INSTITUTE: National Cancer Institute

STUDY NUMBER: 15-C-0166 PRINCIPAL INVESTIGATOR: Ramaprasad Srinivasan, M.D., Ph.D.

STUDY TITLE: Phase 2 Study of Everolimus Therapy in Patients with Birt-Hogg-Dubé Syndrome (BHD)-Associated Kidney Cancer

Continuing Review Approved by the IRB on 05/08/17

Amendment Approved by the IRB on 04/19/17 (B) Date posted to web: 05/25/17

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?

This study is being done in order to find out if the drug everolimus is safe and is effective in people who have Birt-Hogg-Dubé Syndrome (BHD)-associated kidney cancer.

Studies in the laboratory suggest that a protein called mTOR may be activated in BHD associated tumors.

The study drug, everolimus, supplied by Novartis Pharmaceuticals Corporation, works by inhibiting the activity of this protein.

Experiments have shown that everolimus can prevent cancer cells from growing in number and clinical trials have shown that this drug is active in many human cancers.

Everolimus has been FDA approved for adults with advanced kidney cancer (Renal Cell Carcinoma). Everolimus received approval for patients with subependymal giant cell astrocytoma (SEGA), a brain tumor seen with genetic conditions called tuberous sclerosis complex (TSC) who require therapy, but are not candidates for surgery. Everolimus was approved for pancreatic neuroendocrine tumor (PNET) in patients with unresectable, locally advanced, or metastatic disease. Everolimus received approval for the treatment of postmenopausal women with advanced hormone receptor-positive, HER2- negative breast cancer (advanced HR+ BC) in combination with exemestane, after failure of treatment with letrozole or anastrozole. Everolimus also received approval for the treatment of patients with TSC who have renal angiomyolipoma not requiring immediate surgery.

Everolimus has been used to treat patients in clinical studies since 2002 and approximately 30,582 patients (as of 30-Sep-2013) have been treated with everolimus.

Everolimus has not been specifically approved for Birt-Hogg-Dubé Syndrome (BHD)-associated kidney cancer and the studies used to obtain FDA approval for this agent in Renal Cell Carcinoma were performed largely in patients with clear cell renal cell carcinoma, the most common variant of kidney cancer.

Why are you being asked to take part in this study?

You are being asked to take part in the study because you have been diagnosed with Birt-Hogg-Dubé Syndrome (BHD)-associated kidney cancer.

How many people will take part in this study?

Approximately 18 people will be enrolled in this study.

Description of 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. However, there are some extra exams, tests and procedures that you will need to have if you take part in this study. If you have had some of them recently, they may not need to be repeated.

These tests include:

- History and physical evaluation including vital signs
- Routine blood and urine tests
- Serum pregnancy test (if you are female and can have children)
- CT scan of chest/abdomen/pelvis or MRI
- Brain MRI or brain CT
- CT scan of neck (if it is suspected that your tumor has spread to your neck)
- Bone scan (if it is suspected that your tumor has spread to your bones)
- FDG-PET (if your cancer is known or suspected to have spread outside the kidneys)
- Tests to measure how well your lungs function
- Electrocardiogram (EKG)
- Tests for hepatitis if your doctor determines that you are at risk

During the study

If you join this study, you will be given tablets to be taken by mouth. It is very important for you to take the study drug just as the study doctor tells you. Do not skip any doses unless your study doctor tells you to skip doses. If you throw up after taking the study drug, you should NOT take another tablet that day. Let your study doctor know that you got sick. If you do forget to take the study drug one day, do not take any extra doses the next day. Call your study doctor and ask for advice.

You will be asked to take one tablet once a day. You will take everolimus for up to 52 weeks. You should take everolimus about the same time each day, either consistently with or without food.

You should only take the study medicine as the doctor tells you to, and should not do anything else with it.

During the study, you must talk to the study doctor before you take any drug other than the study drug. This includes homeopathic, alternative, or herbal medicines, and vitamins or other over-the-counter medications. Please avoid eating grapefruit, star fruit, and Seville oranges or drinking their juices while in the study. The juices in these fruits can change the way your body treats or breaks down everolimus.

The amount of study drug you take and the time when you take it may be changed during the study. This may be because of test results or side effects that you experience. Your study doctor

may also ask you to stop taking your study drug for a brief time. If this happens, you will be told when it is safe to start taking the study drug again. If study drug is stopped for a while, you may have to go to extra visits at the clinic for your safety. If you have any side effects that do not get better after stopping the study drug for a while, your study doctor may decide to discontinue the drug permanently.

During the study, you may discuss with a doctor or health care professional, who is not directly involved in the study, health issues or medical problems related to the study treatment or disclose information related to the study treatment. In this case you should tell your doctor or health care professional that the Novartis drug which is part of the study treatment and information relating to it is Novartis' property and is confidential.

Your study doctor will tell you about any changes needed in the way you take the medicine. You must always remember not to throw away your empty study drug containers. Instead, keep them in a safe place and bring them back to the doctor's office whenever your study doctor or nurse asks you to. At the end of the study, any study medicine or empty containers you still have should be given back to the study doctor.

In order to monitor your progress during the study, we will divide the time you are on the study into cycles. One cycle = 4 weeks or 28 days.

You will need the following tests and procedures that are part of regular cancer care.

- Physical evaluation and weight measurement will be done during week 1 of each cycle
- Serum pregnancy test (if you are female and can have children) will be done during week 1 of each cycle.
- Urine tests will be done during week 1 of each cycle.
- Vital signs will be taken every 2 weeks.
- Blood tests will be performed at 2 weeks until the end of cycle 3 and then during week 1 of each cycle.
- CT scan of chest/abdomen/pelvis or MRI with or without a bone scan will be performed every 12 weeks.
- FDG-PET (if your cancer is known or suspected to have spread outside the kidney) and bone scan (if it is suspected that your tumor has spread to your bones) at the start of the study. This may be repeated at one or more times while you are on the study if considered important to make clinical decisions about the management of your cancer.

- Tests for hepatitis if your doctor determines that you are at risk as needed for the duration of the study and during follow-up.

You will need the following tests or procedures that are not usually part of regular cancer care to help us monitor your safety

- Record when you take your medication and any symptoms that you experience in a diary provided by the study team

You will also need the following tests for research to see how the drug is affecting your body and other research studies.

- Tumor biopsy (optional) will be collected at the beginning of the study before you have taken any study drug and then at approximately 8 weeks (the end of cycle 2). The tumor samples we obtain will be used to look for special markers that may be helpful in the study of kidney cancer and in understanding the effect of the study drugs on the tumor. Results of research done on your specimens and data will not be available to you or your doctor. A separate consent form will be provided to you at the time of the biopsy for you to grant permission to that procedure if you agree to the biopsies.
- At the beginning of the study, we would like to obtain your previously collected tumor tissue if it is available. We would like to test your tissue for genes that may be linked to cancer.

When you are finished taking the drugs (treatment)

We would like to see you again within 4 to 5 weeks after you have finished taking the study drug in order to perform the following tests:

- Physical evaluation and blood tests
- CT or MRI for chest, abdomen, pelvis, bone scan if your doctor determines that you may need it.
- Tests for hepatitis if your doctor determines that you are at risk.

After you have completed this visit, we would also like to contact you by telephone approximately every 3-6 months to find out how you are doing.

Birth Control

Women who are pregnant or nursing a child cannot participate in this trial. You must confirm, to the best of your knowledge, that you are not now pregnant, and that you do not intend to become pregnant during the trial.

The risks to an unborn human fetus or a nursing child from everolimus are not known. Based on animal studies, everolimus exposure may result in birth defects or infant death, and may impact fertility in both male and female patients. **Women of childbearing potential** must use a highly effective method of contraception while receiving everolimus, and for up to 8 weeks after ending treatment. Highly effective contraceptive methods are also required for female partners of male patients who are sexually active and may become pregnant.

Please discuss with your Study Doctor the most appropriate birth control method for you that also respect your cultural and religious situation.

Examples of highly effective birth control methods are:

- Total abstinence, when this is in line with your preferred and usual lifestyle. Periodic abstinence like calendar, ovulation, symptothermal, post-ovulation methods, and withdrawal are not acceptable methods of contraception.
- Female sterilization, when you have been already surgically sterilized prior to the study by surgical bilateral removal of ovaries (woman's reproductive system that stores and releases eggs for fertilization and produces female sex hormones), or tubal ligation (getting your "tubes tied") at least six weeks ago.
- Your male partner has already been sterilized (with the appropriate documentation). The sterilized male partner should be your sole partner.

Use of a combination of any two of the following (a+b or a+c or b+c):

a. Use of oral, injected or implanted hormonal methods of contraception. Use of oral, injected or implanted hormonal methods of contraception or other forms of hormonal contraception that have comparable efficacy (failure rate <1%), for example, hormone vaginal ring or transdermal hormone contraception (in case of oral contraception you should have been using the same pill on a stable dose before taking study treatment),

b. Placement of an intrauterine device (IUD) or intrauterine system (IUS),

c. Use of an occlusive cap (diaphragm or cervical/vault cap) by you, or a condom by your male partner combined with a spermicidal foam/gel/film/cream/vaginal suppository.

If you become pregnant or suspect being pregnant during study treatment or within 8 weeks after completing study treatment, you must inform the Study Doctor immediately, and you have to stop ongoing study treatment immediately. You will not be allowed to continue study treatment if you are pregnant.

As a male participant in the study you must agree to use a condom during intercourse and not father a child during the study and for the period of 8 weeks following stopping of study treatment. In addition, it is advised that your female partner uses a highly effective form of birth control method (contraception) if she is sexually active and may become pregnant.

In case you father a child while in this study you will be asked to report the pregnancy to the Study Doctor.

General Information on pregnancy and contraception

85 out of 100 sexually active women who do not use birth control can expect to become pregnant in a year. No matter which birth control you are using from the list above, it is important to follow the manufacturer directions. If you don't, you raise your chance of getting pregnant.

Hormonal contraception is available in the form of pills which need to be taken every day, injections, which lasts approximately 3 months and as implanted devices. Hormonal methods are associated with some risks like changes in your cycle, nausea, headache, changes in mood, weight gain, breast tenderness, and blood clots.

Implanted devices are inserted into the uterus and can stay there for several years. They can cause cramps, bleeding, and infertility. It is important to know that not all women experience all of the adverse effects listed above.

Risks or Discomforts of Participation

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

While on this study, you may feel side effects. These may be side effects of the study drug, or another medicine. They could also be because of what happens during a study visit, including taking blood. You should discuss any symptoms with the study doctor or your regular doctor. Very common (≥10%), common (1% to < 10%), and uncommon (<1%) side effects are listed in this document, but they will be different from person to person. Many side effects go away shortly after the study drug is stopped. In some cases, the side effects may be serious, last a long time or be permanent, and may even cause death.

Because certain drugs may increase or decrease the levels of the study drug in your blood, it is important that you follow your study team's instructions about drugs you may or may not take while you are on this study. Please check with your study doctor before taking ***any*** medications, including over the counter drugs and herbal medications.

Your study doctor will closely follow you during this study, and answer any questions you may have about risks, worries, and side effects. You should talk to your study doctor about any **s**ymptoms that you experience while in the study.

This research study may involve unknown risks. Problems or side effects that are not now known could also occur. You will be given any available new information that may affect your desire to start or continue in the study. Other side effects not mentioned below or observed in previous studies with the drug are also possible.

All problems or side effects need to be reported to the study doctors or study nurses looking after you either by phone or at the next visit.

For more information about risks and side effects, you should feel free to ask your study doctor. If you are concerned about your health between visits due to being in this study, please call the emergency telephone numbers provided at the end of this document.

Adverse Drug Reactions

One of the most common possible side effects of the study drug is mouth lining tenderness (called stomatitis) ranging from redness, irritation, and swelling, to mouth ulcers (sores in the mouth). This side effect is found in more than half of patients treated with everolimus.

Additional very common side effects of everolimus occurring in more than 10% of patients include: fatigue, weakness (feeling weak or tired), chills, nausea and vomiting, loss of appetite, weight loss, skin problems such as rash or itching, diarrhea, pain or swelling of the arms or legs, bleeding of the nose, cough, shortness of breath, and headache. High levels of sugar in the blood, high levels of lipids (cholesterol) in the blood, abnormal or loss of taste, low levels of red blood cells, infections, and spontaneous bleeding or bruising could occur while taking everolimus.

Everolimus may cause changes in the lungs. Very commonly, everolimus may be associated with inflammation in the lungs (pneumonitis). Generally mild, it has been severe in a few cases, although it resolves once the treatment is stopped. The consequences of these changes in patients with BHD associated lung cysts has not been previously studied and may be different from that in the general population. Rarely, everolimus is associated with a blood clot or blockage in your lungs or extremities. Tell your doctor right away if you experience new or worsening lung or breathing symptoms like cough or shortness of breath, even when symptoms are mild, as this might have life-threatening consequences. If you experience these symptoms, your study doctor may ask you to undergo chest CT scans and/or a pulmonary function test to evaluate the cause and seriousness of these symptoms.

Common side effects (1% to <10%) of everolimus include: dry mouth, dehydration, skin changes (acne, rash, redness, dryness or irritation, itching and skin inflammation), abdominal pain, stomach virus, passing gas, constipation, irritability, nail disorders, increased blood pressure, joint stiffness or pain, mouth pain, difficulty swallowing, (heartburn), fever, insomnia, inflammation of the lining of the digestive system and other mucous membranes such as the sinus, stomach pain, bleeding, and low white blood cells (leukopenia, lymphopenia and neutropenia).

As noted above, there could be a lowering of the number of your blood cells that help fight infection. This could lead to an infection (which could be potentially life-threatening). Examples of infections are common colds (sore throat, runny nose), throat infections, pneumonia, urinary tract infections, and ear infections. Therefore, it is important that your blood counts be regularly checked by your study doctor.

In addition, there could be a lowering of the blood cells that help the blood to clot (which could cause you to bleed more easily), and a lowering of the protein in your blood (hemoglobin) that helps carry oxygen; this could lead to anemia.

Drugs like everolimus can cause the patient's immune system not to work as well as usual. A patient with hepatitis B or hepatitis C who takes everolimus could be susceptible to the virus becoming more active. If you have active hepatitis B or C, you will not be allowed into the study.

Changes to the levels of blood sugar (glucose), which could lead to diabetes, could occur while taking everolimus, so your blood sugar levels will be checked often during the study. If you are taking another medicine which may increase blood sugar levels, more frequent monitoring may also be required. Another diabetes test (Hemoglobin A1c) will be checked at the beginning of the study.

Everolimus may have an effect on the liver. There could also be an increase in your blood of a waste product of your liver (bilirubin), which could mean that your liver is not working as well. These will be tested regularly during the study. The levels of cholesterol and triglycerides (fats in your blood) could increase. Increased levels of cholesterol and triglycerides are an important factor of risk for heart disease, so your blood cholesterol and triglyceride levels will be regularly checked in this study. Also, your doctor may prescribe medical treatment as appropriate. The levels of liver enzymes (transaminases), which are signs of liver function/damage, may also increase. Everolimus may cause toxicity to your kidneys and cause the levels of creatinine in your blood and protein in your urine to increase. These increases are an indication that the kidneys are not working as well as they did before. This toxicity could lead to kidney failure. Therefore, your blood creatinine levels and urine protein levels (and other urine tests) will be regularly monitored in this study. In addition, there could be a lowering of electrolytes (potassium, phosphate), which are also markers of kidney function, and will be monitored during the study.

Everolimus may contribute to increased levels of an enzyme called blood lactate dehydrogenase which gives information about the health of certain organs.

Other, uncommon side effects (<1%) include the following: Severe decrease in red blood cells or all blood cells, loss of taste, rash of small blisters, bronchitis, coughing up of blood and congestive heart failure (fluid build-up and shortness of breath) as well as non-cardiac chest pain and impaired wound healing, increased daytime urination, inflammation of the gallbladder known as cholecystitis, and elevated number of white cells in the colon with inflammation

known as eosinophilic colitis. An eye condition known as Anterior Uveitis (inflammation of the eye) has been observed in a very small number of patients.

For women of child-bearing potential taking everolimus, changes to your menstrual period (menstruation) may occur. These changes may include: delayed or missing one or more menstrual period (secondary amenorrhea), increased or decreased blood flow during menstruation, or any other irregular change to your menstrual cycle. Also, a hormone called luteinizing hormone (LH) and follicle stimulating hormone (FSH) may be increased due to everolimus. Fertility may be affected.

If you experience any hypersensitivity or signs of serious allergic reaction such as rash, itching, hives, difficulty breathing or swallowing, dizziness, signs of serious allergic reaction, please contact your doctor.

You should not receive live vaccines and have close contact with people who have received live vaccines within 7 days of starting everolimus and while on this study without consultation with your study doctor. Examples of live vaccines include intranasal influenza, measles, mumps, rubella, oral polio, BCG, yellow fever, varicella (Chicken Pox), and typhoid vaccines.

Blood sampling risks

Taking blood may cause some discomfort, bleeding or bruising where the needle enters the body, and in rare cases, it may result in fainting. There is a small risk of infection. Some people have not felt well when having their blood taken. Some people have felt dizzy while having their blood drawn or after. Let the nurse know if you would prefer to lie down while you have your blood drawn.

Tumor Biopsy Risks

The biopsy procedure usually causes only brief discomfort at the site from which the biopsy is taken. Rarely, infection or bleeding may occur at the needle site.

Research Radiation Risks

The biopsy may be done under CT guidance. If that is the case, then this research study involves exposure to radiation from up to 2 CT scans. 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 0.29 rem which is below the guideline of 5 rem (or 0.5 rem in children) 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. It is best to avoid radiation exposure to unborn or nursing infants since they are more sensitive to radiation than adults.

Side Effects Diary

You will be asked to keep a diary of any side effects, when they occurred, how long they lasted, and what if anything helped to relieve the side effect. This diary will be reviewed by the study team during each visit.

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. The benefits of everolimus are not established for people with your medical condition. 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 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 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.

Will your 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. 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), which are involved in keeping research safe for people.
- Governmental agencies in other countries where the study drug may be considered for approval.
- National Cancer Institute Institutional Review Board.
- Qualified representatives from Novartis, the pharmaceutical company who produces everolimus.

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.

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

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 Novartis 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 can**not** be recalled and destroyed.

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.

The National Institutes of Health and the research team for this study are using a drug developed by Novartis through a joint study with your researchers and the company. The company also provides financial support for this study.

Use of Specimens and Data for Future Research

To advance science, it is helpful for researchers to share information they get from studying human samples. They do this by putting it into one or more scientific databases, where it is stored along with information from other studies. A researcher who wants to study the

information must apply to the database and be approved. Researchers use specimens and data stored in scientific databases to advance science and learn about health and disease.

We plan 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 stripped of identifiers such as name, address or account number, so that they may be used for future research on any topic and shared broadly for research purposes. Your specimens and data will be used for research purposes only and will not benefit you. 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 do not want your stored specimens and data used for future research, please contact us in writing 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. However, it may not be possible to withdraw or delete materials or data once they have been shared with other researchers.

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, Ram Srinivasan, M.D., Ph.D., Building 10, Room 2-5940, Telephone: 240-760-6251. You may also call the Clinical Center Patient Representative at 301-496-2626. If you have any questions about the use of your specimens or 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

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.

Signature of Adult Patient/ Legal Representative | Date

Print Name

B. Parent's Permission for Minor Patient.

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.

(Attach NIH 2514-2, Minor's Assent, if applicable.)

Signature of Parent(s)/ Guardian | Date

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 MAY 08, 2017 THROUGH MAY 07, 2018.

Signature of Investigator | Date | Signature of Witness | Date

Print Name | Print Name