INSTITUTE: National Cancer Institute

STUDY NUMBER: 13-C-0032 PRINCIPAL INVESTIGATOR: Naoko Takebe, MD, PhD

STUDY TITLE: A Phase I Study of Single-agent AZD1775 (MK-1775), a Wee1 Inhibitor, in Patients with Advanced Refractory Solid Tumors

Continuing Review Approved by the IRB on 10/22/19
Amendment Approved by the IRB on 08/12/19 (U) Date posted to web:10/26/19

Standard

## INTRODUCTION

We invite you to take part in a research study at the National Institutes of Health (NIH). First, we want you to know that:

Taking part in NIH research is entirely voluntary.

You may choose not to take part, or you may withdraw from the study at any time. In either case, you will not lose any benefits to which you are otherwise entitled. However, to receive care at the NIH, you must be taking part in a study or be under evaluation for study participation.

You may receive no benefit from taking part. The research may give us knowledge that may help people in the future.

Second, some people have personal, religious or ethical beliefs that may limit the kinds of medical or research treatments they would want to receive (such as blood transfusions). If you have such beliefs, please discuss them with your NIH doctors or research team before you agree to the study.

Now we will describe this research study. Before you decide to take part, please take as much time as you need to ask any questions and discuss this study with anyone at NIH, or with family, friends, or your personal physician or other health professional.

**Why is this study being done?**
We are doing this study to try to develop better treatments for cancer. In this study and experimental drug, AZD1775 (formerly known as MK-1775), will be given to you. The purpose of this study is to test the safety of AZD1775 and find out the dose of the drug that can be safely given to humans. We are trying to understand how AZD1775 works in humans, how your body handles this drug, what side effects the drug causes, and the safety of the drug at the given dose. AZD1775 is thought to work by blocking a protein that affects other proteins inside the cell that are known to be important in the growth of cancer. It is an experimental drug that has shown some anti-

cancer effects against tumor cells in the laboratory and in experimental animals. This drug is in the beginning stages of being tested in humans.

**Why are you being asked to take part in this study?**
You are being asked to take part in this research study because you have advanced cancer that has progressed after receiving standard treatment, or for which no effective therapy exists.

**How many people will take part in this Study?**
Up to 72 patients will take part in this study. As of November 2016, 49 patients have taken part. The first part of this study tested different doses of AZD1775. Since that part of the study has been completed, all patients joining the study now will be given the same dose and will have tumor biopsies collected. This is to learn more about how the drug affects cancer cells. Up to 20 patients will participate in this next part of the study.

**Description of Research Study**

**What will happen if you take part in this research study?**
Before you begin the study
You will need to have the following examinations, tests, or procedures to find out if you can be in the study. These tests are part of your regular cancer care and should be done by your health care team even if you do not join the study. If you have had them recently, they may not need to be repeated. This will be up to your study doctor. Willingness to give blood and urine samples for research is required for taking part in this study.

If you decide that you would like to participate in this study, you will be asked to sign this consent form. You will then have the examinations, tests, and procedures listed below done to see if you can take part in the study (this is called the screening/baseline evaluation).

- **Complete medical history.**
- **Physical examination,** including height, weight, blood pressure, pulse, and temperature.
- **Standard blood tests** (requiring about 1 tablespoon of blood in total), which include measurement of your white blood cells, red blood cells, platelets, blood sugar and electrolytes, and how your liver and kidneys work.
- **Pregnancy test** in women who are able to become pregnant.
- **CT scans (a computerized x-ray examination)** or other imaging tests to measure your tumor(s).
- **Pathology slides:** Before starting on the study, we will request tumor slides or blocks to confirm your diagnosis.

**During the study**
If you are accepted and you choose to take part, you will take study drug on the following dosing schedule:

- **Once a day for two weeks per cycle:** AZD1775 by mouth once a day for five days each week

The drug is given in cycles; each cycle is 21 days (3 weeks) long. Each patient may receive a different dose based on when he or she entered the study. Your dose of study drug may be increased if it is determined that the dose is safe to be increased one level up and you tolerate it well, or it may be decreased by the study doctor if you are not tolerating it well.

You will be asked to keep a diary to record the exact time you took the study drugs, and to report any side effects you may have. If you miss a dose or vomit the dose, please make a note of this in your diary and contact your team immediately to receive further instructions. Please bring the study diary with you to each clinic visit.

You will also have tests and procedures done because you are in the study to see how AZD1775 is affecting your body. This will include repeating some of the imaging studies (for example, CT scans, a computerized x-ray examination) every 6 weeks (every 9 weeks if you have been on study for more than a year, or every 12 weeks if you have been on study for more than 3 years) to find out if your cancer has responded. Descriptions of the tests and procedures that will be performed during the study are listed below. Please see the Study Chart below for more details.

**Clinical Center Visits:** We will ask that you come to the Clinical Center for 1 day at the beginning of cycle 1, and for at least 1 additional day during the second week of cycle 1, and then for 1 or 2 days at the beginning of all other cycles. While you are at the Clinical Center we will perform study tests and procedures to see how the study drugs are affecting your body. If you develop any side effects, you may be asked to visit more often.

**Standard procedures being done because you are in this study; these may be done more often because you are in the study:**

- **Clinic visit:** to ask how you are feeling and to evaluate you with a physical examination during week 1 and 2 of cycle 1, and then at the beginning of each cycle.
- **Vital signs and physical examinations:** will be performed during the clinic visits.
- **Blood tests:** Measurement of your white blood cells, red blood cells, platelets, blood sugar, electrolytes, and of how your liver and kidneys work will be done every week during cycle 1, and then at the beginning of every cycle. Approximately 1 tablespoon (15 mL) of blood will be drawn per visit.
- **CT scans** or other imaging tests such as ultrasound (an examination using sound waves) or MRI (an examination using magnetic field and radio waves) that detect your tumor will be done before the study and every 6 weeks while you are receiving study drugs (every 9 or 12 weeks if you have been on study for a year or 3 years). This is done so that any benefit of the treatment can be determined, and if your cancer is not responding to the treatment, the study team can tell you and discuss other treatment options (discussed further below).

**Tests and procedures that are either being tested in this study or being done to see how the drug is affecting your body:**

- **Measurement of AZD1775 in your blood:** We will collect blood samples to measure the amount of study drug in the blood and to help us find out how the body handles the drug. Blood will be collected at multiple time points during cycle 1 only. Please see the study

chart for more details. The total blood for all these tests will be about 6 tablespoons (90 mL). Willingness to give these blood samples is required for taking part in this study. Any blood samples remaining after analysis of AZD1775 may be used for analyses of other compounds related to how the body handles AZD1775 or how the drug affects the body.

- **Other research blood samples:** We will also be collecting optional blood samples from some patients to find out the effects of the drug on any tumor cells in the blood. Blood samples will be collected at the following times during every cycle: day 1, day 4, day 8 (both before and after receiving drug), and day 11, and then every time we do a CT scan to find out how your tumor is responding to the treatment. Each blood collection is about 2 teaspoons (8 mL). In addition, we will be collecting optional blood samples to find out if there are any effects from the drug on your immune system at the beginning of the study and on day 8 of cycle 1. The total amount of blood collected for this optional study is approximately 18 tablespoons (270 mL), though this will vary depending how long you are on study. We will tell you when blood for research will be collected.
- **Tumor Biopsy:** After you are accepted to take part in the study, you will be asked to undergo imaging-directed biopsy of your tumor (removal of a small bit of tissue for microscopic examination) once before you receive the study drug and a second time a few days later. We are collecting biopsy samples to study the effects of AZD1775 on your tumor. Biopsies are an important part of this trial and are done for research purposes. If you have already had a recent tumor biopsy for research we may be able to use this instead for your before-study biopsy if you haven't had any treatment since it was collected and it is of good quality. During the early stage of the study only, a patient may choose to not undergo biopsies, and this will not affect his or her taking part in this study. During that time, if a patient decides not to have one or both biopsies collected, he or she will still receive AZD1775 and other tests that are part of the study and detailed above. **However, at a certain point in this study, willingness to undergo tumor biopsies will be required for taking part in this study.** We will tell you if biopsies are required before you decide to take part in the study.

  We may also ask you for an optional third biopsy if your disease comes back or shows signs of coming back during treatment. You will be asked to sign a separate consent form for each biopsy procedure.

  Tumor biopsies are only collected by trained personnel. Biopsies are collected using a small needle under imaging guidance (CT, MRI, or ultrasound as deemed appropriate by the interventional radiologist performing the biopsy). Imaging helps the specialized radiologist know that the needle has been placed into the tumor mass.

  Typical risks of biopsy collection include, but are not limited to, bleeding, infection, pain, and scarring. If you experience any complications from the biopsy, medical care will be offered to you. You will be counseled in more detail about biopsies, and you will be asked to sign a separate consent form that will describe the procedures and risks at that time. Your safety is the most important thing at all times. If upon attempting the first biopsy, no tissue can be obtained or it has caused you harm, further biopsies will not be done. After you are enrolled in this study, if for any reason the biopsies cannot be done safely, you may still receive the study drugs but the biopsies will not be done.

I agree to allow biopsies for research purposes:

Yes ____ No _____ Initials_____

**Study chart**

The study drug is given over 21-day periods of time called cycles. You will take AZD1775 by mouth on an empty stomach, either 2 hours before or 2 hours after a meal, at about the same time each day.

Some patients will be asked to undergo research tumor biopsies to take part in the study, for others it is optional. Blood samples for research will be taken from all patients; however, some patients may be asked to provide multiple blood samples for research. The chart below shows what will happen to you during cycle 1 and future cycles after you sign the consent form and start the study. Each cycle is numbered. The left-hand column shows the day in the cycle, and the right-hand column tells you what will happen on that day.

| Day | What to do and what will happen to you |
|---|---|
| **Before starting study drug** | • Check in at the Outpatient Clinic<br>• Get routine blood tests and electrocardiogram of your heart<br>• Pregnancy test for women who are able to become pregnant<br>• Have a history taken of how you feel and undergo a physical examination by a Health Care Provider<br>• CT or MRI scan will be done<br>• Tumor biopsies may be taken from some patients |
| **Cycle 1, Day 1** | • Be admitted to the Clinical Center<br>• Optional blood samples for research will be taken before the first dose<br>• Begin taking AZD1775 by mouth once a day for 5 days<br>• Blood samples to measure AZD1775 will be taken at several times (before the first dose and 2 and 4 hours after the dose) |
| **Cycle 1, Day 4** | • Check in at the Outpatient Clinic<br>• Optional blood samples for research will be taken after the day 4 dose |
| **Cycle 1, Day 8** | • Check in at the Outpatient Clinic<br>• Have a history taken of how you feel and undergo a physical examination by a Health Care Provider<br>• Get routine blood tests<br>• A blood sample to measure AZD1775 will be taken before you take the drug<br>• Optional blood samples for research will be taken before and after the day 8 dose<br>• Tumor biopsies may be taken from some patients<br>• Start taking AZD1775 by mouth once a day for 5 days<br>• An electrocardiogram will be done after you take the drug |
| **Cycle 1, Day 11** | • Check in at the Outpatient Clinic<br>• Optional blood samples for research will be taken after the day 11 dose |
| **Cycle 2 and** | • Check in at the Outpatient Clinic |

| Day | What to do and what will happen to you |
|---|---|
| **onwards, Day 1** | • Have a history taken of how you feel and undergo a physical examination by a Health Care Provider<br>• Get routine blood tests<br>• Pregnancy test for women who are able to become pregnant<br>• Optional blood samples for research will be taken before the first dose<br>• Take AZD1775 by mouth once a day for 5 days, each week, for two weeks |
| **Cycle 2 and onwards, Day 4** | • Check in at the Outpatient Clinic<br>• Optional blood samples for research will be taken after the day 4 dose |
| **Cycle 2 and onwards, Day 8** | • Check in at the Outpatient Clinic<br>• Optional blood samples for research will be taken before and after the day 8 dose |
| **Cycle 2 and onwards, Day 11** | • Check in at the Outpatient Clinic<br>• Optional blood samples for research will be taken after the day 11 dose |
| **Cycle 3 and onwards, Day 1** | • Check in at the Outpatient Clinic<br>• Have a history taken of how you feel and undergo a physical examination by a Health Care Provider<br>• Get routine blood tests<br>• Pregnancy test for women who are able to become pregnant<br>• CT scan to determine how your tumor is responding to the drug will be done every 6 weeks (9 weeks if you have been on study for more than a year, 12 weeks if for more than 3 years)<br>• Optional blood samples for research will be taken when CT scans are done at restaging<br>• Take AZD1775 by mouth once a day for 5 days, each week, for two weeks |
| **Cycle 4 or later** | • Optional tumor biopsy for research will be obtained if your disease comes back or shows signs of coming back<br>• Optional blood draw for research will be obtained if your disease comes back or shows signs of coming back |

**Risks or Discomforts of Participation**

**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 lose time at work or home 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

The AZD1775 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 study drug(s)/study approach.

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 the study drugs to try to reduce side effects.

We do not know if taking AZD1775 will cause any other medications you may be taking to work differently. It is very important that you tell a member of the research team before starting any new drugs, over-the-counter medications, or alternative therapies. You will also receive a list of medications, vitamins, and supplements that should be avoided while taking part in the study. All herbal supplements and medications should be avoided while participating in the study. Grapefruit and Seville oranges and their products (including marmalade, juice, etc.) should be avoided while taking part in the study.

The tables 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.

Some patients on this study have experienced anaphylaxis, or a severe allergic reaction, possibly related to the study drug. This condition can cause difficulty breathing, increased heart rate, decreased blood pressure, skin rash, dizziness, nausea, and vomiting. Anaphylaxis can be life-threatening.

The risks and side effects associated with AZD1775 are presented below and are based on 3 completed studies. You will be closely followed for these risks and side effects.

| **COMMON, SOME MAY BE SERIOUS**<br>In 100 people receiving AZD1775 (adavosertib), more than 20 and up to 100 may have: |
|---|
| • Diarrhea, nausea, vomiting<br>• Tiredness |

| **OCCASIONAL, SOME MAY BE SERIOUS**<br>In 100 people receiving AZD1775 (adavosertib), from 4 to 20 may have: |
|---|
| • Anemia which may require blood transfusion<br>• Pain<br>• Constipation, heartburn<br>• Sores in the mouth which may cause difficulty swallowing<br>• Swelling of the body<br>• Fever<br>• Infection, especially when white blood cell count is low<br>• Bruising, bleeding<br>• Loss of appetite, dehydration<br>• Dizziness, headache<br>• Difficulty sleeping<br>• Cough, shortness of breath<br>• Rash |

| **RARE, AND SERIOUS**<br>In 100 people receiving AZD1775 (adavosertib), 3 or fewer may have: |
|---|
| • Abnormal heartbeat<br>• Bleeding from multiple sites<br>• Internal bleeding which may cause black tarry stool, blood in vomit<br>• Damage to the liver<br>• Change in the heart rhythm<br>• Bleeding in the brain which may cause confusion |

**Reproductive Risks:**
If you are a woman who is breastfeeding or pregnant, you may not take part in the study because we do not know how AZD1775 would affect your baby or your unborn child. If you are a woman on this study who may become pregnant, you should not become pregnant while on this study and for 2 months after you stop taking the drug because the drugs in this study can affect an unborn baby. It is important you understand that women who may become pregnant need to use birth control for at least two weeks before the start of this study, while on this study, and for 2 months after the study.

If you are a man on this study, you should not father a baby or donate sperm while on this study or for 3 months after you stop taking the drug because the drugs in this study can affect an unborn baby. It is important you understand that men on this study and their female partners who may become pregnant need to use birth control while on this study and for 3 months after the study. If you are a man with a female partner who is pregnant or not using effective birth control, you should abstain while on this study and for 3 months after you stop taking the drug. If you are a man who wishes to father children while on this study, you should arrange for the freezing of sperm samples prior to the start of the study.

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. If you think that you or your partner is pregnant, you should tell your study doctor or nurse at once. Patients who become pregnant while taking part in the study will be taken off the study.

Effective forms of birth control include:

- abstinence
- hormonal [birth control pills, injections, or implants]
- vasectomy
- intrauterine device (IUD)
- tubal ligation
- barrier methods (condoms)

**Potential Risks Related to Research-Related Imaging Studies:**
This research study involves exposure to radiation from up to 3 CT scans (used in biopsy collections). This radiation exposure is not required for your medical care and is for research purposes only. The amount of radiation you will receive in this study is 2.4 rem, which is below the guideline of 5 rem per year allowed for research subjects by the NIH Radiation Safety Committee. The average person in the United States receives a radiation exposure of 0.3 rem per year from natural sources, such as the sun, outer space, and the earth's air and soil. If you would like more information about radiation, please ask the investigator for a copy of the pamphlet, An Introduction to Radiation for NIH Research Subjects.

While there is no direct evidence that the amount of exposure received from participating in this study is harmful, there is indirect evidence it may not be completely safe. There may be a very slight increase in the risk of cancer.

Please tell your doctor if you have had any radiation exposure in the past year, either from other research studies or from medical tests or care, so we can make sure that you will not receive too much radiation. Radiation exposure includes x-rays taken in radiology departments, cardiac catheterization, and fluoroscopy as well as nuclear medicine scans in which radioactive materials were injected into your body.

If you are pregnant you will not be permitted to participate in this research study.

**Potential Benefits of Participation**

**Are there benefits to taking part in this study?**

The aim of this study is to see if this experimental treatment will cause your tumors to shrink. We do not know if you will receive personal, medical benefit from taking part in this study. These potential benefits could include shrinking of your tumor or lessening of your symptoms, such as pain, that are caused by the cancer. Because there is not much information about the drug's effect on your cancer, we do not know if you will benefit from taking part in this study, although the knowledge gained from this study may help others in the future who have cancer.

**Alternative Approaches or Treatments**

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

Instead of being in this study, you have these options**:**

- Getting treatment or care for your cancer without being in a study
- Taking part in another study
- Getting comfort care, also called palliative care. This type of care helps reduce pain, tiredness, appetite problems, and other problems caused by the cancer. It does not treat the cancer directly. Instead, it tries to improve how you feel. Comfort care tries to keep you as active and comfortable as possible.

Please talk to your doctor about these and other options.

**Research Subject's Rights**

**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 this study. If you decide to take part, 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 medical care from our institution if you are eligible and choose to participate in another trial. 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. In the case of injury resulting from this study, you do not lose any of your legal rights to seek payment by signing this form.

**What are the costs of taking part in this study?**

If you choose to take part in the study, the following will apply, in keeping with the NIH policy:

- You will receive study treatment at no charge to you. This may include surgery, medicines, laboratory testing, x-rays, or scans done at the Clinical Center, National Institutes of Health (NIH), or arranged for you by the research team to be done outside the Clinical Center, NIH if the study related treatment is not available at the NIH.

- There are limited funds available to cover the cost of some tests and procedures performed outside the Clinical Center, NIH. You may have to pay for these costs even if they are not covered by your insurance company.
- Medicines that are not part of the study treatment will not be provided or paid for by the Clinical Center, NIH.
- Once you have completed taking part in the study, medical care will no longer be provided by the Clinical Center, NIH.
- The study agent, AZD1775, will be provided free of charge while you are participating in this study. Even though it is unlikely, there is a possibility that at some point the supply of study agents may run out, necessitating taking you off-study.

**Stopping Therapy**

Your doctor may decide to stop your therapy for the following reasons:

- if he/she believes that it is in your best interest
- if your disease comes back during treatment
- if you have side effects from the treatment that your doctor thinks are too severe
- if new information shows that another treatment would be better for you
- if too many patients in the study experience severe side effects
- if you become pregnant

In this case, you will be informed of the reason therapy is being stopped.

You can stop taking part in the study at any time. However, if you decide to stop taking part in the study, we would like you to talk to the study doctor and your regular doctor first.

If you decide at any time to withdraw your consent to participate in the trial, we will not collect any additional medical information about you. However, according to FDA guidelines, information collected on you up to that point may still be provided to the Cancer Therapy Evaluation Program (CTEP) at the National Cancer Institute (NCI) or designated representatives. If you withdraw your consent and leave the trial, any samples of yours that have been obtained for the study and stored at the NCI can be destroyed upon request. However, any samples and data generated from the samples that have already been distributed to other researchers or placed in the research databases cannot be recalled and destroyed.

**Follow-up**

You will be followed for 30 days after taking the last dose of study drugs. We will call you between days 27-30 to ask about any side effects that were ongoing when you stopped therapy, or any new side effects that might be related to the study therapy. If you have side effects that might be related to the study drugs that have not gotten better after 30 days, we will call you every 2 weeks until the side effects have become stable or gotten better. The follow-up period will end if you enroll in another study or start receiving standard therapy.

**Conflict of Interest**

The National Institutes of Health (NIH) reviews NIH staff researchers at least yearly for conflicts of interest. This process is detailed in a Protocol Review Guide. You may ask your research team for a copy of the Protocol Review Guide or for more information. Members of the research team who do not work for NIH are expected to follow these guidelines but they do not need to report their personal finances to the NIH.

Members of the research team working on this study may have up to $15,000 of stock in the companies that make products used in this study. This is allowed under federal rules and is not a conflict of interest.

**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.

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

- The National Cancer Institute (NCI) and other government agencies, like the Food and Drug Administration (FDA), involved in keeping research safe for people.
- Pharmaceutical collaborator (AstraZeneca)

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.

**Where can I get more information?**

You may call the National Cancer Institute's Cancer Information Service at: 1-800-4-CANCER (1-800-422-6237). You may also visit the NCI Web site 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.

**Use of Specimens and Data for Future Research**

We would like to keep some of your specimens and data that we collect and use them for future research and share them with other researchers. We will not contact you to ask about each of these future uses. These specimens and data will be identified by a number and not your name. Your specimens and data will be used for research purposes only and will not benefit you. Researchers use specimens and data stored in scientific databases to advance science and learn about health and disease. It is also possible that the stored specimens and data may never be used. Results of research done on your specimens and data will not be available to you or your doctor. It might help people who have cancer and other diseases in the future.

If you decide now that your specimens and data can be kept for research and shared, you can change your mind at any time. Just contact us and let us know that you do not want us to use your specimens and/or data. Then any specimens that have not already been used or shared will be destroyed and your data will not be used for future research.

Please read the sentence below and think about your choice. After reading the sentence, circle and initial the answer that is right for you. No matter what you decide to do, it will not affect your care.

My specimens and data may be kept and shared for use in research to learn about, prevent, or treat cancer or other health problems.

Yes No Initials_____

## OTHER PERTINENT INFORMATION

**1. Confidentiality.** When results of an NIH research study are reported in medical journals or at scientific meetings, the people who take part are not named and identified. In most cases, the NIH will not release any information about your research involvement without your written permission. However, if you sign a release of information form, for example, for an insurance company, the NIH will give the insurance company information from your medical record. This information might affect (either favorably or unfavorably) the willingness of the insurance company to sell you insurance.

The Federal Privacy Act protects the confidentiality of your NIH medical records. However, you should know that the Act allows release of some information from your medical record without your permission, for example, if it is required by the Food and Drug Administration (FDA), members of Congress, law enforcement officials, or authorized hospital accreditation organizations.

**2. Policy Regarding Research-Related Injuries.** The Clinical Center will provide short-term medical care for any injury resulting from your participation in research here. In general, no long-term medical care or financial compensation for research-related injuries will be provided by the National Institutes of Health, the Clinical Center, or the Federal Government. However, you have the right to pursue legal remedy if you believe that your injury justifies such action.

**3. Payments.** The amount of payment to research volunteers is guided by the National Institutes of Health policies. In general, patients are not paid for taking part in research studies at the National Institutes of Health. Reimbursement of travel and subsistence will be offered consistent with NIH guidelines.

**4. Problems or Questions.** If you have any problems or questions about this study, or about your rights as a research participant, or about any research-related injury, contact the Principal Investigator, Dr. Naoko Takebe, 31 Center Drive, Building 31, room 3A44, Bethesda, Maryland, Telephone: 240-781-3398. You may also call the Clinical Center Patient Representative at 301-496-2626. If you have any questions about the use of your specimens and data for future research studies, you may also contact the Office of the Clinical Director, Telephone: 240-760-6070.

**5. Consent Document.** Please keep a copy of this document in case you want to read it again.

| **COMPLETE APPROPRIATE ITEM(S) BELOW:** | |
|---|---|
| **A. Adult Patient's Consent**<br>I have read the explanation about this study and have been given the opportunity to discuss it and to ask questions. I hereby consent to take part in this study.<br><br>_____ _____<br>Signature of Adult Patient/ Legal Representative Date<br><br>_____<br>Print Name | **B. Parent's Permission for Minor Patient.**<br>I have read the explanation about this study and have been given the opportunity to discuss it and to ask questions. I hereby give permission for my child to take part in this study.<br>(Attach NIH 2514-2, Minor's Assent, if applicable.)<br><br>_____ _____<br>Signature of Parent(s)/ Guardian Date<br><br>_____<br>Print Name |

**C. Child's Verbal Assent (If Applicable)**
The information in the above consent was described to my child and my child agrees to participate in the study.

_____ _____ _____
Signature of Parent(s)/Guardian Date Print Name

**THIS CONSENT DOCUMENT HAS BEEN APPROVED FOR USE FROM OCTOBER 22, 2019 THROUGH NOVEMBER 12, 2020.**

| | |
|---|---|
| _____ _____<br>Signature of Investigator Date | _____ _____<br>Signature of Witness Date |
| _____<br>Print Name | _____<br>Print Name |