NCI Community Oncology Research Program – Kansas City (NCORP-KC)

Study Title for Study Participants:

Testing the effects of palbociclib and fulvestrant or letrozole for patients 70 years of age and older with metastatic breast cancer

Official Study Title for Internet Search on http://www.ClinicalTrials.gov:

A Phase II Trial Assessing the tolerability of Palbociclib in combination with letrozole or fulvestrant in patients aged 70 and older with estrogen receptor positive, HER-2 negative metastatic breast cancer

This study is conducted by the Alliance for Clinical Trials in Oncology, a national clinical research group supported by the National Cancer Institute. The Alliance is made up of cancer doctors, health professionals, and laboratory researchers, whose goal is to develop better treatments for cancer, to prevent cancer, to reduce side effects from cancer, and to improve the quality of life of cancer patients.

What is the usual approach to my breast cancer?

We are asking you to take part in this study because you are 70 years old or over and have been recently diagnosed with estrogen receptor positive, HER2 negative metastatic breast cancer. Patients with this metastatic breast cancer are usually treated with a drug called palbociclib along with a hormonal agent, either fulvestrant or letrozole, as determined by your doctor. Palbociclib and letrozole are given by mouth and fulvestrant is an injection. This study follows the usual FDA-approved treatment, but we are conducting this study because we don't know if older patients have more side effects than younger patients.

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 without being in a study.
- You may choose to take part in a different study, if one is available.
- You may choose not to be treated for cancer and may want to receive comfort care to relieve symptoms.

Why is this study being done?

The purpose of this study is to find out the side effects that the standard, FDA-approved combination treatment of letrozole or fulvestrant and palbociclib has on patients 70 years old and over. Palbociclib given along with letrozole or fulvestrant instead of letrozole or fulvestrant

alone seems to prevent the cancer from getting worse. However, few patients aged 75 and older participated in previous studies. There will be about 88 people taking part in this study.

What are the study groups?

In this study, all study participants will get the same treatment. You will take one capsule of palbociclib once a day with food for 21 days. You will not take palbociclib for the next 7 days. This 28 day period is called a cycle. You should try to take the palbociclib capsules at about the same time each day. You should not have grapefruit or grapefruit juice while on this study. You should also check with your doctor or pharmacist before using any new medicines, including over-the-counter drugs because of possible drug interactions.

During this period, you will also be given either letrozole or fulvestrant based on what your doctor decides. If your doctor prescribes letrozole, you will take one pill daily for 28 days. If your doctor prescribes fulvestrant you will receive injections on the first day and fifteenth day of the first cycle and then on the first day of every cycle after that. You will continue on this treatment plan until your cancer progresses or if you have side effects that may prevent you from continuing to take the treatment.

Each cycle is 28 days (4 weeks)

Palbociclib plus Letrozole

	Week 1	Week 2	Week 3	Week 4	Week 5+
Palbociclib	1 capsule every day	1 capsule every day	1 capsule everyday	No capsule	1 capsule every day for 21 days, then 7 days no capsules
Letrozole	1 pill every day	1 pill every day	1 pill every day	1 pill every day	1 pill every day for 28 days

If you forget to take a capsule of palbociclib or letrozole, do not make up the missed dose. Skip that dose and take the drug on the next day.

Or

Palbociclib plus Fulvestrant

	Week 1	Week 2	Week 3	Week 4	Weeks 5+
Palbociclib	1 capsule every day	1 capsule every day	1 capsule everyday	No capsule	1 capsule every day for 21 days, then 7 days no capsules
Fulvestrant	Injection on Day 1	No injection	Injection on Day 15	No injection	Injection on Day 1 of every 28-day cycle

If you forget to take a capsule of palbociclib, do not make up the missed dose. Skip that dose and take the capsule on the next day.

How long will I be in this study?

You will receive the study treatment for as long as you do not have severe side effects and your cancer does not get worse. If you develop severe side effects or your cancer gets worse, your doctor may decide to remove you from the study treatment. After you stop the study treatment, your doctor will continue to follow your progress every year for up to five years.

What extra tests, and procedures will I have if I take part in this study?

Most of the exams, tests, and procedures you will have are part of the usual approach for your cancer. However, there are some extra questionnaires that you will need to complete if you take part in this study.

You will be asked to complete five questionnaires and perform some tasks as part of this study. The questionnaires will be used in this study in order to find out more about how you feel during cancer treatment and what the effect of the treatment may be.

The questionnaires will be completed at the following time points:

Geriatric Assessment: You will be asked to complete the geriatric assessment before you begin treatment, prior to cycle 4, and at the end of your treatment period. It will take about 30 minutes to complete. The geriatric assessment involves a questionnaire, an interview and a task. Some questions will be asked by a member of the health care team. You will complete other questions on your own. If you have difficulty completing any of the questions or tasks, a member of the team will help you. You may skip any questions you do not wish to answer. The walking task involves minimal risk. It will involve you getting up from a chair, walking 10 feet, and returning to the chair. Possible risks include feeling tired, dizziness, increased heart rate, and falling. To minimize this risk you will be closely monitored by a member of the health care team during this task. If you are uncomfortable with walking, you may skip this task.

You will be asked to complete four other questionnaires, two of which will be required at the beginning of every cycle for the first 6 cycles of treatment, and at the end of your treatment period. These questionnaires will involve questions about the side effects you are experiencing from your treatment and about your general quality of life. They will take about fifteen to twenty minutes to complete. The other two questionnaires will only need to be completed at the end of your treatment. They will ask questions regarding how the study helped you. They will take about five minutes to complete.

Pill Diary
You will also be completing a pill diary every day, for the first three cycles. You will be asked to bring the completed pill diary at the end of every cycle, to make sure you are taking the correct dose and not more than the standard dose.

You will receive routine scans every 12 weeks to see if your cancer is getting worse or better, as part of your cancer care. Your doctor will send copies of these scans to the Alliance, so that researchers can evaluate whether the treatment you are receiving may cause loss of muscle tissue.

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 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

The 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 side effects from the study drugs.

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 be serious and may even result in death.

You can ask the study doctor questions about side effects at any time. 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 tables below show the most common and the most serious side effects that researchers know about. Keep in mind that 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.

Possible side effects of Palbociclib, Letrozole and Fulvestrant:

Possible Side Effects for Palbociclib (PD-0332991)

COMMON, SOME MAY BE SERIOUS In 100 people receiving palbociclib (PD-0332991), more than 20 and up to 100 may have:
• Anemia which may require blood transfusion • Nausea • Tiredness • Infection, especially when white blood cell count is low

OCCASIONAL, SOME MAY BE SERIOUS In 100 people receiving palbociclib (PD-0332991), from 4 to 20 may have:
• Blurred vision, watering eyes • Dry eye, skin • Constipation, diarrhea, vomiting • Sores in the mouth which may cause difficulty swallowing • Fever • Bruising, bleeding • Loss of appetite • Changes in taste • Headache • Nose bleed • Hair loss, rash

Possible Side Effects of Fulvestrant

COMMON, SOME MAY BE SERIOUS In 100 people receiving Fulvestrant, more than 20 and up to 100 may have:
• Pain • Tiredness • Increased sweating • Hot flashes, flushing • Swelling and redness at the site of the medication injection

OCCASIONAL, SOME MAY BE SERIOUS In 100 people receiving Fulvestrant, from 4 to 20 may have:
• Constipation, diarrhea, nausea, vomiting, loss of appetite, heartburn • Swelling of the body • Loss of bone tissue, broken bone, or decreased height • Dizziness, headache • Difficulty sleeping • Fluid around lungs

OCCASIONAL, SOME MAY BE SERIOUS In 100 people receiving Fulvestrant, from 4 to 20 may have:
• Swelling of the liver which may cause belly pain • Worry, depression, mood swings • Hair thinning • Cough

RARE, AND SERIOUS In 100 people receiving Fulvestrant, 3 or fewer may have:
• Allergic reaction which may cause rash, low blood pressure, wheezing, shortness of breath, swelling of the face or throat • Liver damage which may cause yellow eyes and skin • Vaginal bleeding • Blood clot which may cause swelling, pain, shortness of breath • Heart attack or heart failure which may result in chest pain, shortness of breath, swelling of ankles, and tiredness • Stroke which may cause weakness, paralysis

Possible Side Effects of Letrozole

COMMON, SOME MAY BE SERIOUS In 100 people receiving Letrozole, more than 20 and up to 100 may have:
• Pain • Tiredness • Increased sweating • Hot flashes, flushing

OCCASIONAL, SOME MAY BE SERIOUS In 100 people receiving Letrozole, from 4 to 20 may have:
• Constipation, diarrhea, nausea, vomiting, loss of appetite, heartburn • Swelling of the body • Loss of bone tissue, broken bone, or decreased height • Dizziness, headache • Difficulty sleeping • Fluid around lungs • Swelling of the liver which may cause belly pain • Worry, depression, mood swings • Hair thinning

RARE, AND SERIOUS In 100 people receiving Letrozole, 3 or fewer may have:
• Allergic reaction which may cause rash, low blood pressure, wheezing, shortness of breath, swelling of the face or throat • Liver damage which may cause yellow eyes and skin • Vaginal bleeding • Blood clot which may cause swelling, pain, shortness of breath • Heart attack or heart failure which may cause shortness of breath, swelling of ankles, and tiredness • Stroke which may cause weakness, paralysis

Risks from questionnaires
You may become tired from the amount of time needed to fill out the questionnaires and do the other evaluations. The questionnaire will focus on life issues that could cause you to become emotionally upset. If you become distressed a member of the study team will talk with you. If needed, you can be referred to your doctor to determine how best to handle your concerns.

What possible benefits can I expect from taking part in this study?
This study may or may not help you. However, this study may help us understand how this study drug works in older adults, and may help researchers learn things that may help other older people in the future.

Can I stop taking part in this study?
Yes. You can decide to stop at any time. If you decide to stop for any reason, it is important to let the study doctor know as soon as possible so you can stop safely. If you stop, you can decide whether or not to let the study doctor continue to provide your medical information to the 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.

In turn, the study doctor may remove you from the study, if:
- Your health changes and the study is no longer in your best interest
- New information becomes available
- You do not follow the study rules
- The study is stopped by the sponsor, Institutional Review Board, 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 Central Institutional Review Board at 888-657-3711.

What are the costs of taking part in this study?

Your Potential Costs:

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

You and/or your health plan/insurance company will be responsible for:

- Palbociclib, letrozole or fulvestrant and all premedications, fluids and procedures.
- Exams, tests, and procedures that may be needed to manage side effects and to monitor your safety.

Costs Paid by the Study

Exams, tests, and procedures done for research purposes only will not be billed to you or your insurance plan. These include blood collections for the optional studies and submission of images to the Alliance for evaluating whether the treatment you are receiving may cause loss of muscle tissue.

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

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 tell your study doctor. 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, you would be responsible for any costs.

If you feel this injury was a result of medical error, you have legal rights to receive payment for this injury 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. However, 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 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. Your health information in the database may also be shared with these organizations. They are required to make sure your information is kept private, unless required by law to provide information. Some of these organizations are:

- The Alliance for Clinical Trials in Oncology
- The Institutional Review Board, 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.

The Alliance has received a Certificate of Confidentiality from the federal government, which will help us to protect your privacy. The Certificate protects against the involuntary release of information about you collected during the course of the study. The researchers involved in this project may not be forced to identify you in any legal proceedings (criminal, civil, administrative, or legislative) at the federal, state or local level. However, some information may be required by the Federal Food, Drug, and Cosmetic Act, the U.S. Department of Health and Human Services, or for purposes of program review or audit. Also, you may choose to voluntarily disclose the protected information under certain circumstances. For example, if you or your guardian requests the release of information about you in writing (through, for example, a written request to release medical records to an insurance company), the Certificate does not protect against that voluntary disclosure.

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. Once the study is over, the site may include a summary of the results. This summary will not include any information that can identify you.

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 doctor _____ *(insert name of study doctor[s])* at _____ *(insert telephone number).*

Additional Studies Section:
This section is about optional studies 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.

Neither you nor your insurance will be billed for these optional studies. You can still take part in the main study even if you say "no" to any or all of these studies. If you sign up for but cannot complete any of the optional studies for any reason, you can still take part in the main study.

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

1. Optional sample collections for laboratory studies and biobanking for possible future studies

Researchers are trying to learn more about cancer and other health problems using samples from people's tissue, blood, urine, or other fluids. By conducting research on these samples, researchers hope to find new ways to prevent, detect, treat, or cure health problems.

Some of these studies may be about how genes affect health and disease and how people respond to treatment. Genes carry information about features that are found in you and your family, from the color of your eyes to health conditions for which you may be at risk. Research that studies your genes is known as genomics or genetics.

If you choose to take part in these optional studies, the study doctor for the main study would like to collect blood for research on why patients have different side effects from the treatment.

In addition, the researchers ask your permission to store and use your samples and related health information (for example, your response to cancer treatment, results of study tests and medicines you are given) for medical research. The additional research that may be done is unknown at this time. Storing samples for future studies is called "biobanking". The Biobank is being run by the Alliance and supported by the National Cancer Institute.

What is involved?

If you agree to take part, here is what will happen next:

1) About 6 teaspoons of blood will be collected from a vein in your arm. Four teaspoons of blood will be drawn before you begin treatment, and two teaspoons will be drawn after you have taken three cycles of treatment.

2) Your baseline blood sample and some related health information will be sent to a researcher for use in the study described above. Remaining baseline blood samples may be stored in the Biobank, along with samples from other people who take part. The samples will be kept until they are used up.
3) Only qualified researchers can receive samples from the biobank. There will be scientific and ethics reviews to ensure that the research is necessary and proper. Researchers will not be given your name or any other information that could directly identify you.
4) Neither you nor your study doctor will be notified when research will be conducted. You will not receive reports or other information about any research that is done using your samples.
5) Some of your genetic and health information may be placed in central databases that will be available to qualified researchers. Information that could directly identify you will not be included.

What are the possible risks?

1) The most common risks related to drawing blood from your arm are brief pain and maybe a bruise.
2) Even without your name or other identifiers, your genetic information is unique to you. There is a risk that someone outside of the research could get access to your personal information in your medical records or trace information in a database back to you. The researchers believe the chance that someone could re-identify you is very small, but the risk may change in the future as people come up with new ways of tracing information.
3) In some cases, this information could be used to make it harder for you to get or keep a job or insurance. There are laws against the misuse of genetic information, but they may not give full protection. There can also be a risk in knowing genetic information. New health information about inherited traits that might affect you or your blood relatives could be found during a study. The researchers believe the chance these things will happen is very small, but cannot promise that they will not occur.

How will information about me be kept private?

Your privacy is very important to the researchers and they will make every effort to protect it. Here are just a few of the steps they will take:

1) When your samples are sent by the biobank to the qualified researchers, no information identifying you (such as your name) will be sent. Samples will be identified by a unique code only.
2) The list that links the unique code to your name will be kept separate from your sample and health information. Any biobank and Alliance staff with access to the list must sign an agreement to keep your identity confidential.
3) Researchers to whom the Alliance sends your sample and information will not know who you are. They must also sign an agreement that they will not try to find out who you are.

4) Information that identifies you will not be given to anyone, unless required by law.
5) If research results are published, your name and other personal information will not be used.

What are the possible benefits?

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?

There are no costs to you or your insurance. You will not be paid for taking part. If any of the research leads to new tests, drugs, or other commercial products, you will not share in any profits.

What if I change my mind?

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 researchers know. Then, any sample that remains in the biobank will no longer be used and related health information will no longer be collected. This will not apply to those samples or related information that have already been given to or used by qualified researchers.

What if I have questions?

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 to show whether or not you would like to take part in each option:

Samples for the laboratory studies:

1. I agree to have my specimen collected and I agree that my specimen sample(s) and related information may be used for the laboratory studies described above.

   YES NO

Samples for future research studies:

2. My samples and related information may be kept in a biobank for use in future health research.

   YES NO

3. I agree that my study doctor, or their representative, may contact me or my physician 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 main 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 copy of this form. I agree to take part in the main study *and any additional studies where I circled 'yes'. (Note to protocol authors – remove italicized text if not applicable. Remove italics, if the text does apply.)*

Participant's signature_____

Date of signature_____

Signature of person(s) conducting the informed consent discussion_____

Date of signature_____