UAB IRB
Approved
03-May-2023
until
02-May-2024

CONSENT FORM

Title of Research:	**RAD 1805/UAB 1917(I3Y-US-001):** Phase II Clinical Trial of Abemaciclib in Combination with Androgen Deprivation Therapy for Locally Advanced Prostate Cancer
UAB IRB Protocol #:	IRB-300004706
Principal Investigator:	Andrew McDonald, MD, MS
Sponsor:	University of Alabama at Birmingham (UAB), Department of Radiation Oncology
Sponsor Protocol #:	**RAD 1805/UAB 1917(I3Y-US-001)**

Purpose of the Research Study

You are being asked to take part in a medical research study. As required by federal regulations, this research study has been reviewed and approved by an Institutional Review Board (IRB), a University committee that reviews, approves and monitors research involving humans. Before a knowledgeable decision about whether to participate in a research study can be made, the possible risks and benefits related to the study should be understood. This process of learning and thinking about a study before deciding to participate is known as *informed consent* and includes:

- Receiving detailed information about this research study;
- Being asked to read, sign and date this consent form once the nature of the study is understood and a decision is made to participate. If there is anything about the study you don't understand or if there are questions, you should ask for explanations before signing this form;
- Being given a copy of the signed and dated consent form to keep.

A patient who joins a research study has a relationship with the study doctor that is different than the relationship with a treating or personal doctor. A treating doctor treats a specific health condition with the goal of improving that condition. A study doctor treats subjects according to a research plan to obtain information about the experimental drug, device or procedure being studied and with the understanding that there may or may not be benefit from being in the study. The study doctor and study staff can provide more information about research as opposed to treatment.

The type of study you are being asked to join is known as a Phase II study. Phase II research studies are designed to determine the percentage of patients that will respond well to a combination of a new or experimental drug alone or in combination with Food and Drug Administration (FDA)

approved drug for a particular cancer. Phase II studies of anti-cancer drugs are done on patients with cancer.

The main purpose of this study is to evaluate the safety, tolerability, and effectiveness of an experimental drug called Abemaciclib when it is combined with a Food and Drug Administration (FDA) approved androgen deprivation therapy (ADT) drugs like goserelin and leuprolide in patients with localized or locally advanced Prostate Cancer who have and have not received prior radiotherapy or chemotherapy. Abemaciclib is an investigational drug, meaning it has not been approved by the U.S. Food & Drug Administration (FDA) for patients with your type of cancer. It is approved for treatment of patients with breast cancer. In this phase II study, all patients will receive same doses of both the study drug, abemaciclib and FDA approved androgen deprivation therapy.

Androgen Deprivation Therapy (ADT) is given in patients with prostate cancer to prevent spread of disease and it is FDA approved. This may be started before or after administration of radiation therapy or surgical removal of prostate. Since prostate cancer is driven prominently by high testosterone levels, ADT will act to reduce the levels of testosterone and thus slow the growth of prostate cancer. ADT appears to increase survival when added to radiation treatment. This study will evaluate if Abemaciclib will work with ADT to control growth and spread of prostate cancer so as to make the patient's tumor better receptive to radiation therapy and improve outcomes to radiation therapy.

Abemaciclib will be administered orally (by mouth) at a dose of 150 mg and patients can take these pills at their homes twice a day, while ADT is administered through the veins or subcutaneously and hence, this will be given to patients in clinic.

A total of 30 patients with localized or locally advanced prostate cancer will be enrolled at University of Alabama at Birmingham (UAB), over a period of 5 years.

Study Participation & Procedures

If you agree to participate in this trial by signing this informed consent, the following will occur:

Study Design:

- The **Screening Period** consists of evaluation for study eligibility.
- The **Treatment/Intervention Period** consists of Abemaciclib in combination with ADT to evaluate safety, tolerability, and effectiveness of the treatment.

Depending on how well you tolerate Abemaciclib, every 4 weeks you will take Abemaciclib for 3 cycles (4 weeks=1 cycle), then not take it for a week. You will also receive first dose of ADT on cycle 1 day 1 of Abemaciclib. After 12 weeks, you will be scheduled for radiation therapy (once a day for about 5.5weeks for a total of 28 treatments). You will stop Abemaciclib 2 weeks before radiation

therapy and restart combination therapy (Abemaciclib and ADT) one month after completing radiation therapy. Then, you will continue to take Abemaciclib by itself and ADT in clinic at regular intervals of 3 months, until you have progression (spread) of disease, you are unable to tolerate it, or you decide you want to stop taking it. The maximum amount of time you will take Abemaciclib by itself and ADT under supervision will be two years after the end of radiation therapy.

Screening Period
You will undergo screening procedures to determine if you can be in the study. The following procedures and tests will be done during this time:

- Obtain informed consent and research authorization.
- Review and collection of information from your medical records and demographic data (age, race, ethnicity).
- A physical examination and vital signs (body temperature, blood pressure, pulse, respiratory rate, weight, height).
- ECOG performance status score: This is a scale used to assess how your cancer is progressing, and how your cancer affects your daily living abilities.
- Review of medications you are currently taking.
- An electrocardiogram (EKG) to record the activity of your heart.
- Imaging tests: Chest CT (computed tomography), Abdomen/pelvis (CT or MRI [magnetic resonance imaging]), and bone scan.
- Blood draw for laboratory tests: CBC (complete blood count), metabolic panel, PSA (Prostate Specific Antigen), testosterone, testosterone levels, hepatitis B and C. Approximately 3-4 tablespoons of blood taken during the screening period.
- Urine sample will be taken (about 5 tablespoons).
- Tumor archived tissue or biopsy, if unavailable.

Treatment/Intervention Period
If you are a subject participating in this study, you will return to the clinic at regular intervals of 28 days on day 1 of each cycle.

The following assessments will be performed C1D1, and Day 1 cycle 2 onwards:

- A physical examination and vital signs
- ECOG performance status
- Review of medications you are currently taking
- Review of any side-effects you may be experiencing
- An electrocardiogram (EKG) to record the activity of your heart (Day 1 of each cycle).
- Blood draw for laboratory tests: CBC, metabolic panel, PSA (at the beginning of each new cycle) and testosterone levels starting first day of second cycle and then first day of subsequent cycles. You will need to have approximately 3-4 tablespoons of blood taken during the treatment/intervention period at each visit.

    - You will need to come in for blood draws for laboratory tests more frequently in the beginning of the study to monitor your liver enzyme levels and blood counts. You will be asked to come in every 2 weeks for the first 2 months, and then monthly for the next 2 months, and then your physician will make a decision about the most appropriate frequency for monitoring.
- Urine sample will be taken (about 5 tablespoons).
- Imaging tests: Chest CT, Abdomen/pelvis (CT or MRI), and bone scan every 8 weeks when restarting treatment after radiation therapy.

You will take the prescribed dose of Abemaciclib twice daily. You will receive ADT at the prescribed clinic visits every 3 months once before radiation therapy and then every 3 months when restarting one month after radiation therapy to a maximum of 24 months.

End of Study Visit
If you complete all of the treatment/intervention cycles or if you are discontinued from study treatment at any time, you will come in for an end of study visit to have the following procedure done:

- Physical exam and vital signs
- ECOG performance status
- Review of medications you are currently taking
- Review of any side-effects you may be experiencing
- An electrocardiogram (EKG) to record the activity of your heart (Day 1 of each cycle).
- Blood draw for laboratory tests: CBC, metabolic panel, PSA, testosterone. You will need to have approximately 3-4 tablespoons of blood taken during the End of Study Visit.

Follow-up Visits
You will come in for a study visit every 12 weeks following the End of Study visit for a total of up to 4 visits. The following procedures will occur at Follow-Up Visits:

- Physical exam and vital signs
- ECOG performance status
- Review of any side-effects you may be experiencing
- Blood draw for laboratory tests: CBC, metabolic panel, PSA. You will need to have approximately 1-2 tablespoons of blood taken during the Follow-Up Visits.
- Imaging tests: Chest CT, Abdomen/pelvis (CT or MRI)
- Optional tumor biopsy of prostate cancer site.

Additional Information
Your de-identified private information and de-identified biospecimens (private information and biospecimens with all identifiers removed) may be used for future research studies. This is only when there are no identifiers associated with the data or biospecimens.

The clinical results (including individual research results) will not be returned to you.

Risks and Discomforts

Taking medication before surgery or radiation is not standard of care. While androgen deprivation therapy (ADT) plus radiation can cure prostate cancer in some patients, the addition of abemaciclib to ADT may not increase cure rates. This could mean that if you have any side effects from the drug for which recovery time is required, this could delay radiation, which could lead to your cancer getting worse. Elevated lipase has been observed as a possible side effect although the relationship to study treatment is uncertain.

Tell the study doctor or research team as soon as possible if any of the side effects, risks or discomforts listed below occur or if you think a side effect that is not listed may be happening.

If your condition worsens, if side effects become very severe, or if it turns out that being in this study is not in your best interest, you will be taken out of the study.

If questions come up about side effects, ask the study doctor or staff at any time during or after the study.

Possible Side Effects and Risks of Abemaciclib

The possible side effects related to abemaciclib treatment are not all known. The risks of combining abemaciclib with ADT in prostate cancer patients have not been reported before. Some side effects may be serious and may require treatment or additional testing and may be life threatening. If you have any side effects during your participation in this study, you should let your study doctor know right away.

Most common side effects experienced by patients taking Abemaciclib:

The following side effects were experienced by 10% (10 or more patients in 100) or more patients who took Abemaciclib with hormone therapy for breast cancer:

- Diarrhea (occurred in 90% of patients receiving abemaciclib)
- Nausea
- Fatigue
- Vomiting
- Decreased lymphocytes
- Decreased platelets
- Decreased neutrophils
- Decreased hemoglobin

- Increased Lipase and Amylase (pancreatic enzymes used to break down fats in food for absorption)
- Increased creatinine level (The drug elevates the serum creatinine levels but does not damage the kidney or affect its function.)
- Weight loss

The following side effects were experienced by 3-6% (3 to 6 patients in 100) who took Abemaciclib as a single drug therapy:

- Lung inflammation (interstitial lung disease), which was sometimes severe or fatal
- Blood clots in the legs or lungs
- Elevated liver enzymes more than 5 times normal

You may or may not have more side effects depending on what group you are assigned to.

At study visits or at other times if the study doctor decides it is necessary, blood tests will be done to check the function of your heart, lungs, liver, kidneys, pancreas and bone marrow (where blood cells are produced). Abnormal tests will be assessed by the study doctor who will determine if further testing is necessary. The study doctor will discuss test results with you.

Potential for Drug Interactions: The drugs used in this study may interact with other drugs you are taking. The medications you are taking will be closely monitored while you are participating in this study. It is very important to tell your study doctor about all of the medicines you take before you start this study. It is also very important to tell them if you stop taking any regular medicine, or if you start taking a new medicine while you take part in this study. When you talk about your medicine with your study doctor, include medicine you buy without a prescription at the drug store (over-the-counter remedy), or herbal supplements.

Potential Risks of Drug Combination: Since this is the first time Abemaciclib and ADT are being used together, there may be unforeseen risks.

Radiation risks:
If a CT guided tumor localization is necessary, there will be additional radiation exposure for the imaging. Please see below for information regarding the radiation risks due to imaging exposure.

Possible side effects of CT scans: In this study, you will be exposed to some radiation from the CT scan(s). The total radiation from each (combined chest, abdominal and pelvic) CT scan is approximately equal to five years of exposure to natural background radiation. Background radiation is radiation normally received from sources such as cosmic rays and natural radioactivity in building materials and the ground. There is a small risk that the radiation may cause cancer or other radiation effects in several years.

To prepare you for your CT scan, a liquid called a "contrast dye" may be injected into your veins to improve the quality of the image. There is a small possibility that you could have a severe allergic reaction to this dye that could cause injury or death. If you have any kidney problems, the dye may cause other medical problems.

If you have any kidney problems or have ever had an allergic reaction to contrast dye, you must let the study physician know as soon as possible.

MRI scanning is a painless procedure that only requires that you lie quietly on a padded table that gently glides you into the magnet. The MRI scanning procedure requires that you be confined in a small partially enclosed space. Some individuals find this to be uncomfortable and may feel claustrophobic (fearful of being closed in) or experience nervousness, sweating or other minor discomfort. The sound of the MRI scanner can be quite loud. You will be given special earplugs to minimize the noise. In addition, the magnetism of the machine attracts certain metals; therefore, people with these metals within their bodies (such as pacemakers, infusion pumps, aneurysm clips, metal prostheses, joints, rods, some implanted metallic or electrical devices or plates) will be excluded from the study. The “metal” in dental fillings is less responsive to magnetism and is therefore allowed. The MRI technician will ask you if you have any metals within your body. You will be expected to notify the investigator conducting the study of any metal in your body, other than dental fillings. There are no other known side effects resulting from exposure to the MRI scan.

Bone Scan uses a small amount of a radioactive material injected into your vein to allow doctors to see changes in your bones. After the injection, you will wait 2-3 hours. You will then lie on a table for 12-20 minutes while a special camera moves over and under you. [There is no special preparation for this test. You can eat and drink normally.] The radiation from each scans is approximately equal to 1.5 years of exposure to natural background radiation.

Risks from blood draw include slight pain at the site of needle prick, occasional bruising at local site and rarely infection. Blood draw will be done from veins on either of your forearms but on some occasions, in presence of port for infusion, this port will be used for blood draw as well.

Risks from Prostate Biopsy: You may experience bleeding from biopsy site, increased risk of infection and complications related to anesthesia for the procedures.

Information for Men Capable of Fathering a Child

The effect of the study drug on your sperm is unknown. You should not father a baby while on this study because the drugs in the study can affect a fetus. To be in this study you and your partner must practice adequate birth control measures because of potential adverse effects on sperm. The study doctor will discuss acceptable methods of birth control with you.

From when you start taking the study drug until 180 days after your last dose of study drug, you must use a condom with spermicidal when you have sex. This is done to prevent pregnancy and drug exposure to your partner. You must not donate sperm during the study and for 180 days after your last dose of study drug.

If your partner becomes pregnant in the time between when you start taking the study drug until 180 days after your last dose, you must tell the study doctor immediately. The sponsor may ask you and your partner to allow them to collect information about her pregnancy and the health of the infant.

If you are a person in a same sex relationship, it is not necessary for you to practice birth control.

Benefits

There may be no benefit from being in this research, but we hope that what we learn may be helpful to future patients or society in general.

Alternatives

Participation in this study is entirely voluntary. There may be other alternatives that could be considered. These alternatives would include:

- Getting treatment or care for your cancer without being in a study, which usually would involve surgery or radiation with ADT
- Taking part in another study
- Getting no treatment
- Receiving ADT alone is an appropriate standard of care to treat your type of prostate cancer if your life expectancy is 5 years or less and you have no symptoms related to your prostate cancer.

The study doctor will provide information about the study and any alternative treatments available.

Confidentiality and Authorization to Use and Disclose Information for Research Purposes

Federal regulations give you certain rights related to your health information. These include the right to know who will be able to get the information and why they may be able to get it. The study doctor must get your authorization (permission) to use or give out any health information that might identify you.

What protected health information may be used and/or given to others?
All medical information, including but not limited to information and/or records of any diagnosis or treatment of disease or condition, which may include sexually transmitted diseases (e.g., HIV, etc.) or communicable diseases, drug/alcohol dependency, etc.; all personal identifiers, including but not limited to your name, social security number, medical record number, date of birth, dates of service, etc.; any past, present, and future history, examinations, laboratory results, imaging studies and reports and treatments of any kind, including but not limited to drug/alcohol treatment, psychiatric/psychological treatment; financial/billing information, including but not limited to copies of your medical bills; any other information related to or collected for use in the research study, regardless of whether the information was collected for research or non-research (e.g., treatment) purposes; records about any study drug you received or about study devices used; and consent forms from past studies that might be in your medical record.

Your consent form will be placed in your medical record at UAB Health System or Children's of Alabama. This may include either a paper medical record or electronic medical record (EMR). An EMR is an electronic version of a paper medical record of your care within this health system. Your EMR may indicate that you are on a clinical trial and provide the name and contact information for the principal investigator.

If you are receiving care or have received care within this health system (outpatient or inpatient), results of research tests or procedures (i.e. laboratory tests, imaging studies and clinical procedures) may be placed in your existing medical record.

If you have never received care within this health system (outpatient or inpatient), a medical record will be created for you to maintain results of research tests or procedures.

All information within your medical record can be viewed by individuals authorized to access the record.

What protected health information may be used and/or given to others?
All medical information related to your participation in this study. This may include your name, medical record number, date of birth, dates of service, etc.; any past, present, and future history related to this research study, examinations, laboratory results, imaging studies and reports and treatments; any other information related to or collected for use in the research study, regardless of whether the information was collected for research or non-research (e.g., treatment) purposes; records about any study drug you received or about study devices used.

A description of this clinical trial will be available on www.ClinicalTrials.gov, as required by U.S. 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 this website at any time.

Who may use and give out this information?
Information about your health may be used and given to others by the study doctor and staff. They might see the research information during and after the study.

Who might get this information?
All individuals/entities listed in the informed consent document(s), including but not limited to, the physicians, nurses and staff and others performing services related to the research (whether at UAB or elsewhere). Your information may also be given to the sponsor of this research. "Sponsor" includes any persons or companies that are working for or with the sponsor, or are owned by the sponsor, or are providing support to the sponsor (e.g., contract research organization).

Information about you and your health which might identify you may be given to:

- The Office for Human Research Protections (OHRP)
- The U.S Food and Drug Administration (FDA)
- Department of Health and Human Services (DHHS) agencies
- the University of Alabama at Birmingham - the physicians, nurses and staff working on the research study (whether at UAB or elsewhere); other operating units of UAB, UAB Hospital, UAB Highlands Hospital, University of Alabama Health Services Foundation, Children's of Alabama, Eye Foundation Hospital, and the Jefferson County Department of Health, as necessary for their operations; the UAB IRB and its staff
- the billing offices of UAB and UAB Health Systems affiliates and/or Children's of Alabama and its billing agents
- Eli Lilly and Company Pharmaceuticals (drug supplier), which is providing funds to University of Alabama at Birmingham to conduct this research.

Why will this information be used and/or given to others?
Information about you and your health that might identify you may be given to others to carry out the research study. The sponsor will analyze and evaluate the results of the study. In addition, people from the sponsor and its consultants will be visiting the research site. They will follow how the study is done, and they will be reviewing your information for this purpose.

What if I decide not to give permission to use and give out my health information?
By signing this consent form, you are giving permission to use and give out the health information listed above for the purposes described above. If you refuse to give permission, you will not be able to be in this research.

May I review or copy the information obtained from me or created about me?
You have the right to review and copy your health information. However, if you decide to be in this study and sign this permission form, you will not be allowed to look at or copy your information until after the research is completed.

May I withdraw or revoke (cancel) my permission?
Yes, but this permission will not stop automatically. The use of your personal health information will continue until you cancel your permission.

You may withdraw or take away your permission to use and disclose your health information at any time. You do this by sending written notice to the study doctor. If you withdraw your permission, you will not be able to continue being in this study.

When you withdraw your permission, no new health information which might identify you will be gathered after that date. Information that has already been gathered may still be used and given to others. This would be done if it were necessary for the research to be reliable.

Is my health information protected after it has been given to others?
If you give permission to give your identifiable health information to a person or business, the information may no longer be protected. There is a risk that your information will be released to others. Including others outside of UAB, without your permission.

Voluntary Participation and Withdrawal

Whether or not you take part in this study is your choice. There will be no penalty if you decide not to be in the study. If you decide not to be in the study, you will not lose any benefits you are otherwise owed.

You are free to withdraw from this research study at any time. Your choice to leave the study will not affect your relationship with this institution. However, you should return to see the study doctor for safety reasons so you can be taken off the study drug and referred for follow-up care. Contact the study doctor if you want to withdraw from the study.

You may be removed from the study without your consent if the sponsor ends the study, if the study drug is approved by the FDA, if the study doctor decides it is not in the best interest of your health, or if you are not following the study rules. The study doctor will remove you from the study if any of the following occur:

- Disease progression
- You are not compliant with study procedures
- We lose you to follow-up
- You withdraw your consent
- You experience a treatment-limiting adverse event

If you are a UAB student or employee, taking part in this research is not a part of your UAB class work or duties. You can refuse to enroll, or withdraw after enrolling at any time before the study is over,

with no effect on your class standing, grades, or job at UAB. You will not be offered or receive any special consideration if you take part in this research.

Cost of Participation

Research Procedures
There are no charges to you or your insurance carrier for study visits or tests that are part of this research. Items considered research include research blood tests including the circulating tumor cell tests and tumor and bone marrow biopsies. The investigational agent, Abemaciclib will be provided by Eli Lilly Pharmaceuticals, free of charge.

Standard Testing Procedures
Standard of care procedures and doctor visits will be billed to your health insurance carrier. These also include administration of ADT and Radiation therapy which are otherwise considered standard of care in your cancer type. These are charges that would be billed to insurance whether you are in a research study or not. It is possible that insurance coverage may be denied. If that happens you may be responsible for some or all of these charges. The study doctor will explain which procedures, tests and doctor visits are considered standard of care.

If a bill is received that you think is wrong, please discuss it with the study doctor or research coordinator.

If you are in Medicare Advantage (Medicare managed care plan), you should contact someone at your plan before you start a clinical trial. They can provide more information about additional costs you could incur from participating in clinical trials.

Payment for Participation

There is no payment for participating in this study.

Payment for Research-Related Injuries

UAB has not provided for any payment if you are harmed as a result of taking part in this study. If such harm occurs, treatment will be provided. However, this treatment will not be provided free of charge.

In the event of a research-related injury, necessary and available medical care (including hospitalization) will be provided. A research-related injury is a physical injury or illness that is directly caused by any procedure or treatment used in this study that is different from the treatment you

would receive if not participating in a research study. If physical injury occurs due to any drug/substance or procedure properly given under the plan for this study, medical expenses for treating the injury will be billed to your insurance carrier. You should be aware that some costs may not be covered by insurance and may become your responsibility. There is no plan to provide compensation for loss of wages, lost time from work, personal discomfort, or for injuries or problems related to your underlying medical condition(s).

If a bill related to a research-related injury is received that seems wrong, please discuss it with the study doctor or research coordinator.

Significant New Findings

Anything learned during the study, beneficial or not, that may affect your health or willingness to continue in the study, will be explained.

Optional Research

Storage of Specimens for Future Use

About Using Blood and Tissue for Research
Samples of your blood and tissue will be collected at certain visits during the study. We would like to keep some of the blood and tissue that is left over for future research. If you agree, this blood and tissue will be kept and may be used in research to learn more about cancer and other diseases. The blood and tissue may be tested for markers that may be associated with side effects or response to therapy.

While you are on this study, samples of your blood and tissue will be stored for future research and will be kept in a secure location with restricted access at the University of Alabama at Birmingham (UAB). No personal identifiers (for example, name, address, phone number, etc.) will be placed on the sample container, so your sample will not be able to be identified by anyone other than personnel conducting the analysis.

Your blood and tissue may be helpful for research. The research that may be done with your blood and tissue is not designed specifically to help you. It might help people who have cancer and other diseases in the future.

Reports about research done with your blood and tissue will not be given to you or your doctor. These reports will not be put in your health record. The research will not have an effect on your care.

Things to Think About
The choice to let us keep the left over blood and tissue for future research is up to you. No matter what you decide to do, it will not affect your care.

If you decide now that your blood and tissue can be kept for research, you can change your mind at any time. Just contact us and let us know that you do not want us to use your blood or tissue. Then any blood or tissue that remains will no longer be used for research.

Sometimes blood or tissue is used for genetic research (about diseases that are passed on in families). Even if your blood or tissue is used for this kind of research, the results will not be put in your health records.

Your blood and tissue will be used only for research and will not be sold. The research done with your blood and tissue may help to develop new products in the future.

Initial your choice below:

___ I agree to allow my identifiable private information and identifiable biospecimens to be kept and used for future research.

___ I do not agree to allow my identifiable private information and identifiable biospecimens to be kept and used for future research.

Questions

If you have any questions, concerns, or complaints about the research or a research-related injury including available treatments, please contact the study doctor. You may contact Dr. Andrew McDonald at (205) 934-5670.

If you have questions about your rights as a research participant, or concerns or complaints about the research, you may contact the UAB Office of the IRB (OIRB) at (205) 934-3789 or toll free at 1-855-860-3789. Regular hours for the OIRB are 8:00 a.m. to 5:00 p.m. CT, Monday through Friday.

Legal Rights

You are not waiving any of your legal rights by signing this consent form.

Signatures

Your signature below indicates that you have read (or been read) the information provided above and agree to participate in this study. You will receive a copy of this signed consent form.

_____

Signature of Participant Date

_____

Signature of Person Obtaining Consent Date