CHILDREN'S ONCOLOGY GROUP

The world's childhood cancer experts

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A National Cancer Institute-funded group member of the National Clinical Trials Network

November 30, 2021

Martha Kruhm, M.S., RAC
Protocol and Information Office (PIO) Head
National Cancer Institute
Executive Plaza North Room 730
Bethesda, MD 20892

Dear Ms. Kruhm,

Please find attached Amendment #4 to **APEC1621I**, *NCI-COG Pediatric MATCH (Molecular Analysis for Therapy Choice)- Phase 2 subprotocol of Palbociclib in Patients with Tumors Harboring Activating Alterations in Cell Cycle Genes*.

The protocol and ICD have been amended in preparation for Stage 2 of Pediatric MATCH. Descriptions of screening and enrollment procedures have been revised to align with Amendment #4 of APEC1621SC to implement Stage 2.

Several other administrative changes have been made; specific changes are detailed below. Minor administrative updates (such as the correction of typographical errors or updates to the numbers of referenced sections) are tracked in the protocol but not specified below.

Please contact us if you have any further questions.

Sincerely,

Lee Baker, MPH, Protocol Coordinator (for)
Rajen Mody, MD, APEC1621I Study Chair, and
Douglas S. Hawkins, MD, Group Chair, Children's Oncology Group

SUMMARY OF CHANGES: ICD

In accordance with the above discussion, the following specific revisions have been made to the protocol. Additions are in **boldfaced** font and deletions in strikethrough font.

#	Section	Comments
1.	Throughout	• Updated version date. • Ensured all hyperlinks are included and functioning.
2.	Why am I being invited to take part in this study?	Revised language to be consistent with AMD #4 of APEC1621SC, where tumor tissue pathology results are reviewed by the Molecular Review Committee (MRC) for eligibility into the subprotocol.

This model informed consent form has been reviewed by the DCTD/NCI and is the official consent document for this study. Local IRB changes to this document are allowed. (Institutions should attempt to use sections of this document which are in bold type in their entirety.) Editorial changes to these sections may be made as long as they do not change information or intent. If the institutional IRB insists on making deletions or more substantive modifications to the risks or alternatives sections, they must be justified in writing by the investigator and approved by the IRB.

SAMPLE INFORMED CONSENT / PARENTAL PERMISSION FOR PARTICIPATION IN RESEARCH

APEC1621I

NCI-COG Pediatric MATCH (Molecular Analysis for Therapy Choice)- Phase 2 subprotocol of Palbociclib in Patients with Tumors Harboring Activating Alterations in Cell Cycle Genes

If you are a parent or legal guardian of a child who may take part in this study, permission from you is required. The assent (agreement) of your child may also be required. When we say "you" in this consent form, we mean you or your child; "we" means the doctors and other staff.

Why am I being invited to take part in this study?

You are being asked to take part in this research study because your tumor testing results submitted for the NCI-COG Pediatric MATCH screening protocol make you a candidate to receive the investigational drug (or "study drug") palbociclib that we are testing in this study.

This study is called a clinical trial. A clinical trial is a research study involving treatment of a disease in human patients. This study is organized by Children's Oncology Group (COG). COG is an international research group that conducts clinical trials for children and adolescents with cancer. More than 200 hospitals in North America, Australia, New Zealand, and Europe are members of COG. Only hospitals in the United States will participate in this study.

It is common to enroll children and adolescents with cancer in a clinical trial that seeks to improve cancer treatment over time. Clinical trials include only people who choose to take part.

Please take your time to make your decision. You may want to discuss it with your friends and family. We encourage parents to include their child in the discussion and decision to the extent that the child is able to understand and take part.

What is the current standard of treatment for this disease?

When a cancer comes back (relapses) or does not respond to therapy (is refractory), your doctor may recommend other anti-cancer drugs (chemotherapy), surgery, or radiation therapy. For certain cancers, a combination of one or more of these approaches is considered standard treatment. However, for other cancers such as cancers that recur, or for cancer for which therapy is no longer working, the best treatment is not known.

You are being asked to participate in this study because you have a relapsed or refractory tumor without a proven treatment strategy for cure.

Why is this study being done?

This is a Phase 2 study of a drug called palbociclib. In a Phase 2 study, the goal is to find out what effects, good and/or bad, a drug has on your tumor or type of cancer.

We are using palbociclib in this study because it has been shown to block the growth of cancer cells with mutations in an important biological pathway in test tubes and in animals. You are eligible for this study because your tumor was found to have a mutation in this pathway. Palbociclib is considered a study drug in the treatment of your tumor or type of cancer. Although palbociclib has been given to a small number of adults and children, we do not know if it will work against the type of tumor you have.

A Phase 1 study of palbociclib has been completed in children and adolescents with cancer. The goal of Phase 1 studies is to find the highest dose of a study drug that can be given without too many side effects. In the Phase 1 study, researchers determined the dose of palbociclib for children and adolescents that can be given without too many side effects. That same dose will be used for patients enrolled on this study. If you have bad side effects, your dose may be decreased.

The goals of this study are:

- **The main goal of this study is to test any good and bad effects of the palbociclib on your tumor.**
- **A second goal of the study is to evaluate side effects that might be caused by palbociclib.**

How many people will take part in the study?

There will be between 20 and 49 patients participating in APEC1621I. About ___ will be treated at this hospital.

What will happen if I take part in this research study?

Before you begin the study…

You will need to have the following exams, tests or procedures to find out if you can be in the study. These exams, tests or procedures are part of regular cancer care and may be done even if you do not join the study. If you have had some of them recently, they may not need to be repeated. This will be up to your study doctor.

- A medical history
- Physical and neurological exam
- Vital signs (blood pressure, pulse, temperature)
- Blood tests
- Urine tests
- Pregnancy test (if you are a woman who could have children)
- Bone marrow examinations if needed for your type of tumor

We will also perform the necessary X-rays, CT scans, or other tests are needed to check your tumor.

In addition to the above exams, tests or procedures, your study doctor will confirm that you are able to swallow intact capsules whole, capsules should not be opened, chewed or crushed.

During the study…

If the exams, tests and procedures show that you can be in the study, and you choose to take part, palbociclib will be given by mouth once daily for 21 days, followed by a rest period of 7 days. This entire 4 week period is called a cycle. You may continue to receive palbociclib for up to 2 years unless you develop serious side effects or your tumor worsens.

You will be given specific instructions regarding how to take this study drug. You will also be given a medication diary to fill out at home each time palbociclib is taken. Use the diary to record the date and time you take the drug, and any side effects you experience. Also record in the diary other medications and/or supplements you are taking and whether you vomited or missed a dose. This diary should be returned to the clinic, along with the medication bottle (even if it is empty) weekly during Cycle 1 and then at the end of every cycle. This will help us know how much of the study drug you take and how it made you feel.

During the study you will have tests and procedures to check for side effects and see how your tumor is doing. These tests are part of regular cancer care, but you may have them more often because you are on the study:

- Physical and neurological exam
- Vital signs (blood pressure, pulse, temperature)
- Blood tests
- MRI, X-rays. CT scans, or other tests that are needed to check your tumor
- Bone marrow examinations, if needed for your type of tumor

Copies of the scans used to diagnose your cancer and some of the tissue that was previously collected may be sent to a central review center. COG does this to double check the hospitals' results for research purposes only.

Circulating Tumor DNA Studies

We would like to collect blood samples (10-20 mL, or about 2-4 teaspoons) at Cycle 5 Day 1 and end of protocol therapy (only if you receive 5 or more cycles of therapy), to see if a blood test can show whether or not the tumor DNA has changed from when the tumor was biopsied.

_____/_____ Yes, I agree to participate in these additional circulating tumor DNA studies.

_____/_____ No, I do not agree to participate in these additional circulating tumor DNA studies.

How long will I be in the study?

You may be in the study for up to 2 years. Your doctor may decide to take you off study if any of the following occur:

- Your tumor gets worse
- The side effects of palbociclib are too harmful for you
- You need a treatment that is not allowed on this study
- You are not able to follow study-related treatment instructions
- New information becomes available
- The study is not in your best interest
- The study is stopped
- You get pregnant

Can I stop being in the study?

Yes. You can decide to stop at any time. Tell the study doctor if you are thinking about stopping or decide to stop. He or she will tell you how to stop safely.

It is important to tell the study doctor if you are thinking about stopping so any risks from palbociclib can be evaluated by your doctor. Also, your doctor can discuss what follow-up care and testing could be most helpful for you.

What side effects or risks can I expect from being in the study?

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

- **You may lose time at school or home or work and spend more time in the hospital or doctor's office than usual**
- **You may be asked sensitive or private questions which you normally do not discuss**
- **May not be able to take part in future studies**

The drug 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 be testing your blood and will let you know if changes occur that may affect your health.

There is also a risk that you could have side effects from the palbociclib.
Here are important points about side effects:

- **The study doctors do not know who will or will not have side effects.**
- **Some side effects may go away soon, some may last a long time, or some may never go away.**
- **Some side effects may interfere with your ability to have children.**
- **Some side effects may be serious and may even result in death.**

Here are important points about how you and the study doctor can make side effects less of a problem:

- **Tell the study doctor if you notice or feel anything different so they can see if you are having a side effect.**
- **The study doctor may be able to treat some side effects.**
- **The study doctor may adjust palbociclib to try to reduce side effects.**
- **The study doctor will provide you with information about other drugs you may need to avoid while receiving the study drug.**

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

Risks and side effects related to palbociclib include those which are:

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**
RARE, AND SERIOUS **In 100 people receiving Palbociclib (PD-0332991), 3 or fewer may have:**
• **Damage to the lungs which may cause shortness of breath**

Some drugs or supplements may interact with your treatment plan. Talk to your doctor, pharmacist, or study team before starting any new prescription or over-the-counter drugs, herbals, or supplements and before making a significant change in your diet. Supplements may come in many forms, such as teas, drinks, juices, liquids, drops, capsules, pills, or dried herbs. All forms should be avoided.

If you have a drop in your red blood cell count, the cells that carry oxygen around the body, you may feel tired. If your red blood cell count drops very low you may need a blood transfusion.

If you have a decrease in your white blood cell count, the cells that fight infection, you may be more likely to get an infection, including a serious infection that spreads through the blood stream (sepsis). If this happens, you will have to come to the hospital to be treated with antibiotics. If your white blood cell count is very low and you get a fever, you may have to come to the hospital to get treated with antibiotics.

If you have a low platelet count, particles in the blood that help with clotting, you may have easy bruising or bleeding. If the count is very low and there is bleeding, you might need platelet transfusions to help stop the bleeding.

Transfusions can have a small risk of causing a fever and/or reactions that can cause kidney failure, heart failure, anemia, hepatitis, or infections; including HIV (Human Immunodeficiency Virus) which can cause A.I.D.S (acquired immune deficiency syndrome).

Reproductive risks:
Women should not become pregnant during the study and for at least 3 weeks after the last dose of palbociclib, because palbociclib can affect an unborn baby. Men should avoid fathering a child or donating sperm for at least 3 months after the last dose of palbociclib, because palbociclib can affect an unborn baby. Check with your study doctor about what kind of birth control methods to use and how long to use them. Some methods might not be approved for use in this study. **Women should not breastfeed a baby while on this study.**

Risks of blood drawing or placing an intravenous catheter for blood drawing:
Risks associated with drawing blood are slight, but some risks include: pain, excessive bleeding, fainting or feeling lightheaded, bruising, infection (a slight risk any time the skin is broken), and multiple punctures to locate veins.

For more information about risks and side effects, ask your study doctor.

Are there benefits to taking part in the study?

The potential benefit of the treatment with palbociclib is that it may cause your cancer to stop growing or to shrink for a period of time. It may lessen the symptoms, such as pain, that are caused by the cancer. It is extremely unlikely that this treatment will cure your cancer. Because there is not much information about the effect of palbociclib on cancers in humans, we do not know if you will benefit from taking part in this study. Information learned from this study may help future patients with cancer.

What other choices do I have if I do not take part in this study?

Your other choices may include:

- **Getting treatment or care for your cancer without being in a study**
- **Taking part in another study**
- **Focusing on comfort care and quality of life instead of drugs to treat the tumor**

Talk to your doctor about your choices before you decide if you will take part in this study.

Will my medical information be kept private?

We will do our best to make sure that the personal information in your medical record will be kept private. However, we cannot guarantee total privacy. Your personal information may be given out if required by law. If information from this study is published or presented at scientific meetings, your name and other personal information will not be used.

The Children's Oncology Group has received a Certificate of Confidentiality from the federal government, which will help us protect the privacy of our research subjects. The Certificate protects against the involuntary release of information about subjects collected during the course of our covered studies. The researchers involved in the studies cannot be forced to disclose the identity or any information collected in the study in any legal proceedings at the federal, state, or local level, regardless of whether they are criminal, administrative, or legislative proceedings. However, the subject or the researcher may choose to voluntarily disclose the protected information under certain circumstances. For example, if the subject or his/her guardian requests the release of information in writing, the Certificate does not protect against that voluntary disclosure. Furthermore, federal agencies may review our records under limited circumstances, such as a DHHS request for information for an audit or program evaluation or an FDA request under the Food, Drug and Cosmetics Act.
The Certificate of Confidentiality will not protect against the required reporting by hospital staff of information on suspected child abuse, reportable communicable diseases, and/or possible threat of harm to self or others.

Organizations that may look at and/or copy your medical records for research, quality assurance, and data analysis include:

- **The Children's Oncology Group**
- **Representatives of the National Cancer Institute (NCI), Food and Drug Administration (FDA), and other U.S. governmental regulatory agencies involved in overseeing research**
- **The Institutional Review Board (IRB) of this hospital**
- **The Pediatric Central Institutional Review Board (CIRB) of the National Cancer Institute**
- **The drug company partner (the company that makes palbociclib) or their designated reviewers**

What are the costs of taking part in this study?

You and/or your health plan/ insurance company will need to pay for some or all of the costs of treating your cancer in this study. Some health plans will not pay these costs for people taking part in studies. Check with your health plan or insurance company to find out what they will pay for. Taking part in this study may or may not cost your insurance company more than the cost of getting regular cancer treatment.

The NCI will provide palbociclib at no charge while you take part in the study. The NCI does not cover the cost of getting palbociclib ready and giving it to you, so you or your insurance company may have to pay for this. If, during the study, palbociclib becomes approved for use in your cancer, you or your health plan may have to pay for study drug needed to complete this study.

Even though it probably won't happen, it is possible that the NCI may not be able to continue to provide the palbociclib for some reason. If this would happen, the study may have to close. Your study doctor will talk with you about this, if it happens.

You will not be charged for the costs of the special blood studies that are being done for research purposes only, such as the tumor DNA analysis.

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

For more information on clinical trials and insurance coverage, you can visit the National Cancer Institute's Web site at **http://www.cancer.gov/clinicaltrials/learningabout.**

Another way to get the information is to call 1-800-4-CANCER (1-800-422-6237) and ask them to send you a free copy.

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

It is important that you tell your study doctor, _____ *[investigator's name(s)],* if you feel that you have been injured because of taking part in this study. You can tell the doctor in person or call him/her at _____ *[telephone number].*

You will get medical treatment if you are injured as a result of taking part in this study. You and/or your health plan will be charged for this treatment. There are no plans for the study to pay for medical treatment for injuries. In the case of injury resulting from this study do not lose any legal rights to seek compensation by signing this form.

What are my rights if I take part in this study?

Taking part in this study is your choice. You may choose either to take part or not to take part in the study. If you decide to take part in this study, you may leave the study at any time. No matter what decision you make, there will be no penalty to you and you will not lose any of your regular benefits. Leaving the study will not affect your medical care. You can still get your regular medical care from our institution.

We will tell you about new information or changes in the study that may affect your health or your willingness to continue in the study. Whether you participate or not, you will continue to get the best medical care this hospital can provide.

Who can answer my questions about the study?

You can talk to your study doctor about any questions or concerns you have about this study. Contact your study doctor _____ *[name(s)]* at _____ *[telephone number].*

For questions about your rights while taking part in this study, call the _____ *[name of center]* Institutional Review Board (a group of people who review the research to protect your rights) at _____ *(telephone number). [Note to Local Investigator: Contact information for patient representatives or other individuals in a local institution who are not on the IRB or research team but take calls regarding clinical trial questions can be listed here.]*

Where can I get more information?

The **COG Family Handbook for Children with Cancer** has information about specific cancers, tests, treatment side effects and their management, adjusting to cancer, and resources. Your doctor can get you this Handbook, or you can get it at https://www.childrensoncologygroup.org/index.php/cog-family-handbook

You may call the National Cancer Institute's Cancer Information Service at:
1-800-4-CANCER (1-800-422-6237)

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

You may also visit the NCI website at http://cancer.gov/

- For NCI's clinical trials information, go to: http://cancer.gov/clinicaltrials/
- For NCI's general information about cancer, go to http://cancer.gov/cancerinfo/

You will get a copy of this form. If you want more information about this study, ask your study doctor.

Signature

I have been given a copy of all _____ pages of this form.
I have read it or it has been read to me.

I have reviewed the information and have had my questions answered. I agree to take part in this study.

Participant:_____ Date:_____

Signature of Participant / Parent (or Guardian): Date:_____
_____

Physician or Responsible Investigator: Date:_____
_____

Signature of Physician or Responsible Investigator: Date:_____
_____