth control or pregnancy prevention to use during the study and for 1 month after you have completed the study.

Participants of child-bearing potential must agree to use adequate contraception (hormonal or barrier method of birth control; abstinence) during study therapy and for 1 month following the completion of study therapy.

This study will use a sample of your tissue. Generally, your hospital will keep some of your tissue. This tissue may be used to help treat your cancer in the future. Because this study will need to use some of this tissue, there is a small risk that it could be used up.

Side Effect Risks
The study drugs used in this study may affect how different parts of your body work such as your liver, kidneys, heart, and blood. The study doctor will test your blood and let you know if changes occur that may affect your health.

There is also a risk that you could have other side effects from the study drugs.

Here are important things to know about side effects:

1. The study doctors do not know who will or will not have side effects.
2. Some side effects may go away soon, some may last a long time, and some may never go away.
3. Some side effects may be mild. Other side effects may be very serious and even result in death.

You can ask your study doctor questions about side effects at any time. Here are important ways to make side effects less of a problem:

- If you notice or feel anything different, tell your study doctor. He or she can check to see if it is a side effect.

- Your study doctor will work with you to treat your side effects.
- Your study doctor may adjust the study drugs to try to reduce side effects.

This study is looking at a different combination of drugs to treat your type of cancer. This different combination of drugs may increase your side effects or may cause new side effects.

Drug Risks
The tables below show the most common and most serious side effects doctors know about. Keep in mind that there might be other side effects doctors do not yet know about. If important new side effects are found, the study doctor will discuss these with you.

Risk Profile for Darolutamide (BAY 1841788)
(CAEPR Version 2.0, September 23, 2020)

OCCASIONAL, SOME MAY BE SERIOUS In 100 people receiving darolutamide (BAY 1841788) from 4 to 20 may have:
• Anemia which may require blood transfusion • Constipation, diarrhea, nausea • Swelling of arms, legs • Tiredness • Fall • Weight loss • Pain • Dizziness, headache • Blood in urine • Increased urination • Difficulty emptying the bladder • Hot flashes • High blood pressure which may cause headaches, dizziness, blurred vision

RARE, AND SERIOUS In 100 people receiving darolutamide (BAY 1841788), 3 or fewer may have:
• Liver damage which may cause yellowing of eyes and skin, swelling

Possible Side Effects of Leuprolide
(Table Version Date: October 14, 2022)

COMMON, SOME MAY BE SERIOUS In 100 people receiving Leuprolide, more than 20 and up to 100 may have:
• Swelling of the body • Pain, such as pain in muscles and joints • Nausea, vomiting • Vaginal discharge • Depression, mood swings • Difficulty sleeping • Flu-like symptoms including fever, chills, body aches, muscle pain • Cold symptoms such as stuffy nose, sneezing, sore throat

COMMON, SOME MAY BE SERIOUS In 100 people receiving Leuprolide, more than 20 and up to 100 may have:
• Swelling and redness of the throat and sinuses which may cause difficulty breathing and swallowing • Headache, migraine • Flushing, hot flashes, increased sweating • Tiredness • Pain, redness, bruising, itching, or swelling at the site of injection

OCCASIONAL, SOME MAY BE SERIOUS In 100 people receiving Leuprolide, from 4 to 20 may have:
• Heart attack or heart failure, which may cause shortness of breath, swelling of ankles, and tiredness • Blood clot which may cause swelling, pain, shortness of breath • Abnormal heartbeat which may cause fainting • Change in the heart rhythm • High blood pressure which may cause headaches, dizziness, blurred vision • Blockage of the airway which may cause shortness of breath, cough, wheezing • Cough • Anemia, which may require blood transfusions • Bruising, bleeding, delayed wound healing • Infection, especially when white blood cell count is low • Damage to the liver which may cause bleeding • Blood in urine • Painful urination, increased urination, difficulty urinating • Pain in belly, constipation • Diarrhea, dehydration • Damage to the muscles which may cause weakness • Breast tenderness, pain, or change in breast size • Shrinkage of the testis • Broken bone, bone pain • Thoughts of suicide • Dizziness, confusion • Trouble with memory, memory loss • Feelings of “pins and needles” in arms and legs • Weight changes, changes in appetite • Acne • Rash, blisters • Decrease in sexual desire or drive

RARE, AND SERIOUS In 100 people receiving Leuprolide, 3 or fewer may have:
• Damage to or scarring of the lungs which may cause shortness of breath • Low blood pressure which may cause feeling faint • Seizure • Blockage of the bowels which may cause pain, vomiting • Diabetes • Allergic reaction which may cause rash, low blood pressure, wheezing, shortness of breath, swelling of the face or throat

Possible Side Effects of Exemestane
(Table Version Date: October 17, 2019)

COMMON, SOME MAY BE SERIOUS In 100 people receiving Exemestane, more than 20 and up to 100 may have:
• Hot flashes, flushing • Increased sweating • Pain • Tiredness
OCCASIONAL, SOME MAY BE SERIOUS In 100 people receiving Exemestane, from 4 to 20 may have:
• Swelling of the liver which may cause belly pain • Constipation, diarrhea, nausea, vomiting, loss of appetite, heartburn • Loss of bone tissue, broken bone, or decreased height • Swelling of the body • Dizziness, headache • Difficulty sleeping • Worry, depression, mood swings • Hair thinning
RARE, AND SERIOUS In 100 people receiving Exemestane, 3 or fewer may have:
• Heart attack or heart failure which may cause shortness of breath, swelling of ankles, and tiredness • Stroke which may cause weakness, paralysis • Liver damage which may cause yellow eyes and skin • Allergic reaction which may cause rash, low blood pressure, wheezing, shortness of breath, swelling of the face or throat • Vaginal bleeding

Additional Drug Risks
The study drug could interact with other drugs or food so check with your study doctor or pharmacist before starting any new medications or stopping old medications. You will be provided with a study specific wallet card. Share this information with your family members, caregivers, other health care providers, and pharmacists.

Rarely, there are problems getting enough supplies of the study drug. If that happens, your doctor will talk with you about your options.

What are my responsibilities in this study?
If you choose to take part in this study you will need to:

- Keep your study appointments.
- Tell your doctor about:
    - all medications and supplements you are taking
    - any side effects
    - any doctors' visits or hospital stays outside of this study
    - if you have been or are currently in another research study.
- Write down in your medication diary when you take the study drug at home.

Do not get pregnant or breastfeed while taking part in this study. Tell your study doctor right away if you think that you have become pregnant during the study or within 90 days after your last dose of study drug.

What are the costs of taking part in this study?
You and/or your insurance plan will need to pay for the costs of medical care you get as part of the study, just as you would if you were getting the usual care for your cancer. This includes:

- the costs of tests, exams, procedures, and drugs (exemestane and leuprolide acetate)
- that you get during the study to monitor your safety, and prevent and treat side effects.
- the costs of getting the darolutamide ready and giving it to you.
- your insurance co-pays and deductibles.

Talk to your insurance provider and make sure that you understand what your insurance pays for and what it doesn't pay for if you take part in this clinical trial. Also, find out if you need approval from your plan before you can take part in the study.

Ask your doctor, nurse or study staff for help finding the right person to talk to if you are unsure which costs will be billed to you or your insurance provider.

You and/or your insurance provider will not have to pay for exams, tests, and procedures done for research purposes only or that are covered by the study. These include:

- Submission of tumor tissue for research purposes

You or your insurance provider will not have to pay for the darolutamide while you take part in this study.

Taking part in this study may mean that you need to make more visits to the clinic or hospital than if you were getting the usual approach to treat your cancer. You may:

- Have more travel costs.
- Need to take more time off work.
- Have other additional personal costs.

You will not be paid for taking part in this study. The research may lead to new tests, drugs, or other products for sale. If it does, you will not get any payment.

What happens if I am injured because I took part in this study?

If you are injured as a result of taking part in this study and need medical treatment, please talk with your study doctor right away about your treatment options. The study sponsors will not pay for medical treatment for injury. Your insurance company may not be willing to pay for a study-related injury. Ask them if they will pay. If you do not have insurance, then you would need to pay for these medical costs.

If you feel this injury was caused by medical error on the part of the study doctors or others involved in the study, you have the legal right to seek payment, even though you are in a study. Agreeing to take part in this study does not mean you give up these rights.

Who will see my medical information?

Your privacy is very important to us. The study doctors will make every effort to protect it. The study doctors have a privacy permit to help protect your records if there is a court case. However, some of your medical information may be given out if required by law. If this should happen, the study doctors will do their best to make sure that any information that goes out to others will not identify who you are.

Some of your health information, such as your response to cancer treatment, results of study tests, and medicines you took, will be kept by the study sponsor in a central research database. However, your name and contact information will not be put in the database. If information from this study is published or presented at scientific meetings, your name and other personal information will not be used.

There are organizations that may look at or receive copies of some of the information in your study records. Your health information in the research database also may be shared with these organizations. They must keep your information private, unless required by law to give it to another group.

Some of these organizations are:

- The study sponsor and any company supporting the study now or in the future. This would include any organization helping the company with the study.

- The NCI Central IRB, which is a group of people who review the research with the goal of protecting the people who take part in the study.
- The FDA and the groups it works with to review research.
- The NCI and the groups it works with to review research.
- The NCI's National Clinical Trials Network and the groups it works with to conduct research, including NRG Oncology.

In addition to storing data in the study database, data from studies that are publicly funded may also be shared broadly for future research with protections for your privacy. The goal of this data sharing is to make more research possible that may improve people's health. Your study records may be stored and shared for future use in public databases. However, your name and other personal information will not be used.

Some types of future research may include looking at your information and information from other patients to see who had side effects across many studies or comparing new study data with older study data. However, right now we don't know what research may be done in the future using your information. This means that:

- You will not be asked if you agree to take part in the specific future research studies using your health information.
- You and your study doctor will not be told when or what type of research will be done.
- You will not get reports or other information about any research that is done using your information.

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.

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 doctor (*insert name of study doctor[s]*) at (*insert telephone number, and email address if appropriate*).

For questions about your rights while in this study, call the (*insert name of organization or center*) Institutional Review Board at (*insert telephone number*).

Optional studies that you can choose to take part in

This part of the consent form is about optional studies that you can choose to take part in. They are separate from the main study described above. These optional studies will not benefit your health. The researchers leading these optional studies hope the results will help other people with cancer in the future. The results will not be added to your medical records and you or your study doctor will not know the results.

Taking part in these optional studies is your choice. You can still take part in the main study even if you say "no" to this study. There is no penalty for saying "no." You and your insurance company will not be billed for these optional studies. If you sign up for, but cannot complete any of these studies for any reason, you can still take part in the main study.

Circle your choice of "yes" or "no" for the following study.

Optional sample collections for storage for possible future studies

Researchers are trying to learn more about cancer and other health problems using blood and tissue samples from people who take part in clinical trials. By studying these samples, researchers hope to find new ways to prevent, detect, treat, or cure diseases.

Some of these studies may be about how genes affect health and disease. Other studies may look at how genes affect a person's response to treatment. Genes carry information about traits that are found in you and your family. Examples of traits are the color of your eyes, having curly or straight hair, and certain health conditions that are passed down in families. Some of the studies may lead to new products, such as drugs or tests for diseases.

Unknown future studies

If you choose to take part in this optional study, a sample of tissue from your previous biopsy will be collected and stored. Storing samples for future studies is called "biobanking." The biobank is being run by NRG Oncology and is supported by the NCI. This is a publicly funded study. Samples from publicly funded studies are required to be shared as broadly as possible. However, we will protect your privacy. The goal of this is to make more research possible that may improve people's health.

The biobank is a public research resource. It has controlled access. This means that researchers who want to get samples and data from it must submit a specific research request. The request identifies who they are and what their planned research project is. Before getting the samples and data, the researchers must agree to keep the data private, only use it for their planned research project, and never use it to try to identify you.

Right now, we don't know what research may be done in the future using your tissue samples. This means that:

- You will not be asked if you agree to take part in the future research studies.
- You and your study doctor will not be told when or what type of research will be done.
- You will not get reports or other information about any research that is done using your samples.

Unknown future research studies may include sequencing of all or part of your DNA. This is called genomic sequencing. Sequencing allows researchers to identify your genetic code. Changes in your genetic code may just be in your tumor tissue. These are called somatic changes. Changes may also be in your normal tissue and passed down through your family. For example, these genetic changes may be passed down to your children in the same way that eye

and hair color are passed down. These are called germline changes. If only tumor tissue is sequenced, we will not know if a genetic change in your tumor is also in your normal tissue. This is why sometimes both normal tissue and tumor tissue are sequenced. This helps researchers understand if a genetic change happened only in your cancer tissue, or in your normal tissue as well.

What is involved in this optional sample collection?
If you agree to take part, here is what will happen next:

1. A sample from the tissue that was collected at the time of your surgery will be sent to the biobank.
2. Your sample will be stored in the biobank. There is no limit on the length of time we will keep your samples and research information. The samples will be kept until they are used for research or destroyed.
3. Researchers can only get samples from the biobank after their research has been approved by experts. Researchers will not be given your name or contact information.
4. Some of your genetic and health information may be placed in central databases for researchers to use. The databases will not include your name or contact information.

What are the risks in this optional sample collection?

- Generally, hospitals will keep some of your tissue. This tissue may be used to help treat your cancer in the future. There is a small risk that when this tissue sample is submitted to the biobank for this optional sample collection, your tissue could be used up.
- Your medical and genetic information is unique to you. There is a risk that someone outside of the research study could get access to your study records or trace information in a database back to you. They could use that information in a way that could harm you. Researchers believe the chance that someone could access and misuse your information is very small. However, the risk may increase in the future as people find 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 and get or keep health insurance.

How will information about me be kept private?
Your privacy is very important to the study researchers and biobank. They will make every effort to protect it. Here are just a few of the steps they will take:

1. They will remove identifiers, such as your initials, from your sample and information. They will replace them with a code number. There will be a master list linking the code numbers to names, but they will keep it separate from the samples and information.
2. Researchers who study your sample and information will not know who you are. They also must agree that they will not try to find out who you are.
3. Your personal information will not be given to anyone unless it is required by law.
4. If research results are published, your name and other personal information will not be used.

What are the benefits to taking part in this optional sample collection?

You will not benefit from taking part.

The researchers, using the samples from you and others, might make discoveries that could help people in the future.

Are there any costs or payments to this optional sample collection?
There are no costs to you or your insurance. You will not be paid for taking part in this study. The research may lead to new tests, drugs, or other products for sale. If it does, you will not get any payment.

What if I change my mind about this optional sample collection?
If you decide you no longer want your samples to be used, you can call the study doctor, (*insert name of study doctor for main trial*), at (*insert telephone number of study doctor for main trial*), who will let the biobank know. Then, any sample that remains in the biobank will be destroyed or returned to your study doctor. This will not apply to any samples or related health information that have already been given to or used by researchers.

What if I have questions about this optional sample collection?
If you have questions about the use of your samples for research, contact the study doctor, (*insert name of study doctor for main trial*), at (*insert telephone number of study doctor for main trial*).

Please circle your answer below to show if you would or would not like to take part in each optional study:

Samples for unknown future studies:
I agree that my samples and related health information may be kept in a biobank for use in future health research.

YES NO

Contact for Future Research

I agree that my study doctor, or someone on the study team, may contact me or my doctor to see if I wish to participate in other research in the future.

YES NO

This is the end of the section about optional studies.

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 study doctor and my questions have been answered. I will be given a signed and dated copy of this form. I agree to take part in the main study. I also agree to take part in any additional studies where I circled "yes".

Participant's Printed Name _____

Participant's signature _____

Date of signature _____

Signature of person(s) conducting the informed consent discussion

Printed Name _____

Signature _____

Date of signature _____