Seattle Children's
HOSPITAL • RESEARCH • FOUNDATION

UNIVERSITY OF WASHINGTON
DEPARTMENT OF PEDIATRICS
SEATTLE, WASHINGTON
Telephone: 987-2106
Nights/Weekends: (206) 987-2000
(Ask for the "oncology fellow on call")

TREATMENT FOR EWING SARCOMA

Your child has recently been diagnosed with a Ewing sarcoma (ES), a cancerous tumor in the bone or soft tissue. Treatment for ES consists of chemotherapy (anti-cancer drugs), possibly with radiation therapy and/or surgery to remove the tumor. The chemotherapy is given so that the tumor will decrease in size and to eliminate any metastatic tumor cells (cells which may have traveled to another location within the body).

PROCEDURES

Because your child will receive chemotherapy treatment for a long period of time, and because we will need to monitor the response to treatment and side effects with frequent blood draws, we recommend the surgical placement of an indwelling central line prior to starting treatment. This means that we will put a plastic catheter tube into one of your child's big blood vessels in the chest. This central line will be used to administer chemotherapy drugs and to draw blood in order to minimize the need for individual needle pokes.

TREATMENT

Induction Chemotherapy

During the first phase of treatment (called the induction phase) your child will receive 12 weeks of chemotherapy. Starting on week 1 of treatment, your child will receive vincristine (given as a rapid infusion through the catheter), cyclophosphamide (given as a 1 hour infusion through the catheter), and doxorubicin (given as a 15 minute infusion through the catheter). Because we need to monitor your child closely for any side effects from treatment and administer a lot of fluids, your child will receive these drugs while in the hospital (about 2 days). Your child will also receive a drug, MESNA, which helps to reduce the side effects of cyclophosphamide. About one and a half weeks later (on treatment week 3) your child will receive ifosfamide (given as a 1 hour infusion through the catheter) and etoposide (given as a 1 hour infusion through the catheter). Your child will again receive a drug, MESNA, which helps to reduce the side effects of ifosfamide. Again, your child will need to be in the hospital for 5 days for close monitoring and to receive a lot of fluids. The vincristine/doxorubicin/cyclophosphamide treatment will be repeated on weeks 5 and 9. The ifosfamide/etoposide treatment will be repeated on weeks 7 and 11.

SO IFOSFAMIDE + ETOPOSIDE MUST BE BAD

Surgery/Radiation Therapy

If your child responds well to the chemotherapy treatment and the tumor has shrunk enough in size, it may be surgically removed following recovery from week 11 of treatment. Surgically removing the primary tumor is a common procedure for patients with ES, if the tumor can be removed. Depending upon the completeness of surgery, your child may also receive radiation therapy following surgery. If the tumor can not be removed by surgery, your child will receive radiation therapy instead around week 15 of treatment. If the tumor has spread to other parts of the body, radiation therapy will be given to those locations around week 15 of treatment. Your doctor and surgeon will discuss the timing and choice of surgery and radiation therapy around week 11 of treatment.

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Continuation Chemotherapy

If your child has surgery following week 11 of treatment, chemotherapy will resume approximately 2 weeks after surgery. If your child does not have surgery following week 11 of treatment, chemotherapy will continue 2 weeks after week 11 of treatment. The second phase of chemotherapy is called the Continuation phase and lasts for 16 weeks. During the Continuation phase, your child will receive the vincristine/doxorubicin/cyclophosphamide treatment on weeks 15 and 19. To help protect your child's heart, they will also receive dexrazoxane at weeks 15 and 19. The ifosfamide/etoposide treatment will be repeated on week 17, 21, 25, and 29. During weeks 23 and 27 of treatment, your child will receive vincristine/cyclophosphamide, which will be given in clinic rather than in the hospital. *However, if your child receives radiation at week 19, doxorubicin will not be given at week 19 and will instead be given at week 27.

Treatment Schema

WEEK	1	3	5	7	9	11	15	17	19	21	23	25	27	29
	V	I	V	I	V	I	V	I	V	I	V	I	V	I
	D	E	D	E	D	E	D	E	D*	E		E	*	E
	C		C		C		C		C		C		C	
							Surgery and/or Radiation							

V = Vincristine
D = Doxorubicin
C = Cyclophosphamide
I = Ifosfamide
E = Etoposide

OTHER PROCEDURES

Prior to, during, and following treatment, your child will have various tests and examinations done to assess the benefits and to monitor the side effects of this treatment. These tests and exams are standard care. These tests will include medical history and physical exams, blood draws, kidney evaluation (iothalomate or creatinine clearance), heart evaluation (echocardiogram), bone marrow aspiration and biopsies, urinalysis, and radiographic imaging tests such as x-rays, bone scans, CT scans of the chest and affected bones, and MRI and PET scans of the affected bones. Blood tests will be done at least once each week during treatment. Approximately 1 teaspoon of blood will be drawn each time.

It is important to continue to monitor your child's progress; therefore, medical histories, physical exams, and some radiographic imaging tests will need to be done routinely for about five years after the completion of therapy, then once each year indefinitely.

RISKS, STRESS, OR DISCOMFORT

Chemotherapy

There is potential for toxicity with all chemotherapeutic agents. In addition to killing cancer cells, chemotherapy drugs can produce side effects by damaging normal tissues. Although every precaution will be taken to minimize the side effects, their development is unpredictable in nature and severity and they may be life-threatening. By carefully adjusting the doses of chemotherapy, severe side effects can usually be avoided. Problems, which do arise, are usually reversible when the medication is stopped, but occasionally they can persist and cause serious complications.

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Your child's doctor is experienced in giving chemotherapy and in detecting and handling its possible side effects. Your child will be closely watched during therapy for these and any other side effects, which may occur, and changes will be made in your child's treatment to prevent any undue risk. The Hematology/Oncology staff may be contacted to answer any questions or deal with any unexpected side effects that your child may have during or after treatment.

Many chemotherapy drugs cause bone marrow depression. The bone marrow is the site of blood cell production and developing blood cells are susceptible to destruction by a number of chemotherapy drugs. Bone marrow depression results in a decreased production of red cells causing anemia, a decreased platelet production causing bruising and an increased bleeding tendency, and a decrease in white cell production that results in a tendency toward infection. During periods of low white blood counts, patients frequently require hospitalization for several days if signs of infection, such as fever, develop. To reduce the risk of severe infection during periods of low white cell counts, patients receive a medication called G-CSF. G-CSF helps stimulate the production of white blood cells. Anemia can be corrected by the use of red blood cell transfusions and platelets may be replaced with platelet transfusions, but white cell replacement has not been satisfactory and a risk of infection usually persists while the white cell count is low. Medications and blood transfusions will be available to your child if needed. Bone marrow depression is usually temporary, but can vary in severity.

Nausea and vomiting are common side effects of chemotherapy. Your child will receive medications prior to chemotherapy to prevent or lessen the nausea and vomiting. Sometimes additional medicines are needed to treat unusually severe nausea and vomiting.

Mucositis (sores in the mouth and esophagus or swallowing tube) are a common side effect, particularly following doxorubicin. Mucositis is frequently severe enough to require strong pain medications and often makes it difficult to swallow. Nausea and vomiting are common side effects of chemotherapy. Your child will receive medications prior and during chemotherapy to prevent or reduce the severity of chemotherapy. Because of these complications, it is common for patients to receive supplemental nutrition either through the catheter or through a nasogastric tube (a plastic tube from the nose into the stomach used for feeding).

After 2 weeks
Hair loss (alopecia) is a universal side effect but is temporary. Other potential side effects are specific to each chemotherapeutic agent and are described in the attached drug information sheets.

The risks of treatment to an unborn child would be severe. Patients of childbearing age should use reliable means of birth control to avoid pregnancy during treatment. Pregnancy testing may be done before starting treatment.

It is possible that a second form of cancer known as acute myelogenous leukemia (AML) may result from this treatment. This risk is associated with the combination of chemotherapy agents. Experience so far suggests that the chance of this happening is very small. Early data in adults shows that one in every 400-800 patients may be affected, depending on the specific combination of chemotherapy used. However, not enough information has been gathered in children to be able to give an accurate prediction, although it may be in the range of one in every 50 to 800. Data is now being collected on all studies using these drugs in order to find out the relationship between the drug and the development of second cancers. Patients will be provided with all new information as it becomes available.

1050 chance = 2%

Radiation Therapy

Side effects associated with radiation therapy include hair loss if the part of body receiving radiation has hair. The hair usually grows back, but it may take six or more months. Radiation therapy also causes reddening of the skin and, rarely, skin blisters like a severe sun burn. Patients may experience nausea, vomiting, loss of

appetite, a lowering of white blood cell counts which may make them less resistant to fighting infection, and/or a lowering of platelet counts which may require delays in therapy. Additionally, some side effects are not seen until years later, for example, if bones or other soft tissues are irradiated, they may not grow as much as non-irradiated bones and soft tissues. As with any kind of radiation therapy received, there is always the chance that another tumor may appear later in tissue near the area that received radiation therapy.

Other risks

Other risks include temporary discomfort while taking blood samples. A bruise may form at the point where the needle enters the skin. There is a small risk of infection at the site where the needle enters the skin. Patients usually experience pain during bone marrow aspirate and biopsy procedures and there may be soreness, pain or discomfort for a few days following these procedures. There is a small risk of infection with these procedures.

For both males and females, the use of radiation therapy and/or chemotherapy for the treatment of cancer is a risk to fertility. Inability or difficulty in conceiving a child as a result of these therapies may be temporary or permanent. A number of factors, including the individual's gender, age at the time of treatment, type of chemotherapy drugs used, location of radiation, total dose of chemotherapy and/or radiation, and length of time since treatment all influence the ability to have a child after cancer treatment. Predicting the outcome for any individual patient is difficult. Your oncologist can discuss the fertility risk of this particular treatment regimen with you.

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Possible side effects of Vincristine

	Common Happens to 21-100 children out of 100	**Occasional** Happens to 5-20 children out of every 100	**Rare** Happens to <5 children out of 100
Immediate: Within 1-2 days of receiving drug	Damage to nearby tissue if the medication leaks from a vein	Jaw pain	
Prompt: Within 2-3 weeks, prior to the next course)	Hair loss	Weakness, constipation	Absent intestinal activity resulting in intestinal blockage, drooping eyelid, hoarseness, decrease in the number of red and white blood cells and platelets made in the bone marrow, abnormal hormone function affecting levels of salt in the blood and urine, causing too much or too little urine to be produced, seizures
Delayed: Any time later during therapy, excluding the above conditions	Loss of deep tendon reflexes How long does this last?	Numbness, tingling, clumsiness, and extremity pain	
Late: Any time after the completion of treatment			

(L) Toxicity may also occur later.

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Possible side effects of Cyclophosphamide

	Common Happens to 21-100 children out of every 100	**Occasional** Happens to 5-20 children out of every 100	**Rare** Happens to <5 children out of every 100
Immediate: Within 1-2 days of receiving drug	Loss of appetite (L), nausea (L), vomiting (L)	Metallic taste (L), abnormal hormone function affecting levels of salt in the blood and urine, causing too much or too little urine[1], seizures	Temporary blurred vision[1], nasal stuffiness, heart damage with abnormal heart rhythms[1]
Prompt: Within 2-3 weeks, prior to next course	Decrease in the number of red and white blood cells and platelets made in the bone marrow, hair loss	Bleeding and inflammation of the urinary bladder (L)	Damage of muscle tissue in the heart[2]
Delayed: Any time later during therapy, excluding the above conditions	Decreased ability of the body to fight infection or disease, absence of sperm or stopped monthly periods, inability to have children (L)		Damage/scarring of lung tissue[3] (L)
Late: Any time after completion of treatment			A new cancer or leukemia resulting from this treatment, damage/scarring of bladder tissue
Unknown frequency and timing: This agent may be toxic to developing fetuses (unborn children) and to breast fed children			

[1] *Less common with lower doses.*
[2] *Only with very high doses.*
[3] *Risk increased in someone who has had chest radiation..*
(L) Toxicity may also occur later.

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Possible side effects of Doxorubicin

	Common Happens to 21-100 children out of every 100	**Occasional** Happens to 5-20 children out of every 100	**Rare** Happens to <5 children out of every 100
Immediate: Within 1-2 days of receiving drug	Abnormal heart rhythm[1], nausea, vomiting, worsening of side effects due to radiation treatments, damage to the skin if the medication leaks from a vein; pink or red color to urine, sweat, tears, or saliva		Allergic reaction (sometimes life-threatening), rash (L)
Prompt: Within 2-3 weeks, prior to the next course	Decrease in the number of red and white blood cells and platelets made in the bone marrow (L), hair loss (L)	Mouth sores (L), damage to the liver (L)	
Delayed: Any time later during therapy, excluding the above conditions	Reduced function of the immune system	Weakness of the heart muscle, the chance of which is higher with higher doses or when radiation therapy to the chest is given (L)	Dark discoloration under fingernails
Late: Any time after completion of treatment			A new cancer or leukemia resulting from this treatment

[1] *Rarely causes a problem (L) Toxicity may also occur later.*

Possible Side Effects of Ifosfamide:

	Common Happens to 21-100 children out of every 100	**Occasional** Happens to 5-20 children out of every 100	**Rare** Happens to <5 children out of every 100
Immediate: Within 1-2 days of receiving drug	Nausea (L), vomiting (L), loss of appetite	Drowsiness, confusion, weakness, abnormal hormone function affecting levels of salt in the blood and urine, causing too much or too little urine[1], seizure	Damage to brain tissue (L)
Prompt: Within 2-3 weeks, prior to the next course	Decrease in the number of red and white blood cells and platelets made in the bone marrow	Bleeding and inflammation of the urinary bladder, damage to the heart with abnormal heart beat or rhythm[2]	Damage to the heart tissue (2) with very high doses
Delayed: Any time later during therapy, excluding the above conditions	Hair loss, difficulties or complete inability to conceive children	Abnormal kidney function, body loss of certain important salts and minerals (such as sodium, potassium and bicarbonate), abnormal bone development	Numbness, tingling, clumsiness, sudden kidney failure, damage/scarring to lung tissue (L)
Late: Any time after completion of treatment			A new cancer or leukemia resulting from this treatment, damage/scarring to bladder tissue

[1] ***Less common with lower doses***
[2] ***Extremely rare at doses of ≤ 10 g/m²/course***
(L) Toxicity may also occur later.

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Possible side effects of Etoposide

	Common Happens to 21-100 children out of every 100	**Occasional** Happens to 5-20 children out of every 100	**Rare** Happens to <5 children out of every 100
Immediate: Within 1-2 days of receiving drug	Nausea, vomiting	Decrease in or loss of appetite, decreased blood pressure during the infusion	Low blood pressure, allergic reactions
Prompt: Within 2-3 weeks, prior to next course	Decrease in the number of red and white blood cells and platelets made in the bone marrow	Hair loss, worsens side effects due to radiation treatments, diarrhea	Numbness, tingling, clumsiness, mouth sores, damage to liver
Delayed: Any time later during therapy, excluding the above conditions			
Late: Any time after completion of treatment			A new cancer or leukemia resulting from this treatment

(L) Toxicity may also occur later.

Possible side effects of MESNA: (Anti Nausea)

	Common Happens to 21-100 children out of every 100	**Occasional** Happens to 5-20 children out of every 100	**Rare** Happens to <5 children out of every 100
Immediate: Within 1-2 days of receiving drug	Bad taste when taken by mouth	Nausea, vomiting, stomach pain	Headache*, pain in arms, legs, and joints*; tired feeling*, rash*, temporary low blood pressure*, allergic reaction
Prompt: Within 2-3 weeks, prior to the next course			diarrhea
Delayed: Any time later during therapy, excluding the above conditions			
Late: Any time after completion of treatment			

** These side effects have been reported only at high doses*
Note:Young children receiving high doses of benzyl alcohol (> 99 mg/kg/day) may develop the gasping syndrome manifested by gasping, metabolic acidosis and multiple organ system failure. Benzyl alcohol is the preservative in multidose vials of MESNA.

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Possible side effects of G-CSF (Neulasta)

	Common Happens to 21-100 children out of every 100	**Occasional** Happens to 5-20 children out of every 100	**Rare** Happens to <5 children out of every 100
Immediate: Within 1-2 days of receiving drug		Local irritation at injection site	Allergic reaction, low fever
Prompt: Within 2-3 weeks, prior to the next course		Ache or pain inside the bones, increased levels of liver enzymes and uric acid in the blood, low number of platelets in the blood	Enlargement of the spleen, worsening of pre-existing skin rashes, hair loss
Delayed: Anytime later during therapy, excluding the above conditions			Inflammation of a blood vessel in the skin
Late: Anytime after the completion of treatment			

Possible side effects of Dexrazoxane

	Common Happens to 21-100 children out of every 100	**Occasional** Happens to 5-20 children out of every 100	**Rare** Happens to <5 children out of every 100
Immediate: Within 1-2 days of receiving drug		Mild nausea and/or vomiting, loss of appetite, feeling tired, diarrhea, damage to the skin if the medication leaks from a vein, pain in the vein through which the medication is given	Increase in triglyceride level, increase in amylase
Prompt: Within 2-3 weeks, prior to the next course	Decrease in the number of red and white blood cells and platelets made in the bone marrow	Temporary increases in the blood of iron and decreases in the blood of calcium and zinc, temporary elevation in the blood of certain enzymes and bilirubin found in the liver, may take longer for the blood to clot	
Delayed: Anytime later during therapy, excluding the above conditions			
Late: Anytime after the completion of treatment			A new cancer or leukemia resulting from this treatment