INSTITUTE: National Institute of Dental and Craniofacial Research

STUDY NUMBER: 18-D-0086 PRINCIPAL INVESTIGATOR: Rachel I. Gafni, M.D.

STUDY TITLE: BGJ398 for the Treatment of Tumor-Induced Osteomalacia

Continuing Review Approved by the IRB on 02/11/19
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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.

Purpose of the Study

The purpose of this study is to see how treatment with the medication BGJ398 affects people with Tumor-induced Osteomalacia (TIO).

Background

You have a disorder called Tumor-induced Osteomalacia (TIO). People with this disorder have a small tumor that makes a hormone called FGF23. FGF23 is normally only made by bone cells. FGF23 helps to control the amount of phosphorus and active vitamin D (calcitriol) in the blood. When the FGF23 level is too high, calcitriol and phosphorous levels go down and sometimes become very low. Low levels of phosphorous in the blood can cause a person to feel sick. It can cause weak muscles and broken bones. A very low blood phosphorous can cause abnormal heart beats and confusion. The standard treatment for TIO is to find the tumor and have it removed by a surgeon, which can often results in a cure. However, these tumors are often very small and can be hard to find. Sometimes, the tumor cells have spread all over the body and there are many small tumors in different places. When this happens it is hard to remove all the tumors. In addition, some people with TIO may not be able to have surgery or the TIO tumor is surgically difficult to remove. Treatment of patients whose tumors cannot be located or that cannot be removed is difficult. It involves taking phosphorus

many times a day. This treatment often causes diarrhea. Treatment also includes taking active vitamin D. Blood and urine tests must be done often to adjust medication doses and prevent side effects. Side effects of phosphorus and vitamin D include: high levels of parathyroid hormone, high levels of calcium in the blood and urine, and calcium deposits in the kidney.

FGF23 in the blood goes to the kidneys and attaches to receptors called FGFR1 which cause the effects of FGF23 described above. BGJ398 is being studied as a new drug for other cancers. It blocks the FGFR1 receptors in the kidney. Blocking this receptor may stop or slow phosphate from being lost into the urine, which may increase the blood phosphorous levels. TIO tumors may also have these FGFR1 receptors – BGJ398 may cause TIO tumors to make less FGF23. Early results of BGJ398 treatment in two patients with TIO tumors are promising. Both patients had normal blood phosphorous levels while taking BGJ398. In the patient who had many tumors all over his body, BGJ398 treatment decreased the size of many of the tumors. However, how BGJ398 affects people with TIO is not well studied. This study will look at the effects of BGJ398 treatment on TIO tumors that cannot be found, have spread in the body, or cannot be easily taken out by surgery.

Study Population

This study will enroll 10 people diagnosed with a TIO tumor(s) that cannot be found, have spread in the body, or cannot be easily taken out by surgery.

Who Can Be In This Study

You may be eligible to participate if you are:

1. Enrolled into NIH protocol, 01-D-0184 Evaluation and Treatment of Bone and Mineral Disorders
2. Diagnosed with a TIO and:
   - your tumor has not been found after evaluation on protocol 01-D-0184 OR
   - your tumor has spread to different parts of your body OR
   - surgery would be dangerous for you OR
   - your tumor is in a place that would make it hard to take out
3. 18-85 years old
4. Able to understand this consent document and are willing to participate in the study
5. Able to swallow capsules
6. Post-menopausal or not able to have children – for example, you have not had a period for 12 months in the setting of menopause symptoms OR have had your uterus or ovaries removed have had your tubes tied at least 6 weeks ago.
7. Able to get pregnant but verbally agree to use one of the effective methods of birth control listed below during BGJ398 treatment and for 3 months after the last dose of the study drug.
   - Total abstinence (when this is in line with the preferred and usual lifestyle of the subject. Periodic abstinence (e.g., calendar, body temperature, etc…) and withdrawal are not acceptable methods of birth control.
   - Male sterilization (at least 6 months prior to screening). For female subjects on the study the sterilized male partner should be the only partner for that subject.
   - Combination of the following (a+b or a+c, or b+c):
     a. Use of oral, injected, implanted, patch, or other hormonal methods of birth control that have a failure rate of less than 1%.
     b. An intrauterine device (IUD) or intrauterine system (IUS)
     c. Barrier methods of birth control: Condom or diaphragm/cervical caps used with spermicide

8. Sexually active men, including those that have had a vasectomy, must verbally agree to use a condom during sex while taking BGJ398 and for 3 months after the last dose of the study drug and should not father a child in this period.
9. If you have taken BGJ398 previously, you must be off the medication for at least 2 weeks before enrolling in this study.

Who May Not Be In This Study

You may not be eligible to be in this study if you:

1. Have another medical reason for low blood phosphorus levels
2. Have a history of another cancer that has not been in remission for at least 5 years.
3. Have a history of receiving a drug similar to BGJ398.
4. Have a problem with your corneas or retinas
5. Have a history of gastrointestinal disease such as ulcers, colitis, uncontrolled nausea, vomiting, or diarrhea.
6. Are taking the medications that may interfere with BGJ398
7. Eat or drink food with grapefruit, grapefruit juice, pomegranates, star fruits, or Seville oranges within 7 days before the first dose of BGJ398.
8. Are taking certain medications that may cause heart rhythm changes
9. Are taking warfarin or a similar medication.
10. Have a low white cell, red cell, or platelet count
11. Have abnormal liver function
12. Have abnormal kidney function
16. Have a significant history of or current heart disease
17. Are pregnant (determined by blood test), nursing, or planning to become pregnant during the study.

Pre-Study Requirements

Before enrolling in this study, you will have already been enrolled onto protocol 01-D-0184, "Evaluation of Bone and Mineral Disorders," to confirm the diagnosis TIO and attempt to locate the tumor with standard methods.

Study Visits and Procedures

Study visits are described in this section. A full description of the exams, tests and procedures can be found in the section Research Tests/Procedures, on page 5.

If you qualify and agree to participate in this study you will be asked to come to the NIH Clinical Center for 8 or 9 visits over a nine-month period. These visits will include:

·One inpatient or outpatient visit to determine if you are eligible (Screening Visit)

·One inpatient visit for examinations, testing and to give BGJ398 and monitor you after the first dose of the drug (Baseline Visit) – this visit may be combined with the screening visit.

·One NIH visit (inpatient or outpatient depending upon where you live) after your last dose of BGJ398 for examinations, testing, and daily blood and urine tests

·Eight outpatient visits

·5 visits every 4 weeks while taking BJG398

·3 outpatient visit 4 weeks after the last dose of BJG398

In between NIH visits you will also need to have regular blood and urine tests done at a doctor's office or laboratory near your home.

Informed Consent (done at Screening Visit)

As part of the screening visit, one of the researchers will explain the study to you. If you are willing, you will be asked to sign this consent form. You will not be allowed to participate in any part of the study until you have signed and dated this form and received a copy of the signed and dated form.

Screening Visit

For the screening visit you will come to the NIH Clinical Center for 1-3 days for either an inpatient or outpatient visit. You and the investigator will determine which type of visit would be best for you. Once you have signed the consent form we will discuss your medical history and do tests to see if you qualify for the study. The tests and exams you can expect during this visit include:

·history and physical exam, heart rhythm test, blood and urine tests

·other tests may include a radiology studies to find the tumor if not done in the last 6 months.

If, after the testing, you qualify and agree to participate and would like to begin drug immediately, the evaluation at the screening visit may also serve as the baseline evaluation. If you decide that you do not want to start BGJ398 at the screening visit you will be asked to return to the NIH for the baseline admission scheduled within 6 weeks after the screening visit.

Baseline Visit

This inpatient visit at the NIH Clinical Center will last 5-7 days. During this visit, you will receive your first dose of BGJ398. After the first dose of BGJ398 is given you will have blood and urine collected every 2 - 4 hours for 24 hours. This is to monitor if there are changes in your body's minerals, such as calcium and phosphorus, after you have taken BGJ398.

Other procedures or tests done at this visit include: history and physical exam, blood and urine tests, questionnaires, Rehabilitation Medicine Consultation, and eye exam.

Follow-up Visits

You will come to the NIH for a follow-up visit every 4 weeks while you are taking BGJ398 for 24 weeks and also every 4 weeks when you are off BGJ398 for 12 weeks (total 36 weeks). The 24-week visit will last up to 7 days and may be done as inpatient or outpatient. At each visit we will perform blood and urine tests to make sure your BGJ398 dose is correct and to see if you are feeling better and/or having any side effects of the drug. We may also adjust your other medications or add medications based on the results of the blood and urine testing.

All tests and procedures performed at the baseline visit will be repeated at the follow-up visits as noted below in the Research Tests/Procedures section.

Research Tests/Procedures

This section describes the tests and procedures that will be done on this study. The section also clarifies at which visits they will be done.

1. **Medical History, Vital Signs and Physical Exam (each study visit)**. The study doctor will ask you about your health and check your vital signs including heart rate, blood pressure, temperature, and breathing rate. You will also have a physical exam and have your height and weight measured. This will take about 60-90 minutes.

2. **Blood tests (each study visit).** Blood will be drawn to check for response to the drug and side effects. We will also draw blood for research. Blood will be drawn through a needle in your arm. We will draw no more than 2 tablespoons of blood at any one time. You will be asked not to eat (fast) after midnight the night before these are done. The total blood drawn during most study visits is approximately 2 tablespoons. On most visit days, there will be only one blood draw per day. The most blood to be drawn will be during the Baseline Visit and the amount for this entire visit will be about 6 tablespoons.

3. **24-Hour Blood Sampling (baseline visit only)**. On the day you start taking BGJ398 you will have blood drawn every 2 hours over a 24-hour period. You may have up to 12 blood draws throughout the day. The amount of blood drawn over the 24-hour period will be about 3 tablespoons.

   An intravenous catheter (IV) will be placed for the purpose of painless blood draws through the day. For the IV, a needle will be used to guide a thin plastic tube (catheter) into one of your veins. The needle will be removed, leaving only the catheter in the vein. The catheter will be taped to the skin to hold it in place. Occasionally, there is trouble placing the IV and we may need to place a longer catheter called a PICC line, into one of your larger veins.

4. **Glucose tolerance test (baseline and 8-week visit only).** This is the same test that is sometimes used to see if a person has diabetes. This test will tell us how high your blood sugar and insulin levels go after you drink a standard glucose load. This drink tastes like very sweet soda. Very rarely, some people may feel nausea after they drink this. The test lasts two hours. We will take blood samples through the plastic tube described above in your arm.

5. **Urine Pregnancy Test (each study visit)**. Women who are able to become pregnant will have a urine sample collected for a pregnancy test at each study visit.

6. **Urine Collection (each study visit)** – you will be asked to provide a urine sample in a cup provided by NIH. This sample will be used to test your urine.

7. **24-hour Urine Collection (each study visit).** At every visit we will ask you to save and collect your urine for 24 hours. You will be given a special container to use to collect the urine. You will be able to carry the container around with you. When you are an inpatient at the NIH Clinical Center the container may be stored in the bathroom of your hospital room and a nurse will collect the urine throughout the day.

8. **2-hour Urine Collection (baseline visit only)** Urine samples will be collected every 2 hours for 24 hours starting after your first dose of BGJ398.

9. **Electrocardiogram (EKG) (screening visit and every 4-12 weeks as indicated while on BGJ398)** The EKG records the electrical activity of the heart. For the EKG, we will place small metal discs or sticky pads on your chest. You will be asked to lie still for a few minutes while the EKG is recorded. If you take certain other medicines that can cause heart rhythm changes, you will also need to get an EKG done by your local doctor within 7-10 days of increasing your dose of BGJ398 or the other medicine.
10. **Echocardiogram (baseline and 24-week visit)** This is an ultrasound to look for heart problems. For this test, you will need to lie on a table for about 15-30 minutes while a technician moves a wand over your chest to look at your heart.
11. **Kidney Ultrasound (baseline and 24-week visit)** To look for calcium deposits. For this test, you will need to lie on a table for about 15-30 minutes while a technician moves a wand over your back to look at your kidneys.
12. **Nuclear Medicine Tests** - These tests can help show sometimes very small tumors that cause TIO. One or more of these tests may be performed at the screening visit if they have not been done within 6 months of the screening visit.
13. **Questionnaires (screening, baseline, and follow-up visits).** You will be asked to answer questions for four surveys. One survey will ask you questions about your overall health and the others will ask you about your pain, mobility, and fatigue. These questionnaires may be completed on paper or on a computer. It should take you less than an hour to complete these questionnaires.
14. **Physical Therapy/Rehabilitation Medicine Evaluation (baseline, 24-week, and 36-week visits).** TIO can impact your activities of overall functioning. We will be looking at the activity of your upper and lower body for strength. A physical rehabilitation doctor will exam you and will ask you to perform several activities to test for strength. These will include asking you to sit and stand-up, grip a tool several times, and do a few other exercises using your arms and legs.
15. **6-Minute Walk Test. (baseline, 24-week, and 36-week visits)** You will be asked to complete a 6-minute walking test. For the walking test, you will be asked to walk back and forth on an indoor walking course. You will be asked to walk as briskly as is comfortable for you. The walk will continue for 6 minutes or until you are unable to continue. You will be monitored by a rehabilitation specialist throughout the test.
16. **Ophthalmology (eye) Exam (screening, monthly and as needed)**

    An exam of your eye and possibly a test to look at the inside of your eye may be done. This would be done at the NIH by a doctor that specializes in the evaluation and testing of eyes known as an ophthalmologist.

17. **BGJ398 Administration**

    The first dose of BGJ398 will be given to you when you are at NIH.

    BGJ398 comes in hard gelatin capsules which are to be swallowed whole, not chewed. You will need to take the capsule(s) each morning at the same time every day, 1 hour before or 2 hours after a meal. You should take it with a large glass of water and completely swallow it as quickly as possible.

18. Tests at Your Local Laboratory (every 2 weeks between NIH visits)

Between NIH visits you will be asked to go to your local laboratory for blood and urine tests every 2 weeks. You or your local laboratory will send the laboratory results to the NIH study staff. One of the study doctors will contact you to adjust your medications, if needed.

Extension of treatment with BGJ398

If you have responded well to BGJ398 during the study, but develop low phosphorus at any time after the 24 weeks of ending BGJ398 treatment, we may give you the option of restarting BGJ398. will continue to need tests at your local laboratory at least once every 4 weeks and will be seen at the NIH for the tests noted above at least once every 12 weeks. Continuing to take BGJ398 is voluntary. You may decide to stop participating in the study at any time and for any reason. You will not lose any benefits to which you are otherwise entitled. Investigators may also take you off of the drug when the study is closed or at any other time if they feel that it is in your best interest to do so or if you cannot follow the study requirements. If you become pregnant, do not respond well to BGJ398, or develop certain conditions then the study doctor will withdraw you from the study. The study doctor can tell you more about these conditions.

If you or the study doctor elects to discontinue the study medication you may be asked to return to the NIH for follow-up tests or exams to monitor you. You have the right to refuse these tests and exams.

Risks, Inconveniences and Discomforts

Some of the known risks and discomforts of the study drug and procedures are listed below. As with all studies, there may be risks or discomforts we don't know about.

Medical History and Exams/ Evaluations

There is little medical risk or discomfort from the following: medical history and physical exam including vital signs, height and weight, questionnaires, EKG, Physical Therapy/Rehabilitation Medicine exam and testing, Ophthalmology exam and testing.

Blood Tests

You may have discomfort and bruising at the site of the needle stick. There is a very small risk of fainting. Infection in the area of the needle stick is rare.

The risks of having an intravenous (IV) catheter line include bleeding, infection, or inflammation of the skin and vein with pain and swelling. If any of these occur they will be treated.

Having blood drawn every 2 hours at the baseline visit may be inconvenient to you and may disrupt your sleep.

Urine collections

Urine collections are an inconvenience but do not involve risk.

Nuclear Medicine Tests

Imaging tests may involve lying on a hard table for different lengths of time which may be uncomfortable and boring. These studies involve radiation, however, they are clinically necessary to evaluate your tumor(s). Radiation exposure will be kept as low as possible.

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.

BGJ398

BGJ398 has not been approved by the Food and Drug Administration (FDA). It is currently being studied in patients with kidney and gall bladder cancers. The most common side effects of the drug are constipation, decreased appetite, diarrhea, mouth and throat ulcers, nausea, fatigue, and hair loss. In some patients with different cancers treated with BGJ398, there was a decrease in heart muscle function that did not cause symptoms and went away when the drug was stopped. The known risks of taking BGJ398 for TIO are described below. There may be additional risks from taking BGJ398 that are not yet known.

Some patients developed eye problems when taking BGJ398. However, their eye condition returned to normal after the drug was temporarily stopped. Symptoms did not re-occur after the drug was restarted at a lower dose. On this study you will be closely monitored by an eye specialist. You will also have blood work checked every 2-4 weeks with frequent exams at NIH. The table below summarizes the more common side effects seen in patient who have taken BGJ398 in other studies.

Side Effects	Percent of patients with this side effect
Constipation	39.6%
Decreased Appetite	36.2%
Fatigue	34.3%
Mouth, lip ulcers	33.3%
Nausea	31.4%
Slight decrease in kidney function	28.5%
Diarrhea	27.5%
Hair Loss	26.1%
Dry Mouth	23.7%
Vomiting	20.8%
Anemia	20.3%
Skin and Nail Changes	55.2%
Eye Problems	~47%
Decrease in heart function	~20%
Abdominal Pain	~15%

Some people may not respond to BGJ398 therapy. In that case, we will increase the dose of BGJ398 to keep the phosphorous at the proper level. If the blood phosphorous levels do not become normal while you are on the highest tolerated dose of BGJ398, then the drug will be stopped and you will have to go back to taking standard treatment.

When it is time to stop BGJ398, we will put you back on phosphorous and calcitriol treatment to maintain normal blood levels. We will need to check your blood levels frequently at your local laboratory during that time. Some people need to take higher or lower doses of phosphorous and calcitriol than they did before joining the study while they are switching off of the BGJ398. We will monitor you for 12 weeks after BGJ398 is stopped to make sure that your phosphorous levels are stable off of the BGJ398 before we refer you back to your local primary care physician and/or Endocrinologist.

QED is the drug company that is supplying the NIH with BGJ398. They may be provided with samples or findings collected on this study, however, your personal information will be removed and they will not be able to link these findings to you. QED will not pay any money to you or your medical bills if you experience an injury while on this study.

Use of Stored Samples

Your blood and urine samples will be stored in secured freezers on the NIH campus. Your name and identifying information will not be on the samples; we will assign them a code. The key to the code will be kept in a separate, secure area.

Your sample may be used for other research projects, including those not related to TIO if you agree. The samples may be shared with researchers at NIH and outside of NIH. Please initial on the line below that reflects your choice:

_____ My samples may be used for other research projects including those not related to TIO.

_____ I do not want my samples used for other research projects. Please destroy my samples once this project is complete.

If you withdraw from this research project before it is complete, you may request that any remaining samples you have be discarded. Results obtained before you withdraw will be kept and your privacy will be protected.

The results from this study may appear in medical magazines, books or presented at medical conferences. No individual private information will be shared. Your research samples will not be sold to anyone. There is a chance that medical or lab products could be developed in the future. These products may help in finding the diagnosis or may be treatment of a medical condition. These products may be developed and patented based on our research. If this happens you will not be paid if a product, process or service is developed from the use of your samples.

Anticipated Benefits

The aim of this study is to see if your TIO disease is better managed on BGJ398 compared to the standard treatment of phosphorous and calcitriol. Because there is not much information about the drug's effect on TIO 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 TIO.

Right of Withdrawal and Conditions for Early Withdrawal

Participation in this research study is voluntary. You may decide to stop participating in the study at any time and for any reason. You will not lose any benefits to which you are otherwise entitled.

Investigators may also discontinue your participation in the study at any time without your permission, if they feel that it is in your best interest to do so or if you cannot comply with study requirements. If you become pregnant, do not respond well to BGJ398, or develop certain conditions then the study doctor will withdraw you from the study. The study doctor can tell you more about these conditions.

If you or the study doctor elects to discontinue the study medication you may be asked to return to the NIH for follow-up tests or exams to monitor you. You have the right to refuse these tests and exams.

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 QED and its authorized agents. If you withdraw your consent and leave the trial, any samples of yours that have been obtained for the study and stored at NIH 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.

Results from This Study

You will be informed of any new findings that develop during this study that might affect your willingness to continue to participate. You will be informed of any new information about TIO that might affect your health.

Study Termination

If the study is stopped early, you will not continue to receive BGJ398 from the NIH. The study may be stopped early for several reasons, including subject safety.

Alternatives to Participation or Treatment

You do not have to be in this study to get treatment for your TIO. If you do not participate in this study you have the following options:

- Getting treatment or care for TIO without being in a study. The standard treatment is oral phosphorous and calcitriol. You may receive this standard treatment from doctors who treat patients with TIO.
- You may also be eligible for participation in other clinical trials that are evaluating other treatments.

Compensation and Travel Costs

You will not be paid to participate in this study. However, 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. Travel/subsistence expenses and research-related co-pays will be reimbursed. This is based on to the NIH policy established January 5, 2009.

Posting of Research Results on www.ClinicalTrials.gov

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.

Conflicts of Interest

The National Institutes of Health reviews NIH staff researchers at least yearly for conflicts of interest. The following link contains details on this process: https://ethics.od.nih.gov/procedures.htm#protocol. You may ask your research team for additional information or a copy of the Protocol Review Guide.

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, Rachel I. Gafni, MD, Building 30, Room 228, Telephone: 301-594-9924. You may also call the Clinical Center Patient Representative at (301) 496-2626.

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 FEBRUARY 11, 2019 THROUGH MARCH 11, 2020.

Signature of Investigator _____ Date _____ Signature of Witness _____ Date _____

Print Name _____ Print Name _____