

Dr Shivam Shingla

Consultant Medical Oncologist
MBBS, MD, DNB Medical Oncology
MNAMS MRCP UK (SCE)
Lung Cancer Fellowship From
Zurich Switzerland

 www.drshivamshingla.com

 +91 98925 96286

 drshivamshingla@gmail.com

#Reference From NCCN Guidelines

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National Comprehensive Cancer Network (NCCN) and NCCN Foundation
3025 Chemical Road, Suite 100, Plymouth Meeting, PA 19462 USA

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Guideline basics

- 5 What is primary CNS lymphoma?
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- 8 How is primary CNS lymphoma diagnosed?
- 8 Can primary CNS lymphoma be cured?
- 9 What's next?
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Being diagnosed with a brain tumor can be frightening and overwhelming. This book will help you make sense of all the information that's out there. It will also describe your options for treatment. Taken together, you'll have the confidence to make well-informed decisions.

What is primary CNS lymphoma?

Primary central nervous system lymphoma is a rare and aggressive cancer that affects the central nervous system (CNS).

Let's break it down word by word to understand it better:

Primary – Primary means first. When talking about cancer, primary refers to the place where cancer first started. Primary CNS lymphoma starts in the central nervous system.

Central nervous system – The CNS is made up of the brain and spinal cord. Primary CNS lymphoma occurs more often in the brain than in the spinal cord, but it can also involve the cerebrospinal fluid (CSF), and/or the eyes.

Lymphoma – Lymphoma is cancer that forms from lymphocytes. Lymphocytes are white blood cells that fight infections. Cancer is what happens when cells grow out of control. So, a lymphoma is an abnormal overgrowth of lymphocytes.

Now let's put it all together:

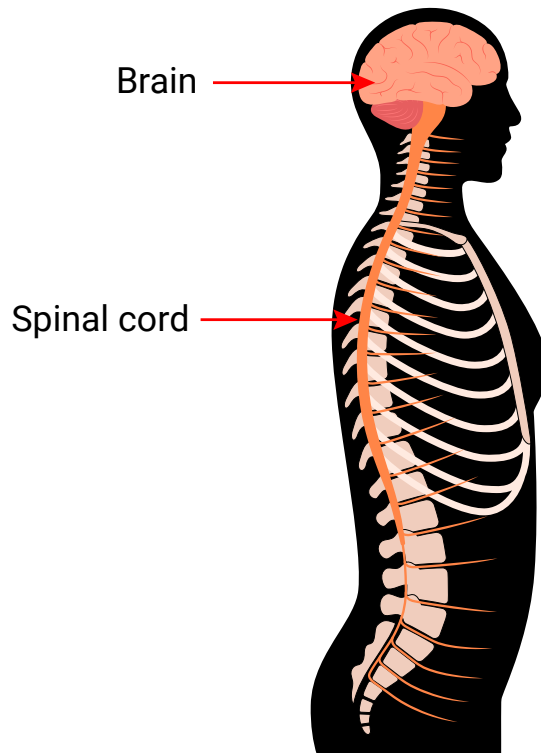
Primary CNS lymphoma is a cancer that begins when lymphocytes in the brain and spinal cord grow out of control.

Primary CNS lymphoma starts in lymphocytes in the immune system. The immune system is your body's natural defense against infection and disease. Having an impaired immune system may increase the risk of developing this cancer.

Primary CNS lymphoma can spread to other areas within the nervous system. For example, it may spread from the brain to the eyes. But it rarely spreads to other areas of the body. However, a different kind of lymphoma—called secondary CNS lymphoma—starts in another part of the body but then spreads to the brain or spinal cord.

This book is only about **primary CNS lymphoma**.

What is the CNS?



The central nervous system (CNS) receives signals from your senses, processes information, and controls your body's responses. The CNS includes:

- **The brain**, which controls functions of the body such as feeling, moving, thinking, and learning. The eyes are connected directly to the brain and are also part of the CNS.
- **The spinal cord**, which transmits messages between the brain and the body.

Because the CNS is so important, your body has parts that protect it. These include:

- **Meninges**, which are membranes that cover your brain and spinal cord.
- **Cerebrospinal fluid**, which is a liquid that surrounds your brain and spinal cord.
- **Bones** including the skull that shields your brain and the vertebrae that surround your spinal cord.

What causes primary CNS lymphoma?

Every person diagnosed with cancer wants to know how they got it. Although no one knows exactly what causes a lymphoma, we do know that lymphomas often start with a genetic abnormality (mutation) in certain lymphocytes. This abnormality causes these lymphocytes to grow out of control (become cancerous). The abnormality occurs on its own. It's not a mutation that occurs in other cells or organs in your body. And it's not typically passed down in families (hereditary mutation).

Although primary CNS lymphoma is rare, it could happen to almost anyone. However, some people with certain risk factors have a greater chance.

Risk factors

A risk factor is something that increases your chance of developing a disease. For example, having a reduced immune system increases the risk of developing primary CNS lymphoma.

Risk factors don't necessarily cause a disease (and just because you have risk factors, it doesn't mean you'll definitely get the disease). But people with primary CNS lymphoma often have one or more of these risk factors:

- **Carrying the Epstein-Barr virus**, which is the virus that causes mononucleosis ("mono") and other illnesses. Epstein-Barr is one of the most common viruses in humans. Most people are infected with it. After you're infected, the virus remains dormant (inactive or "sleeping") in your body for life.
 - **Having an autoimmune disease**, such as lupus, in which the immune system overreacts and attacks healthy tissues and organs.
 - **Having an organ transplant**, which requires medications that suppress the immune system. This leads to a higher risk of infections.
 - **Being an older adult**. Although primary CNS lymphoma can occur at any age, the majority of people diagnosed with it are in their 60s or 70s.
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- **Having an immunodeficiency disorder**, which is an illness that weakens the immune system's ability to fight infections and diseases. Primary CNS lymphoma is frequently linked to HIV, the immunodeficiency virus that causes AIDS.

How is primary CNS lymphoma diagnosed?

Primary CNS lymphoma is often found when a person develops symptoms. A symptom is a feeling or problem that may be a sign of disease. Symptoms usually develop over several weeks. Primary CNS lymphoma can cause a variety of symptoms.

Symptoms are often related to the lymphoma's location in the central nervous system. The most common location is in the central part of the brain. A lymphoma located here may cause specific nerve changes such as leg or arm weakness, or problems with coordination or movement.

Other such symptoms may include changes in personality or behavior, depression, confusion, memory problems, loss of bladder control (incontinence), or difficulty speaking or swallowing.

As the lymphoma tumor grows, it puts pressure on the CNS. This pressure often leads to neurological symptoms and difficulties, including headaches, nausea, vomiting, or seizures. Changes in eyesight, such as blurry vision or double vision, can also occur.

You'll need several tests to confirm whether you have primary CNS lymphoma or a lymphoma that started in another part of your body, or a different disease with similar symptoms. Important tests include a neurological exam, imaging (MRI or CT scan), and biopsies. A biopsy means taking a sample of fluid or tissue from your body to look for cancer. You'll also have blood tests, an eye exam, and other tests.

If these tests show that you have primary CNS lymphoma, your care team should discuss your treatment options with you. If possible, seek care at a center with experience in treating lymphomas in the brain.

Can primary CNS lymphoma be cured?

Curing primary CNS lymphoma is rare, but it may be possible if it's diagnosed early and treated immediately. Sometimes the bigger problem is managing the major side effects of the intense treatment. People who are younger, healthier, and more physically fit have a better chance for a cure.

In most people, primary CNS lymphoma can't be cured, but it can be treated. Treatment can slow down its growth and reduce its symptoms for a period of time, and prolong life. The main treatments for primary CNS lymphoma include chemotherapy, radiation therapy, stem cell transplant, or a combination of these treatments. Joining a clinical trial of a potential new therapy is another recommended option.

Treatment may be able to put primary CNS lymphoma into remission. Remission means there are no symptoms or signs of cancer. Remission may last for months or years. However, even with the best treatment, primary CNS lymphoma often comes back (relapses) in the brain, spinal cord, or the eye.

It's true that primary CNS lymphoma is fatal for some patients. Anyone diagnosed with primary CNS lymphoma has a difficult road ahead. Still, there's hope. In the past few years, improved detection methods have shortened the time

to diagnosis and led to better outcomes, even in people with weakened immune systems. Therapies specifically designed to treat primary CNS lymphoma are currently being studied in clinical trials. The number of these trials has increased in recent years, offering more hope to people living with this disease.

What's next?

This chapter provides only a brief overview of primary CNS lymphoma. The next chapters explain:

- Tests needed to diagnose the disease
- Different treatment options and what they do
- Which treatment options are right for you
- What happens after treatment
- Thoughts on next steps

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Don't Google your diagnosis and assume that statistics define your life! Every person's brain tumor story and situation is different. My motto is to 'live fearlessly' and ignore those fears the internet can give you.”

In most people, primary CNS lymphoma can't be cured, but it can be treated. Treatment can slow down the lymphoma's growth, reduce its symptoms, and prolong life.



Key points

- Cancer is what happens when cells grow out of control.
- Lymphocytes are white blood cells that fight infections. A lymphoma is an abnormal overgrowth (cancer) of lymphocytes.
- Primary CNS lymphoma is a rare and aggressive cancer that most often affects the brain. But it can also occur in the spinal cord, cerebrospinal fluid (CSF), and/or the eyes.
- Primary CNS lymphoma can spread to other areas in the nervous system but it rarely spreads to other areas of the body.
- A risk factor is something that increases your chance of developing a disease.
- Having an impaired immune system is a risk factor for developing primary CNS lymphoma.
- A lymphoma located in the central part of the brain can cause leg or arm weakness, coordination or movement difficulties, changes in personality or behavior, memory problems, and other symptoms.
- If possible, seek care at a center with experience in treating brain lymphomas.
- Not everyone with primary CNS lymphoma can be cured, but all can be treated. Treatment can slow down the lymphoma's growth, reduce symptoms, and prolong life.
- The main treatments for primary CNS lymphoma include chemotherapy, radiation therapy, stem cell transplant, or a combination of these treatments.
- Another recommended option is receiving treatment in a clinical trial.

A message to caregivers and loved ones

This book is for you, too. This book will help you understand this disease and the challenges it presents. People with lymphoma in the central nervous system (the brain and spinal cord) commonly develop problems with brain function. This can show itself in multiple ways, such as slower thinking, memory loss, difficulty moving or walking, trouble speaking, inability to do everyday activities, changes in behavior, losing one's sense of self, and other problems.

Helping a person with primary CNS lymphoma can be challenging and time-consuming. You may be providing physical, mental, emotional, and hands-on support. You may be taking the patient to appointments, helping to lessen side effects, and even assisting with treatment decisions. Gather as much help as you can. Start with the online resources listed in the back of this book.

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Tests for primary CNS

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Different tests are needed to identify primary CNS lymphoma and to make a treatment plan. The key to confirming the diagnosis is removing a small sample of the tumor tissue and testing it.

Many diseases have signs and symptoms similar to primary central nervous system (CNS) lymphoma, including neurological illnesses and other types of brain cancer. So it's important to have tests to confirm your diagnosis. If you're given a diagnosis of primary CNS lymphoma, you'll have more tests to find out how far the cancer extends within the central nervous system or if it has spread to another area of the body. Tests are also used to help plan your treatment.

Tests for diagnosis

If you haven't yet been diagnosed with primary CNS lymphoma, you'll first have a physical examination and some general assessments of your health. These include a neurological exam and an evaluation of your level of activity. After these, you'll have imaging scans and one or more biopsies.

Neurological exam

This exam involves some simple tests to check your alertness, balance, coordination, reflexes, hearing, and other senses. Your doctor may also perform an eye exam to look at the health of the nerves in the back of your eye.

Performance status

Your care team will want to know how well you can do ordinary day-to-day activities—like taking a walk, climbing stairs, cooking dinner, carrying laundry, or taking a bath or shower. This evaluation is called performance status. The more activities you can do, the better your performance status. Your care team uses this evaluation to get a sense of the level of treatment you may be able to handle and whether you may be eligible for a clinical trial.

Imaging

Imaging tests take pictures (images) of the insides of your body. The images show areas in the body that might have cancer. The images can reveal a lymphoma's location, size, and other features.

MRI

Magnetic resonance imaging (MRI) is the most useful imaging technique for identifying primary CNS lymphoma. An MRI scan is good at showing the spine and soft tissues, including the brain, as well as other details that are helpful for planning surgery.

MRI uses radio waves and powerful magnets to take pictures of the inside of the body. During an MRI, you'll lie on a table that slides into the scanning machine. (An open MRI scanner may be an option at some health care centers.) It's important to lie still during the test to get the best pictures. The machine makes loud noises but you can wear earplugs.

An MRI of the brain or spinal cord usually requires a contrast agent (also called contrast dye or just contrast). Contrast highlights areas in organs, blood vessels, or other tissues to make them easier to see. The contrast

is injected into the bloodstream through an intravenous (IV) line before or during the imaging test and later flushed out in urine. The contrast agent used for primary CNS lymphoma is called gadolinium.

You'll have multiple MRI tests throughout diagnosis and treatment. An MRI should be done early on if your symptoms suggest a brain tumor. It's also used right after treatment to see how well the treatment worked. You'll have more MRIs during follow-up to watch for any recurrence or new growth.

CT

If MRI is unavailable or not recommended for you, you might have a computed tomography (CT or CAT) scan instead. A CT scan uses x-rays to take many images of your body from different angles. A computer then combines the pictures to make a 3D image.

After imaging

After the MRI or CT scan, your images will be studied by a radiologist, an expert in analyzing images of the nervous system. The radiologist will convey the imaging results to your care team. This information helps your team plan what the next steps of your care should be.

If your imaging results suggest a primary CNS lymphoma, the next step is a biopsy.

MRI of the brain

Magnetic resonance imaging (MRI) is the most useful imaging technique for identifying primary CNS lymphoma. It's important to lie still during the test to get the best images. Straps or other devices may help you avoid moving.



Biopsy

If imaging scans show something that may be a primary CNS lymphoma, your care providers will want to take a sample and test it. A procedure that removes a small piece of tissue for testing is called a biopsy. Getting a biopsy is the only way to be certain that you have cancer. A biopsy also gives your care team clues on how to treat it.

The standard method for diagnosing primary CNS lymphoma is a stereotactic biopsy. It's the recommended procedure when a brain tumor is in a hard-to-reach or vital area. It aims to remove only enough of the tumor to make a diagnosis.

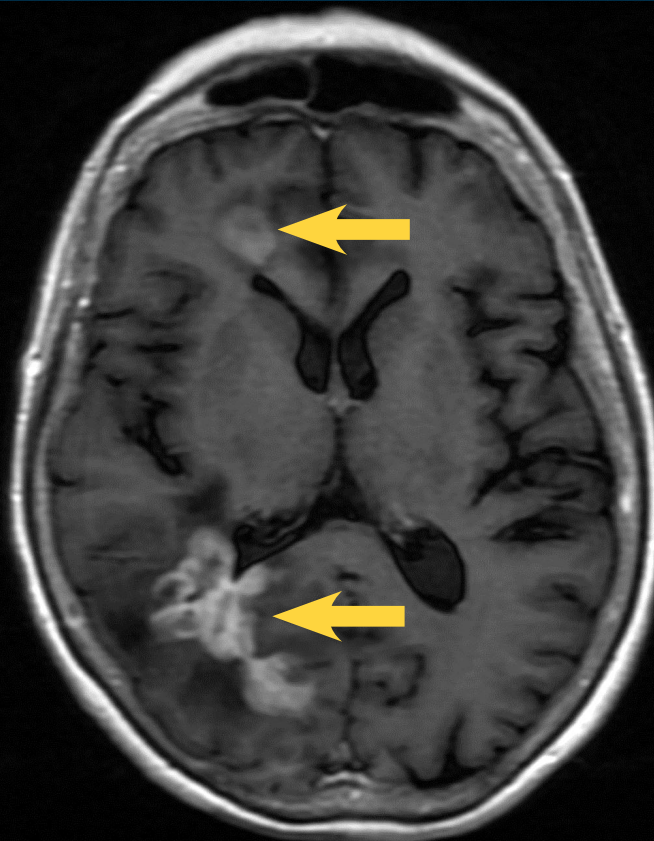
A stereotactic biopsy is done by a neurosurgeon in an operating room. First, you'll be fitted with a frame or several tiny markers around your head to aid the surgery. Next, you'll be given anesthesia to go to sleep. A small area of your hair will be shaved down to the scalp.

The neurosurgeon will then make a little opening in your skull and insert a thin, hollow needle into the brain to remove a sliver of the tumor. A computerized navigation system, connected to MRI or CT imaging, will allow the surgeon to target and remove the sample with a high degree of precision. After removal, the opening in your scalp will be closed with sutures and you'll be able to go home.

What an MRI shows

An MRI scan highlights primary CNS lymphoma in the brain. People with primary CNS lymphoma may have one or multiple tumors appear on their scan.

Image: Stephanie E. Weiss, MD, FASTRO



The tissue sample will be sent to a laboratory for analysis. A specialist called a pathologist will examine the tissue under a microscope. If the tissue is cancerous, the pathologist will identify the type and grade of the cancer. The testing process will take about a week to complete.

If stereotactic biopsy is unavailable at your hospital or medical center, ask to be referred to a specialized center where it can be performed.

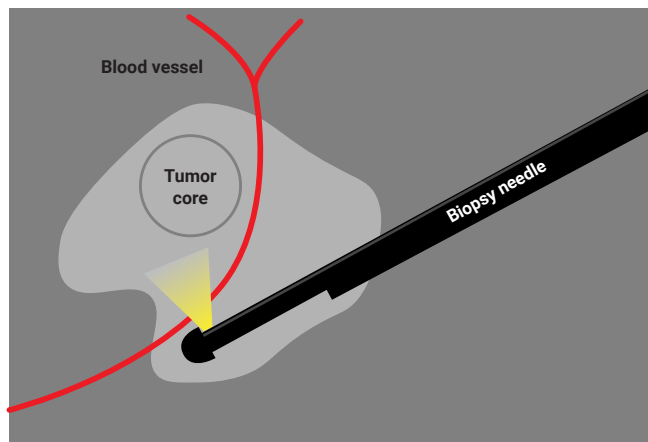
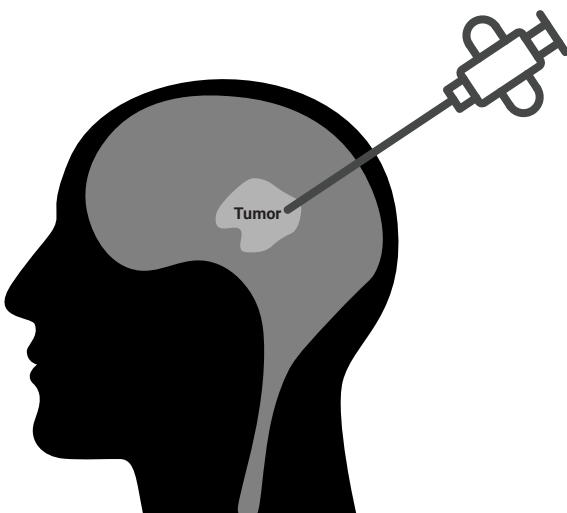
share with us.

**Take our survey,
and help make the
NCCN Guidelines for Patients
better for everyone!**

[NCCN.org/patients/comments](https://www.nccn.org/patients/comments)

Stereotactic biopsy

A stereotactic biopsy is needed to diagnose primary CNS lymphoma. In this procedure, a thin, hollow needle is inserted into the brain to remove a sliver of the tumor. The sample is sent to a lab to be tested for cancer cells.



Tests after diagnosis

After an MRI scan and a stereotactic biopsy have confirmed a diagnosis of lymphoma in the central nervous system, a few more tests are needed to find out how far the cancer has grown in the CNS and if it may have spread to other areas of the body. Although many people with primary CNS lymphoma have only one visible tumor, others have multiple tumors on their scan.

Testing after diagnosis also checks for signs of cancer in the eyes, cerebrospinal fluid, blood, chest, abdomen, and pelvis, and possibly the bone marrow and testicles. These tests include:

Eye exam

Your eyes are connected directly to the brain by the optic nerves. So primary CNS lymphoma doesn't travel far to spread from the brain to the eyes. (Very rarely it starts in the

eyes and spreads to the brain.) If lymphoma occurs in the eye, it often forms in the back of the eye, called the retina. The retina converts what you see into signals, which it sends through the optic nerves to the brain. Lymphoma cells can also invade the vitreous, the clear gel that fills the eye. When primary CNS lymphoma involves the eyes, it's called vitreoretinal lymphoma.

Everyone diagnosed with primary CNS lymphoma should have a thorough eye exam. This is done at an eye doctor's office using a slit lamp, a microscope with a bright light. You'll first be given drops in your eyes to widen (dilate) your pupils. This gives the eye doctor a better view inside your eyes. The eye doctor will use the lamp's bright light to examine the retina, optic nerve, and other parts of your eyes.

If the vitreous looks unusual or you have visual symptoms, you may need a biopsy of the vitreous. For this procedure (called

CNS lymphoma in the eye

Primary CNS lymphoma can occur in the brain, the spinal cord, and sometimes in the eyes. Everyone diagnosed with primary CNS lymphoma should have a thorough eye examination. Here, an ophthalmologist uses a special microscope called a slit lamp to take a close-up look at a patient's eye.



a vitrectomy), your eye is first numbed with anesthetic. Then a thin needle is inserted into the eye. The needle removes a tiny amount of vitreous, which is then tested for cancer cells. In some cases, a vitrectomy alone can confirm the diagnosis of primary CNS lymphoma without the need for brain biopsy.

Lumbar puncture

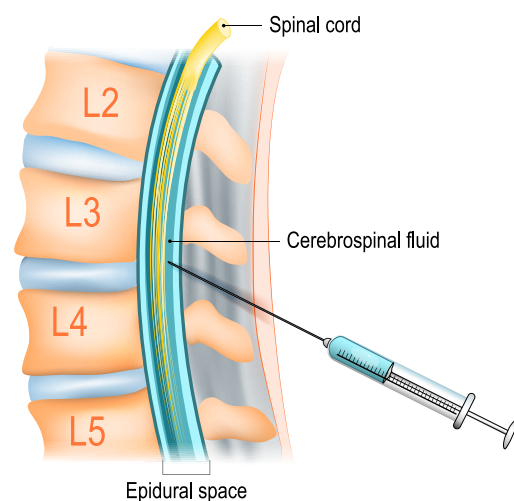
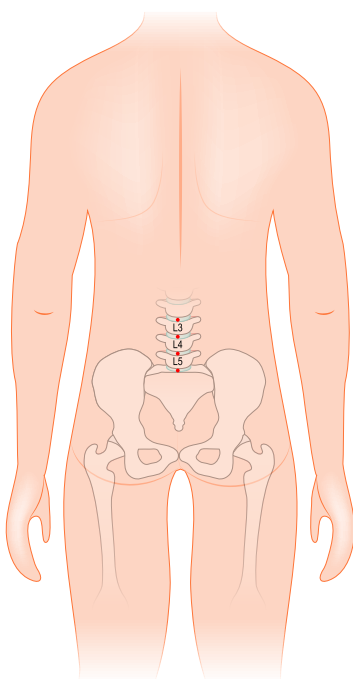
A lumbar puncture (also called a spinal tap) is a procedure that removes a small amount of cerebrospinal fluid (CSF) for testing. CSF is a liquid that flows in and around the hollow

areas in the brain and spinal cord. This fluid protects and nourishes the central nervous system. Testing the CSF can help confirm a diagnosis of primary CNS lymphoma. Testing also provides other helpful information needed for planning treatment.

A lumbar puncture is done only if it can be performed safely and it won't delay treatment. If cancer cells are found in the spinal fluid, or if you're having symptoms, another MRI may be needed to find out if there are any lesions in the spine.

Lumbar puncture

Cancer cells in the spinal fluid may or may not cause symptoms. A lumbar puncture is used to learn whether cancer has spread to the spinal cord. First, the lower back is numbed. Then a long, thin needle is inserted into the lower part of the spinal column to remove cerebrospinal fluid. The fluid is then sent to a lab for testing.



More imaging

It's uncommon for primary CNS lymphoma to spread outside of the central nervous system or the eyes. Still, it's important to have a look at the rest of your body just to be sure. The imaging methods most commonly used for this are positron emission tomography (PET) and/or computed tomography (CT).

PET imaging uses a small amount of a radioactive drug to find cancer cells in the body. After the radioactive drug is injected into a vein, it causes cancer cells to show up as bright spots on PET scans.

A CT scan takes many x-rays of the same body part from different angles. A computer combines all the x-ray pictures to make a single detailed image. A CT scan of the chest, abdomen, and pelvis is recommended to look for cancer that has spread to these areas. A contrast agent is injected into the bloodstream before the scan to make the areas of cancer easier to see.

Sometimes PET is combined with CT (a PET/CT scan). PET/CT imaging may be done with one or two machines depending on the cancer center. A PET/CT scan takes images of the whole body to find cancer.

Imaging after diagnosis may also include an ultrasound of the testicles. However, if the whole-body PET/CT scan didn't find anything, then this imaging test may not be needed.

Blood tests

Blood tests can also help establish the extent of the cancer and provide other information needed for planning your treatment. The following blood tests are recommended:

- **Complete blood count (CBC)** is a common blood test that measures the number of red blood cells, white blood cells, and platelets in a blood sample.
- **Comprehensive metabolic panel (CMP)** is a group of 14 different blood tests that provides information about your blood sugar, calcium, and electrolyte levels, and the health of your liver and kidneys.
- **Lactate dehydrogenase (LDH)** is an enzyme involved in converting food into energy for the body. An LDH test measures the level of this enzyme. A high level of LDH can be a sign of cell damage caused by cancer or other health problems.
- **Human immunodeficiency virus (HIV) blood test** is needed for everyone with primary CNS lymphoma. HIV that's related to primary CNS lymphoma requires specialized care and treatment with antiretroviral therapy in addition to cancer treatment.
- **Hepatitis B testing** will be necessary if you're having immunotherapy treatment and you've had this virus before (or you're at risk of getting it). Immunotherapy can "reawaken" the hepatitis B virus and cause illness that interferes with treatment.

Bone marrow biopsy

Most bones have a spongy center called marrow. The marrow is where new blood cells are made. It's uncommon to find cancer cells in the bone marrow of people diagnosed with primary CNS lymphoma. But if imaging suggests the possibility of lymphoma in the bones, your care team may recommend a bone marrow biopsy.

In this procedure, a hollow needle is inserted into the bone (usually at the back of the hip bone) and a sample of marrow is removed. The marrow sample is then sent to a lab for testing.

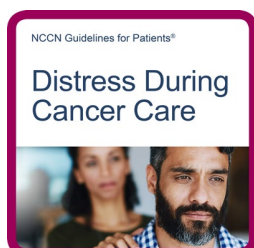
What's next?

After you've been diagnosed and have gone through further testing to find out the extent of your lymphoma, your treatment team will discuss your results with you. You'll also talk about your choices for treatment. The next chapter explains the different options for treating primary CNS lymphoma.

Don't dismiss your distress

Depression, anxiety, and distress are very common in people with cancer (and their caregivers, too). About 1 in 3 patients with primary brain tumors develop clinical depression and anxiety at some point. Up to 3 out of 4 people with primary brain tumors experience psychological distress. Tell your treatment team if you're feeling stressed or overwhelmed. Ask them for help. You don't have to cope with it by yourself.

Read more about cancer and distress in *NCCN Guidelines for Patients: Distress During Cancer Care*, available at [NCCN.org/patientguidelines](https://www.nccn.org/patientguidelines) and on the [NCCN Patient Guides for Cancer](#) app.



Key points

- A biopsy is the main test to diagnose primary CNS lymphoma.
- Imaging tests take pictures that show areas in the body that might have cancer as well as the extent of the disease.
- A biopsy is a procedure that removes a small piece of a tumor, which is tested for cancer cells.
- The standard biopsy method for diagnosing primary CNS lymphoma is a stereotactic biopsy.
- A stereotactic biopsy is a precise technique that's used when a brain tumor is in a hard-to-reach or vital area.
- After primary CNS lymphoma is diagnosed, more tests are needed to find out how far the cancer has grown and if it has spread to any other area of the body.
- Everyone diagnosed with primary CNS lymphoma should have a thorough eye examination to look for lymphoma in the eyes.
- A lumbar puncture is a procedure that removes a small amount of cerebrospinal fluid, which is tested for cancer cells.
- HIV that's related to primary CNS lymphoma requires specialized therapy in addition to cancer treatment. So everyone with primary CNS lymphoma needs to have an HIV blood test.

List all your drugs and supplements

Your treatment team will ask you to write a list of all the prescription drugs you take and how often you take them. Make copies of this list, which you can give to the many other providers or specialists you may see.

Also be sure to tell your treatment team if you're using any over-the-counter medicines (including antacids, aspirin, or NSAIDs like ibuprofen) or supplements, vitamins, or herbs. Some of these can interfere with your cancer treatment. For example, some supplements or herbs can raise or lower the levels of chemotherapy drugs in your body. This may cause more side effects or make your treatment less effective.

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Treatment options

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This chapter lists the different treatment options for primary CNS lymphoma. Ask your care team about the risks and benefits of each option. Together, you and your team can make a treatment plan.

There's no single drug or procedure that's best for treating primary central nervous system (CNS) lymphoma. The best treatment is the one that works best for you.

Treatment options include corticosteroids, chemotherapy, radiation therapy, targeted therapy, immunotherapy, and stem cell rescue. Receiving treatment in a clinical trial is also a recommended option.

Therapies are often combined to treat cancer. For example, chemotherapy may be given with an immunotherapy drug, or several chemotherapy drugs may be given together. Chemotherapy is also an essential part of having a stem cell rescue.

Surgery is not normally an option. Because primary CNS lymphoma usually develops deep within the brain tissue, removing it with surgery is risky and may be more harmful than helpful.

Treatment is usually given in phases (which are discussed in the next chapter).

Clinical trial

NCCN experts recommend that everyone with primary CNS lymphoma consider joining a clinical trial for treatment.

A clinical trial is a type of medical research study. Clinical trials are a key way to assess new treatment approaches. After being developed and tested in a laboratory, potential new ways of fighting cancer need to be studied in people. If found to be safe and effective in a clinical trial, a drug, device, or treatment approach may be approved by the U.S. Food and Drug Administration (FDA).

Talk to your treatment team about whether a clinical trial makes sense for you. Everyone with cancer should carefully consider all the treatment options available for their type of cancer, including standard treatments and clinical trials.

Who can enroll?

Every clinical trial has rules for joining, called eligibility criteria. The rules may be about age, cancer type and stage, treatment history, or general health. These requirements ensure that participants are alike in certain ways in order to compare how their disease responds to a specific treatment.

Informed consent

Clinical trials are managed by a group of experts called a research team. The research team will review the study with you in detail, including its purpose and the risks and benefits of joining. All of this information is also provided in an informed consent form. This is an agreement that confirms you've been fully

told about your part in the trial. Read the form carefully and ask questions before signing it. Take time to discuss it with family, friends, or other people you trust. Keep in mind that you can leave and seek treatment outside of the clinical trial at any time.

Start the conversation

Don't wait for your treatment team to bring up clinical trials. Start the conversation and learn about all your treatment options. Ask if a clinical trial is available for your situation. If you find a study that you may be eligible for, ask your treatment team if you meet the requirements. Try not to be discouraged if you cannot join. New clinical trials are always becoming available.

Frequently asked questions

There are many myths and misconceptions surrounding clinical trials. The possible benefits and risks are not well understood by many with cancer.

Will I get a placebo?

Placebos (inactive versions of real medicines) are almost never used alone in cancer clinical trials. It's common to receive either a placebo with a standard treatment or a new drug with a standard treatment. You'll be informed if a placebo is part of a clinical trial before you enroll.

Are clinical trials free?

There's no fee to enroll in a clinical trial. The study sponsor pays for research-related costs, including the study drug. You may, however, have costs indirectly related to the trial, such as the cost of transportation or childcare due to extra appointments and the costs of routine



Finding a clinical trial

In the United States

NCCN Cancer Centers
[NCCN.org/cancercenters](https://www.nccn.org/cancercenters)

The National Cancer Institute (NCI)
[cancer.gov/about-cancer/treatment/clinical-trials/search](https://www.cancer.gov/about-cancer/treatment/clinical-trials/search)

Worldwide

The U.S. National Library of Medicine (NLM)
clinicaltrials.gov

Need help finding a clinical trial?

NCI's Cancer Information Service (CIS)
1.800.4.CANCER (1.800.422.6237)
[cancer.gov/contact](https://www.cancer.gov/contact)

patient care during the trial. Depending on the trial, you may continue to receive standard cancer care. The standard therapy is billed to—and often covered by—insurance. You're responsible for copays and any costs for this care that aren't covered by your insurance.

NCCN experts recommend that everyone with primary CNS lymphoma should consider joining a clinical trial for treatment.

Steroids

Corticosteroids (often just called steroids) can shrink lymphomas and decrease swelling in the brain. This can rapidly reduce the signs and symptoms of the lymphoma. However, steroids lose their effectiveness and cause side effects when given long-term. So steroids are only given for a short period of time usually in newly diagnosed patients.

Importantly, steroid therapy shouldn't start until after you have a biopsy and get a diagnosis. This is because steroids can change the appearance of lymphoma cells, making it difficult for the pathologist to reliably diagnose the disease.

Side effects of steroids

Common side effects of steroids are feeling hungry, trouble sleeping, slow wound healing, upset stomach, mood changes, and swelling in the ankles, feet, and hands. Steroids may also significantly increase blood sugar levels. Most side effects of steroids go away after the drug is stopped.

Chemotherapy

Chemotherapy is a drug treatment that damages and destroys rapidly dividing cells throughout the body. Because cancer cells divide and multiply rapidly, they're a good target for chemotherapy. But chemotherapy harms healthy cells, too. The damage to healthy cells can cause side effects.

Treatment may include a single chemotherapy drug or a combination of drugs. A combination of drugs is sometimes chosen because the drugs work better when they're used together.

Most chemotherapy drugs for primary CNS lymphoma are given intravenously (IV). This means the medicine is slowly infused through a tube into a vein in your arm or another part of your body. The medicine travels in the bloodstream to reach cells throughout the body. Some chemotherapy drugs are taken by mouth as a tablet or capsule.

Chemotherapy is given in cycles. One cycle involves a few treatment days followed by several days of rest. Different chemotherapy drugs have different cycles. Common cycles are 14, 21, or 28 days long. Having chemotherapy in cycles gives your body a chance to recover after receiving the treatment.

Intrathecal chemotherapy

If cancer cells are found in the cerebrospinal fluid (CSF) or if an MRI of the spine shows cancer, chemotherapy may be infused directly into the CSF in some cases. This is known as intrathecal or intra-CSF chemotherapy. Intrathecal chemotherapy may be used in select cases or as part of specific treatment program for primary CNS lymphoma.

Intraocular chemotherapy

In rare cases, primary CNS lymphoma may occur in the eye. In these situations, the chemotherapy may be infused into a vein or directly into the eye. Possible side effects from intraocular chemotherapy include eye irritation, infection, inflammation, and cataracts. Cataracts can be treated with a routine operation by an eye surgeon.

Side effects of chemotherapy

Like other therapies, the side effects of chemotherapy depend on many factors. These include the drug, the dose, and the person. Chemotherapy, especially in high doses, may not be the right treatment for people who are frail or older. These individuals may have a difficult time dealing with the harsh side effects.

The main chemotherapy drug used to treat primary CNS lymphoma is high-dose methotrexate. Methotrexate is one of the most effective drugs for treating many kinds of cancers. But when given in high doses, methotrexate may cause damage to the kidneys, liver, and other organs. In severe cases, kidney failure is possible. To reduce this risk, you'll have to stay at the hospital during methotrexate treatment and receive fluids through a vein in your arm. You may also be given medicine to reduce the toxicity of methotrexate and to prevent severe problems in your kidneys and other organs.

Many cancer treatments, including chemotherapy, can lead to birth defects. So avoid becoming pregnant or getting someone pregnant while on chemotherapy treatment. Other side effects of chemotherapy include nausea, vomiting, diarrhea, mouth sores, loss of appetite, hair loss, low blood cell counts,

What about side effects?

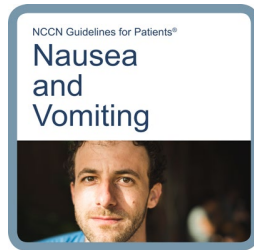
A side effect is an unhealthy or unpleasant physical or emotional condition caused by treatment. Every treatment for primary CNS lymphoma can cause side effects.

Side effects depend on many factors, such as the drug, the amount taken, the length of treatment, and the person. Each person has an individual response to a drug. Some people have many side effects. Others have few. Some side effects can be very serious. Others are not serious but are still unpleasant. Most side effects appear shortly after treatment starts and stop after treatment. Other side effects are long-term or may even appear years later.

Your treatment team will monitor your side effects during and after your treatment. Ask your team for a complete list of common and rare side effects of each treatment. If a side effect bothers you, let them know. There may be ways to prevent or avoid some side effects and help you feel better.

and feeling very tired or weak (fatigue). Additional side effects are also possible. Medicines are available during chemotherapy treatment to help control most of these side effects.

Read more about nausea and vomiting side effects in *NCCN Guidelines for Patients: Nausea and Vomiting*, available at [NCCN.org/patientguidelines](https://www.nccn.org/patientguidelines) and on the [NCCN Patient Guides for Cancer](#) app.



x-rays used for imaging, you won't see or feel anything during treatment. The total dose of radiation is usually divided into small doses given over several weeks. By giving a little every day, the radiation damages the tumor while better preserving the healthy tissue.

The most commonly used radiation technique for primary CNS lymphoma is treatment of the entire brain, called whole-brain radiation therapy (WBRT). Because primary CNS lymphoma can occur in multiple spots anywhere in the brain, WBRT is used to treat the entire brain all at once. WBRT can also reach the upper part of the spine and a part or all of the eyeballs. WBRT even treats microscopic tumors in the CNS that aren't visible on an MRI scan.

You'll need to remain as motionless as possible during each scan. You may be fitted with a mask or supports to help you keep still.

Side effects of radiation therapy

Your radiation oncologist will discuss the possible side effects of WBRT. Side effects

Radiation therapy

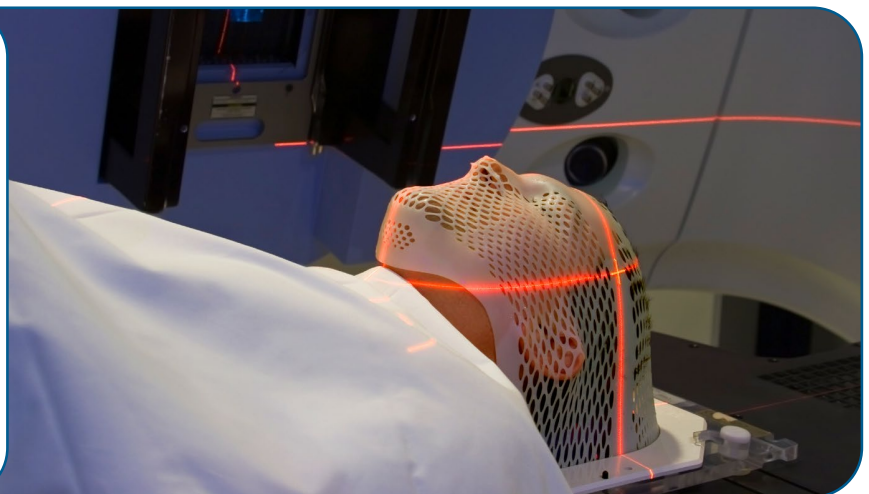
Before effective chemotherapy became available to treat primary CNS lymphoma, radiation therapy was the most commonly used treatment. It's still an option for treating primary CNS lymphoma in people who can't have chemotherapy in the first phase of treatment (induction).

Another situation in which radiation is sometimes used is in the second phase of treatment (consolidation) to kill cancer cells left over after induction treatment.

Radiation therapy uses high-energy x-rays or other radiation to kill cancer cells. Like

Radiation therapy

Radiation therapy sends beams of intense energy to kill cancer cells. You'll need to remain as motionless as possible during each scan. You may be fitted with a mask or supports to help you lie still.



differ among people. Common side effects include headaches, nausea, vomiting, and loss of appetite. Fatigue may begin after the treatment has finished and last for several weeks. Most of these symptoms can be controlled by medications during treatment.

Radiation therapy may be more likely to damage the nervous system than chemotherapy, especially in older adults. Months or years after WBRT, patients may develop memory problems, slowed thinking, and trouble speaking. Fine motor skills, such as handwriting or tying shoes, may also be affected.

Talk to your treatment team about the benefits of radiation therapy compared with the risk of nervous system damage, including long-term problems with cognition.

Radiation therapy for the eyes

Radiation therapy is also used to treat primary CNS lymphoma in the eyes. WBRT can be expanded to include the eyes. Or the radiation can be focused only on the eyes but at a lower dose. With either method, usually both eyes are treated at the same time. Possible side effects include vision problems that may be temporary or permanent. Radiation therapy may cause cataracts, for instance, which can be treated with a routine operation by an eye surgeon.

Targeted therapy

Targeted therapy is another treatment for primary CNS lymphoma that can be combined with chemotherapy. Targeted therapy drugs attack specific parts of cancer cells to kill these cells or to slow their growth and spread.

Side effects of targeted therapy

Because targeted therapy aims at cancer cells while mostly avoiding healthy cells, it may have fewer side effects than chemotherapy. Some common side effects include allergic reactions, fever, chills, muscle aches, fatigue, weakness, infections, nausea, and diarrhea. These medications may also reduce the number of blood-clotting cells (platelets) in the body, increasing the risk of bruising and bleeding. Medicines are available during treatment to help reduce most of these side effects.

Immunotherapy

Immunotherapy uses your body's immune system—your natural defense against infection and disease—to fight cancer. Immunotherapy treats cancer cells throughout the body.

The main immunotherapy drug used for primary CNS lymphoma is rituximab (Rituxan). Rituximab is a type of immunotherapy called a monoclonal antibody. Monoclonal antibodies hunt for specific proteins on the surface of cancer cells. Cancerous blood cells (and some healthy blood cells) have a protein on their surface called CD20. Rituximab finds and attaches itself to CD20 proteins. This helps your immune system locate and then destroy the cancer cells. Rituximab is given through an IV infusion.

Side effects of immunotherapy

Rituximab and other immunotherapies may cause drowsiness, fatigue, constipation, joint pain, loss of appetite, low blood cell counts, serious blood clots, and rashes.

Keep track of your symptoms and side effects

Think about ways to keep track of your symptoms and side effects when they happen. You can make notes in a weekly diary, on a calendar, or in a smartphone app. Or create your own way to record the symptoms or side effects you experience. Some things to track include:

- Each treatment and any side effects it caused
- How long the side effect lasted
- How the side effect affected your quality of life
- If you're given a treatment for a side effect, note how well the treatment worked

Show this information to your treatment team at each visit. Tracking your side effects gives your care team a better sense of how you're doing. This can help your providers know how to manage your symptoms better.

Stem cell rescue

A stem cell is a basic cell that can develop into any kind of cell. Stem cells that become blood cells are called hematopoietic stem cells. Hematopoietic means “blood-forming.” Blood-forming stem cells are made in the bone marrow. But cancer and its treatment can damage and destroy cells in the bone marrow. When hematopoietic stem cells are damaged, they may not supply all the blood cells that the body needs.

A stem cell rescue is a way to jumpstart the bone marrow to make more healthy blood cells. Also called a hematopoietic stem cell transplant, stem cell rescue uses your own blood-forming stem cells to regrow your bone marrow.

A stem cell rescue has 3 key steps:

- **Stem cell removal** – First, some of your healthy stem cells will be removed from your blood or bone marrow. You may need a few visits to collect enough stem cells. These collected stem cells are then frozen and stored for later.
- **High-dose chemotherapy** – Next, you'll receive intensive chemotherapy to kill any lymphoma cells in your body. The chemotherapy also kills all the stem cells in your bone marrow. Because your blood count will be low, your body will be very vulnerable to infections at this time and you will feel very fatigued.
- **Stem cell replacement** – After chemotherapy, your healthy stem cells will be thawed and returned back into your body to “rescue” your damaged bone marrow. Your transplanted stem cells will

3 Treatment options » Stem cell rescue

migrate to the bone marrow and start to grow new blood stem cells. This will also begin to restore your body's ability to protect itself from infection.

You'll grow back blood cells and bone marrow in a few weeks, but it may take a year for your body to fully recover. During this time, you'll have frequent blood tests and health checkups until your bone marrow is restored and your blood cell counts return to normal.

Stem cell rescue can be an intense procedure. It's not for everyone with primary CNS lymphoma. And it's only used after you've had other treatments or if the lymphoma comes back after earlier treatment (relapse).

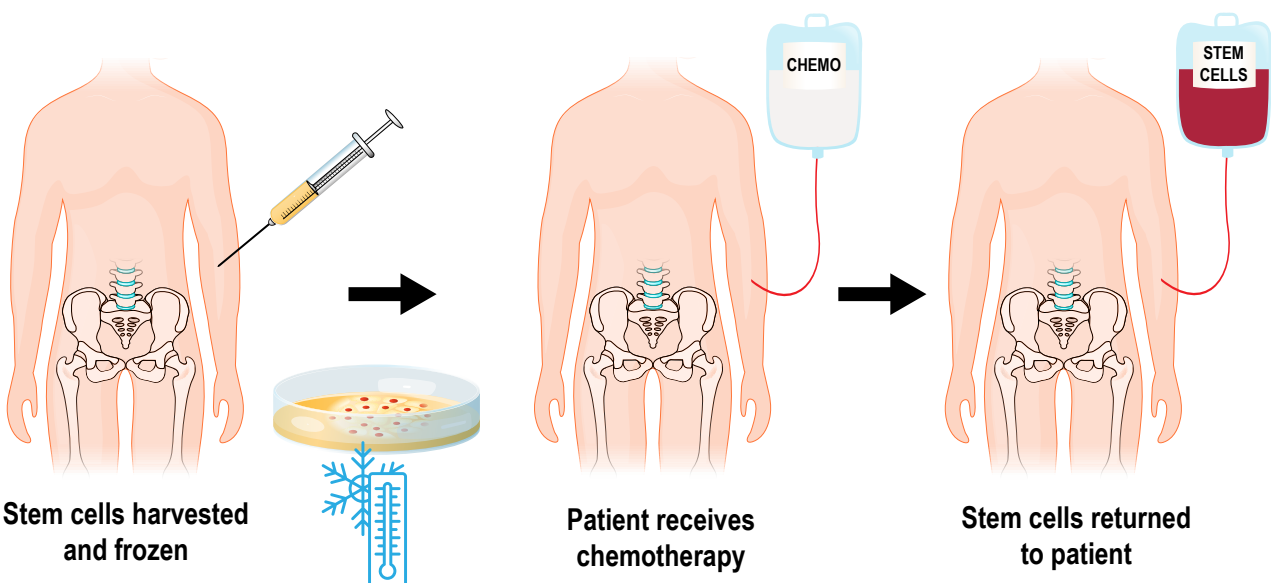
Your treatment team will consider many factors to decide if a stem cell rescue is right for you. Some of these factors include your fitness level, health status, organ function, cancer stage, previous treatments, other medical conditions, available supportive care, and

High-dose chemotherapy and stem cell rescue

First, stem cells are removed (harvested) from the patient's blood or bone marrow. The harvested stem cells are concentrated and frozen for preservation.

Next, the patient receives high-dose chemotherapy to destroy any cancer cells in your body. This also kills all the stem cells in the bone marrow.

Lastly, the harvested stem cells are returned (transfused) to the patient, where they'll grow new, healthy blood-forming stem cells in the bone marrow.



additional factors—including your goals and preferences. Because the procedure can be risky and the side effects harsh, it may not be a useful option for people who are older or frail. Ask your team about the benefits and risks of having a stem cell rescue.

Side effects of stem cell rescue

Most side effects of stem cell rescue come from the chemotherapy. High-dose chemotherapy can result in nausea, vomiting, diarrhea, hair loss, mouth sores, and other side effects. Medicines are available during chemotherapy to help reduce most of these side effects.

You'll also likely feel tired and weak after the procedure and while waiting for the new blood stem cells to grow in the bone marrow. This should get better over time as you recover.

Supportive care

Supportive care (also called palliative care) is for relieving the symptoms of cancer and the side effects of cancer therapies, and other health issues related to the cancer.

Supportive care is given at any stage of disease, not just at the end of life. It isn't meant to treat the cancer, but rather to relieve symptoms and make you more comfortable.

While one goal of treatment is to control cancer, that should be balanced with the other goal of treatment: maintaining quality of life. For older patients who have other diseases or conditions and aren't able to fully perform ordinary daily activities, supportive care by itself may be a reasonable option.

What's next?

Now that you've been introduced to the various treatment options for primary CNS lymphoma, the first step toward treatment is to come up with the best possible treatment plan. This plan involves a number of different health care providers.

Multidisciplinary care

During the course of your diagnosis and treatment, you'll be cared for by numerous doctors, specialists, and allied health providers.

These may include a neuro-oncologist, neurosurgeon, radiation oncologist, medical oncologist, pathologist, ophthalmologist, nurses, primary care doctor, nurse practitioners, physician assistants, palliative care specialist, pain specialist, psychologist, social workers, nutritionist, and rehabilitation specialists like physical, occupational, and speech therapists.

When all these providers are working and communicating as a team to help you, it's called multidisciplinary care.

It's helpful to understand the role that each team member plays. Keep a list of names and contact information for each member of your team. This will make it easier for you and anyone involved in your care to know who to contact with questions or concerns.

Ask who will coordinate your care and what efforts can be made to schedule appointments together.

3 Treatment options » What's next?

Your multidisciplinary care team should clearly discuss your care goals with you. Removing or reducing the size of your lymphoma is one goal of your team. But you and your team's other goals may include improving your overall well-being, maintaining your ability to do day-to-day activities, reducing pain, getting good nutrition, and lowering stress and anxiety. Your multidisciplinary team will meet to discuss your treatment and which options are best for you.

The next chapter explains the phases of treatment and what your individual treatment plan may be.

Quality of life

Quality of life refers to a person's overall enjoyment of life, including their sense of well-being and ability to participate in their usual activities. Your quality of life should be the main priority that guides your treatment and care. Successful treatment isn't just about reducing the cancer. Other goals include minimizing cognitive problems, reducing pain, lowering anxiety and stress, carrying out regular activities, being with friends and family, and enjoying life as best as you can.

Your multidisciplinary team

When all of your doctors, specialists, and allied health providers are working and communicating as a team to help you, it's called multidisciplinary care. Be clear about your treatment goals when you talk with your multidisciplinary team.



Key points

- A recommended treatment option for primary CNS lymphoma is participating in a clinical trial.
- Other treatment options include corticosteroids, chemotherapy, radiation therapy, targeted therapy, immunotherapy, and stem cell rescue. Often, some of these therapies are combined to treat primary CNS lymphoma.
- Chemotherapy is a drug treatment that damages and destroys rapidly dividing cells throughout the body. The main chemotherapy drug used to treat primary CNS lymphoma is methotrexate.
- Whole-brain radiation therapy (WBRT) is the most commonly used radiation technique for primary CNS lymphoma.
- Targeted therapy drugs attack specific parts of cancer cells to slow their growth and spread.
- Immunotherapy uses your body's immune system to fight cancer. The main immunotherapy drug for primary CNS lymphoma is rituximab.
- High-dose chemotherapy and stem cell rescue uses your own blood-forming stem cells to jumpstart the bone marrow to make more healthy blood cells.
- Supportive care is for relieving the symptoms of cancer and the side effects of cancer treatment.
- Supportive care is given at any stage of cancer, not just at the end of life.



Ask about clinical trials available to you and the services your hospital and other facilities provide to cancer patients, such as counseling, nutritional advice, meditation, physical therapy, palliative care, and integrative medicine. Don't be shy. Be your own advocate—or ask someone close to be one for you.”

- Multidisciplinary care means that a number of doctors, specialists, and allied health providers are working and communicating as a team to help you.
- Quality of life refers to a person's overall enjoyment of life, including their sense of well-being and ability to participate in their usual activities.

4

Phases of treatment

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- 36 Consolidation
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- 39 Key points

Treatment should start soon after being diagnosed with primary CNS lymphoma. This chapter describes what to expect from the treatment process and explains the options for each phase of treatment.

Although there are different treatment options for primary central nervous system (CNS) lymphoma, the treatment approach is often a two-step process.

The first step is the **induction phase**, which aims to wipe out all lymphoma cells or as many as possible. The goal of the second step, the **consolidation phase**, is to destroy any cancer cells that may remain in the body after the first phase. Consolidation is also for preventing the lymphoma from returning.

Induction

The first (induction) phase of treatment can last several months. Treatment typically requires multiple courses of chemotherapy, which are given while in the hospital. The options for induction treatment are listed in **Guide 1** and discussed here:

Clinical trial

Clinical trials allow you to receive treatment while also helping researchers learn more about this uncommon cancer. Everyone with primary CNS lymphoma is encouraged to consider enrolling in a clinical trial. The treatment you receive in the trial may or may

not work better than the standard treatments for primary CNS lymphoma. Ask your care team if there is a clinical trial you may be eligible for.

If you don't want to join a clinical trial or none are available for you, the recommended induction treatment is high-dose methotrexate chemotherapy, often given with other chemotherapies.

High-dose chemotherapy

The most effective chemotherapy drug for primary CNS lymphoma is methotrexate. Methotrexate has been used for many years to treat a variety of cancers. It works by blocking the body's use of folate, a form of vitamin B. Lymphoma cells can't multiply and spread as quickly without folate.

High doses of methotrexate are needed to overcome the blood-brain barrier and still have enough strength to kill lymphoma cells. The blood-brain barrier is a protective layer around the brain that prevents germs, infections, and other toxins from getting in. But it also blocks some chemotherapy drugs like methotrexate from reaching the brain.

For induction therapy, high-dose methotrexate is given together with the immunotherapy drug rituximab (Rituxan). Rituximab can be given on its own but it usually works better when given with chemotherapy.

In addition to methotrexate and rituximab, one or more other chemotherapy medicines such as temozolomide, vincristine, and procarbazine may also be included.

Alternatives to methotrexate

High-dose methotrexate (with or without additional medicines) is the preferred induction therapy for primary CNS lymphoma. But it's not the best option for everyone. Your treatment team may recommend a different induction therapy if:

- Your kidneys aren't working well
- High-dose chemotherapy is too intense or risky for you
- Cancer was found in your spine or spinal fluid

If you can't have high-dose methotrexate, other options for induction therapy include:

- Ibrutinib (Imbruvica) or similar medication
- Temozolomide (Temodar)
- Rituximab with or without temozolomide
- Lenalidomide with or without rituximab
- High-dose cytarabine
- Pemetrexed
- Pomalidomide

Guide 1 Options for induction treatment

Treatment options	Drugs included in treatment
Preferred options	
Treatment in a clinical trial	Depends on the individual trial
High-dose chemotherapy + immunotherapy	Methotrexate with or without temozolomide + rituximab
	Methotrexate, vincristine, and procarbazine + rituximab
Other option	
High-dose combination chemotherapy + immunotherapy	Methotrexate, cytarabine, and thiotepa + rituximab

Whole-brain radiation therapy

If you're unable to have chemotherapy or another anticancer medicine, whole-brain radiation therapy (WBRT) may be an option for induction treatment.

Supportive care

Supportive care is available for everyone with cancer. It isn't meant to treat the cancer, but rather to relieve symptoms and make you more comfortable. Speak to your care team about how you're feeling and if you're having any symptoms or side effects.

Consolidation

Consolidation is the second phase of treatment. The purpose of consolidation is to kill any cancer cells that may be left behind after induction and to prevent them from coming back. Not everyone with primary CNS lymphoma will need consolidation treatment.

Before starting consolidation, you'll have a few tests such as imaging and blood tests to find out how well your induction treatment worked. The results of your induction treatment will guide your options for consolidation treatment.

Induction result: Complete response

If there are no signs of cancer after induction therapy, you've had a complete response. The next best outcome is an "unconfirmed" complete response, which means that there are minimal signs of cancer left in the body. If you have a complete response or unconfirmed complete response to induction, you may

have several options for consolidation. These options are listed in **Guide 2** and described here:

High-dose chemotherapy with stem cell rescue

In people who are healthy and strong enough, high-dose chemotherapy and stem cell rescue is a consolidation option. The preferred chemotherapy combinations are:

- Cytarabine and thiotepa followed by carmustine and thiotepa
- Thiotepa, busulfan, and cyclophosphamide

However, if you have a higher risk of infection or your body can't handle a stem cell transplant for other reasons, high-dose chemotherapy with stem cell rescue may not be a good option for you.

High-dose chemotherapy

Chemotherapy without stem cell rescue may be a better fit for someone who isn't suited to receive a stem cell transplant. For this consolidation option, the recommended treatment is high-dose cytarabine with or without etoposide.

Maintenance therapy

Continuing induction therapy with high-dose methotrexate and rituximab is also an option. Other options are rituximab alone or temozolomide alone. When these treatments are used for consolidation, they're typically given once a month for up to 1 year. This is called maintenance therapy.

Guide 2**Options for consolidation treatment**

Treatment options	Drugs included in treatment
Complete response to induction therapy	
High-dose chemotherapy and stem cell rescue	<ul style="list-style-type: none"> • Cytarabine and thiotepa followed by carmustine and thiotepa and stem cell rescue • Thiotepa, busulfan, and cyclophosphamide and stem cell rescue
High-dose chemotherapy	<ul style="list-style-type: none"> • High-dose cytarabine and etoposide • High-dose cytarabine
Maintenance therapy	<ul style="list-style-type: none"> • High-dose methotrexate and rituximab • High-dose methotrexate • Rituximab • Temozolomide
Low-dose whole-brain radiation therapy	<ul style="list-style-type: none"> • Radiation therapy
Incomplete response to induction therapy	
High-dose chemotherapy that does not include methotrexate	<ul style="list-style-type: none"> • High-dose cytarabine and etoposide • High-dose cytarabine
Whole-brain radiation therapy	<ul style="list-style-type: none"> • Radiation therapy
Supportive care	<ul style="list-style-type: none"> • Treatment for symptom relief • Treatment for side effects of lymphoma therapy

Radiation therapy

If more chemotherapy seems too harsh or isn't recommended for other reasons, low-dose WBRT may be an option. Lower doses of radiation cause fewer side effects. So a lower dose is typically used when WBRT is given for consolidation.

Induction result: Incomplete response

If results show that cancer cells remain after methotrexate-based induction therapy, you've had an incomplete response. The next step is to consider a different treatment to kill leftover cancer cells, prevent neurologic damage, and maintain quality of life. These options are listed in **Guide 2** and discussed here:

High-dose chemotherapy

You could have a different chemotherapy medicine than methotrexate for your consolidation treatment. The recommended chemotherapy is high-dose cytarabine with or without etoposide.

Radiation therapy

If you want to avoid more chemotherapy or if chemotherapy is no longer a good option for you, whole-brain radiation therapy is recommended. Although radiation therapy has risks, it can relieve symptoms and may control the cancer for a while.

Supportive care

If your body isn't able to handle either chemotherapy or WBRT, supportive care is always an option. Supportive care can help with cancer-related pain and discomfort as well as medication-related side effects.

Treatment for the spine

If testing finds cancer cells in the spine or spinal fluid, and if treatment with high-dose methotrexate is thought to be too harsh for you, your care team may recommend intrathecal chemotherapy and possibly radiation therapy to the spine.

What is the blood-brain barrier?

Your brain is a very important organ. It needs special protection to keep it safe and healthy. To block germs, infections, and other toxins from getting in, the brain has a unique security system. This protective layer is called the blood-brain barrier. It's like a moat that surrounds and protects a castle.

The blood-brain barrier does its job well—maybe too well. One problem with the barrier is that it won't permit most drugs in the blood to reach the brain. This includes many chemotherapy drugs. However, scientists have learned that some chemotherapy drugs can cross the blood-brain barrier more easily than others.

In intrathecal chemotherapy, an anticancer medicine is injected directly into the spinal fluid. Intrathecal chemotherapy options for primary CNS lymphoma include methotrexate, cytarabine, and rituximab.

Treatment for the eyes

If tests find cancer cells in the eyes after induction therapy, further treatment is needed. Recommended options are intraocular (eye) chemotherapy or radiation therapy.

Intraocular chemotherapy involves injecting anticancer medicine, such as methotrexate or rituximab, directly into the eyes. For this procedure, you may need to go to an ophthalmologist who specializes in this type of treatment. If intraocular chemotherapy isn't fully effective or if you can't have intraocular chemotherapy, radiation therapy focused only on the eyes may be another option.

What's next?

After induction and consolidation treatments, your primary CNS lymphoma may be undetectable for months or perhaps years. During this time, you'll need regular imaging tests and checkups to see if the cancer shows signs of coming back. When cancer comes back after a period of remission, it's called a relapse.

Lymphoma that remains (or gets worse) even after induction and consolidation treatments is called refractory.

Read about relapsing and refractory lymphoma in the next chapter.

Key points

- Treatment for primary CNS lymphoma is often a two-step process that includes an induction phase and a consolidation phase.
- The induction phase aims to wipe out as many lymphoma cells as possible. The recommended induction treatment (other than a clinical trial) is high-dose chemotherapy plus immunotherapy.
- The blood-brain barrier blocks toxins like germs and infections from reaching the brain. But it also prevents some chemotherapy and anticancer drugs from reaching the brain.
- The consolidation phase kills any cancer cells left behind after the induction phase. Consolidation also helps prevent the cancer from returning.
- High-dose chemotherapy and stem cell rescue may be a consolidation option for people who are healthy and strong enough to undergo this intense treatment.
- High-dose chemotherapy alone may be a consolidation treatment for those who are unable to have a stem cell transplant.
- If cancer remains after methotrexate-based induction therapy, consolidation therapy may be high-dose chemotherapy (with a medicine other than methotrexate) or radiation therapy. Supportive care is also an option.

5

Follow-up care and further treatment

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After you've finished treatment, it's important to go to follow-up visits to check that the cancer hasn't returned. If the lymphoma does return, you have several options for further treatment.

Follow-up care

After treatment ends, the follow-up phase of care begins. It's important to go to follow-up visits and stay in touch with your treatment team. Follow-up care is for:

- Making sure the lymphoma is in remission
- Watching for signs that the lymphoma may be coming back
- Checking for any unexpected problems related to the lymphoma or treatment

A key test during follow-up of primary CNS lymphoma is brain imaging with MRI. Brain imaging monitors for the return of the lymphoma. NCCN experts recommend follow-up MRIs of the brain:

- Every 3 months for the first 2 years
- Every 6 months for the following 3 years
- Once a year after 5 years

You may need to have brain MRIs more or less often than this. Your treatment team will explain how often you should expect to have them.

If cancer cells were found in your spine or cerebrospinal fluid (CSF), your follow-up care may also include imaging your spine or testing your spinal fluid.

If you received treatment to your eyes for ocular lymphoma, you'll have eye exams with an ophthalmologist as part of your follow-up care.

If cancer remains or returns

Cancer that doesn't improve with treatment is called refractory. Refractory is another word for resistant—the lymphoma has become resistant to treatment.

The return of cancer after a cancer-free period is known as a relapse.

There is no single best way to treat refractory or relapsed primary CNS lymphoma. The best treatment is the one that's best for you. You'll need to consider your quality of life and how treatment and its side effects may impact it. For some, especially those at higher risk of complications, the best option may be no therapeutic treatment at all.

Of course, two options available to those with relapsed or refractory primary CNS lymphoma are:

- **Clinical trial** – Seeking treatment in a clinical trial is strongly encouraged. The treatment you receive may or may not work better than standard cancer care. Ask your care team about current clinical trials you may be eligible for.

- **Supportive care** – Supportive care is for cancer-related pain or discomfort as well as medication-related side effects. The goal of supportive care is not to treat the cancer, but to help with the emotional, physical, and practical demands of living with cancer.

Other treatment options depend in part on your previous treatment or treatments:

You had whole-brain radiation

If cancer resists or returns after initial whole-brain radiation therapy (WBRT), radiation should not be used again because of the risk of damage to the nervous system. Your treatment team may recommend chemotherapy instead. Alternative chemotherapies or anticancer medicines such as rituximab, ibrutinib, or others may be added or substituted for methotrexate. High-dose chemotherapy with stem cell rescue may also be an option in certain cases.

The only type of radiation therapy that may be given after initial WBRT is focal radiation. This is radiation that focuses only on cancerous areas of the brain, not the whole brain. Focal radiation is given mainly to relieve symptoms, not to treat the cancer.

If lymphoma is found in your spine or CSF, you can have chemotherapy injected directly into the spinal fluid.

You had high-dose chemotherapy

If you had high-dose methotrexate-based chemotherapy that resulted in a long remission (more than 1 year), your care team may recommend that you have it again. It's common to have the same type of chemotherapy you had the first time around. High-dose methotrexate can be given by itself or with other chemotherapies. Treatment that doesn't include high-dose methotrexate is also an option.

If high-dose methotrexate-based chemotherapy didn't work or didn't result in a lasting cancer-free period, there's more than one option. Your team may recommend chemotherapies or other anticancer treatment that doesn't include methotrexate. Another option is radiation therapy with or without other chemotherapy or anticancer treatment.

High-dose chemotherapy with stem cell rescue may also be an option for people who can tolerate it.

You had high-dose chemotherapy with stem cell rescue

If high-dose chemotherapy with stem cell rescue led to a complete remission that lasted 1 year or more, your treatment team may suggest you have it again. If that's too much or not possible for you, then another option is chemotherapy or other anticancer therapy that doesn't include methotrexate or stem cell rescue.

If you didn't have a lasting response to high-dose chemotherapy with stem cell rescue, radiation therapy may be an option. WBRT or radiation that's focused only on the lymphoma may be used.

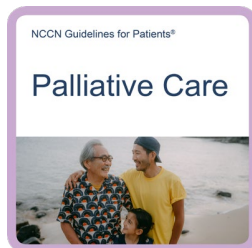
What's next?

You may have several types of treatment for relapsed or refractory primary CNS lymphoma. After any treatment, it's important to go to follow-up visits.

You may eventually reach a point where you want to stop treatment. For some people, how they spend their time is more important than how much time they have left.

Supportive care (also called palliative care) is appropriate for anyone, regardless of age, cancer stage, or the need for other therapies. Although end-of-life care is a part of supportive care, supportive care is much more than that. Supportive care is an important part of high-quality, comprehensive cancer care. Its goal is to control symptoms, relieve emotional and physical suffering that comes from the diagnosis and treatment of cancer, and improve the quality of life for those with cancer and their loved ones and/or caregivers.

For more information, see *NCCN Guidelines for Patients: Palliative Care*, available at [NCCN.org/patientguidelines](https://www.nccn.org/patientguidelines) and on the [NCCN Patient Guides for Cancer](https://www.nccn.org/patientguidelines) app.



Let us know what you think!

Please take a moment to complete an online survey about the NCCN Guidelines for Patients.

[NCCN.org/patients/response](https://www.nccn.org/patients/response)

Key points

- Follow-up visits are for making sure the lymphoma is in remission. Follow-up also looks for signs of its return and checks for any unexpected problems.
 - MRI of the brain is used to monitor for the return of primary CNS lymphoma. Other follow-up testing is needed if cancer cells are found in the spinal fluid or eyes.
 - Cancer that doesn't improve with treatment is called refractory. Cancer that returns after a cancer-free period is known as a relapse.
 - Enrolling in a clinical trial is strongly encouraged for everyone with relapsed or refractory primary CNS lymphoma.
 - Supportive care is available to everyone with relapsed or refractory primary CNS lymphoma. Other treatment options depend in part on what treatment you've had before.
 - If your initial treatment was WBRT, the usual therapy for relapsed or refractory disease is methotrexate-based chemotherapy. Another chemotherapy or anticancer medicine may also be an option. High-dose chemotherapy with stem cell rescue is another possible treatment.
 - If your initial treatment was high-dose methotrexate-based chemotherapy and you had a remission that lasted more than 1 year, the therapy for relapsed or refractory disease may be more methotrexate chemotherapy. This may be given by itself or with other medicines.
- Your comfort and quality of life shouldn't come second to excessive tests and procedures that won't affect your outcome.**
- If initial treatment with high-dose methotrexate-based chemotherapy didn't work or didn't result in a lasting remission, the treatment for relapsed or refractory disease may be therapy that doesn't include methotrexate.
 - Supportive care is appropriate for any person with cancer, regardless of age, cancer stage, or the need for other therapies. Supportive care is more than end-of-life care.

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Making treatment decisions

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It's important to be comfortable with the cancer treatment you choose. This choice starts with having an open and honest conversation with your care team.

It's your choice

Treatment decisions are very personal. What's important to you may not be important to someone else.

In shared decision-making, you and your care team share information, discuss the options, and agree on a treatment plan. It starts with an open and honest conversation between you and your team.

Some things that may play a role in your decision-making:

- What you want and how that might differ from what others want
- Your feelings about certain treatments like radiation or chemotherapy
- Your feelings about pain or side effects
- Cost of treatment, travel to treatment centers, and time away from school or work
- Quality of life and length of life
- Your religious and spiritual beliefs
- How active you are and the activities that are important to you

Think about what you want from treatment. Discuss openly the risks and benefits of specific treatments and procedures. Weigh options and share concerns with your care team. If you can build a relationship with your team, you'll feel supported when considering your options and making treatment decisions.

Second opinion

It's normal to want to start treatment as soon as possible. While cancer treatment shouldn't be put off for too long, there is usually time to have another cancer care provider review your test results and suggest a treatment plan. This is called getting a second opinion, and it's a normal part of cancer care. Even doctors get second opinions!

Seek out a specialist who focuses on cancer in the brain, if you can, because they have more experience with diagnosing and treating people with central nervous system cancers.

Things you can do to prepare for a second opinion:

- Check with your insurance company about its rules on second opinions. There may be out-of-pocket costs to see doctors who are not part of your insurance plan.
- Make plans to have copies of all your records sent to the doctor you will see for your second opinion.

Support groups

Many people diagnosed with cancer and their caregivers find support groups to be helpful. Support groups often include people at different stages of treatment. Some people may be newly diagnosed, while others may be finished with treatment. If your hospital or community doesn't have support groups for people with cancer, check out the online resources listed in the back of this book.

Financial concerns

The financial cost of cancer can be overwhelming. As a result, many people with cancer and their loved ones struggle with the cost of treatment, as well as the stress of paying for it.

If you struggle to pay for food, housing, treatment, follow-up care, and other expenses, or you have difficulty getting to appointments, talk with your care team's social worker, patient navigator, and hospital financial services staff. They can help you find financial support and transportation options.

Questions to ask

Possible questions to ask your care team are listed on the following pages. Feel free to use these or come up with your own. Be clear about your goals for treatment and find out what to expect from treatment. Have a notebook handy to jot down the answers to your questions.



Report any unusual feelings of sadness, loss of interest in activities, anxiety, and sleep problems to your doctor. Many people experience these feelings, and they should not go untreated.”

Resources

Be the Match

bethematch.org/one-on-one

Blood & Marrow Transplant Information Network (BMT InfoNet)

bmtinfonet.org

Cancer Hope Network

cancerhopenetwork.org

Lymphoma Research Foundation

lymphoma.org

National Bone Marrow Transplant Link (nbmtLINK)

nbmtlink.org

National Coalition for Cancer Survivorship

canceradvocacy.org

The Leukemia & Lymphoma Society

LLS.org/PatientSupport

Triage Cancer

triagecancer.org



We want your feedback!

Our goal is to provide helpful and easy-to-understand information on cancer.

Take our survey to let us know what we got right and what we could do better.

NCCN.org/patients/feedback



Words to know

autoimmune disease

An illness in which the immune system overreacts and attacks healthy tissues and organs.

biopsy

A procedure that removes samples of tissue or fluid to be tested for disease.

blood-brain barrier

A cell network that blocks harmful substances but allows nutrients from the blood to enter the central nervous system.

bone marrow biopsy

A procedure that removes samples of bone and marrow to test for disease.

central nervous system (CNS)

The brain and spinal cord.

cerebrospinal fluid (CSF)

A liquid that flows in and around the hollow spaces of the brain and spinal cord. Also called spinal fluid.

chemotherapy

A drug treatment that damages and destroys rapidly dividing cells throughout the body.

clinical trial

A type of research that assesses investigational tests or treatments in people.

computed tomography (CT)

An imaging test that uses x-rays from many angles to make a picture of the inside of the body.

consolidation therapy

Treatment given after initial therapy to kill any leftover cancer cells in the body.

contrast

A substance put into the body to make clearer pictures during imaging tests.

follow-up care

Health care that involves regular check-ups, which begin after treatment has ended.

immune system

The body's natural defense against infection and disease.

immunodeficiency disorder

An illness that weakens the immune system's ability to fight infections and diseases.

immunotherapy

A drug treatment that helps the body's immune system find and destroy cancer cells.

induction therapy

The first phase of treatment, which aims to wipe out all cancer cells or as many as possible.

lumbar puncture

A procedure that removes a small amount of cerebrospinal fluid for testing. Also called a spinal tap.

lymphoma

Cancer that begins in white blood cells (lymphocytes) that are part of the immune system.

magnetic resonance imaging (MRI)

An imaging test that uses radio waves and powerful magnets to view the inside of the body.

performance status

A rating of a person's overall health and ability to do ordinary activities.

Words to know

positron emission tomography (PET)

An imaging test that uses radioactive material to see the shape and function of organs and tissues inside the body.

radiation therapy

A treatment that uses high-energy rays (radiation) to kill cancer cells.

refractory cancer

A cancer that does not improve with treatment.

relapse

The return of cancer after a period of improvement.

remission

The absence of cancer signs and symptoms after treatment.

slit-lamp eye exam

An exam that uses a microscope and a strong beam of light to inspect the inside of the eye.

stem cell rescue

A cancer treatment that uses high-dose chemotherapy to destroy cells in the bone marrow, which are replaced with healthy blood stem cells. Also called a hematopoietic stem cell transplant.

stereotactic biopsy

A procedure that removes a tissue sample using a thin, hollow needle guided by a computerized navigation system.

supportive care

Health care for the symptoms of cancer or for the side effects of cancer treatment. Also called palliative care.

targeted therapy

A drug treatment that identifies and attacks a specific feature of cancer cells with less harm to normal cells.

tumor

A mass of abnormal cells.

ultrasound

A test that uses sound waves to take pictures of the inside of the body.

whole-brain radiation therapy (WBRT)

Cancer treatment that sends small amounts of radiation to the whole brain, including tumors and healthy tissue.

NCCN Contributors

This patient guide is based on the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Central Nervous System Cancers Version 1.2023. It was adapted, reviewed, and published with help from the following people:

Dorothy A. Shead, MS
Senior Director
Patient Information Operations

John Murphy
Medical Writer

Laura Phillips
Graphic Artist

The NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Central Nervous System Cancers Version 1.2023 were developed by the following NCCN Panel Members:

Louis Burt Nabors, MD/Chair
O'Neal Comprehensive
Cancer Center at UAB

Jana Portnow, MD/Vice-Chair
City of Hope National Medical Center

Joachim Baehring, MD
Yale Cancer Center/Smilow Cancer Hospital

Ankush Bhatia, MD
University of Wisconsin
Carbone Cancer Center

Orin Bloch, MD
UC Davis Comprehensive Cancer Center

Steven Brem, MD
Abramson Cancer Center
at the University of Pennsylvania

Nicholas Butowski, MD
UCSF Helen Diller Family
Comprehensive Cancer Center

Donald M. Cannon, MD
Huntsman Cancer Institute
at the University of Utah

Samuel Chao, MD
Case Comprehensive Cancer Center/
University Hospitals Seidman Cancer
Center and Cleveland Clinic
Taussig Cancer Institute

* Milan G. Chheda, MD
Siteman Cancer Center at Barnes-
Jewish Hospital and Washington
University School of Medicine

Andrew J. Fabiano, MD
Roswell Park Comprehensive Cancer Center

Peter Forsyth, MD
Moffitt Cancer Center

Pierre Giglio, MD
The Ohio State University Comprehensive
Cancer Center - James Cancer Hospital
and Solove Research Institute

Jona Hattangadi-Gluth, MD
UC San Diego Moores Cancer Center

* Matthias Holdhoff, MD, PhD
The Sidney Kimmel Comprehensive
Cancer Center at Johns Hopkins

Craig Horbinski, MD, PhD
Robert H. Lurie Comprehensive Cancer
Center of Northwestern University

Thomas Kaley, MD
Memorial Sloan Kettering Cancer Center

Michelle Kim, MD
University of Michigan Rogel Cancer Center

Ryan Merrell, MD
Vanderbilt-Ingram Cancer Center

Maciej M. Mrugala, MD, PhD, MPH
Mayo Clinic Comprehensive Cancer Center

Seema Nagpal, MD
Stanford Cancer Institute

Lucien A. Nedzi, MD
St. Jude Children's Research Hospital/
The University of Tennessee
Health Science Center

Kathryn Nevel, MD
Indiana University Melvin and Bren Simon
Comprehensive Cancer Center

* Douglas E. Ney, MD
University of Colorado Cancer Center

Phioanh L. Nghiemphu, MD
UCLA Jonsson Comprehensive
Cancer Center

Ian Parney, MD, PhD
Mayo Clinic Comprehensive Cancer Center

Toral R. Patel, MD
UT Southwestern Simmons
Comprehensive Cancer Center

Katherine Peters, MD, PhD
Duke Cancer Institute

Vinay K. Puduvalli, MD
The University of Texas
MD Anderson Cancer Center

Chad Rusthoven, MD
University of Colorado Cancer Center

Nicole Shonka, MD
Fred and Pamela Buffet Cancer Center

Lode J. Swinnen, MBChB
The Sidney Kimmel Comprehensive
Cancer Center at Johns Hopkins

* Stephanie Weiss, MD
Fox Chase Cancer Center

Patrick Yung Wen, MD
Dana-Farber Cancer Institute

* Nicole E. Willmarth, PhD
American Brain Tumor Association

NCCN

Mary Anne Bergman
Susan Darlow, PhD
Senem Kurtoglu Lubin, PhD, MBA

* Reviewed this patient guide. For disclosures, visit [NCCN.org/disclosures](https://www.nccn.org/disclosures).

NCCN Cancer Centers

Abramson Cancer Center
at the University of Pennsylvania
Philadelphia, Pennsylvania
800.789.7366 • pennmedicine.org/cancer

**Case Comprehensive Cancer Center/
University Hospitals Seidman Cancer Center and
Cleveland Clinic Taussig Cancer Institute**
Cleveland, Ohio
UH Seidman Cancer Center
800.641.2422 • uhhospitals.org/services/cancer-services
CC Taussig Cancer Institute
866.223.8100 • my.clevelandclinic.org/departments/cancer
Case CCC
216.844.8797 • case.edu/cancer

City of Hope National Medical Center
Duarte, California
800.826.4673 • cityofhope.org

**Dana-Farber/Brigham and Women's Cancer Center |
Mass General Cancer Center**
Boston, Massachusetts
617.732.5500 • youhaveus.org
617.726.5130 • massgeneral.org/cancer-center

Duke Cancer Institute
Durham, North Carolina
888.275.3853 • dukecancerinstitute.org

Fox Chase Cancer Center
Philadelphia, Pennsylvania
888.369.2427 • foxchase.org

Fred & Pamela Buffett Cancer Center
Omaha, Nebraska
402.559.5600 • unmc.edu/cancercenter

Fred Hutchinson Cancer Center
Seattle, Washington
206.667.5000 • fredhutch.org

Huntsman Cancer Institute at the University of Utah
Salt Lake City, Utah
800.824.2073 • healthcare.utah.edu/huntsmancancerinstitute

**Indiana University Melvin and Bren Simon
Comprehensive Cancer Center**
Indianapolis, Indiana
888.600.4822 • www.cancer.iu.edu

Mayo Clinic Comprehensive Cancer Center
Phoenix/Scottsdale, Arizona
Jacksonville, Florida
Rochester, Minnesota
480.301.8000 • Arizona
904.953.0853 • Florida
507.538.3270 • Minnesota
mayoclinic.org/cancercenter

Memorial Sloan Kettering Cancer Center
New York, New York
800.525.2225 • mskcc.org

Moffitt Cancer Center
Tampa, Florida
888.663.3488 • moffitt.org

O'Neal Comprehensive Cancer Center at UAB
Birmingham, Alabama
800.822.0933 • uab.edu/onealcancercenter

**Robert H. Lurie Comprehensive Cancer Center
of Northwestern University**
Chicago, Illinois
866.587.4322 • cancer.northwestern.edu

Roswell Park Comprehensive Cancer Center
Buffalo, New York
877.275.7724 • roswellpark.org

**Siteman Cancer Center at Barnes-Jewish Hospital
and Washington University School of Medicine**
St. Louis, Missouri
800.600.3606 • siteman.wustl.edu

**St. Jude Children's Research Hospital/
The University of Tennessee Health Science Center**
Memphis, Tennessee
866.278.5833 • stjude.org
901.448.5500 • uthsc.edu

Stanford Cancer Institute
Stanford, California
877.668.7535 • cancer.stanford.edu

**The Ohio State University Comprehensive Cancer Center -
James Cancer Hospital and Solove Research Institute**
Columbus, Ohio
800.293.5066 • cancer.osu.edu

**The Sidney Kimmel Comprehensive
Cancer Center at Johns Hopkins**
Baltimore, Maryland
410.955.8964
www.hopkinskimmelcancercenter.org

The UChicago Medicine Comprehensive Cancer Center
Chicago, Illinois
773.702.1000 • uchicagomedicine.org/cancer

The University of Texas MD Anderson Cancer Center
Houston, Texas
844.269.5922 • mdanderson.org

UC Davis Comprehensive Cancer Center
Sacramento, California
916.734.5959 • 800.770.9261
health.ucdavis.edu/cancer

NCCN Cancer Centers

UC San Diego Moores Cancer Center

La Jolla, California

858.822.6100 • cancer.ucsd.edu

UCLA Jonsson Comprehensive Cancer Center

Los Angeles, California

310.825.5268 • cancer.ucla.edu

UCSF Helen Diller Family Comprehensive Cancer Center

San Francisco, California

800.689.8273 • cancer.ucsf.edu

University of Colorado Cancer Center

Aurora, Colorado

720.848.0300 • coloradocancercenter.org

University of Michigan Rogel Cancer Center

Ann Arbor, Michigan

800.865.1125 • rogelcancercenter.org

University of Wisconsin Carbone Cancer Center

Madison, Wisconsin

608.265.1700 • uwhealth.org/cancer

UT Southwestern Simmons Comprehensive Cancer Center

Dallas, Texas

214.648.3111 • utsouthwestern.edu/simmons

Vanderbilt-Ingram Cancer Center

Nashville, Tennessee

877.936.8422 • vicc.org

Yale Cancer Center/Smilow Cancer Hospital

New Haven, Connecticut

855.4.SMILOW • yalecancercenter.org

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DR SHIVAM SHINGLA

BSES MG Hospital (Andheri):

9 am to 10 am (Monday to Friday)

Nanavati Max Hospital (Vile Parle):

10 am to 12 pm (Monday to Saturday)

S. L. Raheja Hospital (Mahim):

12 pm to 4 pm (Monday to Saturday)

Suvarna Hospital (Borivali):

5 pm to 6 pm (Monday and Friday)

Sushrut Hospital (Chembur):

By appointment

Hinduja Hospital (Khar):

By appointment

Galaxy Healthcare (Borivali):

By appointment



www.drshivamshingla.com



drshivamshingla@gmail.com



+91 98925 96286

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