

Primary central nervous system (CNS) lymphoma is an aggressive form of non-Hodgkin lymphoma (NHL) in which malignant (cancer) cells are found only in the CNS (the brain and spinal cord).

Primary CNS lymphoma can start in the brain, spinal cord, meninges (sheets of tissue that protect the CNS) or the eye. When the lymphoma begins in other parts of the body and spreads to the CNS, it is referred to as secondary CNS lymphoma. In more than 95% of patients with primary CNS lymphoma, the cancer starts in white blood cells (cells that help the body fight infections and cancer) called B-cells.

The cause of primary CNS lymphoma is unknown but having a weakened immune system (for example, people with acquired immunodeficiency syndrome [AIDS] or patients who have undergone organ transplant) may increase the risk of developing the disease. Having one or more of these risk factors does not mean a person will develop primary CNS lymphoma. Most people diagnosed with primary CNS lymphoma have never been exposed to any clearly known risk factors.

The symptoms of CNS lymphoma depend on the part of the CNS that is affected. These can occur suddenly or develop over time, and may include:

- Language problems, like difficulties with finding words or forming sentences, and slurred or slow speech.
- Paralysis (inability to move part of the body).
- Loss of vision or blurred vision.
- Confusion.
- Headaches.
- Vomiting.
- Seizures.
- Personality changes.

Early identification of symptoms and diagnosis of CNS lymphoma is important, followed by a quick start of treatment to reverse *neurological deficits* (problems in bodily functions due to damage in the brain, spinal cord or nerves) and improve outcomes (how well the patient will do). Upon diagnosis, tests are done to find out which parts of the CNS are involved as well as to determine if there is cancer elsewhere in the body. These can include computed tomography (CT) or positron emission tomography (PET, an imaging procedure that uses a special dye to locate the cancer in the body) scans of the body, magnetic resonance imaging (MRI, an imaging procedure that uses a powerful magnet and x-rays to take detailed pictures of areas inside the body) of the brain and spinal cord, lumbar puncture (or spinal tap, where a needle is inserted in the lower back to collect a sample of the fluid that surrounds the CNS), eye exams, and bone marrow biopsy (a needle is used to take samples of the spongy tissue inside the bones). Primary CNS lymphoma usually does not spread beyond the CNS or the eye, but it often relapses (disease returns after treatment).

Recognizing the symptoms and diagnosing CNS lymphoma early on is very important. This will allow the healthcare team to start treatment quickly to reverse *neurological deficits* (problems in bodily functions due to damage in the brain, spinal cord and nerves) and improve the patient's outcome (how well the patient will do).

After CNS lymphoma is diagnosed, the doctors conduct tests to find out which parts of the CNS are involved and if the cancer has spread to other parts of the body, including:

- Computed tomography (CT), an imaging procedure that uses X-rays to take detailed pictures of areas inside the body.
- Positron emission tomography (PET), an imaging procedure that uses a special dye to find out where the cancer is in the body.
- Magnetic resonance imaging (MRI), an imaging procedure that uses a powerful magnet and X-rays to take detailed pictures of areas inside the body.
- Lumbar puncture (or spinal tap), where a needle is inserted in the lower back to collect a sample of the fluid that surrounds the CNS.
- Bone marrow biopsy, where a needle is used to take samples of the spongy tissue inside the bones.

Primary CNS lymphoma usually does not spread beyond the CNS or the eye, but it often *relapses* (disease comes back after treatment).

For more information on CNS lymphoma diagnosis and disease staging, please view the *Understanding Lymphoma and CLL Guide* on the Foundation's website (visit [lymphoma.org/publications](http://lymphoma.org/publications)).

### Treatment Options

Until the mid-1990s, radiation was the *standard therapy* (the proper treatment that is widely used by health care providers and accepted by medical experts) for patients with CNS lymphoma. Now, *chemoimmunotherapy* which is a combination (two or more drugs given at the same time) of chemotherapy (drugs that stop the growth of or kill cancer cells) with immunotherapy (drugs that use the body's immune system to fight cancer) is recommended for most patients as induction (initial) treatment. The most common combination

regimen is high-dose methotrexate with the monoclonal antibody (a protein made in the laboratory that binds to cancer cells and helps the immune system destroy them) rituximab (Rituxan). Sometimes, this is given in combination with other chemotherapy agents such as cytarabine (Cytosar), vincristine (Oncovin), procarbazine (Matulane), ifosfamide (Ifex), thiotepa (Tepadina), or temozolomide (Temodar).

The initial treatment is often followed by other regimens or consolidation therapies (treatments given once the cancer has disappeared after initial treatment to kill any cancer cells that may be left in the body), to reduce the risk of relapse. These consolidation therapies include:

- High-dose chemotherapy alone such as cytarabine (Cytosar).
- Chemotherapy with cytarabine (Cytosar) and etoposide (Etopophos, Toposar).
- Stem cell transplantation (SCT, a procedure in which the patient is treated with high-dose chemotherapy or radiation to remove their blood-forming cells or stem cells, and then receives healthy stem cells to restore the immune system and the bone marrow's ability to make new blood cells).
  - *Autologous SCT* (patient's own stem cells are infused after high-dose chemotherapy).
  - For more information about stem cell transplantation, please see the *Understanding Cellular Therapy* guide on the Foundation's website ([lymphoma.org/publications](http://lymphoma.org/publications)).
- Radiation therapy (uses high-energy radiation to kill cancer cells)
  - Whole brain radiation therapy. This type of radiation therapy is rarely used in patients over the age of 65 because of permanent and progressive neurological complications (for example, loss of memory, problems with balance, or muscle coordination).

Table 1: Treatments Under Investigation for Primary CNS Lymphoma Under Phase 2 or 3 Clinical Trials.

Agent (Drug)	Class (Type of Treatment)
Abemaciclib (Verzenio)	Targeted therapy; CDK inhibitor
Ibrutinib (Imbruvica)	Targeted therapy; BTK inhibitor
Lenalidomide (Revlimid)	Immunotherapy; immunomodulatory drug
Nivolumab (Opdivo)	Immunotherapy; immune checkpoint inhibitor, anti-PD-1
Obinutuzumab (Gazyva)	Immunotherapy; monoclonal antibody, anti-CD20
Tafasitamab (Monjuvi)	Immunotherapy; monoclonal antibody, anti-CD19
Pembrolizumab (Keytruda)	Immunotherapy; immune checkpoint inhibitor, anti-PD-1
Acalabrutinib (Calquence)	Targeted therapy; BTK inhibitor
Orelabrutinib (ICP-022)	Targeted therapy; BTK inhibitor
Zanubrutinib (Brukinsa)	Targeted therapy; BTK inhibitor
Paxalisib (GDC-0084)	Targeted therapy; PI3K/mTOR inhibitor
Tirabrutinib (ONO-4059)	Targeted therapy; BTK inhibitor

BTK, Bruton's kinase; CDK, cyclin-dependent kinase; PD-1, programmed cell death protein-1; PI3K/mTOR, phosphatidylinositol-3-kinase/mammalian target of rapamycin.

## Treatments Under Investigation

Many treatments (also referred to as investigational drugs) are currently being tested in clinical trials (a type of research study that tests how well new treatments work) in patients with primary CNS lymphoma. Results from these clinical trials may improve or change the current standard of care (the proper treatment that is widely used by healthcare professionals and accepted by medical experts). The table below lists some of these investigational drugs that can be accessed through a clinical trial.

Treatment options may change as new treatments are discovered and current treatments are improved. Because today's scientific research is continuously evolving, it is important that patients check with their physician or with the Lymphoma Research Foundation for any treatment updates that may have recently appeared. It is also very important that patients consult with a specialist to clear up any questions.

## Clinical Trials

Clinical trials are important in identifying effective drugs and determining the best treatment doses for patients with lymphoma. Because CNS lymphoma is a rare disease, clinical trials are very important to discover treatments that are more effective and less toxic. The rarity of the disease also means that the most recent treatments are often available only through clinical trials.

Patients interested in participating in a clinical trial should view the *Understanding Clinical Trials* fact sheet on the Foundation's website (visit [lymphoma.org/publications](http://lymphoma.org/publications)), and the *Clinical Trials Search Request Form* at [lymphoma.org](http://lymphoma.org), talk to their physician, or contact the Helpline for an individualized clinical trial search by calling (800) 500-9976 or emailing [helpline@lymphoma.org](mailto:helpline@lymphoma.org).

## Follow-up

Patients with CNS lymphoma should have regular visits with their physician. During these visits, medical tests (such as blood tests, MRI scans of the brain and/or spine) and eye (ophthalmological) examination may be required to evaluate the need for additional treatment.

Some treatments can cause long-term side effects (occur **during** treatment and continue for months or years) or late side effects (appear only months, years or decades **after** treatment has ended). These can vary depending on the following factors:

- Duration of treatment (how long was the treatment given).
- Frequency of treatment (how often was the treatment administered).
- Type of treatment given.
- Age and gender of the patient.
- Patient overall health at the time of treatment.

A physician will check for these side effects during follow-up care. Visits may become less frequent the longer the patient remains in *remission* (no sign or symptoms of cancer).

Patients and their care partners are encouraged to keep copies of all medical records. These include test results as well as information on the types, amounts, and duration of all treatments received. Medical records are important for keeping track of any side effects resulting from treatment or potential disease recurrences. The Foundation's award-winning *Focus On Lymphoma* mobile app ([lymphoma.org/mobileapp](http://lymphoma.org/mobileapp)) and the *Lymphoma Care Plan* ([lymphoma.org/publications](http://lymphoma.org/publications)) can help patients manage this documentation.

## Lymphoma Care Plan

Keeping your information in one location can help you feel more organized and in control. This also makes it easier to find information pertaining to your care and saves valuable time. The Foundation's Lymphoma Care Plan document organizes information on your health care team, treatment regimen, and follow-up care. You can also keep track of health screenings and any symptoms you experience to discuss with your health care provider during future appointments. The Lymphoma Care Plan document can be accessed by visiting [lymphoma.org/publications](http://lymphoma.org/publications).

## Patient Education Programs

The Foundation also offers a variety of educational activities, including live meetings and webinars for individuals looking to learn directly from lymphoma experts. These programs provide the lymphoma community with important information about the diagnosis and treatment of lymphoma, as well as information about clinical trials, research advances and how to manage/cope with the disease. These programs are designed to meet the needs of a lymphoma patient from the point of diagnosis through long-term survivorship. To view our schedule of upcoming programs, please visit [lymphoma.org/programs](http://lymphoma.org/programs).

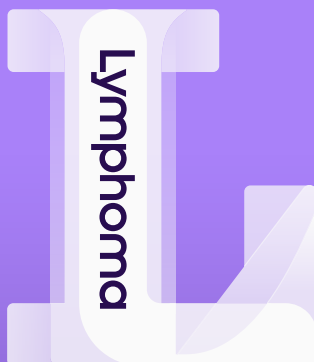
## Helpline

The Foundation's Helpline staff are available to answer your general questions about lymphoma and treatment information, as well as provide individual support and referrals to you and your loved ones. Callers may request the services of a language interpreter. The Foundation also offers a one-to-one peer support program called the Lymphoma Support Network and clinical trials information through our Clinical Trials Information Service. For more information about any of these resources, visit our website at [lymphoma.org](http://lymphoma.org), or contact the Helpline at (800) 500-9976 or [helpline@lymphoma.org](mailto:helpline@lymphoma.org).

Para información en Español, por favor visite [lymphoma.org/es](http://lymphoma.org/es). (For Information in Spanish please visit [lymphoma.org/es](http://lymphoma.org/es)).

## Focus on Lymphoma Mobile App

Focus on Lymphoma is the first app to provide patients and their care partners with tailored content based on lymphoma subtype, and actionable tools to better manage diagnosis and treatment. Comprehensive lymphoma management, conveniently in one secure and easy-to-navigate app, no matter where you are on the care continuum. Get the right information, first, with resources from the entire Lymphoma Research Foundation content library, use unique tracking and reminder tools, and connect with a community of specialists and patients. To learn more about this resource, visit our website at [lymphoma.org/mobileapp](http://lymphoma.org/mobileapp), or contact the Foundation's Helpline at (800) 500-9976 or [helpline@lymphoma.org](mailto:helpline@lymphoma.org).



Research Foundation

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### Helpline

(800) 500-9976

helpline@lymphoma.org

lymphoma.org

lymphoma@lymphoma.org

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