



[cancer.org](https://www.cancer.org) | 1.800.227.2345

Treating Neuroblastoma

If your child has been diagnosed with neuroblastoma, your child's treatment team will discuss the options with you. It's important to weigh the benefits of each treatment option against the possible risks and side effects.

How is neuroblastoma treated?

The types of treatment used for neuroblastoma can include:

- [Neuroblastoma Surgery](#)
- [Chemotherapy for Neuroblastoma](#)
- [Radiation Therapy for Neuroblastoma](#)
- [High-Dose Chemotherapy/Radiation Therapy and Stem Cell Transplant for Neuroblastoma](#)
- [Retinoid Therapy for Neuroblastoma](#)
- [Immunotherapy for Neuroblastoma](#)

Common treatment approaches

Treatment of neuroblastoma depends on the [risk group](#) of the cancer, the child's age, and other factors, and might include more than one type of treatment.

- [Treatment of Neuroblastoma by Risk Group](#)

Who treats neuroblastoma?

Children with neuroblastoma and their families have special needs. These needs can be met best by cancer centers for children, working closely with the child's primary care doctor. These centers have teams of specialists who understand the differences

between cancers in adults and those in children, as well as the unique needs of younger people with cancer. Treating neuroblastoma is complex and often requires the expertise of many different doctors, nurses, and other health professionals.

- [How to Find the Best Cancer Treatment for Your Child](#)
- [Navigating the Health Care System When Your Child Has Cancer](#)

Making treatment decisions

Your child's cancer care team will discuss the treatment options with you. It's important to discuss these options and their possible side effects with your child's doctors so you can make an informed decision. It's also important to ask questions if there's anything you don't understand or are not sure about.

If time allows, getting a second opinion from another doctor experienced with your child's type of tumor is often a good idea. This can give you more information and help you feel more confident about the treatment plan you choose. If you aren't sure where to go for a second opinion, ask your doctor for help.

- [Questions To Ask About Neuroblastoma](#)
- [How to Talk to Your Child's Cancer Care Team](#)
- [Seeking a Second Opinion](#)

Thinking about taking part in a clinical trial

Today, most children and teens with cancer are treated at specialized children's cancer centers. These centers offer the most up-to-date-treatment by conducting clinical trials (studies of promising new therapies). Children's cancer centers often conduct many clinical trials at any one time, and in fact most children treated at these centers take part in a clinical trial as part of their treatment.

Clinical trials are one way to get state-of-the art cancer treatment. Sometimes they may be the only way to get access to newer treatments (although there is no guarantee that newer treatments will be better). They are also the best way for doctors to learn better methods to treat these cancers. Still, they might not be right for everyone.

If you would like to learn more about clinical trials that might be right for your child, start by asking the treatment team if your clinic or hospital conducts clinical trials.

- [Clinical Trials](#)

Considering complementary and alternative methods

You may hear about alternative or complementary methods that your doctor hasn't mentioned to treat your child's tumor or relieve symptoms. These methods can include vitamins, herbs, and special diets, or other methods such as acupuncture or massage, to name a few.

Complementary methods refer to treatments that are used *along with* your regular medical care. Alternative treatments are used *instead of* standard medical treatment. Although some of these methods might be helpful in relieving symptoms or helping people feel better, many have not been proven to work. Some might even be harmful.

Be sure to talk to your child's cancer care team about any method you are thinking about using. They can help you learn what is known (or not known) about the method, which can help you make an informed decision.

- [Complementary and Alternative Medicine](#)

Preparing for treatment

Before treatment, the doctors and other members of the team will help you, as a parent, understand the tests that will need to be done. The team's social worker will also counsel you about the problems you and your child might have during and after treatments such as surgery, and might be able to help you find housing and financial aid if needed.

- [When Your Child Has Cancer](#)

Help getting through cancer treatment

Your child's cancer care team will be your first source of information and support, but there are other resources for help when you need it. Hospital- or clinic-based support services can also be an important part of your care. These might include nursing or social work services, financial aid, nutritional advice, rehab, or spiritual help. For children and teens with cancer and their families, other specialists can be an important part of care as well.

The American Cancer Society also has programs and services – including rides to treatment, lodging, and more – to help you get through treatment. Call our National Cancer Information Center at 1-800-227-2345 and speak with one of our trained

specialists.

- [Finding Help and Support When Your Child Has Cancer](#)
- [Find Support Programs and Services in Your Area](#)

The treatment information given here is not official policy of the American Cancer Society and is not intended as medical advice to replace the expertise and judgment of your cancer care team. It is intended to help you and your family make informed decisions, together with your doctor. Your doctor may have reasons for suggesting a treatment plan different from these general treatment options. Don't hesitate to ask him or her questions about your treatment options.

Neuroblastoma Surgery

Surgery can be used both to help [diagnose](#)¹ neuroblastoma and to treat it. For smaller tumors that have not spread, surgery is often the only treatment that is needed.

Surgical (open) biopsy

In many cases, doctors need to get a sample of the tumor to be sure it is a neuroblastoma before deciding which treatment might work best. Tumor samples are removed during a surgical biopsy to be looked at under a microscope and for other lab tests.

If the tumor is in the abdomen (belly), the surgeon might do the biopsy with a laparoscope. This is a long, thin tube with a tiny video camera on the end. It is put into the abdomen through a small incision to allow the surgeon to see inside. The surgeon then makes a second small incision to reach inside the abdomen with long, thin instruments and remove pieces of tumor.

Surgery as treatment

After neuroblastoma is diagnosed, surgery is often used to try to remove as much of the tumor as possible. In some cases, surgery can remove the entire tumor and no additional treatments are needed.

During the operation, the surgeon looks carefully for signs of cancer spread to other organs. Nearby lymph nodes (small collections of immune system cells to which cancers often spread first) are removed and looked at under a microscope for cancer cells.

If possible, the surgeon will remove the entire tumor. This is less likely if the tumor is near vital structures or wrapped around large blood vessels. Even if some of the tumor is left behind, that doesn't always mean the tumor will come back. Whether chemotherapy and other treatments will be needed after surgery depends on the child's risk group.

If the tumor is very large, chemotherapy may be used before surgery to shrink the tumor and make it easier to remove.

Possible risks and side effects of surgery

The risks from surgery depend on the location and extent of the operation and the child's health beforehand. Serious complications, although rare, can include problems with anesthesia, excess bleeding, infections, and damage to blood vessels, kidneys, other organs, or nerves. Complications are more likely if the tumor is large and growing into blood vessels or nerves. Most children will have some pain for a while after the operation, but this can usually be helped with medicines if needed.

Hyperlinks

1. www.cancer.org/cancer/neuroblastoma/detection-diagnosis-staging/how-diagnosed.html

References

Brodeur GM, Hogarty MD, Bagatell R, Mosse YP, Maris JM. Neuroblastoma. In: Pizzo PA, Poplack DG, eds. *Principles and Practice of Pediatric Oncology*. 7th ed. Philadelphia Pa: Lippincott Williams & Wilkins; 2016:772–792.

National Cancer Institute. Physician Data Query (PDQ). Neuroblastoma Treatment. 2017. Accessed at www.cancer.gov/cancertopics/pdq/treatment/neuroblastoma/healthprofessional on October 12, 2017.

Pinto NR, Applebaum MA, Volchenboum SL, et al. Advances in risk classification and

treatment strategies for neuroblastoma. *J Clin Oncol*. 2015; 30;3008-3017.

Speleman F, Park JR, Henderson TO. Neuroblastoma: a tough nut to crack. *Am Soc Clin Oncol Educ Book*. 2016; 35:e548-557. Accessed at <https://meetinglibrary.asco.org/record/50740/edbook#fulltext> on October 15, 2017.

Last Revised: March 19, 2018

Chemotherapy for Neuroblastoma

Chemotherapy (chemo) uses anti-cancer drugs, which are usually given into a vein. The drugs enter the bloodstream and travel throughout the body to reach and destroy cancer cells. This makes chemo useful for treating neuroblastoma that has spread to the lymph nodes, bone marrow, liver, lungs, or other organs.

Whether a child with neuroblastoma will get chemotherapy depends on their risk group. Some children with neuroblastoma are treated with chemo either before surgery (neoadjuvant chemotherapy) or after surgery (adjuvant chemotherapy). In other cases, especially when the cancer has spread too far to be removed completely by surgery, chemotherapy is the main treatment.

Chemo for neuroblastoma usually includes a combination of drugs. The main chemo drugs used include:

- Cyclophosphamide
- Cisplatin or carboplatin
- Vincristine
- Doxorubicin (Adriamycin)
- Etoposide
- Topotecan
- Busulfan and melphalan (sometimes used during stem cell transplant)
- Thiotepa (sometimes used during stem cell transplant)

The most common combination of drugs includes carboplatin (or cisplatin), cyclophosphamide, doxorubicin, and etoposide, but others may be used. For children in the high-risk group, more combinations are used, and some drugs are given at higher

doses, which may be followed by a [stem cell transplant](#) (described further on).

Doctors give chemo in cycles, which consist of treatment on a few days in a row, followed by time off to allow the body time to recover. The cycles are typically repeated every 3 or 4 weeks. The total length of treatment depends on which risk group the child is in – higher risk groups usually require longer treatment.

Possible side effects of chemotherapy

Chemo drugs attack cells that are dividing quickly, which is why they work against cancer cells. But other cells in the body, such as those in the bone marrow (where new blood cells are made), the lining of the mouth and intestines, and the hair follicles, also divide quickly. These cells are also likely to be affected by chemo, which can lead to side effects.

The side effects of chemo depend on the type and dose of drugs given and the length of time they are taken. General side effects can include:

- Hair loss
- Mouth sores
- Loss of appetite
- Nausea and vomiting
- Diarrhea or constipation
- Increased chance of infections (from having too few white blood cells)
- Easy bruising or bleeding (from having too few blood platelets)
- Fatigue (from having too few red blood cells)

Most of these side effects tend to go away after treatment is finished. There are often ways to lessen these side effects. For example, drugs can be given to help prevent or reduce nausea and vomiting. Be sure to ask your child's doctor or nurse about medicines to help reduce side effects, and let him or her know if your child has side effects so they can be managed.

Along with the effects listed above, some drugs can have specific side effects. For example:

Cyclophosphamide can damage the bladder, which can cause blood in the urine. The risk of this can be lowered by giving the drugs with plenty of fluids and with a drug called mesna, which helps protect the bladder. These drugs can also damage the ovaries or testicles, which could affect fertility (the ability to have children).

Doxorubicin can cause heart damage. Doctors try to reduce this risk as much as possible by limiting the doses of doxorubicin and by checking the heart with an echocardiogram (an ultrasound of the heart) during treatment. This drug can also cause skin damage if it should leak out of the vein while it is being given.

Cisplatin and carboplatin can affect the kidneys. Giving plenty of fluids can help reduce this risk. These drugs can also affect hearing. Your child's doctor may order hearing tests (audiograms) during or after treatment.

Vincristine can damage nerves. Some patients may have tingling, numbness, weakness, or pain, particularly in the hands and feet.

Chemotherapy can also have some longer-term side effects. For example, some drugs can increase the risk of later developing another type of cancer (such as [leukemia](#)¹). While this is a serious risk, it is not common, and the small increase in risk has to be weighed against the importance of chemotherapy in treating neuroblastoma. For more on the possible long-term effects of treatment, see [Late and Long-term Effects of Neuroblastoma and Its Treatment](#)².

For more information on chemotherapy in general, see [Chemotherapy](#)³.

Hyperlinks

1. www.cancer.org/cancer/leukemia.html
2. www.cancer.org/cancer/neuroblastoma/after-treatment/long-term-effects.html
3. www.cancer.org/treatment/treatments-and-side-effects/treatment-types/chemotherapy.html

References

Brodeur GM, Hogarty MD, Bagatell R, Mosse YP, Maris JM. Neuroblastoma. In: Pizzo PA, Poplack DG, eds. *Principles and Practice of Pediatric Oncology*. 7th ed. Philadelphia Pa: Lippincott Williams & Wilkins; 2016:772–792.

National Cancer Institute. Physician Data Query (PDQ). Neuroblastoma Treatment. 2017. Accessed at www.cancer.gov/cancertopics/pdq/treatment/neuroblastoma/healthprofessional on October 12, 2017.

Pinto NR, Applebaum MA, Volchenbom SL, et al. Advances in risk classification and

treatment strategies for neuroblastoma. *J Clin Oncol*. 2015; 30:3008-3017.

Speleman F, Park JR, Henderson TO. Neuroblastoma: a tough nut to crack. *Am Soc Clin Oncol Educ Book*. 2016; 35:e548-557. Accessed at <https://meetinglibrary.asco.org/record/50740/edbook#fulltext> on October 15, 2017.

Last Revised: March 19, 2018

Radiation Therapy for Neuroblastoma

Radiation therapy uses high-energy rays or particles to kill cancer cells. It is sometimes a necessary part of treatment, but because of the possible long-term side effects in children, doctors avoid using it when possible. Most children with neuroblastoma will not need radiation therapy. It is most common for radiation to be used in children with high-risk neuroblastoma after stem cell transplant. It might be used for children with low- and intermediate-risk neuroblastoma only if a child has life-threatening symptoms and needs emergency treatment to shrink the tumor.

Two types of radiation therapy can be used to treat children with neuroblastoma:

- External beam radiation therapy
- Radioisotope based radiation

External beam radiation therapy

External radiation therapy focuses the radiation on the cancer from a source outside the body. This type of treatment might be used:

- To try to shrink tumors before surgery, making them easier to remove
- To treat larger tumors that are causing serious problems (such as trouble breathing) and do not respond quickly to chemotherapy
- As part of the treatment regimen after [stem cell transplant](#) in children with high-risk neuroblastoma to destroy neuroblastoma cells that remain behind. Radiation might involve the primary tumor area and other areas of the body that might have active disease seen on an [MIBG scan](#)¹.

- To help relieve pain caused by advanced neuroblastoma

When radiation is aimed at the whole body, it is known as *total body irradiation* (TBI). Total body irradiation has been used in the past for children with high risk neuroblastoma before a stem cell transplant, but it is more common now for radiation only to be given after a stem cell transplant to the primary tumor site and any other areas of the body that might have active neuroblastoma cells.

Before treatments start, the radiation team takes careful measurements with [imaging tests](#)² such as MRI scans to determine the correct angles for aiming the radiation beams and the proper dose of radiation.

Radiation therapy is much like getting an x-ray, but the dose of radiation is much higher. Your child might be fitted with a plastic mold resembling a body cast to keep him or her in the same position during each treatment so that the radiation can be aimed more accurately.

The number of radiation treatments given depends on the situation. For each treatment session, your child lies on a special table while a machine delivers the radiation from a precise angle. The treatment is not painful. Each actual treatment lasts only a few minutes, but the setup time – getting your child into place for treatment – usually takes longer. Young children may be given medicine to make them sleep so they will not move during the treatment.

Possible side effects: Radiation therapy is sometimes an important part of treatment, but young children's bodies are very sensitive to it, so doctors try to use as little radiation as possible to help avoid or limit any problems. Radiation can cause both short-term and long-term side effects, which depend on the dose of radiation and where it is aimed.

Possible short-term effects

- Effects on skin areas that receive radiation can range from mild sunburn-like changes and hair loss to more severe skin reactions.
- Radiation to the abdomen (belly) can cause nausea or diarrhea.
- Radiation therapy can make a child tired, especially toward the end of treatment.

Radiation can also make the side effects of chemotherapy worse. Talk with your child's doctor about the possible side effects because there are ways to relieve some of them.

Possible long-term effects

- Radiation therapy can slow the growth of normal body tissues (such as bones) that get radiation, especially in younger children. In the past this led to problems such as short bones or a curving of the spine, but this is less likely with the lower doses of radiation used today.
- Radiation can affect the thyroid gland in the neck, causing it to make less thyroid hormone (hypothyroidism). Symptoms of hypothyroidism can vary greatly. In children, hypothyroidism can affect growth and development. Thyroid replacement medicine is usually all that's needed to manage hypothyroidism.
- Radiation that reaches the chest area can affect the heart and lungs. This does not usually cause problems right away, but in some children it may eventually lead to heart or lung problems as they get older.
- Radiation to the abdomen in girls can damage the ovaries. This might lead to abnormal menstrual cycles or problems getting pregnant or having children later on.
- Radiation can damage the DNA inside cells. As a result, radiation therapy slightly increases the risk of developing a second cancer in the areas that get radiation, usually many years after the radiation is given.

Close follow-up with doctors is important as children grow older so that any problems can be found and treated as soon as possible. For more on the possible long-term effects of treatment, see the section [Late and Long-term Effects of Neuroblastoma and Its Treatment](#)³.

MIBG radiotherapy

As described in the section [Tests for Neuroblastoma](#)⁴, MIBG is a chemical similar to norepinephrine, which is made by sympathetic nerve cells. A slightly radioactive form of MIBG is sometimes injected into the blood as part of an imaging test to look for neuroblastoma cells in the body.

A more highly radioactive form of MIBG is also used to treat some children with advanced neuroblastoma, often along with other treatments. Once injected into the blood, the MIBG goes to tumors anywhere in the body and delivers its radiation. The child will need to stay in a special hospital room for a few days after the injection until most of the radiation has left the body. Most of the radiation leaves the body in the urine, so younger children might need to have a catheter in the bladder to help urine leave the body, usually for a couple of days.

Possible side effects: Most of the radiation from MIBG therapy stays in the area of the neuroblastoma, so most children do not have serious side effects from this treatment. MIBG therapy can sometimes cause mild nausea and vomiting. It can also make some children feel tired or sluggish. Some children might have swollen cheeks from the MIBG because it can affect the salivary glands. In rare cases it might cause high blood pressure for a short period of time.

Hyperlinks

1. www.cancer.org/cancer/neuroblastoma/detection-diagnosis-staging/how-diagnosed.html
2. www.cancer.org/cancer/neuroblastoma/detection-diagnosis-staging/how-diagnosed.html
3. www.cancer.org/cancer/neuroblastoma/after-treatment/long-term-effects.html
4. www.cancer.org/cancer/neuroblastoma/detection-diagnosis-staging/how-diagnosed.html

References

National Cancer Institute. Physician Data Query (PDQ). Neuroblastoma Treatment. 2017. Accessed at www.cancer.gov/cancertopics/pdq/treatment/neuroblastoma/healthprofessional on October 12, 2017.

Pappo AS, Navid F, Brennan RC, et al. Solid tumors of childhood: Neuroblastoma. In: DeVita VT, Lawrence TS, Rosenberg SA, eds. *DeVita, Hellman, and Rosenberg's Cancer: Principles and Practice of Oncology*. 10th ed. Philadelphia, PA: Lippincott Williams & Wilkins 2015:

Pinto NR, Applebaum MA, Volchenboum SL, et al. Advances in risk classification and treatment strategies for neuroblastoma. *J Clin Oncol*. 2015: 30;3008-3017.

Last Revised: March 19, 2018

High-Dose Chemotherapy/Radiation

Therapy and Stem Cell Transplant for Neuroblastoma

This type of treatment is often used in children with high-risk neuroblastoma who are unlikely to be cured with other treatments. Before the stem cell transplant, a child has usually had about 5 months of intense chemotherapy and might have had surgery to remove the tumor.

Giving higher doses of [chemotherapy](#) might be more effective in treating these cancers, but normally this can't be done because it would cause severe damage to the bone marrow, where new blood cells are made. This could lead to life-threatening shortages of blood cells.

Doctors can sometimes get around this problem by giving the high-dose treatments, then replacing the patient's bone marrow cells by giving them new blood-making cells (called **stem cells**). This is known as a **stem cell transplant** (SCT). Some children might have 2 stem cell transplants, called **tandem stem cell transplants**.

Collecting stem cells before the transplant

For most children with neuroblastoma, their own stem cells are used for the transplant. These stem cells are collected in a process called **apheresis**.

To help prepare for stem cell collection, doctors give children a medicine called G-CSF that helps bone marrow make more white blood cells and helps stem cells move into the bloodstream.

G-CSF is usually started at the end of a regular cycle of chemotherapy and is given daily. Children often need blood tests every day once their blood cell counts start to increase (this is often about 7 to 10 days after their first dose of chemotherapy). Once part of the white blood cell count (known as the **absolute neutrophil count**, or **ANC**) reaches a certain level, the dose of G-CSF is increased until there are enough stem cells to collect. A special kind of central line will be placed so the stem cells can be collected using apheresis. The collection process is similar to donating blood, but instead of going into a collecting bag, the blood goes into a special machine that filters out the stem cells and returns the other parts of the blood back to the person's body. Apheresis can take 3 to 4 hours and your child will probably need to lie flat and hold still during the procedure. This process may be repeated over a few days. The stem cells are then frozen until the transplant.

How the transplant is done

Typically, the child will be admitted to the SCT unit of the hospital on the day before the high-dose chemo begins. He or she will usually stay in the hospital until after the chemo and the stem cells have been given, and until the stem cells have started making new blood cells again (see below).

The child gets high-dose chemotherapy first. This destroys the cancer cells in the body, as well as the normal cells in the bone marrow. After high-dose chemotherapy, the frozen stem cells are thawed and given as a blood transfusion. The stem cells travel through the bloodstream and settle in the child's bone marrow.

Usually within a couple of weeks, the stem cells begin making new white blood cells. This is later followed by new platelet production and new red blood cell production. Until this happens, the child is at high risk of [infection](#)¹ because of a low white blood cell count, as well as bleeding because of a low platelet count. To help lower the risk of infection, the child stays in a special hospital room, and visitors must wear protective clothing. Blood and platelet transfusions and treatment with IV antibiotics may also be used to help prevent or treat infections or bleeding problems.

The child usually stays in the hospital room until part of the white blood cell count rises to a safe level. The child is then seen in an outpatient clinic almost every day for several weeks. Because platelet counts often take longer to return to a safe level, the child may get platelet transfusions as an outpatient. Patients may need to make regular visits to the outpatient clinic for about 6 months, after which time their regular doctors may continue their care.

A SCT is a complex treatment that can cause life-threatening side effects. If the doctors think your child can benefit from a transplant, the best place to have this done is at a nationally recognized cancer center where the staff has experience with the procedure and managing the recovery period.

Possible side effects

The possible side effects from SCT are generally divided into early and long-term effects.

Early or short-term side effects

The early complications and side effects are basically the same as those caused by high-dose chemotherapy or radiation therapy and can be severe. They are caused by

damage to the bone marrow and other quickly growing tissues of the body, and can include:

- Low blood cell counts (with fatigue and increased risk of infection and bleeding)
- Nausea and vomiting
- Loss of appetite
- Mouth sores
- Diarrhea
- Hair loss
- Problems with liver

One of the most common and serious short-term effects is an increased risk for serious infections. Antibiotics are often given to try to prevent this. [Other side effects](#)², like low red blood cell and platelet counts, might require [blood product transfusions](#)³ or other treatments.

Late or long-term side effects

Some complications and side effects can last for a long time or might not occur until months or years after the transplant. These can include:

- Radiation damage to the heart or lungs
- Problems with the thyroid or other hormone-making glands
- Problems with fertility
- Damage to bones or problems with bone growth
- Development of another cancer (including leukemia) years later

Be sure to talk to your child's doctor before the transplant to learn about possible long-term effects your child might have. For more on the possible long-term effects of this and other treatments, see the section, [Late and Long-term Effects of Neuroblastoma and Its Treatment](#)⁴.

For more information on stem cell transplants in general, see [Stem Cell Transplant for Cancer](#).⁵

Hyperlinks

1. www.cancer.org/treatment/treatments-and-side-effects/physical-side-effects/low-blood-counts/infections.html

2. www.cancer.org/treatment/treatments-and-side-effects/physical-side-effects.html
3. www.cancer.org/treatment/treatments-and-side-effects/treatment-types/blood-transfusion-and-donation.html
4. www.cancer.org/cancer/neuroblastoma/after-treatment/long-term-effects.html
5. www.cancer.org/treatment/treatments-and-side-effects/treatment-types/stem-cell-transplant.html

References

National Cancer Institute. Physician Data Query (PDQ). Neuroblastoma Treatment. 2017. Accessed at www.cancer.gov/cancertopics/pdq/treatment/neuroblastoma/healthprofessional on October 12, 2017.

Pappo AS, Navid F, Brennan RC, et al. Solid tumors of childhood: Neuroblastoma. In: DeVita VT, Lawrence TS, Rosenberg SA, eds. *DeVita, Hellman, and Rosenberg's Cancer: Principles and Practice of Oncology*. 10th ed. Philadelphia, PA: Lippincott Williams & Wilkins 2015: 1465-1562

Pinto NR, Applebaum MA, Volchenboum SL, et al. Advances in risk classification and treatment strategies for neuroblastoma. *J Clin Oncol*. 2015; 30;3008-3017.

Last Revised: March 19, 2018

Retinoid Therapy for Neuroblastoma

Retinoids are chemicals that are related to vitamin A. They are known as **differentiating agents** because they are thought to help some cancer cells mature (differentiate) into normal cells.

In children with high-risk neuroblastoma, treatment with a retinoid called *13-cis-retinoic acid* (isotretinoin) reduces the risk of the cancer coming back after high-dose chemotherapy and stem cell transplant. Most doctors now recommend 6 months of *13-cis-retinoic acid* after the transplant. This drug is taken as a capsule, twice a day for 2 weeks, followed by 2 weeks off.

Researchers are now trying to develop more effective retinoids and to define the exact role of this approach in treating neuroblastoma.

Possible side effects

The most common side effect of 13-cis-retinoic acid is dry and cracked lips. Dry skin or eyes are also possible, as are nosebleeds, muscle and joint pains, and changes in the nails.

References

Brodeur GM, Hogarty MD, Bagatell R, Mosse YP, Maris JM. Neuroblastoma. In: Pizzo PA, Poplack DG, eds. *Principles and Practice of Pediatric Oncology*. 7th ed. Philadelphia Pa: Lippincott Williams & Wilkins; 2016:772–792.

Pinto NR, Applebaum MA, Volchenboum SL, et al. Advances in risk classification and treatment strategies for neuroblastoma. *J Clin Oncol*. 2015; 30:3008-3017.

Last Revised: March 19, 2018

Immunotherapy for Neuroblastoma

Immunotherapy is the use of medicines to help a patient's own immune system recognize and destroy cancer cells more effectively. Several types of immunotherapy are now being studied for use against neuroblastoma (some of which are described in [What's New in Neuroblastoma Research?](#)¹), and some are now being used to treat it.

Anti-GD2 monoclonal antibodies

Monoclonal antibodies are man-made versions of immune system proteins that can be made to attach to a very specific target on cells in the body. These antibodies can be injected into the blood to seek out and attach to cancer cells.

Many neuroblastoma cells have large amounts of a substance called GD2 on their

surfaces. Monoclonal antibodies that attach to GD2 can help the body's immune system find and destroy these cancer cells.

Dinutuximab (Unituxin)

This monoclonal antibody is given together with cytokines (immune system hormones) such as GM-CSF and interleukin-2 (IL-2) to help the body's immune system recognize and destroy neuroblastoma cells.

This drug is given as an infusion into a vein (IV) over many hours, for 4 days in a row. This is done about once a month, usually for a total of about 5 cycles of treatment. Other medicines are given before and during each infusion to help with possible side effects such as pain or allergic reactions.

Dinutuximab is now part of the routine treatment for many children with high-risk neuroblastoma, often after a [stem cell transplant](#).

Possible side effects

Dinutuximab can cause side effects, some of which can be serious. Possible side effects include:

- Nerve pain (which can sometimes be severe)
- Leaking of fluid from small blood vessels in the body (which can lead to low blood pressure, fast heart rate, shortness of breath, and swelling)
- Allergic reactions (which can lead to airway swelling, trouble breathing, and low blood pressure)
- Eye and vision problems
- Fever
- Vomiting
- Diarrhea
- Itching
- Trouble urinating
- Infections
- Low blood cell counts
- Changes in mineral levels in the blood

Other side effects are possible as well. Talk to the treatment team to learn more about the possible side effects and what can be done about them.

Naxitamab (Danyelza)

This monoclonal antibody is given together with the cytokine (immune system hormone) GM-CSF to help the body's immune system recognize and destroy neuroblastoma cells.

This drug is given as an infusion into a vein (IV) over 30 to 60 minutes on days 1, 3, and 5 of each 4-week cycle. Other medicines are given before and during each infusion to help with possible side effects such as pain or allergic reactions.

Naxitamab can be used in patients who are at least one year old and who have high-risk neuroblastoma that is in their bones or bone marrow and that has come back or started to grow again after initially responding to treatment.

Possible side effects

Naxitamab can cause side effects, some of which can be serious. Possible side effects include:

- Nerve pain (which can sometimes be severe)
- Allergic reactions (which can lead to airway swelling, trouble breathing, and low blood pressure)
- Eye and vision problems
- Rapid heartbeat
- Fever
- Vomiting
- Cough
- Nausea
- Diarrhea
- Low blood pressure
- Itching
- Trouble urinating
- Infections
- Low blood cell counts
- Changes in mineral levels in the blood

Other side effects are possible as well. Talk to the treatment team to learn more about the possible side effects and what can be done about them.

Hyperlinks

1. www.cancer.org/cancer/neuroblastoma/about/new-research.html

References

Dome JS, Rodriguez-Galindo C, Spunt SL, et al. Pediatric solid tumors. In: Neiderhuber JE, Armitage JO, Doroshow JH, Kastan MB, Tepper JE, eds. *Abeloff's Clinical Oncology*. 5th ed. Philadelphia, PA. Elsevier: 1804-1847

Pinto NR, Applebaum MA, Volchenboum SL, et al. Advances in risk classification and treatment strategies for neuroblastoma. *J Clin Oncol*. 2015; 30:3008-3017.

Yu AL, Gilman AL, Ozkaynak MF, et al. Anti-GD2 antibody with GM-CSF, interleukin-2, and isotretinoin for neuroblastoma. *N Engl J Med*. 2010;363:1324–1334.

Last Revised: December 2, 2020

Treatment of Neuroblastoma by Risk Group

Treatment for neuroblastoma is largely based on which [risk group](#)¹ a child is in. Generally, older children, children with tumors that have spread throughout the body, and children whose tumors have unfavorable features or extra copies of the *MYCN* gene will be considered high risk. Some infants with neuroblastoma that has spread throughout the body can still be considered low risk, especially if their tumor does not have extra copies of *MYCN* or other unfavorable features.

Low risk

Children at low risk usually don't need very intensive treatment to cure the neuroblastoma. In fact, some children might not need to be treated at all because some of these neuroblastomas will mature or go away on their own. If a child is low risk and the tumor can easily be removed, [surgery](#) can often be their only treatment. Even if

some neuroblastoma is left behind after surgery, the child can usually be watched carefully without further treatment because the remaining tumor will often mature or go away on its own.

If much of the tumor can't be removed, the tumor gets bigger after a surgery, or if a tumor is causing symptoms, [chemotherapy](#) (chemo) is typically given. A common chemo regimen is a combination of carboplatin, cyclophosphamide, doxorubicin, and etoposide. But other combinations may be used.

For those few children that have symptoms from a low-risk tumor that can't safely be treated right away with surgery, a short course of chemo might be given first. For example, if the tumor is pressing on the spinal cord or affecting breathing, chemo may be used to shrink the tumor to control the symptoms. A short course of [radiation therapy](#) usually is only used if the symptoms are not getting better with chemo, are life threatening, or are causing spinal cord compression.

Infants with stage 4S disease and no symptoms can often be watched carefully with no treatment, because these cancers typically mature or go away on their own. If the tumor causes problems such as an enlarged liver, which can be life-threatening for very young infants, chemo that is less intense may be used to shrink the tumor. Radiation therapy may be used if chemo doesn't shrink the liver right away.

Recent research has also shown that infants younger than 6 months with small adrenal tumors (which are assumed to be neuroblastomas) can often be watched closely without needing surgery or other treatments. Many of these tumors will mature or go away on their own, but if a tumor keeps growing or is causing symptoms, surgery or chemo might be used.

Intermediate risk

[Surgery](#) is an important part of treatment for children at intermediate risk, but it is rarely enough on its own. Children are typically given 4 to 8 cycles (about 12 to 24 weeks) of [chemotherapy](#) before or after surgery. The chemo drugs used usually include carboplatin, cyclophosphamide, doxorubicin, and etoposide. If chemo is used first, surgery may then be done to remove any remaining tumor. [Radiation therapy](#) usually is only used if the tumor is not responding well to chemo or if a child's symptoms from the tumor require emergency treatment.

Doctors are looking at the possibility of observing infants and young babies with no symptoms and favorable tumor features instead of treatment with surgery and/or chemotherapy. In this approach, doctors watch the tumor closely using [imaging tests](#)² to

make sure the tumor goes away or does not get bigger. If the tumor does get bigger or a child has symptoms, then treatment with chemotherapy will be started. Some studies have shown promising results using this approach, and more studies are being done now.

Children at intermediate risk who need chemotherapy are monitored closely to see how they respond after every 2 cycles (6 to 8 weeks). The total number of cycles depends on how well chemotherapy shrinks the tumor. Doctors hope that treating with chemotherapy based on a child's results can help children who have tumors that respond quickly get less chemotherapy.

High risk

Children at high risk require more aggressive treatment, which often includes [chemotherapy](#), [surgery](#), [radiation](#), [stem cell transplant](#), [immunotherapy](#), and [retinoid therapy](#). Treatment is often done in 3 phases:

- **Induction:** The goal of this phase is to get the cancer into remission by destroying or removing as much of it as possible. Treatment usually starts with chemotherapy, using alternating regimens of several drugs (typically cisplatin, etoposide, vincristine, cyclophosphamide, doxorubicin, and topotecan) given at higher doses than what is used for other risk groups. Surgery is usually done after induction to try to remove any tumors that are still visible.
- **Consolidation:** This phase uses more intensive treatment to try to get rid of any cancer cells that remain in the body. High-dose chemotherapy is given, followed by one or two stem cell transplants. A recent study showed that giving two stem cell transplants back to back (tandem stem cell transplant) was better than giving one stem cell transplant. Even though long-term results of this study are still being looked at, the short-term results were promising enough that some centers may give two stem cell transplants, followed by immunotherapy. Radiation is often given to the primary tumor site after stem cell transplant (even if the tumor was removed by surgery) and to any other parts of the body that might have active disease, based on [MIBG scan results](#)³.
- **Maintenance:** The goal of this phase of treatment is to try to lower the chance that the cancer will come back. The retinoid drug 13-cis-retinoic acid (isotretinoin) is often given for 6 months after other treatments are completed. Immunotherapy with the [monoclonal antibody](#) dinutuximab (Unituxin), along with immune-activating cytokines (GM-CSF and IL-2), is often given as well.

Recurrent neuroblastoma

If neuroblastoma comes back after initial treatment, it is known as a [recurrence](#)⁴ or relapse. Treatment of recurrent neuroblastoma depends on many factors, including the initial [risk group](#)⁵, where the cancer recurs, and what treatments have been used.

For **low- and intermediate-risk** neuroblastomas that recur in the same area where they started, surgery with or without chemotherapy may be effective.

For **high-risk** cancers or those that recur in distant parts of the body, treatment is usually more intense, and may include a combination of chemotherapy, surgery, and radiation therapy (such as MIBG radiotherapy). Chemotherapy might include drugs that weren't used during the initial treatment. Other options might include intensive treatment with high-dose chemotherapy followed by a stem cell transplant, or treatment with the [monoclonal antibody](#) naxitamab (Danyelza).

Because these cancers can be hard to treat, clinical trials of newer treatments, such as monoclonal antibodies or new anti-cancer drugs, might be another reasonable option. To learn more, see [What's New in Neuroblastoma Research?](#)⁶

Hyperlinks

1. www.cancer.org/cancer/neuroblastoma/detection-diagnosis-staging/risk-groups.html
2. www.cancer.org/treatment/understanding-your-diagnosis/tests/imaging-radiology-tests-for-cancer.html
3. www.cancer.org/cancer/neuroblastoma/detection-diagnosis-staging/how-diagnosed.html
4. www.cancer.org/treatment/survivorship-during-and-after-treatment/understanding-recurrence.html
5. www.cancer.org/cancer/neuroblastoma/detection-diagnosis-staging/risk-groups.html
6. www.cancer.org/cancer/neuroblastoma/about/new-research.html

References

Baker D, Schmidt M, Cohn S, et al. Outcome after reduced therapy for intermediate-risk neuroblastoma. *N Engl J Med*. 2010; 363;1313-1323.

Brodeur GM, Hogarty MD, Bagatell R, Mosse YP, Maris JM. Neuroblastoma. In: Pizzo PA, Poplack DG, eds. *Principles and Practice of Pediatric Oncology*. 7th ed. Philadelphia Pa: Lippincott Williams & Wilkins; 2016:772–792.

National Cancer Institute. Physician Data Query (PDQ). Neuroblastoma Treatment. 2017. Accessed at www.cancer.gov/cancertopics/pdq/treatment/neuroblastoma/healthprofessional on October 12, 2017.

Nuchtern JG, London WB, Barnewolt CE, et al. A prospective study of expectant observation as primary therapy for neuroblastoma in young infants: A Children's Oncology Group study. *Ann Surg*. 2012;256:573–580.

Pappo AS, Navid F, Brennan RC, et al. Solid tumors of childhood: Neuroblastoma. In: DeVita VT, Lawrence TS, Rosenberg SA, eds. *DeVita, Hellman, and Rosenberg's Cancer: Principles and Practice of Oncology*. 10th ed. Philadelphia, PA: Lippincott Williams & Wilkins 2015: 1465-1562

Park JR, Kriessman SG, London WB, et al. A phase III randomized clinical trial of tandem myeloablative autologous stem cell transplant using peripheral blood stem cell as consolidation therapy for high risk neuroblastoma: A Children's Oncology Group study. *J Clin Oncol*. 2016: 34;18_suppl, LBA3-LBA3

Pinto NR, Applebaum MA, Volchenboum SL, et al. Advances in risk classification and treatment strategies for neuroblastoma. *J Clin Oncol*. 2015: 30;3008-3017.

Speleman F, Park JR, Henderson TO. Neuroblastoma: a tough nut to crack. *Am Soc Clin Oncol Educ Book*. 2016; 35:e548-557. Accessed at <https://meetinglibrary.asco.org/record/50740/edbook#fulltext> on October 15, 2017.

Last Revised: December 2, 2020

Written by

The American Cancer Society medical and editorial content team
(www.cancer.org/cancer/acs-medical-content-and-news-staff.html)

Our team is made up of doctors and oncology certified nurses with deep knowledge of cancer care as well as journalists, editors, and translators with extensive experience in medical writing.

American Cancer Society medical information is copyrighted material. For reprint requests, please see our Content Usage Policy (www.cancer.org/about-us/policies/content-usage.html).

cancer.org | 1.800.227.2345