**Official Study Title:** TRIAL TREATING RELAPSED ACUTE LYMPHOBLASTIC LEUKEMIA WITH VENETOCLAX AND NAVITOCLAX

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**Informed Consent for Research**

# A PHASE I/II TRIAL TREATING RELAPSED ACUTE LYMPHOBLASTIC LEUKEMIA WITH VENETOCLAX AND NAVITOCLAX

*Note: When we say "you" in this consent, we mean "you or your child." When we talk about research, it can be called a clinical trial, research study, or research protocol.*

## Key Information

We highlight here the risks and study requirements that we think you should know before deciding if you want to take part in this research study. If you're still interested, we'll then get into more detail in the paragraphs that follow.

A. Why are you being asked to volunteer in this study?

You are being asked to take part in a research study because you have acute lymphoblastic leukemia (ALL) that has come back after treatment (relapsed).

B. What is the usual approach to the condition that you have?

The current standard treatment for children with relapsed or refractory (hard to get rid of) ALL is cytotoxic chemotherapy. Cytotoxic chemotherapy drugs do not specifically kill only leukemia cells, instead the drugs try to kill any cells that are rapidly growing. This type of treatment usually involves combinations of medicines that work in different ways and are often medicines that children with ALL have already received during their initial treatment.

C. Why is this study being done?

The purpose of this study is to learn the effects (good and bad) of treatment with venetoclax and navitoclax in combination with the usual chemotherapy. These therapies may kill leukemia cells directly or make them more sensitive to other chemotherapy.

D. What will happen if you decide to take part in the study?

You will receive multi-drug chemotherapy in courses called "Blocks". This consent will cover Block 1 of chemotherapy, which will last 4-6 weeks, depending on how long it takes your bone marrow to recover. Block 2 and subsequent treatment will be covered in later consents.

**Key Information**

E. What are the research risks and benefits of taking part in this study?

The most common side effects of venetoclax and navitoclax are respiratory infections, decreased white blood cell and red blood cell count, decreased platelets, nausea, vomiting, diarrhea, loss of appetite, constipation, and abdominal pain. Detailed information about the side effects of all the drugs used in this study are described later in this consent.

The potential benefits of treatment on this study are that it may cause your leukemia to stop growing for a period of time or go into remission. It may also lessen the symptoms, such as pain, that are caused by the leukemia or enable future therapies such as hematopoietic stem cell transplant (HSCT).

F. How many people will take part in this study?

Up to 98 children and young adults will take part in this study at St. Jude and other hospitals collaborating on this study. Up to 50 participants will take part at St. Jude.

G. What are your options?

If you decide not to take part in this study, you have choices. For example:

- you may choose to receive other chemotherapy, not part of a research study
- you may choose to take part in a different study, if one is available
- or you could decide not to be treated

If you are still interested in taking part in the RAVEN research study, more detail will be provided in the following pages.

## 1. Why are you being asked to volunteer for this research study?

You are being asked to take part in a research study because you have acute lymphoblastic leukemia (ALL) that did not go into remission after treatment (refractory) or has come back after treatment (relapsed). This is a research study to find out if two new drugs called venetoclax and navitoclax are safe and if they have beneficial effects in children, adolescents and young adults when combined with standard chemotherapy for ALL.

The study drug, venetoclax (also called Venclexta®), is approved by the U.S. Food and Drug Administration (FDA) to treat certain types of leukemia in adults. Venetoclax is not approved by the FDA for treating childhood leukemia. The study drug, navitoclax is not approved by the FDA.

Please take your time in deciding and feel free to discuss it with your family, friends and St. Jude staff. Before agreeing, it is important that you read this consent form that describes the study. After you understand the study and if you agree to take part, you will be asked to sign this consent form. You will be given a copy to keep.

## 2. Who is sponsoring this study?

This study is being sponsored by St. Jude Children's Research Hospital.

The drug manufacturer, AbbVie, is supplying venetoclax and navitoclax at no charge to St. Jude for this study.

Unrelated to this study, St. Jude has received a charitable contribution from AbbVie, Inc. The charitable contribution is not being used for clinical or research activities, including any activities related to this study. The Institution has checks and balances in place to ensure that this charitable donation does not influence the conduct of the study. The outcome of this study will not impact how the charitable contribution is spent or whether St. Jude receives additional charitable funds from AbbVie, Inc. in the future. Your enrolling in this study will not cause any money from this charitable contribution to go to Dr. Karol, the St. Jude Principal Investigator.

The principal investigator (researcher) in charge of this study is Dr. Seth Karol. He may be reached by phone at 901-595-3300. Please feel free to call him at any time if you have questions.

## 3. What is the purpose of this study?

The purpose of this study is to learn the effects (good and bad) of treatment with venetoclax and navitoclax in combination with chemotherapy.

With this research study, we plan to meet the following goals:

- To find out if venetoclax and navitoclax in combination with chemotherapy is an effective treatment for children with relapsed and refractory ALL.
- To determine the highest and safest dose of venetoclax that can be given with new combinations of chemotherapy drugs after Block 1 therapy
- To find out if the treatment is safe for children with relapsed and refractory ALL
- To learn more about the biology and genetics of children with relapsed and refractory ALL who receive this treatment.
- To learn more about the immune response to this treatment.
- To learn more about infections in children with ALL who receive this treatment.

Up to 98 participants will take part at St. Jude and several collaborating institutions. About 50 will take part at St. Jude.

## 4. What will be done in this study?

Before you start treatment

You will need to have the following exams, tests or procedures to find out if you can be in the study. These exams, tests or procedures are part of regular cancer care and may be done even if you do not join the study. If you have had some of them recently, they may not need to be repeated. This will be up to your study doctor.

- History and physical exam
- Blood tests
- Pregnancy test (if you are a female who could have children)
- Bone marrow aspirate and biopsy to check the status of your leukemia
- Lumbar puncture (spinal tap) to check the fluid around your spine and brain for leukemia cells
- Echocardiogram (ECHO) to test the function of your heart
- Imaging scans, if needed, to check the status of your leukemia

If the test results show that you do not meet the study eligibility, you cannot start the study treatment and your study doctor will talk to you about other treatment options.

During the study

If the exams, tests and procedures show that you can be in the study, and you choose to take part, you can start treatment.

Treatment in this study will be given in courses called "Blocks", each lasting about 4-6 weeks, depending on how long it takes your blood counts to recover. This consent will cover Block 1 treatment. Block 2 and subsequent treatment will be covered in later consents.

For the first block of treatment (Block 1), you will take the study drugs, venetoclax and navitoclax, by mouth, in combination with other chemotherapy drugs as shown below.

| Drug | How the drug will be given | No. of doses | Days |
|---|---|---|---|
| Venetoclax | By mouth once a day | 22 | Days 1-22 |
| Navitoclax | By mouth one a day | 20 | Days 3-22 |
| Dexamethasone | By mouth or into the vein (IV) twice a day | 30 | Days 1-7 and 15-22 |
| Vincristine | Into the vein (IV) | 4 | Days 1, 8, 15, 22 |
| Calaspargase* | Into the vein (IV) | 1 | Day 2 |
| Dasatinib** | By mouth once a day | 28 | Days 1-28 |
| Intrathecal chemotherapy (methotrexate, | By lumbar puncture into spinal fluid | 1 to 4 | Between day -7 and Day 1, then weekly. |

| Drug | How the drug will be given | No. of doses | Days |
|---|---|---|---|
| hydrocortisone, cytarabine)*** | | | |
| Leucovorin | By mouth or into the vein (IV) | 2+ | 24 and 30 hours after each lumbar puncture |

** Calaspargase may be replaced by alternative forms of asparaginase due to local practice or prior allergy.* ***If pegaspargase is used, two doses (on days 2 and 15) of 2500units/m$^2$ replace the single day 2 dose of calaspargase****. Some patients will not receive asparaginase at all, or will receive fewer doses, depending on their type of leukemia. Your doctor will talk to you about this.*
***Dasatinib will be given only to patients who have certain genetic changes called ABL-class fusions or have T-cell ALL/LLy.*
****IT medicine may be also given on two other days depending on the presence of leukemia in your spinal fluid (CSF). Your doctor will talk to you about this if it applies.*

The treatment you receive after Block 1 will depend on the following:

- Whether or not the surface of your leukemia cells are positive for a marker called "CD19" (CD19 negative patients will receive Block 2a treatment, those that are positive will receive Block 2b unless their physician determines block 2a is in their best interest).
- Down syndrome participants will receive Block 2b unless CD19 is negative. CD19 negative patients with Down syndrome will go off treatment after Block 1.
- The timing of your first ALL relapse and response to treatment (those who relapsed 3 years or more from diagnosis and are MRD-negative after Block 1will continue on after Block 2a or 2b to receive additional consolidation and maintenance therapies). Other participants will stop after Block 2a or 2b.

<u>Taking venetoclax and navitoclax</u>

You will take venetoclax and navitoclax tablets by mouth on scheduled days. You should take the tablets with food and water at about the same time each day.

You should not drink grapefruit juice, and you should not eat grapefruit, Seville oranges or marmalades, or starfruit while you are taking venetoclax. These foods and drinks may increase the amount of venetoclax in your blood.

Do not stop taking venetoclax or navitoclax unless your study doctor tells you to.

If you miss a dose of venetoclax and navitoclax:

- If the missed dose is by less than 8 hours, take the missed dose right away and take your next dose the following day as usual.
- If the missed dose is by more than 8 hours, do not take the dose that day and take the next dose at your usual time the next day.

If you vomit after taking venetoclax and navitoclax:

- Take an additional dose if 1 hour or less has passed since you took the dose.
- Do not take any additional dose that day if more than 1 hour has passed, and take the next dose at the usual time the next day

Intrathecal (IT) chemotherapy to prevent or treat leukemia in the spinal fluid

You may be familiar with spinal taps if they were done during your initial treatment for leukemia. Whether you decide to take part in this study or not, you will need additional spinal taps to give medicines that are necessary to prevent the leukemia from spreading to your spinal fluid, or to treat the spinal fluid if leukemia cells are present.

All patients will get one IT chemotherapy treatment before or right after starting the first cycle. Additional doses of IT chemotherapy will depend on whether or not you have leukemia cells in your spinal fluid and how many relapses of leukemia you have had before starting this study. You will also receive a vitamin supplement called leucovorin, which will help prevent or lessen side effects of the IT chemotherapy.

You will get some form of sedation or anesthesia (medicine to make you sleep) during this procedure. Spinal taps are painful and may cause headaches. The skin at the site of needle insertion is usually numbed with an anesthetic cream or lidocaine before the procedure is performed. About 1 teaspoon of spinal fluid will be withdrawn before injecting the chemotherapy.

Recovery and leukemia evaluation after treatment

You may need to be in the hospital for the administration of this treatment. It will take 1-2 weeks for your blood counts to fully recover from this treatment. After you recover, a bone marrow exam will be done to evaluate the status of your leukemia.

Standard of care tests and procedures during treatment

During treatment on this study, you will have the following tests and procedures that are part of standard of care for leukemia:

- Physical exam and vital signs will be done regularly during treatment
- Blood tests to check your blood counts and blood chemistry will be done regularly during treatment totaling approximately 40 mL (8 teaspoons)
- Bone marrow exams before and at the end of Block 1 to evaluate comprehensive leukemia genomics (Before Block 1 only) and minimal residual disease (MRD) and your leukemia's response to treatment
- Small skin biopsy (if this has not been done previously) for genetic testing
- Blood and bone marrow to evaluate your immune system function
- Some patients will have a blood test to find out if there is a genetic trait that may put you at higher risk of toxicity from drugs used later in this study

Required research studies during this study

The following tests will be done because you are part of this study. If you were not in the study you would probably not have these tests. The information learned would not change the way you are treated. With the exception of the genetic studies mentioned below, the results of these tests will not be given to you. You and your insurance company will not be charged for the costs of the required research study tests listed below.

- Bone marrow for biomarker studies

  Extra bone marrow will be collected during the bone marrow procedure you will have before you start treatment on this study. The pre-treatment bone marrow procedure is part of standard of care, but an extra sample will be collected for research studies. You will not have an additional bone marrow aspirate done for this research test. If your leukemia relapses again, an extra sample will again be collected for these studies.

  This bone marrow sample will be studied in St. Jude research labs with these goals:

  a) To help predict which participants may respond to treatment
  b) To find out which participants may be at increased risk for leukemia relapse
  c) To learn which participants are at risk for more side effects from treatment
  d) To find out if certain genetic mutations are present in the leukemia cells

- Bone marrow and blood for immune research studies

  At the same time you are having a bone marrow for standard of care, extra samples (about 1 teaspoon) will be drawn to learn more about how this treatment affects your immune system. Bone marrow will be collected before you start treatment and at the end of each block of treatment. Again, you will not have an additional bone marrow aspirate done for this research test.

  Blood will be collected before you start treatment, and on Day 15 of Block 1. Total volume for these blood draws is about 8 mL (less than 2 teaspoons).

- Genetic studies

  In this research study, your tumor and non-tumor DNA will be sequenced. This results in information about all of your genes. We will use your bone marrow and your blood, collected at the same time you are having clinical procedures. These samples will be analyzed to look for specific genetic changes. Researchers are looking for changes in DNA that may be related to the development of leukemia, or that may explain why some patients might respond to certain treatments better than other patients. Some of the changes may be present in every cell of the body, including leukemia cells and normal cells (germline mutations), while other changes may only be present in the leukemia cells (somatic mutations).

In order to perform the DNA sequencing for this study, you will be asked to sign an additional clinical genomics consent that gives more detail about genetic testing. Both leukemia and normal cells will be tested. These results will be provided to your study doctor. They will only receive results that show specific genetic changes that may affect how you respond to the study drugs.

You will also be asked to sign our TBANK consent, which allows the St. Jude "biorepository" to store your blood and tissue, including your DNA, for the research objectives of this study and, beyond this study, for other future research. The TBANK consent also gives more detail on how your genetic results may be used and shared in the future.

## 5. What are the risks and benefits of taking part in this study?

If you choose to take part in this study, there is a risk that you may:

- Lose time at school, work or home and spend more time in the hospital or doctor's office than usual
- Be asked sensitive or private questions which you normally do not discuss

The chemotherapy drugs used in this study may affect how different parts of your body work such as your liver, kidneys, heart, and blood. The study doctor will be testing your blood and will let you know if changes occur that may affect your health. There is also a risk that you could have side effects.

Here are important points about side effects:

- The study doctors do not know who will or will not have side effects.
- Some side effects may go away soon, some may last a long time, or some may never go away.
- Some side effects may interfere with your ability to have children.
- Some side effects may be serious and may even result in death.

Here are important points about how you and the study doctor can make side effects less of a problem:

- Tell the study doctor if you notice or feel anything different so they can see if you are having a side effect.
- The study doctor may be able to treat some side effects.
- The study doctor may adjust the study drugs to try to reduce side effects.

<u>Infection</u>

There is a serious risk of developing an infection while being treated on this research study, including serious infections that may require hospitalization. These infections can include bloodstream infections, meningitis, and other life threatening or fatal infections. To reduce the

risk of developing an infection, you will be required to take antibiotics and antifungal medication. You may be required to be in the hospital for most of the treatment so that your doctors and nurses can monitor you very carefully for any signs or symptoms of infection.

If you experience any of the following signs or symptoms while you are being treated on this research study, it is very important to call your doctor or nurse right away.

- Fever
- Pain (earache, sore throat, headache, pain with urination or having a stool)
- Redness, swelling, pain, or pus at the site of your central catheter

Risks of the study

Harmful reactions or side effects may occur in patients taking part in clinical trials. Some of these will be due to the patient's disease or prior treatment and some may be due to the drug being studied. Everyone taking part in the study will be watched carefully for any side effects. However, doctors don't know all the side effects that may happen. In general, side effects can range from mild to serious. Your health care team may give you medicines to help lessen side effects. Many side effects go away soon after you stop treatment. Although numerous measures are established to protect your health, it is possible that in some cases, side effects can be serious, long lasting, or may never go away.

Patients with leukemia may have a risk of death due to their underlying cancer or as a complication of their cancer treatment. Side effects related to this treatment will be closely monitored. The known and more common possible risks and side effects are discussed below.

Possible side effects of VENETOCLAX include:

| VERY COMMON<br>may affect more than 1 in 10 people | |
|---|---|
| • Upper respiratory tract infection (including runny nose, sore throat, or cough)<br>• Low number of white blood cells and platelets<br>• Low blood levels of calcium<br>• High blood levels of phosphorous<br>• Diarrhea<br>• Sepsis (an extreme immune response to an infection) | • Nausea<br>• Vomiting<br>• Constipation<br>• Anemia<br>• Feeling tired<br>• Fever with low number of white blood cells<br>• Pneumonia |

| COMMON<br>may affect from 1 in 100 to 1 in 10 people |
|---|
| • Urinary tract infection<br>• Fever with low number of white blood cells<br>• Tumor lysis syndrome (described below in detail; may experience fever, chills, nausea, vomiting, diarrhea, confusion, shortness of breath, irregular heartbeat, unusual tiredness, muscle pain, joint discomfort and/or seizure)<br>• High blood levels of urea, phosphorous, potassium, and creatine, which could mean problems with your kidneys<br>• Bacteremia (a bacterial infection that has spread to the blood stream) |

Problems and side effects may occur with the use of venetoclax that are not expected or are unknown at this time. You will be informed in writing in a timely manner of any new information or findings that become available that may affect your choice to continue to take part in this study.

Treatment with venetoclax has been associated with nausea, diarrhea, decreases in lymphocytes and neutrophils (two different types of white blood cells), tumor lysis syndrome (TLS) and infections.

Tumor lysis syndrome (TLS)

TLS is a problem that can happen when cancer/leukemia cells break down rapidly and the body has to get rid of the broken up cell parts. Sometimes your body, especially the kidneys, cannot remove the cell parts quickly enough, so the level of some of these cell products in the blood, such as salts and acids, can rise. This can happen especially in people with large tumors or a high number of cancerous white cells in the blood. TLS is most likely to occur in the first 5 weeks of starting venetoclax.

Tumor lysis syndrome can lead to serious problems such as effects on the kidneys and heart (including abnormal heart rhythms) or seizures. These side effects can result in needing kidney dialysis (a special machine to remove toxins from the blood) or lead to death. If you develop TLS, your study doctor will closely monitor and treat you as needed to try to prevent these complications.

Blood tests have shown TLS in some people after receiving the initial dose of venetoclax or after receiving a higher dose of venetoclax than previously received. Two deaths in patients with chronic lymphocytic leukemia (CLL) who experienced TLS have been reported after receiving venetoclax and one CLL patient with TLS has needed dialysis.

Before starting treatment, your study doctor may ask you to drink plenty of fluids. He/she may also give you medications to help the body get rid of the salts or chemicals or broken up cell parts from your leukemia. Your doctor may hospitalize you before you start venetoclax to give fluids into your vein, do blood tests, and check for TLS. If you develop TLS, your urine may look dark, thick, or cloudy.

You may also experience fever, chills, nausea (feeling sick to your stomach), vomiting, diarrhea, confusion, shortness of breath, irregular heartbeat, unusual tiredness, muscle pain, joint discomfort and/or seizure. If you notice any of these, notify your study doctor or nurse right away.
Your study doctor will closely monitor and treat you as needed to decrease the risk of any serious changes in your blood or other complications of TLS. If blood tests suggesting TLS are seen, extra blood tests or monitoring of your heart rhythm may be recommended by your study doctor.

Second cancer

Some patients with CLL who have been treated with venetoclax and who also had received several previous chemotherapy treatments have developed an aggressive form of lymphoma (cancer of the lymph node) at the time their CLL became worse. It is unknown if venetoclax has contributed to these cases since this type of cancer can happen in people with CLL who have not received venetoclax.

Possible side effects of NAVITOCLAX include:

| VERY COMMON<br>may affect more than 1 in 10 people | |
|---|---|
| • Decreases in circulating platelet counts; platelets are cells of your blood that stop bleeding<br>• Decreases in white blood cell counts. White blood cells are parts of your blood that help fight infection. Some patients may develop infections from unusual germs<br>• Increases in liver enzymes in your blood (substances produced by the liver or released when the liver is damaged or injured and are used to measure liver function) | • Diarrhea<br>• Nausea<br>• Feeling tired (fatigue)<br>• Vomiting<br>• Loss of appetite<br>• Constipation<br>• Abdominal pain<br>• Cough<br>• Decrease in red blood cells. Red blood cells are cells in your blood that carry oxygen. |

Some additional events which have been observed with navitoclax and will be monitored during the study are:

- Heart muscles which take longer than normal to recharge between beats (QT interval prolonged). This type of event may raise the risk of developing an abnormal rhythm of the heartbeat (arrhythmia) or other serious heart problems
- Change in taste
- Increases in pancreatic enzymes (blood test used to measure pancreatic function)

There have been rare reports of decreases in the amount of blood the heart pumps; these changes were reversible and did not result in any problems for the subjects.

There have been reports of thrombotic (clots in the blood vessels) events in subjects receiving navitoclax.

There have been reports of bleeding in subjects receiving navitoclax. These reports have included blood in the urine, bleeding from the nose and digestive tract, and one subject with bleeding inside the head.

One person with advanced CLL who received navitoclax in a clinical study was diagnosed with a viral infection of the brain. Such infections spread rapidly and are often fatal. Signs and symptoms may include headaches, memory loss, changes in thinking, speech and vision difficulties, loss of strength, weakness, seizures, partial paralysis, and loss of coordination.

**Possible side effects of <u>DEXAMETHASONE</u>** include:

| COMMON, SOME MAY BE SERIOUS<br>In 100 people receiving dexamethasone, more than 20 and up to 100 may have: | |
|---|---|
| • High blood pressure which may cause headaches, dizziness<br>• Pain in belly<br>• Infection<br>• Diabetes<br>• Loss of bone tissue<br>• Damage to the bone which may cause joint pain or loss of motion | • Mood swings<br>• In children and adolescents: decreased height<br>• Swelling of the body, tiredness, bruising<br>• Increased appetite and weight gain in belly, face, back and shoulders<br>• Difficulty sleeping<br>• Skin changes, rash, acne |

| OCCASIONAL, SOME MAY BE SERIOUS<br>In 100 people receiving dexamethasone, from 4 to 20 may have: | |
|---|---|
| • Blood clot which may cause swelling, pain, shortness of breath<br>• Kidney stones<br>• Glaucoma<br>• Cloudiness of the eye, visual disturbances, blurred vision<br>• A tear or a hole in the bowels which may cause pain or that may require surgery | • Heartburn<br>• Numbness and tingling of the arms, legs and upper body<br>• Muscle weakness<br>• Non-healing wound |

| RARE, AND SERIOUS<br>In 100 people receiving dexamethasone, 3 or fewer may have: |
|---|
| • Bleeding from sores in stomach<br>• Broken bones |

Possible side effects of <u>VINCRISTINE</u> include:

| COMMON, SOME MAY BE SERIOUS<br>In 100 people receiving vincristine, more than 20 and up to 100 may have: | |
|---|---|
| • Headache, jaw pain and/or bone/muscle pain<br>• Numbness and tingling of fingers or toes<br>• Swelling of lower legs<br>• Muscle weakness and difficulty walking | • Constipation, which may be severe, as a result of a bowel blockage<br>• Nausea, vomiting, diarrhea<br>• Pain or redness at the site of injection<br>• Hair loss |

| OCCASIONAL, SOME MAY BE SERIOUS<br>In 100 people receiving vincristine, from 4 to 20 may have: | |
|---|---|
| • High pressure which may cause headaches, dizziness, blurred vision<br>• Low blood pressure which may cause feeling faint<br>• Anemia which may cause tiredness, or may require blood transfusions<br>• Swelling that may be accompanied by confusion and dizziness<br>• Paralysis | • Difficulty with balance and hearing<br>• Loss of appetite, weight loss<br>• Difficulty emptying the bladder or urinating, excessive, frequent, or painful urination<br>• Hoarseness<br>• Drooping eyelids, abnormal eye movement |

| RARE, AND SERIOUS<br>In 100 people receiving vincristine, 3 or fewer may have: | |
|---|---|
| • Seizure<br>• Coma | • Visual loss with a chance of blindness<br>• Allergic reaction which may cause rash, low blood pressure, wheezing, shortness of breath, swelling of the face or throat |

Possible side effects of different forms of ASPARAGINASE (Pegaspargase, Erwinia asparaginase and calaspargase pegol) include:

| COMMON, SOME MAY BE SERIOUS<br>In 100 people receiving asparaginases, more than 20 may have: | |
|---|---|
| • Nausea, vomiting<br>• Allergic reaction which may cause rash, low blood pressure, wheezing, shortness of breath, swelling of face or throat<br>• Chills, fever<br>• Tiredness<br>• Hives, rash<br>• Pain at the site of injection<br>• Diarrhea<br>• Hyperglycemia (high levels of sugar in the blood) | • Low white blood cell count<br>• Prolongation of a blood test (aPTT) to check blood clotting activity<br>• Increase in an enzyme called lipase that helps break down fats in the body, which may mean that the pancreas is damaged<br>• Pain in the abdomen (belly)<br>• Fever with a low white blood cell count which could mean infection and may require hospitalization and treatment with antibiotics |

| COMMON, SOME MAY BE SERIOUS<br>In 100 people receiving asparaginases, more than 20 may have: |
|---|
| • High levels of bilirubin and ALT in the blood, which can mean inflammation and/or damage to liver cells |

| OCCASIONAL, SOME MAY BE SERIOUS<br>In 100 people receiving asparaginases, 4 to 20 may have: | |
|---|---|
| • Abnormal heartbeat<br>• Blood clot<br>• Infection, especially when white blood cell count is low<br>• Bruising, bleeding<br>• Anemia, which may require blood transfusion<br>• Liver damage, which may cause yellowing of eyes and skin<br>• Headache<br>• Night sweats<br>• Increase in triglycerides and cholesterol (types of fat) in the blood which if prolonged can lead to narrowing blood vessels or blocking them and to heart disease<br>• Low levels of the protein albumin in the blood<br>• Prolongation of a blood test (INR) to check blood clotting activity<br>• Weight loss<br>• An increase in an enzyme (amylase) that helps break down carbohydrates. This could mean that the pancreas is damaged<br>• Increase in the blood level of an enzyme called Gamma-glutamyl transferase (GGT), which may indicate bile duct inflammation or damage.<br>• Inflammation of the pancreas (an organ in the abdomen which makes insulin and certain digestive chemicals) which causes severe pain in the abdomen (belly) and back and may increase the blood sugar.<br>• Nausea<br>• Vomiting<br>• Severe blood infections which may be life threatening | • Dizziness (or sensation of lightheadedness, unsteadiness, or giddiness)<br>• Difficulty speaking or putting words together<br>• Disorder in the nerve responsible for control of the muscles for chewing and feeling in the face<br>• Diarrhea<br>• Occasional sudden sharp pain in the rectal area<br>• Inflammation and/or sores in the mouth (and/or throat and/or esophagus, the tube that leads from the mouth to the stomach) that may make swallowing difficult and are painful (painful mouth sores)<br>• Build-up of fluid in the abdomen (belly)<br>• Vomiting blood<br>• Inflammation or infection of the sinuses (the hollow air spaces within the bones surrounding the nose) which can cause pain, headache and nose drip<br>• Infection of the abdominal cavity, belly, bladder or kidney, body tissue, colon, eye, lung, mouth, spleen, or skin<br>• Infection and swelling of the muscle<br>• Infections including those caused by bacteria, virus, and fungus<br>• Infection which occurs due to a decreased number of a type of white blood cells<br>• Abnormal clotting of the blood<br>• Excessive loss of water from the body<br>• Condition where the blood contains more acid than normal<br>• Abnormal control of blood sugar level<br>• Low levels of oxygen in the blood which may make you feel short of breath, confused dizzy or drowsy |

| OCCASIONAL, SOME MAY BE SERIOUS<br>In 100 people receiving asparaginases, 4 to 20 may have: | |
|---|---|
| • A life-threatening severe form of blood infection that usually results from the presence of bacteria and their toxins in the bloodstream and is characterized especially by persistent low blood pressure with reduced blood flow to organs and tissues and often poor organ function.<br>• Loss of appetite.<br>• Fever (high temperature)<br>• Shortness of breath<br>• A decrease in blood pressure<br>• Lip swelling<br>• Hives; red and sometimes itchy bumps on the skin.<br>• Low levels of certain salts in the body like sodium, calcium, potassium and phosphate<br>• Low levels of sugar in the body which may require that you take replacement doses<br>• Increased levels of a chemical (creatinine) in the blood which could mean kidney damage<br>• Low numbers of white blood cells called lymphocytes that may make it easier to get infections which may be life threatening<br>• An increase in the blood level of the enzyme creatine phosphokinase which could indicate muscle damage<br>• Abnormal levels of magnesium in the body which may require that you take extra magnesium by mouth or vein<br>• A disturbance in the function of the brain or spinal cord that may affect the nerves and muscles of the body<br>• Convulsions<br>• Fainting | • Fluid build-up in between the layer of tissue that line the lungs and chest cavity that can make you feel short of breath<br>• Nosebleed<br>• Inflammation of the lungs which may cause shortness of breath, cough, and high temperature (fever)<br>• A feeling of extreme tiredness not relieved by sleep<br>• Pain – general pain, back pain, joint pain, or pain in arms and legs<br>• Bleeding at the site of an IV line<br>• Muscular inflammation or swelling causing discomfort or pain from infection or an unknown cause<br>• Loss of strength in the muscles<br>• Tiny red or purple spots on skin or mucus membranes caused by localized bleeding<br>• Itching<br>• Feelings of sadness, despair, loss of energy, and difficulty dealing with normal daily life<br>• Restlessness<br>• Anxiety<br>• Psychiatric disorder<br>• Increased need to urinate during the daytime<br>• A condition in which the flow of bile from the liver is blocked and may cause itching, dark colored urine, light colored feces, and yellow eyes or skin |

| RARE AND SERIOUS<br>In 100 people receiving asparaginases, 3 or fewer may have: | |
|---|---|
| • Kidney failure<br>• Severe damage to the brain which may lead to difficulty carrying out normal daily tasks and may progress to coma<br>• Bleeding in the brain<br>• Decrease in the blood flow to the brain due to a blockage in the blood supply which can result in a stroke and can be life threatening<br>• Death of tissue of the pancreas<br>• An abnormal hole in the small intestine<br>• A bleeding disorder in which small blood clots develop throughout the bloodstream blocking small blood vessels and depleting platelets and clotting factors needed to control bleeding. This condition can lead to bleeding from many areas of the body and can be life threatening | • Formation or presence of a blood clot inside a blood vessel<br>• Damage to the lungs that can lead to fluid in the lungs and affect the ability to breathe and the levels of oxygen in the blood<br>• Rash; flaking or sloughing of skin<br>• Severe damage to the kidneys causing them to stop working and resulting in the buildup of waste products, fluids, salts and minerals in the body. The damage may be permanent and can be life-threatening.<br>• Premature opening of a wound along surgical stitches after surgery |

Antibody formation

Although antibodies are not typically formed after repeat dose administrations, there may be a possibility you may form antibodies to the asparaginase. Antibodies are proteins that are part of the body's immune system. There is a chance that if you develop these antibodies, this study medicine or similar drugs will not work for you in the future.

Possible side effects of DASATINIB (Sprycel®) (patients with ABL-class fusions only) include:

| COMMON, SOME MAY BE SERIOUS<br>In 100 people receiving dasatinib, more than 20 may have: |
|---|
| • Diarrhea<br>• Nausea<br>• Headache<br>• Skin rash<br>• Fatigue<br>• Decreased number of white and red blood cells and platelets in the blood<br>  o low number of red blood cells (anemia) can make you feel tired and weak<br>  o low number of white blood cells can predispose to infections<br>  o low number of platelets can cause you to bruise and bleed more easily |

| OCCASIONAL, SOME MAY BE SERIOUS<br>In 100 people receiving dasatinib, from 4 to 20 may have: | |
|---|---|
| • Abnormal collection of fluid between the lung and the rib cage<br>• Shortness of breath, chest pain, and cough<br>• Lung infection (pneumonia)<br>• Swelling, buildup of fluid in the abdomen and around the heart<br>• Bleeding<br>• Muscle, bone, and joint pain<br>• Muscle weakness<br>• Fever<br>• Vomiting, abdominal (belly) pain and distention<br>• Low levels of phosphorous and calcium in the blood<br>• Sores in the mouth or other parts of the digestive system<br>• Upset stomach, constipation | • Inflammation of the tissues lining the stomach and bowel<br>• Pain<br>• Itching of skin, acne, dry skin, hives, excessive sweating<br>• Pain, numbness and tingling especially in hands and feet<br>• Dizziness, sleepiness, difficulty sleeping, depressed mood<br>• Change in taste<br>• Infections with and without low white blood cell count<br>• Weight loss and gain<br>• Decreased appetite<br>• Changes in heart rhythm and heartbeat<br>• High blood pressure<br>• Changes in vision, dry eyes |

| RARE, AND SERIOUS<br>In 100 people receiving dasatinib, 3 or fewer may have: | |
|---|---|
| • Bleeding in the brain or spine<br>• Extreme difficulty with breathing and wheezing<br>• Life-threatening infections<br>• Life-threatening diarrhea and bleeding in the stomach or intestines<br>• Weakness of the heart muscle, damage and enlargement of the heart<br>• Buildup of fluid around the heart and lungs<br>• Sores and inflammation on the skin<br>• Changes in nails, sensitivity to light<br>• Redness, swelling, and pain of the soles of the feet and hands<br>• Tremors, fainting, memory loss<br>• Stroke, seizures<br>• Chest pain related to heart problems<br>• Inflammation of the lining of the heart<br>• Pink eyes | • Changes in electrocardiogram that may be a sign of heart damage<br>• Increases in blood tests that measure liver and kidney function; jaundice<br>• Kidney failure, protein in the urine<br>• Difficulty swallowing<br>• Tears in body tissues<br>• Sores in stomach or intestines<br>• Inflammation of the pancreas or esophagus<br>• Blood clots, low blood pressure<br>• Anxiety and extreme emotional response, confusion<br>• Enlargement of breast tissue<br>• Abnormal menstrual periods<br>• Ringing in the ears<br>• Allergic reactions<br>• High blood pressure in the vessels that carry blood from the heart to the lungs |

Possible side effects of INTRATHECAL TREATMENT (spinal injection of methotrexate, cytarabine and hydrocortisone, or cytarabine alone) include:

| COMMON, SOME MAY BE SERIOUS | |
|---|---|
| • Nausea and/or vomiting<br>• Fever | • Headache |

| OCCASIONAL, SOME MAY BE SERIOUS | |
|---|---|
| • Swelling of the brain, which may cause stiff neck, sensitivity to light, headache, vomiting<br>• Major change in thinking patterns<br>• Difficulty learning | • Confusion<br>• Tiredness<br>• Seizure |

| RARE, AND SERIOUS | |
|---|---|
| • Rash<br>• Bleeding in the brain<br>• Paralysis, weakness | • Dizziness<br>• Damage to the brain, which may cause changes in thinking, blindness<br>• Infection |

Possible side effects of LEUCOVORIN CALCIUM include:

| COMMON, SOME MAY BE SERIOUS<br>In 100 people receiving leucovorin, more than 20 may have: | |
|---|---|
| • Diarrhea, nausea, vomiting<br>• Sores in mouth, which may cause difficulty swallowing | • Tiredness |

| OCCASIONAL, SOME MAY BE SERIOUS<br>In 100 people receiving leucovorin, from 4 to 20 may have: |
|---|
| • Allergic reaction which may cause rash, low blood pressure, wheezing, shortness of breath, swelling of the face or throat |

| RARE, AND SERIOUS<br>In 100 people receiving leucovorin, 3 or fewer may have: |
|---|
| • None |

*Leucovorin is a vitamin supplement that is given to decrease the side effects of methotrexate.*

Additional risks

Some drugs or supplements may interact with your treatment plan. Talk to your doctor, pharmacist, or study team before starting any new prescription or over-the-counter drugs, herbals, or supplements and before making a significant change in your diet. Supplements may

come in many forms, such as teas, drinks, juices, liquids, drops, capsules, pills, or dried herbs. All forms should be avoided.

If your red blood cell count is low, the cells that carry oxygen around the body you may feel tired. If your red blood cell count drops very low you may need a blood transfusion.

If you have a decrease in the white blood cell count, the cells that fight infection, you may be more likely to get an infection, including a serious infection that spreads through the blood stream (sepsis). If this happens, you will have to come to the hospital to be treated with antibiotics. If your white blood cell count is very low and you get a fever, you may have to come to the hospital to get treated with antibiotics.

If you have a low platelet count, particles in the blood that help with clotting, you may have easy bruising or bleeding. If the count is very low or there is bleeding, you might need platelet transfusions to help stop the bleeding.

Unknown risks

The drug combination is experimental and still being tested. There may be other risks, including death, which are not known now.

Loss of privacy

Very rarely, personal information from your records could be given out by accident. This might make you upset, embarrass you, or affect your ability to get insurance. Additional privacy and other risks from genomic testing and data sharing are discussed in the clinical genomics consent. To try to stop this from happening, we:

- Store records apart from names or other personal information
- Only allow members of the study team to see the records
- Store electronic data only on computers protected with a password and encryption software
- Report study results on the whole group and never identify one single person in any reports

**Benefits**

We hope that this study will help you personally, but we do not know if it will.

The potential benefits of treatment on this study include:

- May cause your cancer to stop growing for a period of time or go into remission.
- May lessen the symptoms, such as pain, that are caused by the cancer or enable additional therapies such as HSCT.

With any cancer treatment, sometimes treatment does not make the cancer go away. Or, sometimes treatment makes the cancer go away for a while but the cancer comes back later.

Information learned from this study may benefit other patients in the future.

**6. What are the risks to pregnancy, to an unborn child, and to the ability to have children when taking part in this study?**

You should not become pregnant or father a baby while you are taking part in this study. You should not nurse a baby while receiving treatment on this study because it is unknown if this could affect the baby. Both males and females who are able to have children must use a highly effective means of birth control approved by your study doctor.

Some examples of acceptable birth control for heterosexual partners include the following:

- Surgical sterilization:
  - For females: tubal ligation at least 1 month before study participation, ovaries removed, or uterus removed
  - For males: vasectomy at least 3 month before study participation
- Intrauterine device (IUD)
- Double-barrier method (contraceptive sponge, diaphragm or cervical cap with spermicidal jellies or cream AND a condom);
- Hormonal contraceptives (examples include birth control pills, vaginal rings, or patches), associated with inhibition of ovulation for at least 1 month prior to taking study drug.
- Total abstinence from sexual intercourse as the preferred lifestyle of the subject; periodic abstinence is not acceptable.

Your study doctor will explain what specific hormonal contraceptive methods you can use. You must continue the use of birth control during the entire time of your study participation and for at least 30 days after the last dose of venetoclax and navitoclax. Your study doctor will discuss the need for birth control with you.

If you become pregnant, you must stop taking venetoclax and navitoclax at once and notify your doctor immediately. You will not be allowed to continue in the study. You may be asked questions about the outcome of your pregnancy and the baby.

If you are a male, you are responsible for informing your partner(s) that the effects of venetoclax and navitoclax on an unborn fetus or embryo in humans are unknown. You and your partner(s) are responsible for using acceptable birth control as described above. If your partner becomes pregnant while you are on study, you must notify your doctor immediately. You and your partner may be asked questions about the outcome of the pregnancy and the baby. Written informed consent for release of medical information from your partner will be obtained prior to collecting any information about the pregnancy and baby.

## 7. Can you stop taking part in this study?

a. Can you change your mind about taking part in this research study?

You may change your mind about taking part in this research study or stop at any time. The decision will not affect your care or your relationship with your doctor or St. Jude. If available, you may receive routine medical care at St. Jude Children's Research Hospital.

If you change your mind about participating in this study, samples or related information that have already been given to or used by researchers will not be returned or removed.

b. Can you be taken out of this study without your consent?

Your St. Jude doctor may take you out of the study:

- If your health changes and the study is no longer in your best interest,
- If new information becomes available,
- If you do not follow the study rules,
- If the study is stopped by the sponsor, St. Jude.

## 8. What are your other options?

If you decide not to take part in this study, you have choices. For example:

- you may choose to receive other chemotherapy, not part of a research study
- you may choose to take part in a different study, if one is available
- or you could decide not to be treated

## 9. How much will it cost you?

If you have health care coverage, we will bill your health care insurer for all standard of care services, tests, and procedures. Billing your health care insurer impacts your annual deductible and life-time maximum, if any. This may affect your health care coverage to some extent if you go to another health care provider or institution in the future.

At St. Jude, you will not be responsible for or receive bills for co-pays, co-insurance, deductibles, or similar patient-liability amounts, or for the cost of medical care not covered by your health insurer. This includes research-only costs. Research-only tests and procedures will not be billed to you or your health care insurer.

## 10. Will you be paid for your time or expenses?

You will not be paid for your time or expenses.

## 11. What if there is a problem?

If you have any questions about this study or if you are injured because of this study, contact Dr. Karol, at 901-595-3300 immediately. If you are injured from being in this research study, St. Jude will offer you reasonable and necessary medical treatment for that injury. If you need more care than St. Jude can provide or if you prefer to seek treatment elsewhere, we will help you find medical care somewhere else. St. Jude may bill your insurance company or other third parties, if appropriate. It is not the hospital's policy to provide payment for other types of costs, such as lost wages, disability, or discomfort if you are injured from being in this study. You are not giving up any of your rights by signing this consent form.

## 12. How will new findings related to your participation in this study be shared with you?

The researcher will tell you of any new information learned during your study participation which might cause you to change your mind about continuing the study.

## 13. How will you find out the results of the study?

The researcher will give you information about the overall results of this study. Whether you will know your personal test results will be discussed in another part of this document. St. Jude researchers share information with people in studies in many ways including:

- Articles on www.stjude.org,
- In newsletters,
- In medical or scientific journals,
- In the media,
- A description of this clinical trial will be available on http://www.ClinicalTrials.gov, as required by the U.S. Law. This website will not include information that can identify you. At most the website will include a summary of the results. You can search this website at any time.

Published research results will only describe groups of people who took part in the study. Information that points out a single person will not be in research journals or other reports.

## 14. What about privacy and confidentiality?

Privacy

Information from research testing, imaging, and other procedures or studies, including genomic and genetic and other sensitive information, is relevant to your health and is placed in your medical record unless it is from a research-only laboratory. When you first registered at St. Jude, you received a copy of the St. Jude Notice of Privacy Practices. It tells how your PHI (protected health information), including research information placed in your medical record, may be used or given to someone outside of the hospital. You have the right to read the Notice of Privacy Practices before you sign this form. It may have changed since you first registered at St. Jude. You can find it at the bottom of every page on the St. Jude internet website: www.stjude.org.

A decision to take part in this research means that you agree to let the research team use and share your PHI with other researchers for purposes of the study explained above. This information will be kept indefinitely. You have the right to see, copy, and ask for changes to your protected health information that will be used or given out. However, research information may not be seen until the end of the study.

These groups, agencies or people may view your information from your research and medical records:

- United States Food and Drug Administration (FDA)
- United States Office of Human Research Protections (OHRP)
- United States National Institutes of Health (NIH)
- Other government agencies
- Your insurance company and other health benefits plan
- St. Jude Children's Research Hospital Institutional Review Board (IRB)
- AbbVie Pharmaceuticals (the drug manufacturer of venetoclax and navitoclax)
- Other committees or people involved in overseeing research studies and health care researchers at St. Jude Children's Research Hospital.

Confidentiality

If you consent to take part in this study, information obtained from this study, as well as information about disease signs and symptoms, will be entered into one or more scientific databases maintained by St. Jude Children's Research Hospital and the Federal Government. The information will be held securely electronically at St. Jude Children's Research Hospital. Your name will not be passed on to anyone else outside the research team who is not involved in the study. You will be allocated a study number, which will be used as a code to identify you on all study forms. Any research-related information about you that leaves the hospital will have your name and address removed so that you cannot be recognized.

Your records will be available to people authorized to work on the study. The study is being carried out at St. Jude Children's Research Hospital and other hospitals collaborating with St. Jude. The data collected about you during the study may be sent to study investigators inside and outside the USA. The data will be sent with your unique study number and all personal identifiers will be removed so you likely cannot be identified. By signing this consent form, you agree to this access for the current study and any further research that may be conducted in relation to it, even if you withdraw from the current study. The information collected about you may also be shown to authorized people from the US Regulatory Authority (FDA) to ensure that the study is carried out to the highest possible scientific standards.

Identifiers may be removed from the identifiable private information or identifiable biospecimens and assigned a unique code, except as described above, and then the information or biospecimens may be used for future research studies or distributed to other investigators for research studies without additional contact with you. For this you may also sign the TBANK

consent, which gives you information on how your identifiable data and biospecimens will be stored and used in the future.

Researchers and study staff are required by law to report suspected child abuse, threat of harm to self or others, and certain diseases that spread from person to person.

## 15. Permission to use your data/information: permission/HIPAA

If you sign this document, you give permission to all researchers and their staff at St. Jude Children's Research Hospital to use or disclose (release) your health information that identifies you for the research study described in this document.

The health information that we may use or release for this research includes information from your medical record, results of physical examinations, medical history, lab tests including genomic tests, and medical tests and procedures.

St. Jude Children's Research Hospital is required by law to protect your health information. By signing this document, you give St. Jude Children's Research Hospital permission to use and/or disclose (release) your health information for this research. Those persons who receive your health information may not be required by Federal privacy laws (such as the Privacy Rule) to protect it and may share your information with others without your permission, if permitted by laws governing them.

If you sign this document, you give St. Jude permission to share your information for future research studies and for the placement of information on databases as described in #4 and #14 of this consent form. By signing, you will also give St. Jude permission to put your research information, including testing, imaging, genomic and genetic information, other information and studies, and other sensitive information in your medical record (unless the research information is from a research-only laboratory). Any information placed in the medical record becomes a permanent part of your medical record but is protected like any other part of your medical record as described in the Notice of Privacy Practices. The following entities will disclose information:

- The U.S. Food and Drug Administration (FDA)
- AbbVie Pharmaceuticals (the drug manufacturer of venetoclax and navitoclax)
- St. Jude Children's Research Hospital Institutional Review Board (IRB)

You do not have to sign this document and give your permission, but if you do not, you may not receive research-related treatment.

Please note that you may change your mind and revoke (take back) this permission at any time. Even if you revoke your permission, St. Jude Children's Research Hospital may still use or disclose health information they already have obtained about you as necessary to maintain the integrity or reliability of the current research. To revoke this permission, you must write to:

HIPAA Privacy Officer
St. Jude Children's Research Hospital
262 Danny Thomas Place, Mail Stop 280
Memphis, TN 38105

This permission does not have an expiration date.

## 16. Further Information and Contact Details for Questions About This Research Study

You are encouraged to ask any questions you wish, before, during or after your treatment. If you have any questions about the study, please speak to your study nurse or doctor, who will be able to provide you with up to date information about the drug(s)/procedure(s) involved. If you wish to read the research on which this study is based, please ask your study nurse or doctor.

If there is anything you do not understand, or have any other questions, please contact the researcher listed below.

**IF AT ANY TIME DURING THE STUDY YOU EXPERIENCE ANY DISCOMFORT OR UNUSUAL SYMPTOMS, OR SIDE EFFECTS, PLEASE CONTACT THE DOCTOR LISTED BELOW:**

Principal Investigator, Researcher:
Dr. Seth Karol
St. Jude Children's Research Hospital
262 Danny Thomas Place
Memphis, TN
Telephone: (901) 595-3300

If you require any medical or surgical treatments outside of St. Jude such as with your local doctor or another hospital during this study, your researcher and their team must be informed.

You can get more details about your rights as a research participant by calling a St. Jude Research Participant Advocate at 901-595-4644 or 901-595-1139. The Research Participant Advocate is an individual who is not part of the research study team and is available to you to discuss problems, concerns and questions. The Advocate can help you obtain information and can relay any input you may have concerning the research to the research study team.

If you decide you would like to take part, then please read and sign this consent form. You will be given a copy of this informed consent document to keep. A copy of the consent form will be filed in your patient notes, one will be filed with the study records and one will be retained by St. Jude Children's Research Hospital (the study sponsor).

You can have more time to think this over if you are at all unsure.

Thank you for taking the time to read this informed consent document and to consider this study.

**PARENT/GUARDIAN STATEMENT (Required for participants younger than 18 years):** I have read this document, or it was read to me. I have been encouraged to ask questions and all my questions have been answered. I give permission for my child to be in this research study and any additional studies where I circled 'yes'.

| _____ | _____ | _____ AM/PM |
|---|---|---|
| Parent/Legal Guardian Signature | Date | Time (circle one) |

**ASSENT DISCUSSION (Required for participants 7–13 years old):**

☐ The research was explained to the minor participant in age-appropriate terms and the minor verbally agreed to take part in the study.

☐ Minor declined to take part in the study. The minor declined for the following reason(s):

_____

☐ An assent discussion was not initiated with the minor for the following reason(s):

- ☐ Minor is under 7 years of age.
- ☐ Minor is incapacitated.
- ☐ Minor refused to take part in the discussion.
- ☐ Other_____

**RESEARCH PARTICIPANT STATEMENT (14–17 years old and Adult Participants 18 years and older):** I have read this document, or it was read to me. I have been encouraged to ask questions and all my questions were answered. I agree to take part in this research study and any additional studies where I circled 'yes'.

| _____ | _____ | _____ AM/PM |
|---|---|---|
| Research Participant Signature | Date | Time (circle one) |

**RESEARCHER/DESIGNEE STATEMENT:** I have explained the research to the participant and his/her parent(s) or legal guardian(s). The research participant and parent(s)/guardian(s) were encouraged to ask questions and all questions were answered to their satisfaction. A copy of this form has been given to the participant or his/her representative.

| _____ | _____ | _____ AM/PM |
|---|---|---|
| Researcher/Designee Signature | Date | Time (circle one) |

_____
Print Name

**RESEARCH PARTICIPANT ADVOCATE STATEMENT:** I observed the informed consent process. The research study, intervention/observation, risks, benefits, and alternatives were presented to the research participant and/or legal guardian(s). They were encouraged to ask questions, and research team members answered all their questions. The participant /parent(s) indicated that they: 1) understood the information presented; and 2) voluntarily consented /agreed to take part in the research.

| _____ | _____ | _____AM/PM |
|---|---|---|
| Research Participant Advocate | Date | Time (circle one) |

| _____ | _____ | _____AM/PM |
|---|---|---|
| Interpreter (if needed) | Date | Time (circle one) |

PLEASE UPLOAD COMPLETED CONSENT FORM TO EPIC