Official Study Title: TOTAL THERAPY STUDY XVII FOR NEWLY DIAGNOSED PATIENTS WITH ACUTE LYMPHOBLASTIC LEUKEMIA AND LYMPHOMA

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Informed Consent for Research

TOTAL THERAPY STUDY XVII (TOTXVII) FOR NEWLY DIAGNOSED PATIENTS WITH ACUTE LYMPHOBLASTIC LEUKEMIA AND LYMPHOMA

Note: If you are a parent or legal guardian of a child who may take part in this study, permission from you is required. The assent (agreement) of your child may also be required. When we say "you" in this consent form, we mean you or your child; "we" means the doctors and other staff.

Key Information

To start we want to highlight 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 this section, we will briefly explain the following:

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

You are being asked to take part in this research study because you have been diagnosed with Acute Lymphoblastic Leukemia (ALL) or Acute Lymphoblastic Lymphoma (LLy). ALL and LLy are cancers of blood cells. They are similar cancers and are usually treated in similar ways.

B. What is the usual approach to this cancer?

Both ALL and LLy are fast-growing cancers that need immediate treatment with a combination of chemotherapy drugs. People who are not in a study usually receive intensive treatment with multiple chemotherapy drugs that are given in several stages.

C. Why is this study being done?

The main goal of this study is to try and improve the cure rate and quality of life of children, adolescents and young adults with acute lymphoblastic leukemia and lymphoma, by adding "targeted" treatments that are tailored to each child's specific type of ALL or LLy.

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

You will receive chemotherapy for about 2½ to 3 years.

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

Common side effects of cancer treatment include nausea, vomiting, hair loss, and fatigue (tiredness). Drugs may be given to try to prevent or decrease nausea and

Key Information

vomiting. Hair loss is usually temporary but very rarely it may be permanent. Chemotherapy may make you permanently unable to have children. On rare occasions, leukemia/lymphoma treatment can cause a second cancer to develop, usually years after the treatment is finished.

The most common serious side effect from cancer treatment is lowering of the number of normal blood cells that may result in anemia, increased chance of infection, and/or a bleeding tendency.

The potential benefit of this study is that you may have the same or better chance of long-term remission as children in the earlier studies, with fewer serious side effects.

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

Up to 1,000 children and young adults will take part in this study at St. Jude and up to 9 other hospitals in the US and Australia that are collaborating on this study.

G. What are your options?

- you may choose to have the usual approach described above
- you may choose to take part in a different study, if one is available

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

You are being asked to take part in this research study because you have been diagnosed with Acute Lymphoblastic Leukemia (ALL) or Acute Lymphoblastic Lymphoma (LLy). ALL and LLy are cancers of blood cells. They are similar cancers and are usually treated in similar ways.

ALL develops in the bone marrow, which is the soft, spongy center of the bones that produces the three major blood cells: white blood cells to fight infection; red blood cells that carry oxygen; and platelets that help blood clot and stop bleeding. ALL is a cancer of the white blood cells, where too many underdeveloped (abnormal) white blood cells, called “blasts”, are found in the bone marrow. These blasts crowd out the normal blood cells in the bone marrow and spread to the blood. They can also spread to the brain, spinal cord, and/or other organs of the body.

LLy develops when a specific type of white blood cell, called lymphocytes, become abnormal and grow in an uncontrolled way.

In ALL, the abnormal lymphocytes are mainly in the blood and bone marrow, whereas in LLy, the abnormal lymphocytes are present in the lymph nodes or thymus gland.

This consent form gives you information about the study which will be discussed with you. Please take your time making a decision and feel free to discuss it with your friends, family and St. Jude staff. Before agreeing to take part in this research study, 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. Incyte will provide the study drug ruxolitinib at no charge. Incyte may receive information about you related to the study (if you receive ruxolitinib).

The principal investigator (researcher) in charge of this study is Dr. Hiroto Inaba, who can be reached by phone at 901-595-3300, if you have any questions or concerns about this research.

3. What is the current standard of treatment for this disease?

Both ALL and LLy are fast-growing cancers that need immediate treatment with a combination of chemotherapy drugs. People who are not in a study usually receive intensive treatment with multiple chemotherapy drugs that are given in several stages. In the first stage, called Remission Induction, doctors try to remove all visible signs of leukemia and allow normal blood cells to be restored. This is called remission. In the middle stages, called Consolidation, doctors try to deliver a "knock-out punch" to any remaining leukemia cells. In the final stage, called Continuation, doctors try to keep the leukemia from coming back (disease remission is when the leukemia seems to have disappeared). All stages of treatment are very important.

We have learned from past research studies that 8 or 9 of every 10 children with ALL can have a long-term remission (no evidence of disease) if they get strong chemotherapy with several chemotherapy drugs. Most treatment regimens for ALL and LLy typically last for 2½ to 3 years.

4. What is the purpose of this study?

The main goal of this study is to try and improve the cure rate and quality of life of children, adolescents and young adults with acute lymphoblastic leukemia and lymphoma, by adding "targeted" treatments that are tailored to each child's specific type of ALL or LLy. With this research study, we plan to meet these goals:

- To improve the cure rate and survival of children with ALL and LLy by adding individualized and targeted treatment approaches to chemotherapy drugs that are commonly used to treat ALL and LLy.
- To find out if nerve damage can be reduced and/or made less severe if we decrease the amount of vincristine given to children who have a certain genetic feature that makes them more likely to have nerve damage caused by vincristine. Vincristine is another important drug used in ALL and LLy therapy.

- To continue to build upon knowledge learned in past studies about the biology and genetic features of children with ALL and LLy by performing a number of research studies on blood and bone marrow in laboratories at St. Jude.
- To learn more about how the drugs used in this treatment are processed and eliminated in the body (pharmacokinetics) and how these drugs affect the body (pharmacodynamics).
- To find out if a test called "Minimal Residual Disease or MRD" can help researchers predict which children will be at higher risk of having a relapse of leukemia, and to test new ways of performing MRD.
- To learn more about preventing and treating infections in children being treated for ALL and LLy.
- To find out if using a painless device that delivers low magnitude, high frequency stimulus (a small amount of vibration) can improve bone density and bone strength in children being treated for ALL and LLy.

Up to 1,000 children, adolescents and young adults will take part in this study at St. Jude and several other hospitals in the US and Australia that are collaborating with St. Jude.

5. What are the study groups?

Treatment on this study is based on several disease-specific features that can affect how well a patient with ALL or LLy will respond to treatment.

ALL and LLy are classified into **3 different risk groups**: **Low-, Standard-, and High-Risk**. The term "risk" refers to the chance of the ALL or LLy coming back after treatment.

ALL and LLy are classified into **two main cell type groups**, based on the specific type of white blood cell that is affected: **B-cell or T-cell**.

Participants will receive different treatments according to the risk category and cell-type of their ALL or LLy. The specific treatment that you receive will depend on 3 things:

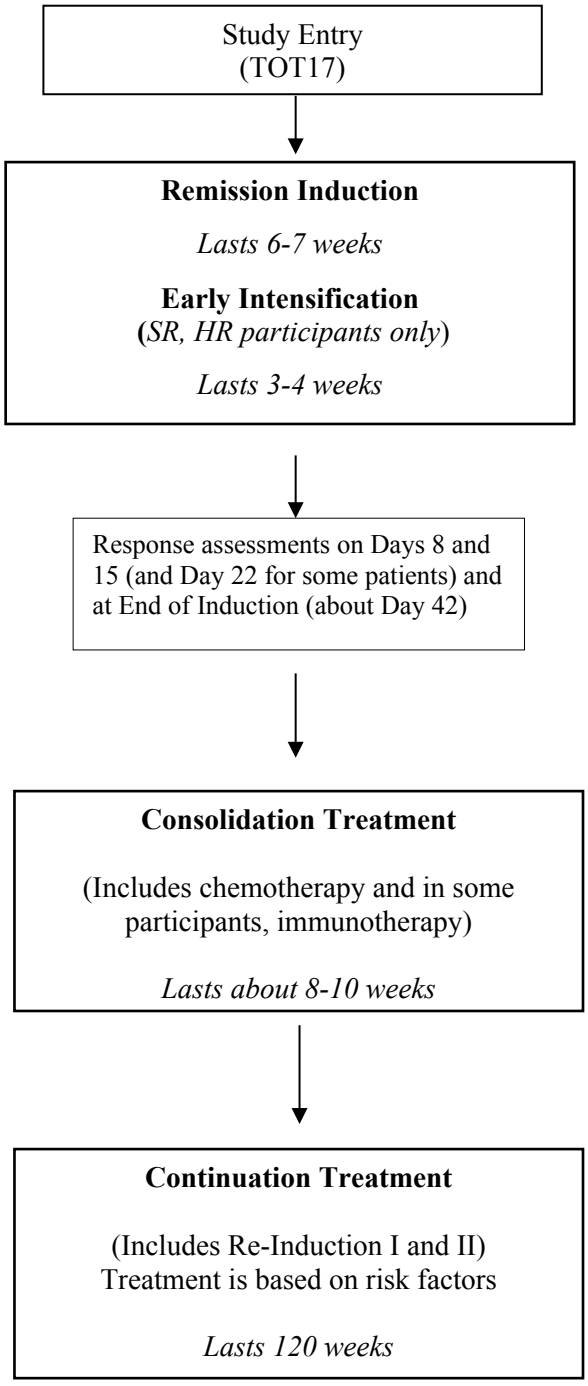
- How well your ALL/LLy responds to the first stage of treatment (Remission Induction)
- Your risk group (Low-, Standard-, or High-Risk)
- Whether your ALL/LLy is B-cell or T-cell type

Patients with a rare type of leukemia called "**mixed phenotype acute leukemia or MPAL**" are also eligible for this study. MPAL has features of both ALL and acute myeloid leukemia. Recent studies show that ALL treatment is effective in MPAL. Throughout this study, participants with B-cell/myeloid MPAL will be treated in the same way as B-ALL and those with T-cell/myeloid MPAL will be treated in the same way as early T cell precursor (ETP) ALL.

This consent form is for Remission Induction therapy. Consolidation and Continuation will be covered in later consents.

Diagram of TOT17 Study

This chart shows the treatments planned in the overall study, which will last about 2½ years.



This consent covers this part of treatment, which includes Day 1 Intrathecal Chemotherapy, followed by 6-7 weeks of intensive chemotherapy (all patients) and 3-4 weeks of additional therapy (SR, HR patients only).

Treatment will depend on the cell type of your leukemia or lymphoma (B-cell or T-cell), and risk group (LR, SR, HR)

You will also be offered participation in our specimen banking and genomic research studies

LR=Low-Risk
SR=Standard-Risk
HR=High-Risk

6. What will be done during Remission Induction Treatment?

Remission Induction chemotherapy will last about 6-7 weeks. You will need to be in the hospital for the first part of this treatment. The remainder of treatment will be given as outpatient.

Before you start treatment

You will have a number of tests, evaluations and procedures to diagnose your leukemia or lymphoma, check your overall health and prepare your body to receive the anti-cancer therapy. Many of these are part of regular cancer care and would be done even if you do not join the study. Some are standard tests that may not be part of regular care, but are being done (or are being done more often) because you are taking part in this study. These tests are described later in this consent under "*What tests and procedures will I have if I take part in this study*?"

Spinal tap and first intrathecal treatment

You will have a spinal tap either right before you are treated on this study, or on Day 1 of treatment. A spinal tap (also called a lumbar puncture) is when fluid surrounding the spinal cord is removed by inserting a needle into the lower back. You will be sedated, or the affected area will be numbed with local anesthetic during the procedure.

This is done to see if there are any leukemia or lymphoma cells in the watery fluid around the brain and spinal cord. You will be given three drugs into the spinal fluid when the spinal tap is done. Giving chemotherapy directly into the spinal fluid is called intrathecal or IT treatment. The three drugs are Methotrexate, Hydrocortisone, and cytarabine (ARA-C); ITMHA. Intrathecal treatment is used to help prevent leukemia and lymphoma in the central nervous system (CNS).

Genetic changes and targeted therapy

Samples of your bone marrow and blood will be sent for the testing described below:

- Clinical genomic sequencing of ALL or LLy cells: After an adequate amount of each of the specimens are sent for routine diagnostic tests, extra samples collected during the procedures done at diagnosis will be sent to different laboratories at St. Jude for special studies to look for specific genetic changes.

- Minimal Residual Disease (MRD): This test detects the number of leukemia or lymphoma cells that are too small to be seen by human eyes.

The results of all the required special and diagnostic studies will be available around the end of your second week of treatment. The information will be given to your doctor and to you and will be part of your medical record. Results of these tests will determine the type and the strength or intensity of the therapy you receive.

If certain changes are present, you will receive an additional drug that has been shown to "target" that change along with the other leukemia or lymphoma drugs. Targeted therapies are drugs that

block the growth and spread of cancer by blocking specific molecules or markers on the cancer cells that are involved in the growth, progression and spread of cancer.

Specifically, patients with the following genetic changes will get these additional drugs during Remission Induction and throughout later treatment on this study:

Genetic change	Targeted Therapy Drug
ABL1-class fusion	Dasatinib*
JAK-STAT signaling and ETP leukemia	Ruxolitinib**
No targetable change	Bortezomib***

**Dasatinib will start on Day 15.*
***Ruxolitinib will start during Early Intensification.*
****If tests show that you do not have a genetic change that can be targeted by any currently known drug, you may get a drug called bortezomib during treatment.*

All three drugs are approved by the Food and Drug Administration (FDA) to treat different types of cancers in adults. Only dasatinib is FDA approved for certain uses in pediatric patients Researchers want to find out if adding these drugs will improve the leukemia/lymphoma response to treatment.

Central line placement

Before you start treatment, you will get a special kind of IV called a "central line." This is a kind of IV placed into a big vein in your chest that can stay in for a long time. The risks connected with central lines will be explained to you and all of your questions will be answered. If you are to have a central line inserted, you will be given a separate informed consent document to read and sign for this procedure.

Methods for giving drugs

Various methods will be used to give drugs:

- PO – Drug is given by tablet or liquid swallowed through the mouth.
- IV – Drug is given using a needle or tubing inserted into a vein. Drugs can be given rapidly over a few minutes ("push") or slowly over minutes or hours ("infusion").
- IM - Drug is given into a muscle using a needle.
- IT – Drug used to treat the brain and spinal cord is given using a needle inserted through the back into the fluid surrounding the spinal cord.
- SubQ – Drug is given as a shot beneath the skin

The treatment tables below and throughout your treatment will show the *plan of treatment*. If you have side effects or complications, the dose and schedule may be adjusted or delayed by your study doctor. In some cases, drugs may be started earlier, for example, if your ALL or LLy is not responding to treatment quickly enough.

If you have Down syndrome, you can be treated on this study, but some of the drugs and dosages will need to be changed to make the treatment safer for you. Your doctor will talk to you about the differences in treatment.

Treatment for B-CELL ALL and LLY

If you have **B-cell** ALL or LLy, you will get a combination of several chemotherapy drugs, as shown below:

Drug	How given	Schedule
Prednisone	PO, 3 times a day	Days 1-28
Vincristine	IV, weekly	Days 1, 8, 15, 22
Daunorubicin	IV	Days 2 and 8
Pegaspargase	IV or IM	Days 3 and 15***
Cyclophosphamide	IV	Day 22
Cytarabine (ARA-C)	IV or SubQ	Days 22-25 and 29-32
Mercaptopurine (6MP)	PO	Days 22-35
Dasatinib*	PO, every day	Starting Day 15
Bortezomib**	IV or SubQ	Days 29 and 32

**Dasatinib - if you have ABL1-class fusion, after first 2 weeks of treatment (Day 15).*
***Bortezomib - if your leukemia or lymphoma cells have no targetable change and you are not in remission (no signs of leukemia/lymphoma) after first 2 weeks of treatment (Day 15).*
****The second dose of pegaspargase will only be given to patients with MRD ≥ 1% on Day 15. Patients with MRD < 1% on Day 15 will not receive second dose of pegaspargase. If you have an allergic reaction to pegasparagase, or if pegaspargase is not available, you may get other forms of asparaginase (for example, Erwinaze, Rylaze or Calaspargase pegol.*

You will also get medications before each dose of asparaginase to help decrease the risk of allergic reactions.

Treatment for T-CELL ALL and LLy

If you have **T-cell** ALL or LLy, you will get a combination of several chemotherapy drugs, as shown below:

Drug	How given	Schedule
Prednisone	PO, 3 times a day	Days 1-28
Vincristine	IV, weekly	Days 1, 8, 15, 22
Daunorubicin	IV	Days 2, 8 and 15
Pegaspargase	IV or IM	Days 3 and 15***
Cyclophosphamide	IV	Day 22
Cytarabine (ARA-C)	IV or SubQ	Days 22-25 and 29-32
Mercaptopurine (6MP)	PO	Days 22-35
Dasatinib*	PO, once a day	Starting Day 15
Bortezomib**	IV or SubQ	Days 29 and 32

**Dasatinib - if you have ABL1-class fusion*
***Bortezomib - if your leukemia or lymphoma cells have no targetable change and you are not in remission (no signs of leukemia/lymphoma) after first 2 weeks of treatment (Day 15).*

****The second dose of pegaspargase will only be given to patients with MRD ≥ 1% on Day 15. Patients with MRD < 1% on Day 15 will not receive second dose of pegaspargase. If you have an allergic reaction to pegasparagase, or if pegaspargase is not available, you may get other forms of asparaginase (for example, Erwinaze, Rylaze or Calaspargase pegol.*

You will also get medications before each dose of asparaginase to help decrease the risk of allergic reactions.

Intrathecal (ITMHA) treatments during Remission Induction – all participants

IT treatments with the drugs methotrexate, hydrocortisone, and Ara-C (ITMHA) will be given on Day 1 and 15 of Remission Induction to all participants (B-cell and T-cell ALL and LLy) on this study. If you are found to be at higher risk of having CNS relapse, you will also receive additional ITMHA treatments on days 8 and 22 (as well as days 4 and 11 for highest risk participants). Leucovorin, a vitamin replacement, will be given by vein or by mouth at 24 and 30 hours after each ITMHA treatment during induction. This drug will help lessen some of the side effects of IT treatment.

Response assessments during and after Remission Induction – all participants

You will have blood drawn and bone marrow procedures to check your disease status. Minimal residual disease (also called MRD) is the measurement of very small amounts of leukemia cells in the blood and bone marrow. Blood will be collected on Day 8. Blood and bone marrow will be collected on Day 15, and in some participants, on Day 22. Treatment after Week 3 will depend on how your leukemia or lymphoma has responded to the first 2-3 weeks of treatment. If you have Low-Risk disease at diagnosis, but your ALL or LLy is not in remission by Day 15, your risk status will change to Standard-Risk.

If you have LLy and your bone marrow exam had a very low number of blasts at diagnosis, then your blood will be checked weekly for MRD and you will not need to have bone marrow exams performed.

After your bone marrow and blood cell counts recover from Remission Induction treatment, your disease will be reassessed between Days 38 and 46. ALL patients will have a repeat bone marrow examination and LLy patients will have repeat imaging scans (CT or PET/CT scans) to evaluate response to Remission Induction Treatment.

Early Intensification Therapy (lasts 3-4 weeks)

Most participants with Standard- or High-Risk disease will get an additional treatment called Early Intensification. This will depend on your MRD response after Remission Induction. Your doctor will talk to you about this treatment and if it is needed or not.

If you have Low-Risk disease, you will move on to the next phase of treatment, called Consolidation (described in another consent form).

Early Intensification will consist of several drugs and will start on Day 43 of Remission Induction, as long as your blood cell counts and bone marrow have recovered.

Drug	How given	Schedule
Intrathecal chemotherapy	IT (into spinal fluid)	Day 43
Cyclophosphamide	IV	Day 43
Cytarabine (ARA-C)	IV or SubQ	Days 43-46 and 50-53
Mercaptopurine	PO	Days 43-56
Dasatinib*	PO, once a day	Continue until end of therapy
Bortezomib**	IV or SubQ	Days 43,46
Ruxolitinib***	PO, twice a day – take 2 weeks on and then 2 weeks off	Start on Day 43-46 and continue until end of therapy

**Dasatinib – if you have ABL1-class fusion*
***Bortezomib – if you have no targetable change and your Day 15 or Day 42 MRD was still positive for leukemia or lymphoma.*
****Ruxolitinib – if you have JAK-STAT signaling that can be inhibited by ruxolitinib and MRD was positive on Day 15, 22 or 42 of Remission Induction, or if you have ETP or T-cell MPAL (regardless of MRD)*

After you complete Early Intensification, you will move to the next phase of treatment, Consolidation.

Interim therapy during Remission Induction and Early Intensification Therapy

If for some reason you cannot receive Remission Induction or Early Intensification therapy, or if these therapies need to be interrupted, you may instead receive 6-MP by mouth daily and methotrexate by vein (or PO or IM) every week. If you cannot take 6-MP and methotrexate, you may get a drug called blinatumomab instead. This is called "interim therapy" and will only be given if you need to have Remission Induction or Early Intensification therapy stopped or delayed.

Additional medicines and supportive care

You will get extra medications and other supportive care (like antibiotics, pain medicine, and anti-nausea drugs) to help fight infection and to manage the side effects of treatment. You will also receive blood and platelet transfusions as needed. These treatments are part of standard care for treatment of leukemia and lymphoma.

7. How long will I be in this study?

Remission induction will last for 6 to 7 weeks (or 9 to 10 weeks if you get Early Intensification). Treatment for the entire study will last for 2½ to 3 years. Follow-up exams after the end of treatment will be done for at least 10 years. This information will be outlined in the consent form for consolidation and continuation treatment.

8. What tests and procedures will I have if I take part in this study?

During Remission Induction, you will have a number of tests, evaluations and procedures. Many of these are part of regular cancer care and would be done even if you do not join the study.

Some are standard tests that may not be part of regular care, but are being done (or are being done more often) because you are taking part in this study:

- Medical history and thorough physical examination
- Blood and urine tests to check your blood cell counts, blood chemistries and how your kidneys are working
- Blood tests to check fats, cholesterol, bone health, thyroid function, and iron content in your blood
- Chest x-ray
- Pregnancy test, if you are female and able to have children
- Blood for MRD and other leukemia/lymphoma markers
- Blood tests to see if you have a genetic defect that makes you more likely to have side effects from some of the drugs used in the study (mercaptopurine and vincristine)
- Imaging scans (CT scan and PET/CT scans) for patients with LLy only
- Bone marrow aspirate and biopsy for MRD and other studies*
- Lumbar puncture (spinal tap) and spinal fluid tests, including MRD deep sequencing to look for the smallest amount of leukemia or lymphoma in the spinal fluid*
- Blood tests to check for any viral or bacterial infections
- Neurocognitive testing at or around Week 120 of Continuation Treatment, and at or around two years after you have completed therapy.
- Other studies your doctor thinks are needed

**You will be asked to sign another consent form for the bone marrow and spinal tap procedures. Your study doctor will also explain these procedures and answer all your questions.*

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

Risks of leukemia/lymphoma treatment

All people who receive cancer treatment are at risk of having side effects. In addition to killing tumor cells, cancer treatments such as chemotherapy can damage normal tissue and produce side effects. Side effects usually get better when the cancer treatment is stopped; but sometimes they last a long time or never go away. Some side effects are not very dangerous, but others can be life-threatening or cause death.

Common side effects of cancer treatment include nausea, vomiting, hair loss, and fatigue (tiredness). Drugs may be given to try to prevent or decrease nausea and vomiting. Hair loss is usually temporary but very rarely it may be permanent. Chemotherapy may make you permanently unable to have children. On rare occasions, leukemia/lymphoma treatment can cause a second cancer to develop, usually years after the treatment is finished.

Remission Induction treatment includes a number of chemotherapy agents, that are commonly used in treating ALL and LLy. The side effects of these drugs are listed in the attachment at the end of this consent. However, the side effects may be increased when these chemotherapy drugs are combined.

The most common serious side effect from cancer treatment is lowering of the number of normal blood cells that may result in anemia, increased chance of infection, and/or a bleeding tendency.

As with any treatment for leukemia or lymphoma, you may become very ill. You may need to be hospitalized and may need special supportive care. There is a 1% to 5% risk that you may die from the complications of treatment.

Risks of this study

The treatment given on this study could be more effective or less effective than the treatment you might receive if you were not on study. The treatment given on this study could have more side effects, less side effects, or different side effects than the treatment you might receive if you were not on study.

The addition of the experimental drugs (ruxolitinib or bortezomib) may cause more complications, but also make the overall treatment more effective.

The experimental treatment that is being studied could be more effective than the standard approach to treatment. The experimental treatment that is being studied could be less effective than the standard approach to treatment.

This study requires testing for leukemia/lymphoma-specific genomic features and MRD testing of your blood, bone marrow and spinal fluid. The results of these tests will be used to help decide whether your leukemia or lymphoma is Low-, Standard- or High-Risk. Because no test is perfectly accurate, there is a small risk that these tests might not be accurate and that you might be assigned incorrectly to a risk group. If you are incorrectly assigned to the High-Risk group then you might receive stronger treatment than is needed. Having stronger treatment may increase the risk of having side effects. If you are incorrectly assigned to the Low- or Standard-risk groups, then you might receive less treatment than is needed. Having less treatment may increase the chance that the leukemia or lymphoma comes back (relapses).

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 clinic than usual
- You may be asked sensitive or private questions that you normally do not discuss

The 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 from this treatment. 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 he/she 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.

The tables below show the most common and the most serious side effects that researchers know about for the experimental drugs used during Remission Induction. The commonly used drugs are listed as an attachment at the end of this consent.

Possible side effects of BORTEZOMIB (Velcade®) – *applies to participants who do not have targetable genetic change only*

COMMON, SOME MAY BE SERIOUS In 100 people receiving bortezomib, more than 20 may have:	
• Anemia which may require blood transfusion • Constipation, diarrhea, nausea, vomiting • Tiredness, fever • Infection	• Bruising, bleeding • Loss of appetite • Muscle weakness • Numbness, tingling or pain of the arms and legs

OCCASIONAL, SOME MAY BE SERIOUS In 100 people receiving bortezomib, from 4 to 20 may have:	
• Pain • Heartburn • Bleeding from multiple sites • Internal bleeding which may cause black tarry stool, or blood in vomit • Chills • Swelling of arms, legs • Weight loss • Dehydration • Muscle spasms	• Dizziness, headache • Feeling of "pins and needles" in arms and legs • Worry • Difficulty sleeping • Cough, shortness of breath, sore throat • Rash • Low blood pressure which may cause feeling faint

RARE, AND SERIOUS In 100 people receiving bortezomib, 3 or fewer may have:	
• Heart failure, which may cause shortness of breath, swelling of ankles, and tiredness • A tear or hole in internal organs that may require surgery which may cause difficulty swallowing • Damage to organs, which may cause shortness of breath, or changes in thinking	• Brain damage, which may cause headache, seizure, blindness (also known as Reversible Posterior Leukoencephalopathy Syndrome or RPLS) • Kidney damage, which may cause swelling, may require dialysis

Possible side effects of RUXOLITINIB (Jakafi®) include – *applies to participants with JAK-STAT signaling that can be inhibited by ruxolitinib and MRD was positive on Day 15, 22 or 42 of Remission Induction or participants with ETP or T-cell MPAL (regardless of MRD)*

COMMON, SOME MAY BE SERIOUS In 100 people receiving ruxolitinib, more than 20 may have:
• Lack of enough red blood cells (anemia) • Decreased number of a type of blood cell that helps to clot blood (platelet) • Increased blood level of a liver enzyme (ALT/SGPT)

OCCASIONAL, SOME MAY BE SERIOUS In 100 people receiving ruxolitinib, from 4 to 20 may have:	
• Decreased number of a type of white blood cell (neutrophil/granulocyte), which can increase your risk of infection • Diarrhea • Fatigue or tiredness • Swelling localized to the arms, legs, and/or some other part of the body • Headache or head pain • Weight gain • Infection of the lung, urinary tract, and/or some other part of the body • Bruising • Dizziness (or sensation of lightheadedness, unsteadiness, or giddiness) • Increased amount of cholesterol (a type of fat) in the blood which if prolonged could lead to narrowing of blood vessels or blocking them and leading to heart disease • Increased blood level of a liver enzyme (AST/SGOT) or a liver pigment (bilirubin) which is often a sign of liver problems	• High blood pressure • Generalized weakness of the whole body • Belly pain • Excess passing of gas • Activation of a virus called herpes zoster that may cause shingles; a painful blistering skin rash • Bleeding in the upper digestive tract and/or in some portion of the lower gastrointestinal tract • Fever • Abnormal increase in sensitivity of the senses to stimulation; increased sensitivity to touch, taste, smell, or sound • Pancreatitis • Group of signs and symptoms due to rapid breakdown of tumor that can occur after treatment of cancer has started that causes increased levels of blood potassium, uric acid, and phosphate, decreased levels of blood calcium, and kidney failure

RARE, AND SERIOUS In 100 people receiving ruxolitinib, 3 or fewer may have:
• A rare disorder* that damages the material that covers and protects nerves in the white matter of the brain. It is caused by the John Cunningham (JC) virus. The disorder may cause headaches, loss of coordination, clumsiness, loss of language ability, memory loss, vision problems, and weakness of the legs and arms that gets worse.

*A rare disease called progressive multifocal leukoencephalopathy (PML) has been reported during ruxolitinib treatment. PML comes from a viral infection that causes brain damage and can be fatal. It is unknown whether this was due to ruxolitinib treatment since PML has occurred in patients with blood cancers who were not treated with ruxolitinib. Tell your study doctor immediately if you have any of the following symptoms or if anyone close to you notices that you have any of these symptoms: confusion or problems thinking, loss of balance or problems walking, clumsiness, difficulty speaking, decreased strength or weakness on one side of your body, blurred and/or loss of vision.

Possible side effects of BLINATUMOMAB include: *applies to B-cell patients receiving Interim Therapy with blinatumomab only*

COMMON, SOME MAY BE SERIOUS In 100 people receiving blinatumomab, more than 10 may have:	
• Anemia (decreased red blood cells) • Thrombocytopenia (decreased platelets, for clotting blood) • Neutropenia (decreased neutrophils, a type of white blood cell that fights infection) • Febrile neutropenia (decreased neutrophils with fever) • Leukopenia (decreased white blood cells) • Increased hepatic enzymes (in the blood, which may be due to inflammation or damage to liver cells) • Tachycardia (rapid heart rate) • Fever • Edema (swelling of hands, legs, ankles, feet, face or trunk) • Back pain • Bone pain • Headache • Insomnia (difficulty falling and/or staying asleep) • Cough • Rash • Weight increase • Low blood pressure	• Infusion related reactions occur during or after the drug is given through the vein. Symptoms of infusion reaction may include headache, rash, itching, flushing, swelling, shortness of breath, nausea and sometimes vomiting. Severe infusion reactions can cause dizziness, severe skin reactions, difficulty breathing or swallowing, a decrease in blood pressure, and could be life threatening. Signs and symptoms of infusion reaction can be very similar to cytokine release syndrome. • Cytokine release syndrome is when your body releases substances called cytokines during the blinatumomab infusion. This can cause fever, chills, headache, decreased blood pressure, increased liver enzymes, nausea, and vomiting. Cytokine release syndrome symptoms generally are mild to moderate but occasionally can be serious or life threatening, or may even lead to death. Your doctor may give you medications such as steroids and/or other medications to prevent or treat cytokine release syndrome

COMMON, SOME MAY BE SERIOUS In 100 people receiving blinatumomab, more than 10 may have:
• High blood pressure • Infections in the blood, including bacteria, fungi, viruses, or infections in other organs. Serious infections can happen during and after treatment and can lead to death. Serious infections such as sepsis (infection in the bloodstream), and pneumonia (severe lung infection) have been reported in patients treated with blinatumomab. Your doctor may give you antibiotics to treat the infection or stop your treatment with blinatumomab

OCCASIONAL, SOME MAY BE SERIOUS In 100 people receiving blinatumomab, from 1 to 10 may have:	
• Leukopenia, lymphopenia (decreased types of white blood cells • Leukocytosis (increased white blood cells) • Lymphadenopathy (swelling in lymph nodes) • Hyperbilirubinemia (high levels of bilirubin in the blood) • Decreased immunoglobulins (in the blood, proteins made by the body's immune system to fight against infections and foreign substances) • Increased alkaline phosphatase (in the blood can be due to problems in your liver or in your bones) • Chills • Chest pain • Pain in the arms, legs and hands • Overdose, accidental overdose • Flushing • Dyspnea (difficulty breathing, wheezing or respiratory failure) • Hypersensitivity, allergic reactions to blinatumomab, including hypersensitivity have been reported. Signs and symptoms of allergic reactions can be very similar to infusion reaction. If you have symptoms of an allergic reaction, you should contact	• Tumor lysis syndrome (a group of complications from release of large amounts of potassium, phosphate, and nucleic acid caused by the breakdown of tumor cells after cancer treatment). Tumor lysis syndrome may cause kidney failure, abnormal heart rhythm, and can even lead to death. Patients with moderate kidney failure showed an increased rate of tumor lysis syndrome compared with patients with mild kidney failure or normal kidney function. However, this did not lead to permanent discontinuation of treatment with blinatumomab. Your doctor may give you medications before your treatment to help prevent tumor lysis syndrome. • Nervous system problems such as tremor (shaking), dizziness, seizures, somnolence (changes in alertness), paresthesia (abnormal skin sensation such as burning, prickling, tingling), hypoesthesia (numbness), aphasia (difficulty speaking or slurred speech), cognitive disorder (difficulty understanding words), encephalopathy (loss of consciousness, brain malfunction), memory impairment (memory loss), confusion and/or disorientation, or loss of balance. Patients with a medical history of neurologic signs

OCCASIONAL, SOME MAY BE SERIOUS In 100 people receiving blinatumomab, from 1 to 10 may have:	
the study doctor or study staff immediately. • Hematophagic histiocytosis can occur with cytokine release syndrome, described above. It is a life threatening overactivity of your immune system caused by releasing large amount of inflammatory cytokines. Your doctor may give you medications such as steroids and/or other medications to prevent or treat cytokine release syndrome	and symptoms had a higher rate of neurologic events (such as tremors, dizziness, confusion, encephalopathy, and poor coordination). Your doctor will be closely monitoring you and may give you medications such as steroids and/or other medications to treat nervous system problems or stop or treatment with blinatumomab.

RARE, AND SERIOUS In 1000 people receiving blinatumomab, 1 and 10 may have:
• Speech disorder • Cytokines storm, a severe form of cytokine release syndrome described above) • Pancreatitis, inflammation of the pancreas that can be life-threatening or may even lead to death. Symptoms can include severe and persistent stomach pain, with or without nausea and vomiting. • Leukoencephalopathy, a rare, serious disorder of the white matter in the brain that can lead to severe disability and death and for which there is no known prevention, treatment or cure. Symptoms can include difficulty thinking, loss of balance, changes in speech or walking, weakness on one side of your body or blurred or lost vision. • Capillary leak syndrome (leakage of fluid from small blood vessels into other body spaces that could cause swelling of the trunk, arms and legs). • Relapse of CD19 negative B-precursor ALL and lineage switch from ALL to AML have been observed in patients with ALL, during or following blinatumomab treatment, in clinical trials and the post marketing setting.

After you start taking blinatumomab, it is possible that your body may make proteins that may stop blinatumomab from working or may cause side effects. In clinical studies of patients treated with blinatumomab, less than 2% tested positive for anti-blinatumomab antibodies. Anti-blinatumomab antibody formation may affect the pharmacokinetics (how much blinatumomab is in your body. Blood tests will be used to check for antibodies during the study.

Tell your doctor if you think you may need any vaccinations in the near future, including those needed to travel to other countries. Some vaccines must not be given within 2 weeks before, at the same time as, or in the months after you receive treatment with blinatumomab. Your doctor will check if you should have the vaccination.

No studies of the effects of blinatumomab on the ability to drive and use machines have been performed. However, due to the potential for nervous system problems, you should not drive or engage in hazardous occupations or activities such as operating heavy or potentially dangerous machinery while blinatumomab is being infused.

Other risks of the study

A possible late side effect is a second cancer. The exact risk is not known but is thought to be 3% to 10% in the first 20 years of follow-up**.**

There are reports of learning and attention problems in children receiving therapy for ALL or LLy. Chemotherapy, the leukemia or lymphoma, and emotional and psychological problems as a result of the illness may cause these problems.

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. 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 of this study

The potential benefit of this study is that you may have the same or better chance of long-term remission as children in the earlier studies, with fewer serious side effects. The research studies of blood and bone marrow may not be of direct benefit to you. However, they may help other children with leukemia in the future.

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

The risks of this treatment to an unborn or nursing child are unknown. Females in the study must not be pregnant or nursing when they start the study and must not get pregnant during the study. If you think you may have become pregnant during the study, you must tell the researcher right away. If you become pregnant, you will be taken out of the study.

Males in the study must not father a child during the study. Males should talk to the researcher about the option of freezing sperm before taking part in this study.

Participants in this study must use effective forms of birth control. The researcher can tell you about the best birth control methods to use during this study. Effective forms of birth control may include birth control pills taken by mouth, condoms, and not having sex. Birth control methods should be continued for 6 months after treatment to avoid pregnancy. We also do not know if there may be unknown long-term effects to your future children.

11. Can you stop taking part in this study?

Yes. You can decide to stop at any time. If you decide to stop for any reason, it is important to let the study doctor know as soon as possible so you can stop safely. If you stop, you can decide whether or not to let the study doctor continue to provide your medical information to the organization running the study.

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

The study 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

13. What are you other options?

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

- you may choose to have the usual approach described above
- you may choose to take part in a different study, if one is available

14. 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.

15. Will you be paid for your time or expenses?

You will not be paid for your time or expenses. Also, your samples and/or information may be used to develop a new product or medical test, which may be sold. If this happens, you will not receive any payments for these new products.

16. 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. Inaba, 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

17. How will new finding 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 that might cause you to change your mind about continuing the study.

18. 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.

19. What about privacy and confidentiality?

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) may be used or given to someone outside 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.

Federal agencies such as the Food and Drug Administration (FDA), the Office for Human Research Protections (OHRP), the National Institutes of Health (NIH), and St. Jude Children's Research Hospital Institutional Review Board (IRB), your insurance company and other health benefits plan (if charges are billed to these plans), Incyte, Amgen, as well as other regulatory agencies, committees, or persons involved in overseeing research studies may review your research and medical record.

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.

If you consent to take part in this study, the records obtained while you are in this study as well as related health records will remain strictly confidential at all times. The information will be held securely on paper and electronically at your treating hospital and the main hospital site managing this research. Your name will not be passed to anyone else outside the research team. You will be allocated a research identification number, which will be used as a code to identify you on all trial forms. Any research-related information about you that leaves the hospital will have your name and address removed so that you cannot be recognized.

To help us protect your privacy, the study has been granted a Certificate of Confidentiality from the federal government. With this Certificate, the researchers cannot be forced to give out your personal information as well as biospecimens that may identify you, even by a court subpoena, in any federal, state, or local civil, criminal, administrative, legislative, or other process. The researchers will use the Certificate to block any demands for information that would identify you, except in the cases listed below.

The Certificate cannot be used to resist a demand for information from the United States Government, if that information is used to audit or check federally funded projects or to meet the needs of the U.S. Food and Drug Administration (FDA).

You should know that a Certificate of Confidentiality does not keep you or a member of your family from choosing to give out information about you or your part in this research. If an insurer, employer, or other person gets your written consent to receive research information, then the researchers cannot use the Certificate to keep that information private.

The Certificate of Confidentiality will not keep researchers or hospital staff from making reports required of them. These include reports about suspected child abuse, about diseases that spread from person to person, or about possible threat of harm to yourself or others.

By signing the 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 (the Food and Drug Administration); this is to ensure that the study is carried out to the highest possible scientific standards.

20. 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, 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:

- the Food and Drug Administration (FDA)
- the Office for Human Research Protections (OHRP)
- the National Institutes of Health (NIH)
- St. Jude Children's Research Hospital Institutional Review Board (IRB)
- Amgen (if you receive blinatumomab)
- Incyte and their designated representatives (if you receive ruxolitinib)
- Cook Children's Medical Center investigators and study team.
- Lucile Packard Children's Hospital investigators and study team.
- The Royal Children's Hospital Melbourne investigators and study team.
- Rady Children's Hospital-San Diego investigators and study team.
- Children's Hospital of Michigan investigators and study team.
- Monash Children's Hospital investigators and study team.
- Hemby Children's Hospital investigators and study team.
- Children's Hospital of Illinois at OSF-Saint Francis Medical Center and study team
- The Children's Hospital at Saint Francis at Tulsa, OK and study team

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.

21. 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. Hiroto Inaba
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 would need to 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 in this research study, please read and sign the consent form. You will be given a copy of this information and the consent form to keep. A copy of the consent form will be put in your patient notes, one will be put with the study records, and one may be sent to the Research 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 information sheet and to consider taking part in this study.

THIS SECTION IS ABOUT OPTIONAL RESEARCH STUDIES YOU CAN CHOOSE TO TAKE PART IN.

You will not get health benefits from any of these optional studies. The researchers leading the optional studies hope the results will help other people with cancer in the future. The results will not be added to your medical records, nor will you or your study doctor know the results.

You can still take part in the main study even if you say 'no' to any or all of these optional studies. If you sign up for but cannot complete any of these optional studies for any reason, you can still take part in the main treatment study.

Blood will be drawn during Remission Induction (and in some cases, Consolidation and/or Continuation Treatment) for the research studies listed below. Every effort will be made to limit the amount of blood drawn at any one time. We will also try to draw blood for research studies at the same time as the regular blood tests and bone marrow procedures to monitor treatment. In most cases, the blood can be drawn from your central line so that multiple needle sticks are not needed.

Please circle your choice of "**YES**" or "**NO**" for each of the following optional research studies, described below and on the next several pages.

1. Optional MRD research

This is being done to use measurements of very small amounts of leukemia cells (Minimal Residual Disease, MRD) to monitor how well the treatment is working. Researchers want to relate the MRD measurements taken during treatment to how well a participant does in the long term and to compare the results of new and different methods used to determine MRD.

Please circle your answer: I agree to allow my bone marrow and blood to be used for MRD research studies.

YES **NO**

2. Optional drug sensitivity research

If you agree to have this extra test, we will use a sample of the bone marrow that was collected during your bone marrow procedure at diagnosis. The bone marrow will be sent to a laboratory at St. Jude for sensitivity to anti-leukemia/lymphoma drugs. If no bone marrow is drawn for routine care, a blood sample drawn at the same time you are having blood drawn for routine care may be used in its place.

Please circle your answer: I agree to allow my bone marrow and blood to be used for drug sensitivity research studies

YES **NO**

3. Optional creation of cell lines for research studies

In addition, samples may be used to create "cell lines" for drug sensitivity studies and genomic profiling for research. Drug sensitivity studies are done when researchers use the cell lines to test many different anti-leukemia/lymphoma drugs, in the hope of finding better treatments for future patients. Genomic profiling is a laboratory method that is used to learn about all the genes in a person, and the way those genes interact with each other and with the environment. Genomic profiling may be used to find out why some people get certain diseases while others do not, or why people react in different ways to the same drug.

Creating a cell line means using a cell from a person to grow more cells with the same genetic information. This process allows us to have a continuing source of genetically similar cells for research. Creating cell lines often involves growing human cells in other species such as mice to provide a suitable environment for cells to grow. Human cells grown in other species are called "xenografts".

Please circle your answer: I agree to allow my bone marrow and blood to be used to create cell lines and xenografts.

YES **NO**

4. Optional genetic research studies and germline DNA

Researchers are looking for changes (also known as mutations) in your DNA that may be related to the occurrence of this type of leukemia and changes that may explain why some patients have more side effects from the drugs used in this study than other patients. DNA is the hereditary material in humans that is passed from parent to child. DNA is organized into units called genes. There are about 20,000 different genes responsible for different functions of human cells. When there is a change in one or more genes, it can *sometimes* mean that a person is at a higher risk of developing a particular condition, such as leukemia or lymphoma. Mutations that are present in every cell of the body (including tumor cells and normal cells) are known as "germline" mutations. Mutations that are only present in the tumor cells (and not in normal cells) are known as "tumor" or "somatic" mutations.

If you agree to participate in this research, researchers will use DNA sequencing information from your non-tumor, "germline" sample. You will have been asked or will be asked to consent to sequencing of tumor and non-tumor DNA to help accurately diagnose your leukemia. Results of tumor sequencing will be provided to your treating doctor. You will also be given the opportunity to consent to receive the results of germline sequencing of genes known to predispose to cancer at a later time. Here, you have the opportunity to consent to the use of your germline sequence information to be used for research.

Privacy risks of genetic research

Your genetic and clinical information will probably be shared with other researchers outside of St. Jude by releasing it into scientific databases. In all cases where this information is placed into databases and shared, your identifying information (such as your name or medical record number) will be removed. These databases are restricted and can only be accessed by approved researchers. Sharing this information will help advance medical research by helping to solve questions about what causes cancer or other diseases and how to treat these conditions better.

Nobody will be able to know just from looking at a database that information belongs to you. However, because your genetic information is unique, there is a small chance that someone could trace the information back to you or your close biological relatives. The risk of this happening is very low but may grow in the future as new ways of tracing the information back to you or your close biological relatives are developed. Thus, the risk that your privacy would be breached may increase over time. Researchers who access your information have a professional obligation to protect your privacy and maintain your confidentiality.

In this study, we will examine the DNA of each individual participant and use the data from all participants to figure out if a gene change is related to leukemia. Because these studies will be done in a research environment and are not qualified as clinical tests, we do not plan to return any of your specific results to you and they will not be placed in your medical record.

Most of the time we do not need to draw a new blood sample. Because this study is focused on leukemia and lymphoma, we do not plan to look at genes associated with other diseases or medical conditions. However, it is possible that, by chance, we will find that you have a variant in a gene that is unrelated to leukemia or lymphoma. This is called an "incidental finding". If we believe that the information about this incidental finding is of medical importance and if you indicated that you wish to be informed about incidental finding(s), we will then contact you and will refer you for genetic counseling at St Jude. Genetic counselors can help you decide if you want to be tested in a clinical lab to determine whether you might or might not carry the gene change that we came across by chance. If you would like to be tested, the counselors and study team will work with you to have your DNA sample analyzed in a separate clinical laboratory.

Please circle your answer: I agree to allow my blood sample to be used for genetic research and germline DNA/RNA studies.

YES **NO**

5. Optional clonal structures of leukemia/lymphoma cells research

If you agree to this research, blood and bone marrow (about 1 teaspoon or less) will be collected at the same time you have blood draws and bone marrow procedures for clinical care. This will be done to monitor any changes in the genetic make-up of your leukemia or lymphoma cells before and during treatment.

Blood or bone marrow will be sent to a laboratory at the following times:

- Pretreatment and Days 1, 3, 8, 15 and 22 of Remission Induction
- At the end of Remission Induction and Early Intensification (if applicable)
- During Continuation Treatment at Weeks 1 (or 3), 7, 33 and 120 (end of treatment)

All patients will have blood or bone marrow sent pretreatment, Days 1 and 3. Only those with a certain subtype of ALL will have the sample collected the remaining days.

Please circle your answer: I agree to allow my blood and/or bone marrow to be used for clone-specific responses of leukemia/lymphoma cells research studies.

YES **NO**

6. Optional asparaginase and biomarker research:

One of the cancer-fighting drugs you will get is called asparaginase. Some children may develop antibodies (blood immunity proteins that fight against the asparaginase) that may keep the drug from working well. These antibodies may affect the levels of asparagine in blood. If you have an allergic reaction to or side effects with asparaginase, about ½ teaspoon blood sample may be collected from your central line if your doctor thinks they would be helpful during your therapy. The blood will be tested to see if antibodies, asparagine levels, and other markers in the blood are related to how well the drug works and side effects of the drug.

To learn more about how the body uses the drug asparaginase, we will collect about ½ to 1 teaspoon of blood at time points listed below. The blood will be tested to see if biomarkers in the blood are related to how well the drug works and side effects of the drug. These blood samples will be collected at the same time blood is collected for routine labs at the following times:

- Days 15 of Remission Induction
- Day 15 of Consolidation Treatment
- Day 1 of Weeks 7, 8 and 17 of Continuation Treatment

Please circle your answer: I choose to take part in the asparaginase and biomarker research studies:

YES **NO**

7. Optional nerve toxicity study

Some patients receiving treatment for leukemia will develop nerve problems from some of the drugs used in this study, particularly vincristine. This can lead to pain, numbness, tingling, swelling, or muscle weakness in different parts of the body. This usually begins in the hands or feet and can get worse over time.

If you agree to take part in this research, you will be asked a series of questions and be tested to check your brain, spinal cord, and nerve function. This evaluation will check your mental status, coordination, ability to walk, and how well the muscles, sensory systems, and deep tendon reflexes work. We will also ask you to walk as fast as possible for six minutes while pushing a measuring wheel that will record how far you walked. Your heart rate will be monitored during this time. Your level of pain will be assessed using a series of questionnaires and pain scales according to your age level.

The neurologic evaluations will be done 8 times:

- One time Remission Induction Treatment (between Day 23-43)
- 4 times during Continuation Treatment (Weeks 1, 17, 49, 101)
- At the end of all therapy (Week 120)
- 2 and 5 years after you stop all therapy

Please circle your answer: I agree to take part in nerve and muscle function research studies:

YES **NO**

8. Optional bone mineral density research (children ages 4 years and older)

Some of the treatment used in this study, especially steroid drugs, such as the dexamethasone and prednisone, are known causes of problems called “osteopenia”. Osteopenia results from the temporary or permanent loss of the bone density.

This research has several parts. Some will start during Remission Induction and will continue in the Consolidation and Continuation Treatment phases. Some will not start until Continuation.

The parts of the research that will begin during Remission Induction Treatment are explained below. The rest of the research tests are explained in the Consolidation and Continuation consent that you will be asked to sign after you complete Remission Induction.

a. Quantitative computed tomography or QCT scan: A QCT is a fast, painless bone mineral density (BMD) exam performed on a CT scanner. It allows doctors to look for low bone mass and monitor the effects of bone mass therapy in patients undergoing treatment. During the exam, your lower spine and tibia (lower leg, shin bone) will be scanned.

If you agree to take part in this research, QCT scans will be done 5 times:

- End of Remission Induction Treatment
- At Week 49 of Continuation Treatment
- At the end of therapy (Week 120) and 2 and 5 years after you stop treatment

b. Bone biomarkers: If you agree to this research, blood samples (about 2 tablespoons) will be collected to measure markers in your blood which indicate the loss and re-growth of bone. Hormones that affect bone growth will also be measured, as well as Vitamin D levels. Blood will be drawn for these tests at these time points:

- End of Remission Induction Treatment
- At Week 49 of Continuation Treatment

If the above tests show that you have suffered bone loss as a result of treatment, you will be referred to the Endocrine clinic for evaluation and treatment. Your doctor may order other tests as needed to monitor your condition, as part of standard care.

c. Measurements and assessments: This part of the research will be done at End of Remission Induction, Weeks 1, 49, and 101 of Continuation Treatment, off therapy (week 120), and 2 and 5 years post therapy.

- *Body measurements*: Your height, weight, waist and hip measurements will be taken by a study team member and recorded.
- *Physical activity questionnaire*: You will be asked about your physical activities over the past 7 days by a study team member.
- *Tibial length*: The length of the bone in your lower leg will be measured using a measuring device that looks like a flexible yard stick.
- *Development staging*: Your stage of pubertal development will also be assessed and recorded. This is done during your routine physical examination by your physician or nurse practitioner.

Please circle your answer: I agree to take part in the bone mineral density research studies as described above:

YES **NO** **N/A** *(participant is < 4 years)*

9. Optional psychological testing

This research is being done to better understand the effects of treatment on neurocognitive function. This research tries to answer the following questions: How does treatment affect a child's ability to think and reason? Will there be later effects on a child's ability to concentrate, learn, remember things, and process information? The measures to be done will depend on the age of the patient. For children 3 years of age and younger, this testing will be shortened and targeted toward early developmental skills. For children over 3 years of age, the psychological

tests will include measures of intelligence, memory, attention, speed of processing information, problem solving, fine motor skills, academic abilities and behavior. These tests are common tests used to evaluate functioning in clinical settings. This testing will occur at three time points [End of Induction/Early Intensification, at the end of therapy (Continuation Week 120) and two years after you complete all protocol therapy]. Parents will be asked to complete questionnaires at the same time points. At each time point, these tests will take about 2-3 hours to complete depending on the child's age and speed at which they can complete the tasks. Brief feedback will be provided including the names of the tests administered, current level of functioning, and any areas of identified problems. If problems are identified, we will also facilitate further clinical testing and provide recommendations for managing these problems.

Please circle your answer: I agree to have psychological testing to learn more about the effects of ALL and LLy treatment on the brain.

YES **NO**

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)

Consent Attachment:

TREATMENT AND PROCEDURES COMMON TO ALL PATIENTS WITH ALL/LLY

Risks of chemotherapy drugs used during Remission Induction

Possible side effects of INTRATHECAL CHEMOTHERAPY (cytarabine, methotrexate, and hydrocortisone) when given into the spinal fluid

COMMON, SOME MAY BE SERIOUS In 100 people receiving intrathecal chemotherapy, more than 20 may have:	
• Nausea, vomiting • Fever	• Headache

OCCASIONAL, SOME MAY BE SERIOUS In 100 people receiving intrathecal chemotherapy, from 4 to 20 may have:	
• Swelling of the brain, which may cause stiff neck, sensitivity to light, headache, vomiting • Major change in thinking patterns • Difficulty learning	• Confusion • Tiredness • Seizure

RARE, AND SERIOUS In 100 people receiving intrathecal chemotherapy, 3 or fewer may have:	
• Rash • Bleeding in the brain • Paralysis, weakness • Dizziness	• Damage to the brain, which may cause changes in thinking, blindness • Infection

Possible side effects of PREDNISONE include:

COMMON, SOME MAY BE SERIOUS In 100 people receiving prednisone, more than 20 and up to 100 may have:	
• Decreased height • Loss of bone tissue • Mood swings • Skin changes, acne • Swelling of the body, tiredness, bruising • Pain in belly	• High blood pressure, which may cause headaches, dizziness, blurred vision • Increased appetite and weight gain • Weight gain in the belly, face, back and shoulders

OCCASIONAL, SOME MAY BE SERIOUS In 100 people receiving prednisone, from 4 to 20 may have:	
• Abnormal heartbeat • Cloudiness of the eye, visual disturbances • Glaucoma • Infection	• High blood sugar, which may lead to diabetes • Damage to the bone, which may cause joint pain and loss of motion

OCCASIONAL, SOME MAY BE SERIOUS In 100 people receiving prednisone, from 4 to 20 may have:	
• Non-healing wound • Heartburn	• Kidney stones

RARE, AND SERIOUS In 100 people receiving prednisone, 3 or fewer may have:
• Bleeding from sores in the stomach • Broken bones

Possible side effects of VINCRISTINE include:

COMMON, SOME MAY BE SERIOUS In 100 people receiving vincristine, more than 20 may have:	
• Constipation • Hair loss • Pain or redness at the site of injection • Numbness and tingling of fingers or toes	• Headache, jaw pain and/or muscle pain • Weakness and difficulty walking • Swelling of lower legs

OCCASIONAL, SOME MAY BE SERIOUS In 100 people receiving vincristine, from 4 to 20 may have:	
• Anemia which may cause tiredness, or may require transfusion • Drooping eyelids	• Hoarseness

RARE, AND SERIOUS In 100 people receiving vincristine, 3 or fewer may have:	
• Seizure • Blurred vision with a chance of blindness	• Difficulty with balance and hearing, hearing loss

Possible side effects of DAUNORUBICIN include:

COMMON, SOME MAY BE SERIOUS In 100 people receiving daunorubicin, more than 20 may have:	
• Hair loss • Nausea, vomiting	• Pink or red colored urine, sweat, or saliva

OCCASIONAL, SOME MAY BE SERIOUS In 100 people receiving daunorubicin, from 4 to 20 may have:	
• Damage to the heart, which may cause shortness of breath, tiredness • Infection, especially when white blood cell count is low • Anemia which may require transfusion • Bruising, bleeding	• Dark discoloration of the nails, skin • Loss of nails • Redness and pain at the site of previous radiation • Swelling and redness at the site of injection • Diarrhea

OCCASIONAL, SOME MAY BE SERIOUS In 100 people receiving daunorubicin, from 4 to 20 may have:
• Pain and sores in mouth and throat

RARE, AND SERIOUS In 100 people receiving daunorubicin, 3 or fewer may have:	
• Cancer of the bone marrow (leukemia) cause by chemotherapy	• 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 In 100 people receiving asparaginases, more than 20 may have:	
• Nausea, vomiting • Allergic reaction which may cause rash, low blood pressure, wheezing, shortness of breath, swelling of face or throat • Chills, fever • Tiredness • Hives, rash • Pain at the site of injection • Diarrhea • Hyperglycemia (high levels of sugar in the blood) • High levels of bilirubin and ALT in the blood, which can mean inflammation and/or damage to liver cells	• Low white blood cell count • Prolongation of a blood test (aPTT) to check blood clotting activity • Increase in an enzyme called lipase that helps break down fats in the body, which may mean that the pancreas is damaged • Pain in the abdomen (belly) • Fever with a low white blood cell count which could mean infection and may require hospitalization and treatment with antibiotics

OCCASIONAL, SOME MAY BE SERIOUS In 100 people receiving asparaginases, 4 to 20 may have:	
• Abnormal heartbeat • Blood clot • Infection, especially when white blood cell count is low • Bruising, bleeding • Anemia, which may require blood transfusion • Liver damage, which may cause yellowing of eyes and skin • Headache • Night sweats	• Dizziness (or sensation of lightheadedness, unsteadiness, or giddiness) • Difficulty speaking or putting words together • Disorder in the nerve responsible for control of the muscles for chewing and feeling in the face • Diarrhea • Occasional sudden sharp pain in the rectal area • Inflammation and/or sores in the mouth (and/or throat and/or esophagus, the tube that leads from the mouth to the stomach)

OCCASIONAL, SOME MAY BE SERIOUS
In 100 people receiving asparaginases, 4 to 20 may have:

- 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
- Low levels of the protein albumin in the blood
- Prolongation of a blood test (INR) to check blood clotting activity
- Weight loss
- An increase in an enzyme (amylase) that helps break down carbohydrates. This could mean that the pancreas is damaged
- Increase in the blood level of an enzyme called Gamma-glutamyl transferase (GGT), which may indicate bile duct inflammation or damage.
- 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.
- Nausea
- Vomiting
- Severe blood infections which may be life threatening
- 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.
- Loss of appetite.
- Fever (high temperature)
- Shortness of breath
- A decrease in blood pressure
- Lip swelling
- Hives; red and sometimes itchy bumps on the skin.
- Low levels of certain salts in the body like sodium, calcium, potassium and phosphate
- that may make swallowing difficult and are painful (painful mouth sores)
- Build-up of fluid in the abdomen (belly)
- Vomiting blood
- Inflammation or infection of the sinuses (the hollow air spaces within the bones surrounding the nose) which can cause pain, headache and nose drip
- Infection of the abdominal cavity, belly, bladder or kidney, body tissue, colon, eye, lung, mouth, spleen, or skin
- Infection and swelling of the muscle
- Infections including those caused by bacteria, virus, and fungus
- Infection which occurs due to a decreased number of a type of white blood cells
- Abnormal clotting of the blood
- Excessive loss of water from the body
- Condition where the blood contains more acid than normal
- Abnormal control of blood sugar level
- Low levels of oxygen in the blood which may make you feel short of breath, confused dizzy or drowsy
- Fluid build-up in between the layer of tissue that line the lungs and chest cavity that can make you feel short of breath
- Nosebleed
- Inflammation of the lungs which may cause shortness of breath, cough, and high temperature (fever)
- A feeling of extreme tiredness not relieved by sleep
- Pain – general pain, back pain, joint pain, or pain in arms and legs
- Bleeding at the site of an IV line
- Muscular inflammation or swelling causing discomfort or pain from infection or an unknown cause
- Loss of strength in the muscles
- Tiny red or purple spots on skin or mucus membranes caused by localized bleeding
- Itching

OCCASIONAL, SOME MAY BE SERIOUS In 100 people receiving asparaginases, 4 to 20 may have:	
• Low levels of sugar in the body which may require that you take replacement doses • Increased levels of a chemical (creatinine) in the blood which could mean kidney damage • Low numbers of white blood cells called lymphocytes that may make it easier to get infections which may be life threatening • An increase in the blood level of the enzyme creatine phosphokinase which could indicate muscle damage • Abnormal levels of magnesium in the body which may require that you take extra magnesium by mouth or vein • A disturbance in the function of the brain or spinal cord that may affect the nerves and muscles of the body • Convulsions • Fainting	• Feelings of sadness, despair, loss of energy, and difficulty dealing with normal daily life • Restlessness • Anxiety • Psychiatric disorder • Increased need to urinate during the daytime • 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 In 100 people receiving asparaginases, 3 or fewer may have:	
• Kidney failure • Severe damage to the brain which may lead to difficulty carrying out normal daily tasks and may progress to coma • Bleeding in the brain • 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 • Death of tissue of the pancreas • An abnormal hole in the small intestine • 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 • 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 • Rash; flaking or sloughing of skin • 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. • 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 CYCLOPHOSPHAMIDE include:

COMMON, SOME MAY BE SERIOUS In 100 people receiving cyclophosphamide, more than 20 may have:	
• Hair loss • Nausea, vomiting, loss of appetite • Sores in mouth	• Infection, especially when white blood cell count is low • Absence of menstrual period, which may decrease your ability to have children • Blood in urine

OCCASIONAL, SOME MAY BE SERIOUS In 100 people receiving cyclophosphamide, from 4 to 20 may have:	
• Damage to the bone marrow (irreversible), which may cause infection, bleeding, may require transfusions • Loss or absence of sperm, which may lead to an inability to father children	• Stuffy nose • Fluid around the heart

RARE, AND SERIOUS In 100 people receiving cyclophosphamide, 3 or fewer may have:	
• Severe skin rash with blisters and peeling, which can involve mouth and other parts of the body • Damage to the heart or heart failure, which may cause shortness of breath, swelling of ankles, cough or tiredness	• A new cancer including cancer of bone marrow (leukemia) caused by chemotherapy • Swelling of the body including the brain, which may cause dizziness, confusion • Scarring of the lungs

Possible side effects of CYTARABINE (ARA-C) include:

COMMON, SOME MAY BE SERIOUS In 100 people receiving cytarabine (Ara-c), more than 20 may have:	
• Blood clot • Rash • Swelling in the rectum, which may cause rectal pain • Diarrhea, loss of appetite, nausea, vomiting	• Sores in mouth, which may cause difficulty swallowing • Anemia, which may cause tiredness, or may require blood transfusions • Fever

OCCASIONAL, SOME MAY BE SERIOUS In 100 people receiving cytarabine (Ara-c), from 4 to 20 may have:	
• Infection, especially when white blood cell count is low • Bruising, bleeding • Allergic reaction, which may cause rash, low blood pressure, wheezing, shortness of breath and swelling of the face or throat • Numbness and tingling of the arms and legs • Severe blood infection	• Kidney damage, which may cause swelling and may require dialysis • Headache • Chest pain • Hair loss • Liver damage which may cause yellowing of skin or eyes • Swelling and redness of the eye

RARE, AND SERIOUS In 100 people receiving cytarabine (Ara-c), 3 or fewer may have:
• Coma • A syndrome called Ara-C syndrome where there is fever, aches, pains, sometimes chest pain, a rash and inflammation of the eye • With higher doses of cytarabine there can be effects on the brain, which can lead to headaches, incoordination of the muscles when walking, rapid jerky eye movements, difficulty with speech, sleepiness, personality changes and coma • With higher doses of cytarabine there can be effects on the heart, which can lead to chest pain and damage to the heart muscle • Muscle breakdown, which can lead to injury to the kidneys and other organs

Possible side effects of MERCAPTOPURINE (6-MP) include:

COMMON, SOME MAY BE SERIOUS In 100 people receiving mercaptopurine, more than 20 may have:	
• Anemia which may cause tiredness, or may require transfusion • Bruising, bleeding • Infection, especially when white blood cell count is low	• Loss of appetite, nausea, vomiting, diarrhea • Fatigue • Rash

OCCASIONAL, SOME MAY BE SERIOUS In 100 people receiving mercaptopurine, from 4 to 20 may have:	
• Damage to the liver which may cause pain, bleeding, confusion • Pain	• Absence or decrease sperm which may impact ability to father children • Fever

RARE, AND SERIOUS In 100 people receiving mercaptopurine, 3 or fewer may have:
• Damage to the lungs which may cause shortness of breath • Damage to the pancreas causing abdominal pain* • A new cancer resulting from treatment of a prior cancer

**If you have damage to the pancreas (also called "pancreatitis"), your doctor may switch you to another drug called thioguanine.*

Possible side effects of THIOGUANINE (*participants with 6MP-related pancreatitis only*)

COMMON, SOME MAY BE SERIOUS In 100 people receiving thioguanine, more than 20 and up to 100 may have:
• Sores in mouth which may cause difficulty swallowing • Nausea, vomiting, loss of appetite

OCCASIONAL, SOME MAY BE SERIOUS In 100 people receiving thioguanine, from 4 to 20 may have:
• Infection, especially when white blood cell count is low • Bruising, bleeding • Anemia which may cause tiredness, or may require transfusion • A tear or a hole in the bowels which may cause pain or that may require surgery • Liver damage which may cause yellowing of eyes and skin, swelling • Damage to the bowels

RARE, AND SERIOUS In 100 people receiving thioguanine, 3 or fewer may have:
• None

Possible side effects of METHOTREXATE (by mouth, intramuscular injection (shot) or by vein) (participants receiving Interim Therapy only)

COMMON, SOME MAY BE SERIOUS In 100 people receiving methotrexate, more than 20 may have:
• Nausea, vomiting, loss of appetite • Increased risk of sunburn, rash • Hair loss

OCCASIONAL, SOME MAY BE SERIOUS In 100 people receiving methotrexate, from 4 to 20 may have:	
• Fluid around heart • Internal bleeding, which may cause belly pain, black tarry stool, blood in vomit • Nausea, vomiting, diarrhea • Sores in mouth, which may cause difficulty swallowing • Liver damage, which may cause yellowing of eyes and skin • Scarring of the liver, hepatitis • Hair loss • Infection, especially when white blood cell count is low	• Anemia, which may cause tiredness, or may require transfusion • Bruising, bleeding • A new cancer resulting from this treatment • Confusion • Seizure • Kidney damage, which may require dialysis • Severe skin rash with blisters and peeling, which can involve mouth and other parts of the body • Blood clot, which may cause swelling, pain, shortness of breath

RARE, AND SERIOUS In 100 people receiving methotrexate, 3 or fewer may have:
• Dizziness • Scarring of the lungs, which may cause shortness of breath

Possible side effects of DASATINIB (Sprycel®) – *applies to participants with ABL1-class fusion only*

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

OCCASIONAL, SOME MAY BE SERIOUS In 100 people receiving dasatinib, from 4 to 20 may have:	
• Abnormal collection of fluid between the lung and the rib cage • Shortness of breath, chest pain, and cough • Lung infection (pneumonia) • Swelling, buildup of fluid in the abdomen and around the heart • Bleeding • Muscle, bone, and joint pain • Muscle weakness	• Inflammation of the tissues lining the stomach and bowel • Pain • Itching of skin, acne, dry skin, hives, excessive sweating • Pain, numbness and tingling especially in hands and feet • Dizziness, sleepiness, difficulty sleeping, depressed mood • Change in taste

OCCASIONAL, SOME MAY BE SERIOUS In 100 people receiving dasatinib, from 4 to 20 may have:	
• Fever • Vomiting, abdominal (belly) pain and distention • Low levels of phosphorous and calcium in the blood • Sores in the mouth or other parts of the digestive system • Upset stomach, constipation	• Infections with and without low white blood cell count • Weight loss and gain • Decreased appetite • Changes in heart rhythm and heartbeat • High blood pressure • Changes in vision, dry eyes

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

Possible side effects of LEUCOVORIN CALCIUM include:

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

OCCASIONAL, SOME MAY BE SERIOUS 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 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.

Risks of study procedures

Lumbar puncture (spinal tap): A lumbar puncture has a small risk of infection, bleeding, nerve damage, or headache. Leakage of spinal fluid into the tissue can cause a severe headache that lasts for days to weeks. You will be given medications to numb the pain and blur the memory before the test since it is painful. The pain is usually brief but occasionally may linger. Most of the time this procedure is done while you are under general anesthesia.

Bone marrow aspiration/biopsy: Pain or discomfort may occur during and after the biopsy, even with the use of local anesthetics. There may be some mild burning sensation when the numbing medicine is injected into the skin. There may be bleeding from the biopsy site, which requires putting pressure on it to stop the bleeding. Rarely, infections can occur at the biopsy site. This can be treated with antibiotics. It is possible but very uncommon to have severe bleeding, infection, nerve damage or other life-threatening complications from a biopsy.

Blood draws: If blood needs to be drawn from a vein in your arm, this will cause some pain and may result in bruising at the site of the needle stick. If a bruise does form at the end of the needle puncture site, it will generally go away on its own without any treatment. If you have a central venous catheter, drawing blood from this line is associated with a small chance of infection, which could require treatment with antibiotics or, rarely, removal of the line.

X-rays and scans: MRI, CT, X-ray, and PET/CT scans are common standard imaging tests used in the diagnosis and monitoring of many diseases. Although these tests have been in use for many years, their long-term effects on the body are still being learned. The most common discomfort is the length of time you must lay still or flat while an X-ray or scan is being performed. Uncommonly, some patients may have allergic reactions to dyes injected for some of these tests. Uncommon allergic reactions may result in rash, difficulty breathing, low blood pressure or other severe complications. Please let your doctor or nurse know if you have previously had an allergic reaction.