INSTITUTE: National Cancer Institute

STUDY NUMBER: 03-C-0304 PRINCIPAL INVESTIGATOR: Wyndham H. Wilson, M.D., Ph.D.

STUDY TITLE: Pilot Trial of Alemtuzumab and Dose-Adjusted Epoch in Chemotherapy Naïve Aggressive T and NK-Cell Lymphomas

Continuing Review Approved by the IRB 05/20/20
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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.

Description of Research Study

Lymphoma and its treatment: You/your child have a disease called T-cell or NK cell non-Hodgkin's lymphoma which your/your child's doctors think would be better treated with chemotherapy than surgery or radiation. For your/your child's particular kind of non-Hodgkin's lymphoma, previous studies have shown that combinations of drugs are much more likely to make the disease go away for appreciable periods of time than single drugs, which have only very limited effectiveness against this group of lymphomas. Studies have also shown that more

intensive (i.e. higher dose) treatments have a greater chance of success than more gentle approaches. In general, mature T-cell and NK cell lymphomas are less responsive to standard therapies than B-cell lymphomas. This protocol is specifically for people with T-cell and NK cell lymphomas, as we are trying to find better treatments for these types of lymphoma. Studies conducted at the National Cancer Institute suggest that certain chemotherapy drugs may be more effective if given by continuous infusion into the vein rather than by the standard method of rapid intravenous injection. One such combination, which we call EPOCH (each letter stands for one of the drugs used in the combination), seems to have a high degree of effectiveness in patients whose tumors have stopped responding to standard regimens. We therefore plan to test this combination in patients who have never received chemotherapy previously. Recent evidence also indicates that the effects of chemotherapy may be improved by combination with monoclonal antibodies. Monoclonal antibodies are purified proteins that are specially made to attach to pieces of foreign substances (such as cancer cells) with the goal of inactivating them. A monoclonal antibody, a drug called Alemtuzumab (the trade name is Campath-1H), has been manufactured to attach to a protein called CD52 that your/your child's type of tumor could contain. We will attempt to determine if your/your child's tumor "expresses" CD52, but you/your child will be eligible for treatment even if the results are unknown. Up to 30 patients will be treated on this study.

Objectives and design of this study:

The general purpose of this study is to develop treatments for lymphoma that are more effective than existing therapies. The experimental part of this treatment program is to test whether giving alemtuzumab in combination with continuous infusion EPOCH chemotherapy with filgrastim is safe and if it improves the outcome of therapy of your/your child's lymphoma. In this study five chemotherapy drugs are given together in an intensive combination called EPOCH. Each series of treatments is called a cycle; a cycle is repeated every three weeks and drugs are administered during the first five days of every cycle. EPOCH consists of prednisone by mouth on days 1-5, and etoposide, doxorubicin, and vincristine as a continuous infusion on days 1 through 5 (total of 96 hours). In addition, cyclophosphamide is given by intravenous injection over about 15 minutes on day 5. You/your child will also receive a dose of alemtuzumab on day 1, immediately before the chemotherapy begins. Each cycle lasts 3 weeks: 5 days of chemotherapy followed by 16 days of no chemotherapy. You/your child will receive repeated cycles of Alemtuzumab and EPOCH until remission (disappearance of tumor) is achieved or until the tumor shows no further evidence of shrinkage. Between cycles of treatment we give another drug, filgrastim, whose purpose is to help your/your child's normal bone marrow cells recover from the chemotherapy and produce normal white cells. The use of filgrastim in this way may help us increase the total amount of chemotherapy you/your child can receive.

Treatment consists of the following drugs:

1. Doxorubicin, etoposide, and vincristine - These three drugs are given by continuous IV infusion over four days, beginning on day 1 and ending on day 5 of each cycle. We deliver these drugs with the aid of one lightweight, portable infusion pump, each about the size of a portable tape recorder; this permits treatment on an outpatient basis. The

pumps deliver the therapy through an intravenous catheter, which is placed in your/your child's vein beforehand. You/your child will be taught about the use and care of the pump and what to do if it stops working.

2. Cyclophosphamide - This is given over about 15 minutes on day 5 of each treatment cycle.

3. Prednisone - These are pills given by mouth twice a day for the first 5 days of every cycle.

4. Alemtuzumab – Administered by vein over approximately twelve hours on the first day of therapy, immediately before the chemotherapy infusion begins.

5. Filgrastim - This is given by injection under the skin once a day starting on day 6 of each cycle and continuing until recovery of the white blood cell count or until day 19 of each cycle. If your/your child's white blood cell count is still very low on the day treatment is due to begin again, the chemotherapy may be deferred and the filgrastim will be given until you/your child have a fuller recovery of the white count. This drug is given to stimulate your/your child's bone marrow to produce neutrophils, one of your/your child's white blood cells. You/your child will be taught how to administer the filgrastim to yourself/your child during the first treatment cycle.

We expect that treatment will be given for 6 cycles (18 weeks), depending on how you/your child's respond to the therapy. In general you/your child will receive two cycles past the point of maximum response. Since several of these drugs can lower your/your child's resistance to infection, we also require that you/your child take a combination antibiotic, trimethoprim/sulfamethoxazole (SeptraR or BactrimR) for three days each week while you/your child are on chemotherapy, acyclovir (or an alternative drug) daily and fluconazole in an attempt to prevent infections. If allergic to these preparations, you/your child will be given other drugs with similar activities in their place.

What happens after treatment is completed:

This depends on how you/your child have responded to the therapy. If all evidence of disease has disappeared, we will schedule periodic visits to the Clinical Center for follow-up examination and tests. If the disease gets worse while receiving therapy, does not disappear entirely or if it should recur after having disappeared for a period of time, then you/your child may need further therapy. At that time you/your child will be given the opportunity of participating in additional research protocols that may be appropriate for you/your child. If no such protocols are available, you/your child will be returned to the care of your/your child's local physician. It is important to stress that participation in this protocol does not constitute a promise of long-term medical care here at the Clinical Center. It is conceivable that participation in this study may make you/your child ineligible to participate in certain other research protocols because the requirements for entry onto these protocols may not allow patients who have already been treated with certain drugs or who have had certain side effects from previous treatment.

You/your child may decide now not to receive treatment on this protocol, or you/your child may choose at any point in time to stop the treatment and withdraw from the protocol; in either case you/your child will be returned to the care of your/your child's referring physician.

Treatment of disease in the nervous system:

It occasionally happens that lymphomas spread to the coverings of the brain (the meninges) at some point during the illness. We will test to see whether there is any evidence of lymphoma in your brain or spinal fluid before you receive any treatment. If this should happen, the treatment usually includes the instillation of one of two chemotherapy drugs (methotrexate and cytarabine) directly into the fluid (the cerebrospinal fluid, or CSF) surrounding the brain. This is usually done by first placing a small reservoir (an Ommaya reservoir) under the skin of the scalp; this reservoir is connected to a catheter that is placed through the brain itself into the fluid. This procedure is performed by a neurosurgeon under general anesthesia. These drugs may also be administered through a spinal tap (also called a lumbar puncture). Depending on how you/your child responds to this therapy, it may be necessary to modify it and to also administer radiation to your/your child's brain and spinal cord. Each of these therapies will be discussed with you/your child if they are needed. Patients who have lymphoma in their bone marrow are at higher risk of developing lymphoma in the brain areas. To reduce this risk, patients at higher risk will receive methotrexate by a spinal tap on days 1 and 5 of cycles 3-6 of their EPOCH chemotherapy. Your/your child's treating physicians will discuss this with you/your child.

Risks or Discomforts of Participation

In order to determine whether this study is suitable for you/your child, a number of tests will have to be done. This period of evaluation may take up to two weeks and is usually done on an outpatient basis. Depending on the tests you/your child have already had before coming here, these may include blood and urine tests, studies of lung function, CAT or MRI scans, radioisotope scans, and biopsies of tumor tissue, bone marrow, liver, or other sites. As reviewed in the section above, you will undergo a lumbar puncture to remove a small amount of spinal fluid (about 1-2 teaspoons) that will be tested for the presence of lymphoma cells. A lumbar puncture is done by inserting a small sterile needle through the skin and muscle, going between the bones of the spine in the lower back until the needle punctures the spinal canal covering. The spinal fluid will then drain out through the needle on its own.

Biopsies will, when possible, be done under local anesthesia. The risks associated with blood draws include pain, blood clots, bruises, infection and nerve damage. The risks associated with bone marrow biopsies include pain, bleeding, and infection. Risks of biopsies include pain, bleeding, infection, and the risks to the particular area undergoing surgery. General anesthesia itself is generally very safe but has a very small risk of major complications such as heart attack or stroke. The surgical and anesthetic risks will be explained to you/your child in more detail at the time of surgery, if this is needed.

In order to receive this therapy you/your child will need to have an intravenous catheter placed. This catheter is usually placed in the arm, chest or neck area into a major vein inside your/your child's chest. We usually remove the catheter after each cycle but on occasion it can be left in for several cycles. The catheter is necessary for infusion of chemotherapy and for the drawing of blood. It is usually inserted under local anesthesia. The risks associated with the procedure include pain, bleeding, infection, and puncture of the underlying lung. Lung puncture can result in lung collapse, which might require that a chest tube be placed into the chest cavity (usually for a day or two) to help the lung reinflate. The long-term risks of the catheter include infection and clotting of the vein in which the catheter sits. If these occur, it may be necessary to remove the catheter. These risks will be explained to you/your child in more detail at the time of the insertion.

Side effects that have been observed with the drugs in this program when they are used individually include the following:

a. Doxorubicin may cause sore mouth, loss of hair, a fall in blood counts with increased risk of serious infection or bleeding, tissue damage if the drug contacts the skin, heart damage and, rarely, death due to heart failure. However, the infusion method used in this study has been shown to reduce the risk of heart damage compared to the standard rapid infusion method.

b. Cyclophosphamide may cause a fall in blood counts with increased risk of serious infection or bleeding, loss of hair, damage to the lining of the urinary bladder with painful and bloody urination, loss of function of the ovaries or testes, and nausea and vomiting. The bladder irritation can be minimized by drinking at least two quarts of fluid each day. Fluid retention with lowering of blood salt levels (known as SIADH) can rarely occur.

c. Vincristine often causes numbness of the hands and feet after several cycles. Patients also may have constipation and medications will be given to reduce this. In most instances, these symptoms resolve when the drug is stopped, but resolution of the numbness in the hands and feet may sometimes take months or even years. The drug can also cause tissue damage if it contacts the skin, low or high blood pressure, frequent or burning on urination, weight loss, rash, fever, headache, jaw pain and eye problems. Fluid retention with lowering of blood salt levels (known as SIADH) can rarely occur.

d. Etoposide may cause nausea and vomiting, diarrhea, loss of hair, lowering of blood pressure during administration, rash, itching, liver abnormalities, allergic reactions, mouth ulcers, and lowering of blood counts.

e. Alemtuzumab has a spectrum of side effects that can be divided into infusional reactions, immune suppression, bone marrow toxicity, and other side effects. These reactions are detailed below.

Acute infusion reactions

Some patients have reactions during the first few treatments that do not occur with later infusions of Alemtuzumab. The administration of Alemtuzumab can cause allergic reactions which may appear as shortness of breath or wheezing. If the shortness of breath becomes severe, you/your child may be required to have a tube placed in your/your child's throat to help you/your child breath. Other types of allergic-like possibilities include severe lowering of blood pressure, fever, chills, rash, hives, itching, or abdominal pain and throat swelling. Lowering of the blood pressure may cause damage to the heart or brain and this damage may be permanent. These reactions can be severe and some patients have died as a result of such reactions. You/your child will be given acetaminophen and diphenhydramine to reduce the severity of these side effects. Your/your child's doctors or nurses will closely monitor you/your child closely throughout the treatment for these side effects.

Immune suppression

The normal cells that fight infection in your/your child's body are killed by this treatment. Without these cells you/your child may develop infections that occur in patients whose immune system does not function. Patients treated with this drug can develop infection with viruses, fungi, parasites and bacteria. You/your child will be treated with oral medications to prevent certain infections and they will be continued until your/your child's doctors have determined that it is safe to discontinue them.

Bone marrow toxicities

Many patients have had low blood counts when Alemtuzumab is given at the doses used in this trial. These effects are even more severe when Alemtuzumab is given to patients with bone marrow abnormalities. Anemia or a low red blood cell count, which causes weakness or fatigue has occurred and may require blood transfusion. Low platelet counts, which may cause a tendency to bleed, may require platelet transfusions and low white blood cell counts may make you/your child susceptible to infection. If the infection fighting white blood cells fall to low levels we may give you/your child G-CSF to stimulate the production of these cells. Occasional patients have had severe depression of all of the normal blood elements, a condition called aplasia.

Miscellaneous toxicities

Other common side effects include loss of appetite, nausea, vomiting, fatigue, headache, diarrhea, muscle or joint pain, ringing in the ears, difficulty with thinking, and damage to the liver. Blood pressure has been seen to increase following administration of Alemtuzumab and may require treatment. Your/your child body may react to the Alemtuzumab by making antibodies to it. These antibodies may rapidly inactivate the injected Alemtuzumab making it ineffective. Infections caused by organisms that normally inhabit your/your child body and cause no disease may become evident as a result of the treatment with Alemtuzumab. You/your child

may also be more susceptible to viral and bacterial infection. In addition the combination of Alemtuzumab and EPOCH chemotherapy may produce toxicities that are unknown.

f. Prednisone may cause ulceration in the stomach or bowel, increased blood pressure, high blood sugar (diabetes), increased risk of infection, a round appearance of your/your child's face, weight gain, change in mood, thinning of your/your child's bones with increase in the risk of fracture, increased pressure in the eye (known as glaucoma) and clouding of the eye (called cataracts). It can also cause or worsen acne.

g. Filgrastim can occasionally cause bone pain by stimulating normal bone marrow. This stops when drug administration stops. It has also been reported sometimes to cause skin rash, skin reddening around the injection site, muscle cramps, decreased platelets (not clinically significant), pain or numbness and tingling around the chin, worsening of certain pre-existing inflammatory conditions (such as psoriasis eczema, or vasculitis), fever, body aches, and alterations in certain laboratory tests. With prolonged administration filgrastim has been associated with hair thinning and enlargement of the spleen. These side effects do not necessarily stop when drug treatment stops.

h. Trimethoprim/sulfamethoxazole can cause a skin rash that goes away when the drug is stopped. It is possible that the rash may not resolve and could indicate a severe reaction (i.e. Stevens-Johnson syndrome). If you/your child are allergic to this drug, you/your child will receive inhaled pentamidine instead. Inhaled pentamidine can cause coughing, wheezing, and burning pain in the throat. All of these symptoms usually go away shortly after the inhalation treatment is finished

i. Acyclovir can cause nausea/vomiting, diarrhea, headache, vertigo, insomina, irritability, depression, skin rash, acne. accelerated hair loss, arthralgia, fever, palpitations, sore throat, muscle cramps, menstrual abnormalities, and lymphadenopathy.

j. Fluconazole can cause nausea. Less common side effects may include: Abdominal pain, diarrhea, headache, skin rash, vomiting and elevated liver enzymes.

k. Methotrexate, when administered into the spinal fluid, may cause low blood counts and ulcerations in the mouth, stomach, and intestines. It can cause acute headache, back pain, stiff neck, and /or fever; it can also cause weakness or paralysis of certain muscles. It can cause seizures and coma. Other side effects it can cause are usually associated with intravenous administration rather than intrathecal (lumbar puncture administration), but these include liver function abnormalities, inflammation and scarring of the lungs, inflammation of the tissue covering the heart, and severe skin reactions.

l. Cytarabine given by lumber puncture can cause nausea, vomiting, fever, and headaches. Rarely, it can cause weakness and seizures. When given into the spinal fluid, it does not usually cause systemic toxicity, but we will monitor you/your child for low blood counts, and liver function abnormalities, which can occur with cytarabine when given by vein.

It is important to emphasize that when you/your child have a decreased white blood cell count, you/your child are at risk of infection. Such infections can be very serious and can even cause death if not quickly and properly treated. Therefore, if you/your child have a temperature greater than 38.3° C (101° F), you/your child must call your doctor immediately. Chemotherapy may also cause your platelets to fall; since platelets are the blood elements that permit blood to clot, this may place you/your child at increased risk of serious bleeding. It may be necessary to give you/your child transfusions of platelets if your/your child's platelet counts reach very low levels. You/your child may also need red blood cell transfusions if your/your child's hemoglobin level drops very low. There is a small chance that damage to the normal bone marrow may eventually result in bone marrow failure, leading to a serious shortage of one or more kinds of cells in the blood, or to leukemia. Because this is a relatively new combination of drugs, it is always possible that unanticipated side effects may occur.

Many of the drugs used in this treatment program are toxic to the cells in the ovary and testicle and may produce sterility. Recovery of normal fertility is not well studied although we know that some patients treated with this combination have remained fertile after the therapy has been completed. For this reason, men who are about to receive this treatment should, if they wish to have children in the future, consider sperm banking before start of the treatment. These drugs may also be very toxic to an unborn child. Therefore, adequate birth control measures (such as the contraceptive pill, condoms, diaphragm with contraceptive foam or ointment, contraceptive sponge, etc.) should be used by participants or their sexual partners while receiving treatment on this study. Women of childbearing age will have a pregnancy test, which must be negative at the time of study entry. This test requires that blood be drawn from a vein one or two days prior to the study. The results of the pregnancy test will be made available to you/your child prior to the initiation of the study. Your/your child's physicians will watch you/your child closely for side effects and will stop treatment if any side effects become a serious threat to your/your child's life or well-being. Your/your child's physicians will also stop the treatments if it becomes clear that the treatment is not successfully controlling your/your child's disease. Complications of Ommaya insertion are uncommon when done by an experienced group but could include infection and bleeding at the operative site or in the brain itself. Complications of lumbar puncture may include pain or bleeding at the site of needle insertion (the low back), infection, and headache. Most patients tolerate this treatment without serious side effects, although drugs placed into the brain fluid (CSF) may cause headache, stiff neck, and confusion that resolve when they are stopped. With long-term treatment, confusion and a slowing of thought processes may occur. If this treatment becomes necessary for you/your child, the complications of the lumbar puncture or Ommaya insertion and methotrexate instillation will be discussed in more detail.

Potential Benefits of Participation

It is likely that most patients will have at least a temporary improvement from treatment with Alemtuzumab and EPOCH chemotherapy. However, we cannot be certain if you/your child will

be cured of your/your child's lymphoma and it is possible that you/your child may not respond to treatment.

Alternative Approaches or Treatments

It should be emphasized that we do not know at this point whether the combination of drugs we propose to give you/your child is superior, inferior, or equivalent to standard combination chemotherapy for your/your child's disease. Alternative procedures that could be used to treat your/your child's disease include:

1. Other combination drug regimens and other schedules of the same drugs used in this study. For example, a chemotherapy called CHOP given in the conventional manner would be suitable standard therapy for your/your child's condition.

2. Treatment with single drugs. This is known to produce brief responses of a few months' duration in many patients but to have little beneficial effect in long-term control of the disease.

3. Radiation (X-ray) treatments. This can stop tumor growth in particular locations, such as bone, abdomen, and other sites but is not successful in controlling the disease overall unless the disease is very localized at the start of therapy.

4. Surgery. As with radiation, surgery can be successful in removing tumor from particular locations but cannot be used successfully to remove all lymphoma cells from the body, since the disease is almost always present in multiple locations. Also, surgery cannot be used against tumor in some of the organs most commonly involved by lymphoma, such as the liver or the lungs.

5. Waiting, without active therapy. Although a period of watchful waiting is appropriate treatment for some kinds of tumors, in lymphomas similar to yours/your child's, the disease will often grow and spread rapidly if no treatment is administered.

6. No treatment. You/your child can choose not to receive any therapy for your/your child's lymphoma. In this case, your/your child's doctor can give you/your child's medications that will make you/your child feel comfortable.

Research Subject's Rights

What are the costs of taking part in this study?

- 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.
- National Cancer Institute Institutional Review Board

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.

Certificate of Confidentiality

To help us protect your privacy, we have obtained a Certificate of Confidentiality. The researchers can use this Certificate to legally refuse to disclose information that may identify you in any federal, state, or local civil, criminal, administrative, legislative, or other proceedings, for example, if there is a court subpoena. The researchers will use the Certificate to resist any demands for information that would identify you, except as explained below.

You should also know that there are several circumstances in which the Certificate does not provide coverage. These include when information:

- will be used for auditing or program evaluation internally by the NIH; or
- must be disclosed to meet the legal requirements of the federal Food and Drug Administration (FDA).
- is necessary for your medical treatment and you have consented to this disclosure;
- is for other research.

In addition, identifiable, sensitive information protected by this Certificate cannot be admissible as evidence or used for any purpose in any action, suit, or proceeding without your consent.

You should understand that a Certificate of Confidentiality does not prevent you or a member of your family from voluntarily releasing information about yourself or your involvement in this

research. If an insurer, employer, or other person obtains your written consent to receive research information, then the researchers will not use the Certificate to withhold that information.

The Certificate of Confidentiality will not protect against the required reporting by hospital staff of information on suspected child abuse, reportable communicable diseases, and/or possible threat of harm to self or others.

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.

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 Wyndham H. Wilson, M.D., Ph.D.; Building 10, Room 4N115, Telephone: 240-760-6092. 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 20, 2020 THROUGH MAY 19, 2021.

Signature of Investigator | Date | Signature of Witness | Date

Print Name | Print Name