Official Study Title: PROTOCOL FOR THE STUDY AND TREATMENT OF PARTICIPANTS WITH IINTRAOCULAR RETINOBLASTOMA

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Informed Consent for Research

PROTOCOL FOR THE STUDY AND TREATMENT OF PARTICIPANTS WITH INTRAOCULAR RETINOBLASTOMA

1. Introduction

We are asking you to allow your child to take part in a research study. Your child is being invited to join this study because he or she has been diagnosed with retinoblastoma, a rare cancer of the retina of the eye. This cancer affects young children.

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 and family. 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.

Before you learn about the study, it is important that you know the following:

- Whether or not you take part in this study is entirely up to you.
- If you decide not to be in the study, or to leave the study at any time, you may still be able to get routine medical care at St. Jude. This study is being sponsored by St. Jude Children's Research Hospital.
- The principal investigator (researcher) in charge of this study is Dr. Rachel Brennan, who can be reached at (901) 595-3300, if you have any questions or concerns.

2. What is the usual approach to my child's type of cancer?

The treatment for retinoblastoma is tailored for each child. The most important goal is always to cure the cancer and save the life of the child. However, treatments are also tailored for each child with the hope of preserving (saving) the child's eye and vision as much as possible, while still trying to completely destroy the tumor(s) and obtain a cure.

Children who are not in a study are usually treated with the same or similar treatments that will be given on this study. The treatment doctors recommend for children with retinoblastoma depends on whether the tumor affects one eye (unilateral) or both eyes (bilateral), and how far the tumor has spread to the structures in and around the eye. Treatment can involve surgery to remove the eye (also called enucleation), chemotherapy drugs, radiation, and other treatments called "focal" treatments. Focal treatments are procedures such as laser therapy, freezing (cryotherapy), or heat treatments that are directed right at the tumor(s) and are meant to shrink and kill the tumor(s). Your doctor will discuss the recommended treatments for your child with you. Again, the treatments are tailored for each child's case. Each of these treatments will also be explained later in this consent.

3. What are our other choices if my child does not take part in this study?

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

- Surgery to remove one or both eyes
- Treatments (surgery, chemotherapy, focal treatments to control the tumor, and/or radiation treatment) like those described in this consent without being on a research study

4. Why is this study being done?

Researchers at St. Jude want to find out if the tumor response can be improved by giving chemotherapy directly to the eye with the first 2 cycles of treatment in children with retinoblastoma who have one or both eyes with advanced tumors. Researchers also want to learn more about the genetics and biology of retinoblastoma, and how these tumors develop (called tumorigenesis). To achieve this goal, we will study tumor samples from children who take part in this study, when part of their treatment requires enucleation (removal of the eye). Many children with retinoblastoma will not have an eye removed and will not take part in the biology research, but they can still receive treatment on this study. With this research study, we also plan to meet these goals:

- To learn more about the makeup of the genes of children with retinoblastoma. Genes are the unit of heredity that is passed from parent to child. We also want to learn about any genetic mutations (abnormalities or mistakes in genes) and what may influence or cause these mutations. This information may help us find better therapies for retinoblastoma in the future.
- To gather additional data (information) about the effectiveness and safety of the different treatments on this study.
- To provide rehabilitation services early in treatment, as well as during and after treatment (especially vision, hearing, and speech therapy). We want to find out if providing these services early will improve the development, learning and quality of life of children with retinoblastoma.
- To learn more about hearing problems in children who receive treatment with a chemotherapy drug called carboplatin as part of this study. We also want to learn more about the best way to test for hearing problems and when to provide hearing services to improve hearing.
- To learn more about how genetic changes may be important in how carboplatin causes hearing loss in some children.
- To learn more about how the drug topotecan is absorbed, distributed and removed from the body (called pharmacokinetics or PK) and also how topotecan affects the body (called pharmacodynamics or PD) of children who receive it on this study.

5. What are the study groups?

As described earlier in this consent, the treatment your child will receive depends on his or her stage and whether or not one or both eyes are involved. Up to 200 children will take part in this study at St. Jude only. While the study is open for enrollment (about 8 years); all children with newly diagnosed retinoblastoma that has not spread beyond the eye will be asked to join.

Each treatment strata or treatment group is described in the following pages.

STRATUM A TREATMENT – EARLY STAGE TUMORS IN ONE OR BOTH EYES

Treatment on stratum A will depend on your child's age. Infants less than 6 months of age will get different treatment than children older than 6 months. Children in stratum A will also receive focal treatments as needed to treat the tumor. Your doctor will talk to you about the treatments your child will need.

Children who are 6 months of age or older will get 8 cycles of chemotherapy using a 2-drug combination (vincristine and carboplatin). Each cycle of chemotherapy will be given every 3 to 4 weeks. Chemotherapy treatment will last about 6-8 months.

Cycles 1-8 – vincristine-carboplatin (VC)

Drug	How given	When given	How often	How many
Vincristine	By vein	Day 1	Every 3-4 weeks	8 cycles
Carboplatin	By vein	Day 1	Every 3-4 weeks	8 cycles

Your child's retinoblastoma will be re-evaluated after 1-2 cycles of this treatment. If the response is very good during therapy, your child's doctor will talk to you about the possibility of stopping chemotherapy after 6 cycles instead of 8.

Infants who are less than 6 months of age will get 6 cycles of chemotherapy, using alternating cycles of vincristine and topotecan, and then vincristine and carboplatin. Each cycle of chemotherapy will be given every 3 to 4 weeks. Chemotherapy treatment will last about 5-6 months.

Cycles 1, 3 and 5 – vincristine-topotecan (VT)

Drug	How given	When given	How often	How many
Vincristine	By vein	Day 1	Every 6-8 weeks	3 cycles
Topotecan	By vein	Daily, days 1-5	Every 6-8 weeks	3 cycles
Filgrastim (G-CSF) or Peg-filgrastim (peg-GCSF)*	Shot just under the skin (SQ)	2-3 days after chemotherapy	Daily (G-CSF) or once (peg-GCSF)	until blood counts recover

We will collect blood samples before and after the topotecan is given to measure the amount of this drug in your child's blood. The study doctor will use this information to give the best dose of topotecan for your child.

Cycles 2, 4 and 6 – vincristine-carboplatin (VC)

Drug	How given	When given	How often	How many
Vincristine	By vein	Day 1	Every 6-8 weeks	3 cycles
Carboplatin	By vein	Day 1	Every 6-8 weeks	3 cycles

Tumor evaluations on stratum A:

Your child's retinoblastoma will be re-evaluated after one to two cycles of chemotherapy, after six cycles and at the end of chemotherapy. If your child is less than 6 months, the end of chemotherapy will be after six cycles. If your child is greater than or equal to 6 months, the end of chemotherapy will be eight cycles.

Focal therapies on stratum A:

The treatment team will decide which of these focal treatments is best for your child. Focal treatments can be given any time after your child is diagnosed with retinoblastoma and may include:

- *Brachytherapy*, a procedure using radioactive material in the form of a plaque (a device that is sort of like a plate). The plaque is positioned on the surface of the eyeball directly over the location of the tumor inside the eye. The plaque gives off radiation constantly while in place on the wall of the eyeball for 3-4 days. Once the plaque is removed, no radioactivity is left inside the body. Brachytherapy requires surgery, first to place the plaque, and then to remove it and your child may have to be in the hospital for monitoring during this time
- *Cryotherapy*, a procedure to freeze-thaw the tumor(s) to shrink and kill it
- *Laser photocoagulation*, when a laser (high intensity light) is used to finely cauterize or seal the blood vessels of the tumor to shrink and kill it
- *Thermotherapy* (a different type of laser that kills the tumor by heat instead of light).

For a few children on this study, the treatment team may decide that the chemotherapy will be given in combination with thermotherapy to get the best results. In these children, carboplatin will be given 1-2 hours before the thermotherapy, and additional doses of carboplatin may be needed beyond the 8 scheduled cycles in order to get the best treatment results for your child

Cryotherapy, laser therapy and thermotherapy are always given while your child is under sedation (given drugs to make him/her sleep).

Children on Stratum A with excellent early response:

There are some children on stratum A who have a very early stage of retinoblastoma that may be treated with focal therapies only. Chemotherapy will not be given right away to these children. However, if there is ever any sign the tumor(s) is getting bigger, or if the tumor(s) does not shrink as well as doctors would like, chemotherapy will be given as described above.

STRATUM B TREATMENT – ADVANCED STAGE TUMORS

Children assigned to stratum B will be split into two groups (Group 1 and Group 2)

Stratum B, Group 1 Treatment

The first Stratum B group is for children who have advanced tumors, but the tumor has not broken apart inside the eye. These children will start treatment with two cycles of vincristine and topotecan, given every 3 to 4 weeks. This will take 6-8 weeks.

Cycles 1 and 2 vincristine-topotecan (VT)

Drug	How given	When given	How often	How many
Vincristine	By vein	Day 1	Every 3-4 weeks	2 cycles
Topotecan	By vein	Daily, days 1-5	Every 3-4 weeks	2 cycles
Filgrastim (G-CSF) or Peg-filgrastim (peg-GCSF)*	Shot just under the skin (SQ)	2-3 days after chemotherapy	Daily (G-CSF) or once (peg-GCSF)	until blood counts recover

**G-CSF or peg-GCSF will be given to help your child's blood counts recover faster.*

We will collect blood samples before and after topotecan is given to measure the amount of this drug in your child's blood. The study doctor will use these results to give the best dose of topotecan.

Response evaluations after each cycle

An exam under anesthesia will be done after both cycles. Further treatment depends on the tumor's response to the first 2 cycles of vincristine/topotecan.

Children in Stratum B, Group 1 with <u>good tumor response</u> to first two cycles of vincristine/topotecan

These children will get 6 cycles of chemotherapy with vincristine and carboplatin given every 3 to 4 weeks, 3 additional cycles of vincristine and topotecan, and carboplatin given "subtenon". Subtenon means that the drug will be injected (a shot) directly into the membranes covering the muscles and nerves of the eyeball, and will only be given if needed to control disease. This is always done when your child is sedated (given drugs to make him or her sleep).

Cycles 3, 4, 6, 7, 9 and 10 - vincristine-carboplatin (VC)

Drug	How given	When given	How often	Duration
Vincristine	By vein	Day 1	Every 3-4 weeks	6 cycles
Carboplatin	By vein	Day 1	Every 3-4 weeks	6 cycles

Cycles 5, 8 and 11 - vincristine-topotecan (VT) and subtenon*** carboplatin

Drug	How given	When given	How often	Duration
Vincristine	By vein	Day 1	Every 9-10 weeks	3 cycles
Topotecan	By vein	Daily, days 1-5	Every 9-10 weeks	3 cycles
Carboplatin	Subtenon***	Days 1, 2, 3, 4 or 5	Every 9-10 weeks	One injection during cycles 5, 8, and/or 11
Filgrastim (G-CSF) or Peg-filgrastim (peg-GCSF)*	Shot just under the skin (SQ)	2-3 days after chemotherapy	Daily (G-CSF) or once (peg-GCSF)	until blood counts recover

***G-CSF or peg-GCSF will be given to help your child's white blood counts recover faster*
****Subtenon administration means the chemotherapy drug (carboplatin) will be injected (a shot) directly into the membranes covering the muscles and nerves of the eyeball, and will only be given if needed to control disease. This is always done under sedation (child is given drugs to make him/her sleep).*

We will collect blood samples before and after topotecan is given to measure the amount of this drug in your child's blood. The study doctor will use these results to give the best dose of topotecan.

Children in Stratum B, Group 1 with <u>poor tumor response</u> to first two cycles of vincristine and topotecan

If your child's tumor did not respond well, the chemotherapy will be changed to an additional 6 cycles using a different 3-drug combination using **v**incristine, **c**arboplatin and **e**toposide (VCE).

Cycles 3-8 – vincristine-carboplatin-etoposide (VCE)

Drug	How given	When given	How often	How many
Vincristine	By vein	Day 1	Every 3-4 weeks	6 cycles
Carboplatin	By vein	Day 1	Every 3-4 weeks	6 cycles
Etoposide*	By vein	Daily, days 1-3	Every 3-4 weeks	6 cycles
Filgrastim (G-CSF) or Peg-filgrastim (peg-GCSF)**	Shot just under the skin (SQ)	2-3 days after chemotherapy	Daily (G-CSF) or once (peg-GCSF)	until blood counts recover
Carboplatin	Subtenon***	One dose on Day 1, 2 or 3	Injection during Cycle 3, 5 and/or 8 as needed	1 injection

**If your child has an allergic reaction to etoposide, this drug will be changed to a similar drug called Etopophos®.*
***G-CSF or peg-GCSF will be given to help your child's white blood counts recover faster*
****Subtenon administration means the chemotherapy drug (carboplatin) will be injected (a shot) directly into the membranes covering the muscles and nerves of the eyeball, and will only be given if needed to control disease. This is always done under sedation (child is given drugs to make him/her sleep).*

Stratum B, Group 2 Treatment

The second Stratum B group is for patients who have advanced tumors AND the tumor has broken apart inside the eye (called subretinal or vitreal seeding). These patients will first get two cycles of topotecan with subtenon injections of carboplatin, given every 3 to 4 weeks. This will take 6-8 weeks.

Cycles 1 and 2 topotecan and subtenon* carboplatin (VT)

Drug	How given	When given	How often	How many
Topotecan	Into the vein over 30 minutes	Daily, days 1-5	Every 3-4 weeks	2 cycles
Carboplatin	Subtenon*	Days 1, 2, 3, 4 or 5	During Cycles 1 & 2	1 injection per cycle
Filgrastim (G-CSF) or Peg-filgrastim (peg-GCSF)**	Shot just under the skin (SQ)	2-3 days after chemotherapy	Daily (G-CSF) or once (peg-GCSF)	until blood counts recover

**Subtenon administration means the chemotherapy drug (carboplatin) will be injected (a shot) directly into the membranes covering the muscles and nerves of the eyeball. This is always done under sedation (child is given drugs to make him/her sleep)*
***G-CSF or peg-GCSF will be given to help your child's blood counts recover faster*

We will collect blood samples before and after topotecan is given to measure the amount of this drug in your child's blood. The study doctor will use these results to give the best dose of topotecan.

Response evaluation after each cycle - An exam under anesthesia will be done after both cycles. Further treatment depends on the tumor's response to the first 2 cycles of topotecan and carboplatin.

Children in Stratum B, Group 2 with <u>good tumor response</u> to first two cycles of topotecan/carboplatin

These children will get 6 cycles of chemotherapy with vincristine/carboplatin given at 3-4 week intervals, 3 additional cycles of vincristine/topotecan, and subtenon carboplatin as needed to control disease.

Cycles 3, 4, 6, 7, 9 and 10 - vincristine-carboplatin (VC)

Drug	How given	When given	How often	Duration
Vincristine	By vein	Day 1	Every 3-4 weeks	6 cycles
Carboplatin	By vein	Day 1	Every 3-4 weeks	6 cycles

Cycles 5, 8 and 11 - vincristine-topotecan (VT) and subtenon*** carboplatin

Drug	How given	When given	How often	Duration
Vincristine	By vein	Day 1	Every 9-10 weeks	3 cycles
Topotecan	By vein	Daily, days 1-5	Every 9-10 weeks	3 cycles
Carboplatin	Subtenon***	Days 1, 2, 3, 4 or 5	During Cycle 5, 8 and/or 11	Injections as needed
Filgrastim (G-CSF) or Peg-filgrastim (peg-GCSF)**	Shot just under the skin (SQ)	2-3 days after chemotherapy	Daily (G-CSF) or once (peg-GCSF)	until blood counts recover

***G-CSF or peg-GCSF will be given to help your child's white blood counts recover faster*
****Subtenon administration means the chemotherapy drug (carboplatin) will be injected (a shot) directly into the membranes covering the muscles and nerves of the eyeball. This is always done under sedation (child is given drugs to make him/her sleep)*

We will collect blood samples before and after topotecan is given to measure the amount of this drug in your child's blood. The study doctor will use these results to give the best dose of topotecan.

Children on Stratum B, Group 2 with <u>poor tumor response</u> to first two cycles of vincristine/topotecan

If your child's tumor did not respond well, the chemotherapy will be changed to an additional 6 cycles using a different 3-drug combination using **v**incristine, **c**arboplatin and **e**toposide (VCE).

Cycles 3-8 – vincristine-carboplatin-etoposide (VCE)

Drug	How given	When given	How often	How many
Vincristine	By vein	Day 1	Every 3-4 weeks	6 cycles
Carboplatin	By vein	Day 1	Every 3-4 weeks	6 cycles
Etoposide*	By vein	Daily, days 1-3	Every 3-4 weeks	6 cycles
Carboplatin	Subtenon***	One dose on Day 1, 2 or 3	One dose during cycle 3, 5 and/or 8	Injections as needed
Filgrastim (G-CSF) or Peg-filgrastim (peg-GCSF)**	Shot just under the skin (SQ)	2-3 days after chemotherapy	Daily (G-CSF) or once (peg-GCSF)	until blood counts recover

**If your child has an allergic reaction to etoposide, this drug will be changed to a similar drug called Etopophos®.*
***G-CSF or peg-GCSF will be given to help your child's white blood counts recover faster*
****Subtenon administration means the chemotherapy drug (carboplatin) will be injected (a shot) directly into the membranes covering the muscles and nerves of the eyeball. This is always done under sedation (child is given drugs to make him/her sleep).*

Some children on Stratum B may also need radiation treatments after chemotherapy to treat tumors that cannot be destroyed with focal therapies alone, or for tumors that have a high risk of coming back (meaning the tumor invades further into the structures around the eye). If your child needs radiation treatment, the radiation oncologist (doctor that specializes in administering radiation therapy) will discuss your child's treatment plan with you and you will be asked to sign another consent document for this treatment.

STRATUM C TREATMENT – ADVANCED TUMOR IN ONE EYE

If your child has an advanced tumor in one eye only (meaning that the tumor is large or it has spread into the structures surrounding the retina) the eye with the tumor will be surgically removed. This surgical procedure is called "enucleation." After the eye is removed, a pathologist will look at the eye under a microscope. If the pathologist finds that the tumor is low-risk (meaning it does not extend beyond the retina), your child will have no further anti-cancer treatment (e.g., no further chemotherapy, focal treatments or radiation therapies). Your child will still be watched closely for any sign of the retinoblastoma coming back.

If the eye is removed and the pathologist finds that the tumor is intermediate risk (meaning it does invade the inner structures next to the retina), your child will need 4 cycles of chemotherapy with a 3-drug combination using vincristine, cyclophosphamide and doxorubicin (VCD).

Cycles 1-4 – VCD for intermediate risk tumors after enucleation

Drug	How given	When given	How often	How many
Vincristine	By vein	Day 1	Every 3-4 weeks	4 cycles
Cyclophosphamide	By vein	Day 1	Every 3-4 weeks	4 cycles
MESNA*	By vein	Day 1 before cyclophosphamide and at 3, 6, and 9 hours	Every 3-4 weeks	4 cycles
Doxorubicin	By vein	Day 1	Every 3-4 weeks	4 cycles
Filgrastim (G-CSF) or Peg-filgrastim (peg-GCSF)**	Shot just under the skin (SQ)	2-3 days after chemotherapy	Daily (G-CSF) or once (peg-GCSF)	until blood counts recover

**MESNA is given with cyclophosphamide to protect the bladder.*
***G-CSF or peg-GCSF will be given to help your child's white blood counts recover faster.*

If the eye is removed and the pathologist finds that the tumor is high risk (meaning it invades further into the outer structures surrounding the retina), your child will need 6 cycles of chemotherapy. This treatment will involve 3 cycles of the 3-drug combination using vincristine, cyclophosphamide and doxorubicin (VCD), alternating with 3 cycles of vincristine, carboplatin and etoposide (VCE).

Cycles 1, 3 and 5 VCE high risk tumors after enucleation

Drug	How given	When given	How often	How many
Vincristine	By vein	Day 1	Every 6-8 weeks	3 cycles
Carboplatin	By vein	Day 1	Every 6-8 weeks	3 cycles
Etoposide	By vein	Daily, days 1-3	Every 6-8 weeks	3 cycles
Filgrastim (G-CSF) or Peg-filgrastim (peg-GCSF)**	Shot just under the skin (SQ)	2-3 days after chemotherapy	Daily (G-CSF) or once (peg-GCSF)	until blood counts recover

***G-CSF or peg-GCSF will be given to help your child's white blood counts recover faster.*

If your child has an allergic reaction to etoposide, this drug will be switched to a similar drug called Etopophos®.

Cycles 2, 4 and 6 for high risk tumors after enucleation (VCD)

Drug	How given	When given	How often	How many
Vincristine	By vein	Day 1	Every 6-8 weeks	3 cycles
Cyclophosphamide	By vein	Day 1	Every 6-8 weeks	3 cycles
MESNA*	By vein	Day 1 before cyclophosphamide and at 3, 6, and 9 hours	Every 6-8 weeks	3 cycles
Doxorubicin	By vein	Day 1	Every 6-8 weeks	3 cycles
Filgrastim (G-CSF) or Peg-filgrastim (peg-GCSF)**	Shot just under the skin (SQ)	2-3 days after chemotherapy	Daily (G-CSF) or once (peg-GCSF)	until blood counts recover

**MESNA is given with cyclophosphamide to protect the bladder*
***G-CSF or peg-GCSF will be given to help bone marrow recover*

STRATUM D TREATMENT – TUMORS IN BOTH EYES WITH AT LEAST ONE EYE SURGICALLY REMOVED

Treatment for children with bilateral retinoblastoma is often more complicated. Some children will need to have one eye removed right after diagnosis because of advanced tumor(s). The treatment of the remaining eye will depend on the group (severity) of your child's tumor(s). The group is determined by the size and number of tumor(s) in the surgically removed eye, if the tumor has grown into the structures in and around the eye, and how the surgically removed eye looks under the microscope (low, intermediate or high risk). It also depends on the group of the tumor(s) in the remaining eye.

Your child will receive one cycle of vincristine, carboplatin and etoposide (VCE) after the surgery. After the final evaluation of the pathology from the enucleated eye is available, further treatment will depend on the final risk and group assignment (intermediate and high risk tumors or low-risk tumors).

If your child is to be treated on Stratum D, and the tumor in the enucleated eye is intermediate or high risk, your child will receive 5 additional cycles of chemotherapy with VCE (even if the other remaining eye is early stage) for a total of 6 cycles.

Cycles 2-6 – stratum D - intermediate and high risk tumors after enucleation (VCE)

Drug	How given	When given	How often	How many
Vincristine	By vein	Day 1	Every 3-4 weeks	5 cycles
Carboplatin	By vein	Day 1	Every 3-4 weeks	5 cycles
Etoposide	By vein	Daily, Days 1-3	Every 3-4 weeks	5 cycles
Carboplatin	Subtenon**	Day 1, 2 or 3	Cycles 1, 3 and 6	1 dose per cycle
Filgrastim (G-CSF) or Peg-filgrastim (peg-GCSF)*	Shot just under the skin (SQ)	2-3 days after chemotherapy	Daily (G-CSF) or once (peg-GCSF)	until blood counts recover

**G-CSF or peg-GCSF will be given to help your child's white blood cell counts recover faster*
***Subtenon administration means the chemotherapy drug (carboplatin) will be injected (a shot) directly into the membranes covering the muscles and nerves of the eyeball, and only if needed to control disease. This is always done under sedation (child is given drugs to make him/her sleep). This will be given as your study doctors think it is needed.*

If your child has an allergic reaction to etoposide, this drug will be changed to a similar drug called Etopophos®.

If the pathologist finds that the tumor in the enucleated eye is low risk, and the tumor in the remaining eye is early stage, your child will get treatment as described above for Stratum A (vincristine -carboplatin for children 6 months of age and older, and vincristine-topotecan alternating with vincristine-carboplatin for infants less than 6 months). Including the first cycle of VCE chemotherapy, children ≥ 6 months will receive a total of 8 courses of chemotherapy. Children < 6 months will receive a total of 6 cycles of chemotherapy. The remaining eye may also need focal therapies, also described in Stratum A above.

If the pathologist finds that the tumor in the enucleated eye is low risk, and the tumor in the remaining eye is more advanced stage, your child will get treatment as described above for Stratum B (with vincristine, topotecan and carboplatin). Including the first cycle of VCE chemotherapy, your child will receive a total of 11 courses of chemotherapy. The remaining eye may also need focal therapies, also described in Stratum A above.

Some children on Stratum D may also need radiation treatments to treat tumors that cannot be destroyed with focal therapies alone, or for tumors that have a high risk of coming back (meaning the tumor invades further into the structures around the eye). If your child needs radiation treatment, the radiation oncologist (doctor that specializes in administering radiation therapy) will discuss your child's treatment plan with you and you will be asked to sign another consent document for this treatment.

6. How long will my child be in the study?

Treatment on this study will last about 6-12 months, depending on which treatment group your child is assigned. After finishing treatment, your child will have regular exams according to this schedule:

First through fifth year after treatment: physical exams including visual acuity (sharpness) every 3-6 months, exam of the eyes under anesthesia (sedation) when your doctor thinks it is needed, speech and occupational therapy every 6 months. ECHO/ECG to check for heart problems will be repeated every 12 months for children who received doxorubicin. An MRI scan will be done 1-2 times per year, depending on the genetic testing, to watch for any sign of the retinoblastoma coming back or spreading to the brain.

At the end of the follow-up visits (after 5 years), your child will be followed as described in the St. Jude Long-Term Follow-up Study (SJLTFU), if you agree to allow your child to take part in that study. The SJLTFU study is being done to help researchers learn more about the health and quality of life of children who survive childhood cancers.

7. What research tests or special studies will be done?

Most of the exams, tests and procedures your child will have are part of the usual approach for retinoblastoma. These tests will be done to watch your child for any side effects of treatment and to measure the response to treatment. These tests will include regular physical exams, eye exams under anesthesia, MRI scans and ultrasounds, blood and urine tests, speech and occupational therapy and hearing tests. If your child is treated with carboplatin, imaging scans will be done regularly to check your child's kidney function. Children who require treatment with chemotherapy will have these routine tests done more often during treatment to watch for possible side effects of the chemotherapy drugs.

From past experience, we know that retinoblastoma can be inherited as a *familial* tumor (meaning the child with retinoblastoma has inherited a mutation from at least one parent and there are likely other cases of retinoblastoma in the family). Retinoblastoma can also be *non-familial* (sporadic or spontaneous with no family history of the disease).

We know that about 6% of newly diagnosed retinoblastoma cases are inherited and 94% are sporadic. Children who have the inherited form of retinoblastoma are born with a mutation (abnormality) in the retinoblastoma gene (also called RB1). These children are at higher risk of developing another retinoblastoma tumor, as well as other types of cancers in their lifetime. They may also pass on this mutation to their offspring, meaning that their children will also have a higher risk of developing retinoblastoma and possibly other cancers.

You will meet with a genetic counselor who can give you all the information about genetic testing. A genetic counselor is a health care provider who specializes in diseases that are caused by abnormal genes at birth.

After you have learned about the risks and benefits of RB1 testing (and are therefore able to make an informed choice), we will offer you the option of having the test to find out if your child has this genetic abnormality. For this test, your child will have an extra blood sample drawn at the same time blood is collected for routine testing. The genetic counselor or your child's study doctor will meet with you to discuss the results.

8. What about returning home during treatment?

It may be possible for your child to return home to your local doctor to receive some care on this study. If your study doctor agrees that this is medically possible, we will request copies of your child's medical records, including documentation that protocol-related treatment was given from your child's local doctor, if applicable. We may also request and receive results of clinic visits, hospitalizations, and laboratory, imaging, or other tests done to evaluate your child's disease or to monitor your child for side effects of treatment. Although this information is obtained as part of standard care for retinoblastoma, some or all of the information may also be included in the research record. By signing this informed consent, you agree to allow your child's local doctor to release this information to us.

9. What risks can I expect from my child taking part in this study?

The treatments that your child will receive on this study are considered standard of care for treating retinoblastoma. There are risks and benefits associated with each of these standard medical treatments. If you choose not to allow your child to take part in this study, he or she would still receive similar treatments without being on a research study.

There is a risk that the retinoblastoma can go away after the treatment and then come back at a later date.

<u>Risks of enucleation (surgery to remove eye), radiation treatments, and focal therapies to treat retinoblastoma tumors</u>

If your child needs any of these treatments, your doctors will discuss them with you in detail. You will be asked to sign a separate consent form for any of these treatments.

<u>Risks of chemotherapy</u>

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

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

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

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

Side effects of the individual standard chemotherapy drugs used in this study are listed in the tables below and on the following pages.

Possible side effects of **TOPOTECAN** (Hycamtin®)

COMMON, SOME MAY BE SERIOUS	

• Diarrhea
• Nausea
• Vomiting
• Constipation
• Fewer white blood cells, red blood cells and platelets in the blood
  o a low number of white blood cells can make it easier to get infections
  o a low number of red blood cells can make you feel tired and weak
  o a low number of platelets can cause you to bruise and bleed more easily and may lead to a need for transfusions
	• Fever including fever with a low white blood cell count. This could mean infection and could require hospitalization and treatment with antibiotics, and rarely could be fatal
	• Pain that can be in the abdomen, back or bones
	• A feeling of weakness and/or tiredness
	• Temporary hair loss

OCCASIONAL, SOME MAY BE SERIOUS	
• Loss of appetite • Elevation in the blood of certain enzymes or bilirubin found in the liver • Headache • Rash, hives, itching or a red bumpy rash • A mild lowering of the blood pressure that usually does not require treatment • Inflammation and/or sores in the mouth, throat and/or esophagus • An infection in the blood that will require admission to the hospital and treatment with antibiotics	• Numbness and tingling in the fingers and toes • Small amount of blood and/or protein in the urine or an elevation in blood creatinine that may indicate mild kidney damage • Shortness of breath • Muscle or joint aches and pains • Chest pain • Shaking chills

RARE AND SERIOUS	
• Severe allergic reaction that can be life threatening with shortness of breath, low blood pressure and a rapid heart rate	• Severe allergic reaction that can be life threatening with rapid build-up of fluid under the skin, in the lining of the intestine and possibly in the throat or swelling of the tongue, making it difficult to breathe

Possible side effects of **VINCRISTINE** (Oncovin®)

COMMON, SOME MAY BE SERIOUS	
• Hair loss • Reversible nerve problem that may affect walking or feelings in the fingers or toes	• Constipation

OCCASIONAL, SOME MAY BE SERIOUS	
• Jaw pain • Headache • Muscle weakness • Pain and bloating in the abdomen • Numbness and tingling in fingers and toes • Wrist or foot drop • Drooping eyelids • Double vision, difficulty seeing at night • Abnormal walk with foot slapping • Difficulty with urination or increased desire to urinate	• Dizziness • Abnormal hormone function that may lower the level of salt in the blood • Seizures • A mild drop in white blood cells, red blood cells and platelets in the blood o a low number of red blood cells can make you feel tired and weak o a low number of white blood cells can make it easier to get infections o a low number of platelets can cause you to bruise and bleed more easily

RARE AND SERIOUS	
• Complete stoppage of intestinal activity that can result in intestinal blockage • If the drug leaks out of the vein when being administered it will cause damage to nearby tissue • Seizures • Vocal cord paralysis • Difficulty breathing • Inability to walk	• Decreased ability to hear clearly • Damage to the nerve to the eye (optic nerve) leading to decreased vision and possible blindness • In combination with other chemotherapy drugs: damage to the liver that can lead to inflammation and/or scarring which could lead to a yellow appearing skin, and fluid collection in the abdomen (belly), making it look larger

Possible side effects of **CARBOPLATIN** (Paraplatin®) – given into the vein (IV)

COMMON, SOME MAY BE SERIOUS	
• Fewer red blood cells and white blood cells and platelets in the blood o a low number of red blood cells can make you feel tired and weak o a low number of white blood cells can make it easier to get infections o a low number of platelets can cause you to bruise and bleed more easily	• Nausea and vomiting • Abnormal levels of certain salts in the body like sodium and potassium

OCCASIONAL, SOME MAY BE SERIOUS	
• Allergic reactions (can be severe and life-threatening causing difficulty in breathing and/or a drop in blood pressure) • Rash • Metallic taste • Numbness and tingling in the fingers and toes • Hair loss • Constipation or diarrhea	• Pain in your abdomen • Temporary changes in vision • Damage to the ear causing hearing and balance problems • A feeling of weakness and/or tiredness • Inflammation and/or sores in the mouth and/or throat and /or esophagus, the tube that leads from the mouth to the stomach that may make swallowing difficult and are painful (painful mouth sores)

RARE AND SERIOUS	
• Damage to the liver • Damage to the kidney	• Leukemia later in life

Possible side effects of **CARBOPLATIN** (Paraplatin®) – given as subtenon injection into the eye

COMMON, SOME MAY BE SERIOUS
• Swelling around the eye • Redness of the eye • Decreased movement of the eyeball

OCCASIONAL, SOME MAY BE SERIOUS
• The eyeball may appear to sink in the socket and this might make it more difficult to fit a false eye, if your child ultimately has to have an enucleation and needs one fitted later

RARE AND SERIOUS
• Damage to the optic nerve leading to decreased vision

Possible side effects of **ETOPOSIDE** (VP-16, Vepesid®)

COMMON, SOME MAY BE SERIOUS

• Nausea and vomiting
• Hair loss
• A feeling of weakness or tiredness
• Fewer red and white blood cells and platelets in the blood
  o a low number of red blood cells can make you feel tired and weak
  o a low number of white blood cells can make it easier to get infections
  o a low number of platelets can cause you to bruise and bleed more easily

OCCASIONAL, SOME MAY BE SERIOUS	
• Loss of appetite • Decreased blood pressure during the infusion that may require treatment • Rashes • Diarrhea • Pain in the abdomen • Mouth sores • Tingling sensation or loss of sensation in fingers or toes	• A feeling of extreme tiredness or weakness • The finger or toe nails may loosen from their nail beds • Inflammation of the vein through where drug was given • Chest pain

RARE AND SERIOUS	
• Damage to the liver • Severe allergic reaction that can be life threatening with shortness of breath, low blood pressure, rapid heart rate, chills and fever • A new cancer or leukemia resulting from this treatment	• Severe rashes that can result in loss of skin and damage to mucous membranes • Absent or decreased monthly periods that may be temporary or permanent and may decrease the ability to have children later in life • Damage to the heart muscle that can make your child feel tired, weak, feel short of breath, and retain fluid

Possible side effects of **ETOPOPHOS** (etoposide phosphate)

COMMON, SOME MAY BE SERIOUS	
• Fewer white blood cells, red blood cells and platelets in the blood: ○ a low number of red blood cells can make your child feel tired and weak ○ a low number of white blood cells can make it easier to get infections ○ a low number of platelets can cause your child to bruise and bleed more easily	• Nausea • Loss of appetite • A feeling of weakness or tiredness • Hair loss • Fever and chills

OCCASIONAL, SOME MAY BE SERIOUS	
• Inflammation and/or sores in the mouth and/or throat and /or esophagus, the tube that leads from the mouth to the stomach that may make swallowing difficult and are painful (painful mouth sores) • Constipation	• Abdominal (belly) pain • Diarrhea • Changes in taste • Dizziness

RARE AND SERIOUS
• If the drug leaks out of the vein when being given, it will cause damage to nearby tissue • Severe allergic reaction that can be life threatening with shortness of breath, low blood pressure, rapid heart rate, chills and fever • Leukemia later in life (very rare)

Etopophos will only be given if your child has an allergic reaction to etoposide.

Possible side effects of **DOXORUBICIN** (Adriamycin®)

COMMON, SOME MAY BE SERIOUS	

• Nausea
• Vomiting
• Fewer white blood cells, red blood cells and platelets in the blood
  ○ a low number of red blood cells can make your child feel tired and weak
  ○ a low number of white blood cells can make it easier to get infections
  ○ a low number of platelets can cause your child to bruise and bleed more easily
	• Temporary hair loss
	• Pink or red color to urine, sweat, tears, saliva
	• Slight damage to the heart muscle that is unlikely to have any noticeable effects on your child's heart function

OCCASIONAL, SOME MAY BE SERIOUS	
• Inflammation and/or sores in the mouth and/or throat and /or esophagus, the tube that leads from the mouth to the stomach that may make swallowing difficult and are painful (painful mouth sores) • Damage to the heart muscle that may make you tired, weak, feel short of breath, and retain fluid • Facial flushing • Fever/chills • Hives • High levels of uric acid in the blood that could damage the kidneys • Dark discoloration of the hands, feet and under the fingernails with possible separation of the nail from the nail bed.	• Damage to the skin if the medication leaks from a vein • Thickening and hardening of the veins through which the medication is given • Reddening reaction of the vein through which the drug is given. • Elevation in the blood of certain enzymes found in the liver • Tearing and inflammation of the eyes • Loss of appetite • Redness and burning at sites that have received radiation in the past • Diarrhea

RARE AND SERIOUS	
• Severe allergic reaction that can be life threatening with shortness of breath, low blood pressure and a rapid heart rate • Ulceration of the lower intestinal tract • An irregular heartbeat that can be life-threatening	• Severe damage to the heart muscle that may lead to severe heart failure • A new cancer or leukemia resulting from this treatment

Possible side effects of **CYCLOPHOSPHAMIDE** (Cytoxan®)

COMMON, SOME MAY BE SERIOUS	
• Loss of appetite • Nausea • Vomiting • Fewer white blood cells in the blood. A low number of white blood cells may make it easier to get infections	• Hair loss • Decreased ability of the body to fight infection • Absence or decrease in the number of sperm that may be temporary or permanent and may decrease the ability to have children

OCCASIONAL, SOME MAY BE SERIOUS	

• Abnormal hormone function that may lower the level of salt in the blood
• Abdominal pain
• Diarrhea
• Fewer red blood cells and platelets in the blood
  ○ a low number of red blood cells can make your child feel tired and weak
  ○ a low number of platelets can cause your child to bruise and bleed more easily
	• Bleeding and inflammation of the urinary bladder
	• Absent or decreased monthly periods that may be temporary or permanent and may decrease the ability to have children
	• Temporary blurred vision
	• Nasal stuffiness with IV infusions
	• Skin rash
	• Darkening of areas of the skin and finger nails
	• Slow healing of wounds
	• Infections

RARE AND SERIOUS	
• Heart muscle damage that may occur with very high doses and may be fatal • Abnormal heart rhythms • Damage and scarring of lung tissue that may make your child short of breath • A new cancer or leukemia resulting from this treatment.	• Damage or scarring of urinary bladder tissue • Severe allergic reaction that can be life threatening with shortness of breath, low blood pressure, rapid heart rate, chills and fever • Infertility or the inability to have children

Possible side effects of **MESNA**

COMMON, SOME MAY BE SERIOUS
• Bad taste when taken by mouth

OCCASIONAL, SOME MAY BE SERIOUS	
• Nausea and vomiting	• Fever
• Stomach pain	• Facial flushing with red cheeks
• Headache	• Nervousness
• Pain in arms, legs and joints	• Dizziness
• Tired feeling	• Confusion
• Rash	• Swelling around the eyes
• Temporary low blood pressure	• Coughing
• Diarrhea	• Rapid heart rate

RARE AND SERIOUS
• Severe allergic reaction that can be life threatening with shortness of breath, low blood pressure, rapid heart rate, chills and fever

Mesna is given to prevent bladder side effects of cyclophosphamide

Possible side effects of **G-CSF** (filgrastim) (Neupogen®) or **PEG-FILGRASTIM** (pegylated filgrastim, PEG-filgrastim, SD-01, Neulasta®)

COMMON, SOME MAY BE SERIOUS
• Aching or pain in the bones

OCCASIONAL, SOME MAY BE SERIOUS	
• Pain, redness, itching, and hardening of the skin and bruising at the site of the injection	• Enlargement of the spleen (an organ in the abdomen/belly that stores blood cells). This may cause pain in the abdomen or left shoulder
• Headache	• Higher than normal white blood count
• Higher than normal levels of liver enzymes in the blood. This may mean liver irritation or damage	• Skin condition marked by fever and painful skin lesions that appear mainly on the face, neck, back and arms
• Increase of uric acid in the blood	• Rash or worsening of rash[1]
• A low number of platelets in the blood. This may cause you to bruise and bleed more easily	• Inflammation of blood vessels in the skin leading to a raised purple rash and bruising has been seen mainly in patient who are treated for a long time[1]
• Low grade fever	• Overall reddening with feelings of warmth[2]

Possible side effects of **G-CSF** – continued

RARE AND SERIOUS	
• Allergic reactions that can be life threatening with shortness of breath, low blood pressure, rapid heart rate, hives, itching, and facial swelling. • Serious allergic reaction that can be life threatening with rapid build-up of fluid under the skin, in the lining of the intestine, and possibly in the throat or swelling of the tongue, making it difficult to breathe[2] • If you are known to have sickle cell disease, filgrastim or pegfilgrastim may cause a sickle cell crisis.	• Severe damage to the spleen (an organ in the abdomen/belly that stores blood cells). This could lead to pain and loss of blood into the abdomen (belly) and may be life-threatening • Difficulty breathing and lung damage that may be due to the white blood cells that are stimulated by filgrastim or pegfilgrastim traveling to the lungs when they are inflamed or infected. • A blood disorder or leukemia that has only been seen in patients with certain immune disorders who are treated for a very long time[1]

[1]Reported with filgrastim
[2]Reported with pegfilgrastim

Filgrastim and peg-filgrastim are given after chemotherapy to help blood cell counts recover more quickly.

Other risks of this study

Second cancers: Children who survive retinoblastoma may develop a second form of cancer later in life, most commonly a tumor of the bone. Some children with retinoblastoma have a higher risk of getting a second cancer even if they are never treated with chemotherapy. You can talk to your child's doctor about whether or not this is true for your child. Chemotherapy drugs may increase your child's risk of getting a second form of cancer. How much that risk is increased is not known.

Loss of privacy: Very rarely, personal information from your child's records could be given out by accident. This might make you upset, embarrass you, or affect your child's 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

Genetic testing: The physical risks related to RB1 genetic testing are very small and include only those related to a blood draw (pain, bruising, lightheadedness, and very rarely, infection).

However, many of the risks related to genetic testing involve the emotional, social, or financial after-effects of the test results. Some people may feel angry, depressed, anxious or guilty about their results. In some cases, genetic testing creates tension within a family because the results can

reveal information about other family members in addition to the person who is tested. The possibility of genetic discrimination in employment or insurance is also a concern.

The RB1 mutation testing can only tell us if your child has this mutation. The test cannot tell us if your child will ever show symptoms of a disorder (such as cancer), how severe the symptoms will be, or whether the disorder will get worse over time.

There is a new federal law called the Genetic Information Nondiscrimination Act (GINA). In general, this law makes it illegal for health insurance companies, group health plans, and most employers to discriminate against you based on your genetic information. However, it does not protect you against discrimination by companies that sell life insurance, disability insurance, or long-term care insurance.

10. What are the possible benefits of the study?

The potential benefit of being in this study is that the treatment may cause your child's retinoblastoma to go into remission (no evidence of active tumor) and may save the eye(s) and preserve sight. Your child may also benefit from the early and frequent rehabilitation services done as part of this study. This study may not help your child directly, but what we learn may help other children with retinoblastoma in the future.

11. Can my child 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 your child can stop safely. If you stop, you can decide whether or not to let the study doctor continue to provide your child's medical information to the organization running the study.

The study doctor will tell you about new information or changes in the study that may affect your child's health or your willingness to continue in the study. The study doctor may take you out of the study:

- If your health changes and the study is no longer in your child's best interest
- If new information becomes available
- If you do not follow the study rules
- If the study is stopped by the sponsor

12. What are my child's rights in this study?

Allowing your child to take part in this study is your choice. No matter what decision you make, and even if your decision changes, there will be no penalty to your child. Your child will not lose medical care or any legal rights.

13. Will my child be paid for time or expenses?

Your child will not be paid for taking part in this study.

14. Who will see my child's medical information?

Your privacy is very important to us and the researchers will make every effort to protect it. Your information may be given out if required by law.

15. Where can I get more information?

You may visit the NCI Web site at http://cancer.gov/ for more information about studies or general information about cancer. You may also call the NCI Cancer Information Service to get the same information at: 1-800-4-CANCER (1-800-422-6237).

OPTIONAL RESEARCH TESTS

These research tests are optional (it is your choice whether you will allow your child to take part or not). The information will only be used to answer research questions. Your child can take part in all, some or none of these research studies. You can still take part in the main study even if you say 'no' to any or all of these studies. If you sign up for but cannot complete any of the studies for any reason, you can still take part in the main study.

This information may be shared with other researchers at St. Jude or other researchers from other institutions; however, any shared information will not include your child's name or other information that could identify your child. The results will not be added to your medical records, nor will you or your study doctor know the results. These research tests will not benefit your child directly but they may help us understand retinoblastoma better and help improve treatment for children with retinoblastoma in the future. If you have questions about these research studies, please talk to the researcher.

Please circle your choice of "YES" or "NO" for each of the following studies.

1. Optional research biology studies with tumor tissue and vitreous

If your child has an enucleation (surgical removal of the eye), and if you agree to this research, a sample of the tumor and of the vitreous (the jelly-like portion of the eye) will be saved for research studies to learn more about the biology of retinoblastoma tumors. In addition, one sample of blood will be drawn at the time of surgery for this research (at the same time blood is drawn for routine care before surgery). We want to learn more about how genes are expressed (meaning how a gene gets activated or "turned on" in a cell to make proteins). We also want to learn more about the tumorigenesis of retinoblastoma (how retinoblastoma tumors develop). Other research biology studies that may be done are described below:

- *Cell line cloning*
  Some of this tissue may be used to make a permanent cell line. A permanent cell line is a "living" tissue sample that can provide an unlimited supply of DNA (that would otherwise be used up) for future research studies. If researchers are able to make a cell line from your child's tumor cells, it will be saved in a research laboratory at St. Jude and

it will be "anonymized." This means that it will be labeled only with a coded identification number, and it will not be linked to your child's name or any other information that could identify your child. Because there will be no link to your child, we cannot destroy this sample later if you change your mind. Also, we will not be able to report to you any possible clinically significant results from this research. However, we will most likely report general results of this research in scientific journals.

- *Xenografts*
  Some of this tissue may be used to make a xenograft. A xenograft is the result of transplanting tissue or cells from one species to another species. For example, researchers may transplant your child's retinoblastoma tissue or cells into an animal model, such as a mouse, to develop new and better ways of treating retinoblastoma tumors in the future.

Optional research biology studies with tumor tissue and vitreous samples *(this includes cell line cloning, xenografts and other biology studies described above).*

I agree to allow my child's tumor tissue to be used for research biology studies

YES **NO**

2. Optional hearing tests - wideband reflectance (WBR) and tympanometry

Some children on this study will get a drug called carboplatin as part of their treatment plan. We know that one of the possible side effects of carboplatin is hearing loss. WBR and tympanometry are non-invasive and painless tools that are used to find hearing loss due to problems of the middle ear.

WBR is done by placing a small probe in the ear canal, applying stimuli (tones and chirps) and then measuring how your child responds. This test is commonly done in hospitals to screen newborns for hearing loss, but is not widely used in older children yet. Tympanometry is a common test that is done to measure the function of the ear drum by creating pressure in the ear canal.

Researchers want to find out if these tests together will be a good way to find hearing loss. We also want to know if these tests are a good way to decide when interventions (for example hearing aids and speech therapy) are needed to correct hearing loss or to lessen the impact of hearing loss.

Optional audiology (hearing) research studies (*WBR and tympanometry tests*).

I agree to allow my child to have audiology research tests to help identify and manage possible hearing loss

YES **NO**

3. Optional occupational and speech therapy questionnaires

Most of the tests and services provided by speech and occupational therapists are standard of care for retinoblastoma patients. However, we will also ask you to complete a series of questionnaires to find out if early and regular interventions with speech and occupational therapists will be of even more help to your child than standard of care. If you agree, you will be asked to complete questionnaires for your child when he or she is enrolled on the study, and then every 6 months for 3 years. You will be asked to complete the questionnaires at the same time your child is having speech and occupational therapy.

Optional rehabilitative services research *(occupational and speech therapy questionnaires).*

I agree to allow my child to take part in research related to rehabilitative research

YES **NO**

SUMMARY OF RESEARCH AND PRIVACY RIGHTS

The following statements describe your rights as a research participant in this study:

1) You may refuse to be in this research study or stop at any time. This decision will not affect your care or your relationship with your doctor or St. Jude. If available, you may receive routine medical care at St. Jude Children's Research Hospital.

2) If you have insurance, TennCare or Medicaid, or other health care coverage such as an employer-sponsored benefit plan, they will be billed for many of the services we provide. However, we do not bill patients or their families for the cost of medical care not covered by their health plans. This includes research costs.

3) Your samples and 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.

4) If you have any questions about this study or if you are injured as a result of this study, contact Dr. Rachel Brennan, at 901-595-3300 immediately. If you are injured from being in this research study, St. Jude will provide reasonable and necessary care for that injury. If you need more care than St. Jude can provide, we will help you find medical care somewhere else. It is not the hospital's policy to provide payment if you are injured from being in this study; however, you are not giving up any of your rights by signing this consent form.

5) A description of this clinical trial will be available on http://www.ClinicalTrials.gov, as required by U.S. Law. This Web site will not include information that can identify you. At most the Web site will include a summary of the results. You can search this Web site at any time.

6) A decision to take part in this research means that you agree to let the research team use and share with other researchers your health information, also called protected health information (PHI), for 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.

7) When you first registered at St. Jude, you received a copy of the St. Jude Notice of Privacy Practices. It tells how your PHI 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 were first registered at St. Jude. You can find it at the bottom of every page on the St. Jude Internet website: *www.stjude.org*.

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

9) Information about you that may be given out includes your complete medical records, including details about diagnosis, illness, treatment, and information that may be recorded about past diagnosis or treatment and information taken as a part of this research study as explained in this informed consent.

10) After your records are given to or used by others, St. Jude Children's Research Hospital cannot promise that information will not be given out again. Also, the information given out may no longer be protected by federal privacy laws.

11) St. Jude uses reasonable safeguards and means to protect your private information. However, St. Jude cannot guarantee the security and confidentiality of e-mail, text messages, fax communications or mail.

12) 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.

13) Your permission to use and give out your child's protected health information will end when your child turns 18 years of age. At that time, we may contact your child for his or her permission to continue using it.

14) You may take back permission for your records to be used or given out at any time, for any reason, except when that information has already been given out or used for the study based on your permission. To take back your permission, please fill out a form called a Revocation of Release of Authorization. You may ask for this form by calling the St. Jude Privacy Officer at 901-595-6141. You must mail the form or hand it to:

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

15) You can get more details about your rights as a research participant by calling the St. Jude Institutional Review Board at 901-595-4357 or the Research Participant Advocate at 901-595-4644. If you are outside of the Memphis area, please call toll-free 1-866-583-3472 (1-866-JUDE IRB).

16) The St. Jude 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. You can reach the Advocate by calling 901-595-4644, or if you are outside of the Memphis area, call toll free at 1-866-583-3472 (1-866-JUDE-IRB).

17) You will be given a copy of this <u>signed</u> consent form.

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_____

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)