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AS MODIFIED
Aug 05, 2013
WIRB®

RESEARCH SUBJECT INFORMATION AND CONSENT FORM

TITLE:	A Feasibility Trial using Molecular-Guided Therapy for the Treatment of Patients with Relapsed and Refractory Childhood Cancer
PROTOCOL NO.:	NMTRC 008 WIRB® Protocol #20121776
SPONSOR:	Giselle Sholler, M.D.
INVESTIGATOR:	Name Address City, State Zip Country
SITE(S):	Name Address City, State Zip Country
STUDY-RELATED PHONE NUMBER(S):	Name Telephone

In this consent form, "you" always refer to the subject. If you are a legally authorized representative, parent or guardian, please remember that "you" refers to the study subject.

This study is a clinical trial (a research study involving subjects). Research studies include only subjects who choose to take part. Your participation in this study is entirely voluntary. Please read the consent form carefully. This consent form may contain words that you do not understand. Please ask the study doctor or study staff to explain any words or information that you do not clearly understand. You will be given a copy of it to keep if you decide to participate in this study. You will be given a copy of this consent form to take home and you may discuss your decision with your friends and family if you would like.

You are being invited to participate in this study because you have recurrent or unresponsive neuroblastoma, brain, or rare tumor that cannot be cured by any other known treatment.

WHY IS THIS STUDY BEING DONE?

You are being invited to participate in a research study conducted by the Neuroblastoma and Medulloblastoma Translational Research Consortium (NMTRC). The NMTRC is a collaboration of academic medical centers and other organizations around the country. Helen DeVos Children's Hospital, a member of Spectrum Health Hospitals, serves as the lead organization of the NMTRC.

The purpose of this study is to test the feasibility (ability to be done) of an experimental test to help plan your cancer treatment. This study plan is not studying the effectiveness of the proposed combinations of therapy for your cancer that you may receive after the experimental testing.

This study will look at experimental technologies to determine a tumor's molecular makeup (gene expression profile) and mutations. This technology called the "Pediatric Gene Analysis Platform" includes the "OncInsights" report (a gene expression profile) and a DNA Mutation Panel Report (generated by the NMTRC) that are being used to discover new ways to understand cancers and potentially predict the best treatments for patients with cancer in the future. The experimental technology has not been approved by the U.S. Food and Drug Administration.

This study is for research purposes only. If you agree to participate in this study, a current specimen obtained from your tumor during a regular (standard of care) surgical biopsy or bone marrow procedure will be sent to the Clinical Research Laboratory, Spectrum Health Molecular Diagnostics department, the Sholler/NMTRC laboratory at Spectrum Health, and to the Translational Genomics Research Institute (TGen). Researchers will attempt to identify the molecular makeup within the specimen, as well as in your blood and bone marrow samples (optional). This additional testing is different than the routine tests currently performed at the hospital for the evaluation of cancer. If we are unable to obtain enough tumor cells for molecular makeup identification you will be unable to continue in the study.

After your tumor has been analyzed, the researchers will use your tumor's genetic information and the OncInsights research technology to generate a report. The report will provide information that predicts which drugs your specific tumor may be most sensitive to. Your personalized research report will be reviewed by a committee made up of at least three oncologists and one pharmacist to decide which combination of drugs might work best against your tumor (the "treatment recommendation board"), and they will recommend a personalized research treatment plan for you. Your referring/primary oncologist will be invited to attend the treatment recommendation board meeting. After the board creates your recommended treatment plan, your study doctor will review this plan and any other possible standard treatment options with you (and your referring/primary oncologist, if applicable) before starting any treatment.

The goals of this part of the study are:

- To determine feasibility (ability to be done) and safety of using tumor samples and the experimental technology to guide therapy decisions in relapsed and refractory neuroblastoma, brain tumor, and rare tumor subjects.

- To determine if our treatment recommendation board (at minimum a panel of 3 oncologists and 1 pharmacist) can use your bone marrow or tumor samples to make real-time treatment recommendations using your specific genetic information and predicted therapies identified in your personalized genetic report.
- To deliver therapy based on molecular guided predictions.
- To determine the activity of treatments chosen based on:
  - How each subject responds to treatment
  - How long a subject lives without their disease progressing

HOW MANY SUBJECTS WILL TAKE PART IN THE STUDY?

We plan to enroll approximately 53-59 subjects in this study nationwide over the next year.

WHAT WILL HAPPEN IF I TAKE PART IN THIS RESEARCH STUDY?

You will undergo a number of standard tests and research-related tests, and then you will undergo treatment for your tumor. You will need to have the following exams, tests and procedures to find out if you can be in the study. Depending on the results of these studies, they may show that you are not eligible to take part in this study. Most of these exams, tests and procedures are part of regular cancer care and may be done even if you do not join the study. If you have had some of them recently, they may not need to be repeated. This will be up to your study doctor.

- Medical history
- Physical exam
- Vital signs (blood pressure, pulse, temperature)
- Blood tests
- Urine tests
- MRI (use of a magnetic field to produce an image) or CT scan (test that produces a picture of your body using radiation) of the tumor(s)
- Any other imaging studies or tests deemed necessary for assessing your tumor by your treating physician

Additional Tests for Neuroblastoma Subjects

- MIBG scan (unless your tumor is pre-determined to not show up on an MIBG scan) or PET scan (An MIBG scan involves injecting a radioisotope into the blood on the first day, and then scanning the whole body on the second day to see where the isotope was absorbed)

Additional Tests for Neuroblastoma Subjects and any Subject with suspected Bone Marrow Disease Involvement:

- Bone marrow examination (this involves using a needle to extract a small amount of your bone marrow from both of your hips usually under anesthesia)

You will need these tests and procedures that are being tested in this study.

- Analysis of your tumor sample and generation of a personalized genetic report
- Review of personalized genetic report with the study doctor
- If you are eligible, you will then be offered and placed on a treatment plan for the entire study.

As a part of your regular (standard of care) treatment you may have a surgical operation to remove as much of the tumor as possible. You will be asked by the pediatric surgeon to sign a separate consent form at the time of that surgery, which will review the risks and benefits of that surgical procedure. If tumor is obtained by surgery, you will be asked if some of the tumor can be saved for special research testing. There is a separate consent section for this at the end of this consent form.

Study Plan:

If the exams, tests and procedures show that you can be in the study, and you choose to take part, a portion of your tumor tissue (either bone marrow biopsy or tissue) will be sent to the Clinical Reference Laboratory and to Spectrum Health Molecular Diagnostics for testing. This testing will generate two personalized genetic reports. The personalized genetic reports will provide information that predicts which of the drugs your specific tumor may be most sensitive to. These reports will be used by the treatment recommendation board to recommend a specific treatment plan for your tumor. Your treating physician will know these recommendations when planning your treatment. Some of the factors that will be taken into account in choosing your treatment may include the safety, mechanism (how the drug works), availability, and cost of the drugs predicted. Once you have completed the pre-study procedures and the Treatment Decision Board has made a treatment recommendation based on the testing results obtained from a portion of your tumor tissue (either bone marrow or tissue), you will be asked to begin a treatment.

Please read the section regarding drug risks for important information relating to this study.

One of the major goals of this study is to identify biologic treatment targets unique to your individual tumor. Therefore the specific treatment plan developed may recommend drugs or combinations of drugs with which there is little or no prior experience in children.

There will be specific testing done while you are on study to monitor your progress and health.

You may participate in this part of the study without agreeing to specific treatment therapy. Deciding not to be in the study or leaving the study will not result in any penalty or loss of benefits to which you are entitled.

You will need tests and procedures that are part of regular cancer care. They may be done more often because you are in this study.

Testing Requirements for Study:

Procedure	Pre-Study	Cycle 1 Day 1	Cycle 1 Day 8	Cycle 1 Day 15	Cycle 1 Day 22 (if applicable)	Subsequent Cycles Day 1	Off Therapy
Informed consent	X						
Medical history	X						
Physical exam	X	X		X		X	X
Vital signs	X	X		X		X	X
Height	X						X
Weight	X	X				X	X
Blood Tests	X	X	X	X	X	X	X
Urine Tests	X	X				X	X
surgical resection &/or diagnostic biopsy	X						
MRI or CT	X	Radiologic measurements will be performed after Cycle 2 and then should be performed every 8 weeks or every other cycle (whichever occurs first)					
MIBG	X						
Bone Marrow (for neuroblastoma and any subject with suspected BM disease)	X	Should be repeated after Cycle 2 and then should be performed every 8 weeks or every other cycle (whichever occurs first) if positive at study entry					
B-HCG (pregnancy test)	X						
EKG (as indicated)	X						

All required scans (MIBG's and MRI/CT's) must be done at your study institution unless otherwise approved by the sponsor.

HOW LONG WILL I BE IN THE STUDY?

As a subject in this study you will remain in this study for as long as you have no disease progression or until you need to come off study.

WHAT SIDE EFFECTS OR RISKS CAN I EXPECT FROM BEING IN THE STUDY?

Drug Risks:
All people who receive cancer treatment are at risk of having side effects. In addition to killing tumor cells, cancer chemotherapy can damage normal tissue and produce side effects. Side effects are usually reversible when the medication is stopped but occasionally persist and cause serious complications. A person can die from these and other complications.

Common side effects include nausea, vomiting, hair loss, and fatigue. Drugs may be given to prevent or decrease nausea and vomiting. Hair loss is usually temporary, but on very rare occasions it may be permanent. Some chemotherapy may lead to sterility. Sterility is the inability to have children. There is also the possibility that a second cancer may develop years later as a result of the chemotherapy.

The most common serious side effect from cancer treatment is lowering of the number of blood cells resulting in anemia, increased chance of infection, and bleeding tendency.

There also may be other side effects that we cannot predict.

There is a risk that the treatment plan will not get rid of the cancer for as long as possible or that the cancer can go away after the treatment and then come back at a later date.

You may be prescribed drugs in a combination that has not been used before or has limited use together. Side effects can be increased when chemotherapy drugs are combined. Information about how these drugs may interact could be based on theoretical knowledge that may not have been tested before. There may be unknown interactions of using these drugs together. These drug combinations may have serious side effects that we may not know about which could occur immediately or at a later time after you have stopped taking the medication. Your study doctor will discuss this with you at the time of your treatment decision.

If you do have side effects, we may recommend medicine or treatments to try to control them and make you comfortable.

You should talk to your study doctor about any side effects that you have while taking part in the study.

Device Risks:
The "Pediatric Gene Target Analysis Platform" test is an investigational test (not FDA-approved) that will be used to select a drug or combination of drugs for your treatment, based on the molecular makeup of your tumor. No test is perfectly accurate and there is a risk that results from this test may incorrectly identify/fail to identify the molecular makeup of your tumor. An incorrect test result (indicating that your tumor has a particular molecular makeup, when it does not) could result in your receiving a study drug, or combination of drugs that may have no benefit to you, and which may have side effects and cause harm.

Bone marrow examination risks:
The test may be painful. There is also a small risk of infection or bleeding. The pain normally lessens within minutes to hours.

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

Reproductive Risks:
Because the drugs in this study can affect an unborn baby, you should not become pregnant or father a baby while on this study. You should not nurse your baby while on this study. Both men and women should use one of the more effective birth control methods during treatment and for six months after treatment is stopped. These methods include

- total abstinence (no sex),
- oral contraceptives ("the pill"),
- an intrauterine device (IUD),
- levonorgestrol implants (Norplant), or
- medroxyprogesterone acetate injections (Depo-provera shots).

If one of these cannot be used, contraceptive foam with a condom is recommended.

A possible effect of this study is the possibility of sterility (inability to have children).

The doctor must be notified if pregnancy occurs during the course of the study.

WHAT IF THERE ARE NEW FINDINGS?

We will tell you if we learn any new information that may affect your health, welfare, or decision to stay in this study. You may be asked to sign a revised consent form if this occurs.

ARE THERE BENEFITS TO TAKING PART IN THE STUDY?

Because there is not much information about molecular guided therapy in your tumor type, we do not know if you will experience personal benefit from taking part in this study. Information learned from this study may help future children with cancer.

WHAT ARE THE COSTS OF TAKING PART IN THIS STUDY?

Taking part in this study may lead to added costs to you or your insurance company. You will be charged for the standard medical treatment you receive while in this study.

You will not have to pay for the tumor sample testing done at the Clinical Reference Laboratory, Spectrum Health, TGen, or at the Sholler/NMTRC laboratory at Spectrum Health.

You will not have to pay for the review conducted by the treatment recommendation board.

Please ask to speak to a financial counselor if you have any questions about the costs of being in this study.

- For more information on clinical studies and insurance coverage, you can visit the National Cancer Institute's Web site at
- http://cancer.gov/clinicaltrials/understanding/insurance-coverage You can print a copy of the "Clinical Trials and Insurance Coverage" information from this Web site. Another way to get the information is to call 1-800-4-CANCER (1-800-422-6237) and ask them to send you a free copy.

WILL YOU BE PAID FOR TAKING PART IN THIS STUDY?

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

WHAT OTHER CHOICES DO I HAVE IF I DO NOT TAKE PART IN THIS STUDY?

This is not a treatment study. Your other choice is to not be in this study and to receive your cancer treatment in the usual way.

Please discuss your options with your study doctor as well as other trusted persons or family members.

WILL MY MEDICAL INFORMATION BE KEPT PRIVATE?

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

Each subject in this trial will be identified by a unique identifier that will be used on all report forms and any other material submitted to the NMTRC. Report Forms for this study will be both paper and electronic. Electronic data will be stored in a HIPAA compliant data center that is housed by a third party. Your medical records are available to those caring for you at this hospital. Other people or groups who may see or copy your medical record because you are participating in this study include:

- The Neuroblastoma and Medulloblastoma Translational Research Consortium (NMTRC), affiliates of the NMTRC, and the NMTRC008 study committee
- Spectrum Health and its affiliates
- The U.S. Food and Drug Administration
- The Western Institutional Review Board® (WIRB®)
- The Spectrum Health Institutional Review Board
- Department of Health and Human Services (DHHS) agencies

Otherwise your name will not be released without your written permission, unless required by law. If results of this study are published, your identity will remain confidential.

Please refer to the separate authorization form that explains more specifically how your personal health information will be used.

Part of these biology studies will be looking at genetic information collected from the samples you provide. A Federal law, called the Genetic Information Nondiscrimination Act (GINA), generally makes it illegal for health insurance companies, group health plans, and most employers to discriminate against you based on your genetic information. This law generally will protect you in the following ways: Health insurance companies and group health plans may not request your genetic information that we get from this research. Health insurance companies and group health plans may not use your genetic information when making decisions regarding your eligibility or premiums. Employers with 15 or more employees may not use your genetic information that we get from this research when making a decision to hire, promote, or fire you or when setting the terms of your employment.

GINA does not protect you against genetic discrimination by companies that sell life insurance, disability insurance, or long-term care insurance. GINA does not prohibit discrimination on the basis of an already manifest genetic disease or disorder.

A description of this clinical trial will be available on 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.

WHAT HAPPENS IF I AM INJURED?

Participating in research may result in an injury. Immediate, short-term medical treatment related to this injury is available at your treating institution, but such treatment will not be free of charge. Your medical insurance may pay for such treatment, but you will ultimately be billed for payment. Any additional, non-emergency treatment related to this injury is also available, but such treatment will not be free of charge.

No compensation will be routinely provided by the sponsors of this study. There are no plans to provide you with financial support for lost wages, disability, pain or discomfort.

By signing this consent form, you are not giving up any legal rights.

WHO WILL PROVIDE FUNDING?

Funding for this research study will be provided by The Neuroblastoma and Medulloblastoma Translational Research Consortium (NMTRC) and Dell, Inc.

CAN I WITHDRAW OR BE WITHDRAWN FROM THE STUDY?

Your participation in this study is voluntary. You may decide not to participate or you may leave the study at any time. Your decision will not result in any penalty or loss of benefits to which you are entitled.

Tell your study doctor if you are thinking about stopping or decide to stop. He or she will tell you how to stop safely. It is important to tell the study doctor if you are thinking about stopping so any risks from treatment can be evaluated by your study doctor. Another reason to tell your study doctor that you are thinking about stopping is to discuss what follow-up care and testing could be most helpful for you.

Your study doctor or sponsor may decide to take you off study at any time without your consent if any of the following occur:

- You do not meet the requirements to take part in the study (for example, there is not enough sample of tumor cells to perform the analysis needed for the personalized genetic reports.)
- The study doctor believes it is in your best interest
- New information becomes available that would suggest that continuing in this study would not be in your best interest
- The study is stopped
- You do not consent to continue in the study after being told of changes in the research that may affect you
- Or for any other reason.

CONTACT INFORMATION

Contact _____ at _____for any of the following reasons:

- if you have any questions about your participation in this study,
- if at any time you feel you have had a research-related injury, or
- if you have questions, concerns or complaints about the research.

If you have questions about your rights as a research subject or if you have questions, concerns or complaints about the research, you may contact:

Western Institutional Review Board® (WIRB®)
3535 Seventh Avenue, SW
Olympia, Washington 98502
Telephone: 1-800-562-4789 or 360-252-2500
E-mail: Help@wirb.com

WIRB is a group of people who perform independent review of research.

WIRB will not be able to answer some study-specific questions, such as questions about appointment times. However, you may contact WIRB if the research staff cannot be reached or if you wish to talk to someone other than the research staff.

Do not sign this consent form unless you have had a chance to ask questions and have received satisfactory answers to all of your questions.

WHERE CAN I GET MORE INFORMATION ABOUT CANCER AND CLINICAL STUDIES?

You may call the National Cancer Institute's Cancer Information Service at: 1-800-4-CANCER (1-800-422-6237) or TTY: 1-800-332-8615. You may also visit the NCI Web site at http://cancer.gov/

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

If you agree to be in this study, you will receive a signed and dated copy of this consent form. You will be given a copy of the protocol (full study plan) upon request. If you want more information about this study, ask your study doctor.

Additional optional tumor biology consent

If you agree to allow your samples to be stored for future research your tumor samples, blood, and/or bone marrow will be stored in a safe and confidential laboratory indefinitely. You have the option to remove the samples from the laboratory at any time because a link will remain between your samples and you. If in future, you ask that your stored samples be destroyed, it is important to know that any research that has already been done on the samples cannot be changed. No matter what you decide to do, it will not affect the care that you will get.

Because these additional tests are for research only, usually your study doctor or you will not know the results. It is very unlikely that the research testing might find important information about your current or future health. If this unlikely event happens, the researchers may contact your study doctor about what the research test results might mean. Only your study doctor will be notified and the information will not become part of your medical record. Your study doctor may discuss this unexpected finding with you, and may recommend that you see a genetic counselor and/or repeat testing in a clinical (not research) laboratory if needed. It is possible that your study doctor may decide that no action is needed.

Please initial your choice on the line below:

I agree to have my tumor samples (including tumor in bone marrow if present), obtained as part of my regular care sent to a laboratory for research studies that will not directly impact my treatment, but the results of these research studies may benefit future children with cancer.

YES_____ NO_____ (initials) Date_____/_____/_____

I agree to have any leftover samples from the above tumor biology studies saved in the laboratory to be used for research in the future.

YES_____ NO_____ (initials) Date_____/_____/_____

Statement of Consent

I have been given and have read a summary of this research study. I have been able to ask questions and my questions have been answered to my satisfaction. Should I have any further questions about the research, I may contact the person conducting the study at the address and telephone number given on page one of this consent form. My participation is voluntary and I may refuse to participate or withdraw at any time without penalty or prejudice to my present and/or future care. I agree to participate in this study.

I authorize the release of my medical records for research or regulatory purposes to the sponsor, the FDA, DHHS agencies, governmental agencies in other countries, [Site Specific] and WIRB®.

By signing this consent form, I have not given up any of my legal rights.

Consent and Assent Instructions:

Consent: *Subjects 18 years and older who can provide consent must sign on the subject line below*
Consent is provided by the Legally Authorized Representative for adult subjects unable to consent
For subjects under 18, consent is provided by the parent or guardian

Assent: *Is not required for subjects 17 years and younger*
Verbal assent is required for adult subjects where possible using the assent section below

_____
Name of Subject Printed

CONSENT SIGNATURE:

_____
Signature of Subject Date

Signature of Legal Guardian or Legally Authorized Representative (applicable for children and subjects unable to provide consent) Date

Name of Legal Guardian or Legally Authorized Representative Printed

Authority of Subject's Legally Authorized Representative or Relationship to Subject

Signature of Person Conducting Informed Consent Discussion Date

Name of Person Conducting Informed Consent Discussion

Signature of Principal Investigator or Designee (if different from above) Date

Name of Principal Investigator or Designee Printed (if different from above)

ASSENT SIGNATURES, For Adult Subjects with a Legally Authorized Representative:

Assent:

For adult subjects who have a legally authorized representative, I confirm that:

- I have explained the study to the extent compatible with the subject's understanding, and the subject has agreed to be in the study.
  OR
- The subject is not able to assent due to lack of mental capacity.

Signature of Person Conducting Assent Discussion Date

---------- Use this witness section only if applicable ----------

If this consent form is read to the subject because the subject is unable to read the form, an impartial witness not affiliated with the research or investigator must be present for the consent and sign the following statement:

I confirm that the information in the consent form and any other written information was accurately explained to, and apparently understood by, the subject. The subject freely consented to be in the research study.

Signature of Impartial Witness Date

Note: This signature block cannot be used for translations into another language. A translated consent form is necessary for enrolling subjects who do not speak English.