

# Understanding Lymphoma: Cutaneous B-Cell Lymphoma

**B-cell lymphomas account for approximately 85%-90% of all non-Hodgkin lymphoma (NHL) cases in the United States. This disease affects men and women at any age group, although most cases are diagnosed in patients older than 60. There are many different forms of B-cell lymphoma.**

Lymphomas that arise in tissues or organs outside of the lymphatic system (tissues and organs that produce, store, and carry white blood cells) are called extranodal lymphomas. When extranodal lymphomas start in the skin and there is no evidence of disease outside of the skin, they are called primary cutaneous lymphomas. Primary cutaneous B-cell lymphomas (CBCLs) occur when the lymphoma originates from B lymphocytes (a type of white blood cells also known as B cells) in the skin.

CBCLs are rare and often indolent (slow-growing), and they may appear on the skin as a rash, reddish bump, lump, or nodule, usually with a raised and smooth appearance. They can appear as a single lesion (area that looks abnormal or different from the surrounding skin) or multiple lesions in either one or several body regions (areas). Many skin conditions may look similar but are not CBCLs. The disease can relapse (return after treatment) or occur in new places on the skin, but it rarely spreads outside the skin. About 50% of patients with single lesions are cured after radiation therapy. However, patients with multiple lesions are more likely to continue to have new lesions appear. This fact does not affect prognosis (how well the patient will do), which remains very good.



## SUBTYPES OF CBCL

**Primary cutaneous follicle center lymphoma** is the most common type of CBCL. This skin lymphoma is indolent, developing slowly over months or years. It usually appears on the head, neck, or torso (upper body or chest) as red pimples, nodules (bumps), or plaques (raised or flat lesions). In some cases, it can be found on the legs. This type of CBCL is usually diagnosed in middle-aged adults and responds well to treatment.

**Primary cutaneous marginal zone B-cell lymphoma** is the second-most common form of CBCL. This indolent lymphoma can have a similar appearance as cutaneous follicle center lymphoma, often as red to purplish large pimples, plaques, or nodules on the arms or upper body. Some cases are linked to an infection with *Borrelia burgdorferi*, a type of bacteria carried by ticks that causes Lyme disease. This type of CBCL is more common in older adults.

**Primary cutaneous diffuse large B-cell lymphoma (CDLBCL), leg type** is a rare type of CBCL but is usually more aggressive (fast-growing), developing over weeks or months. This lymphoma usually appears as solitary or multiple nodules on the lower part of the legs, but it can involve non-leg areas such as the arms and/or torso. The lesions may ulcerate (cause sores on the skin) and spread outside the skin more frequently than slow-

growing CBCLs. This type of CBCL is more common in older women and often requires intensive treatment.

Other types of CDLBCL include a group of very rare, aggressive lymphomas, such as intravascular large B-cell lymphoma, T-cell-rich large B-cell lymphoma, plasmablastic lymphoma, and anaplastic B-cell lymphoma. These lymphomas are not always cutaneous and usually appear on the head, torso, and extremities (arms and legs).



## TREATMENT OPTIONS

Upon diagnosis, appropriate staging work-up (a procedure to evaluate how much the cancer has grown and if it has spread) should be done to make sure that the disease is limited to the skin. In general, this includes routine laboratory tests (like blood testing) and whole-body imaging studies (like computed tomography [CT] scans). Bone marrow biopsies (a needle is used to collect a sample of the soft tissue inside the bones) are not recommended for all patients with indolent CBCLs.

Treatment selection for CBCL depends on the type of CBCL and whether the skin lesion is solitary/regional (single lesion or lesions that are limited to one region of the skin) or multifocal (widespread). Treatment also depends on how fast the lymphoma is growing (indolent vs. aggressive).

For indolent lymphomas with solitary/regional lesions, the most common treatment is local radiation therapy. Surgical treatment can be an option, but it may result in wide, unnecessary scars. Indolent CBCLs that present as multiple lesions may be observed through an approach known as “active surveillance” or “watchful waiting,” in which patients’ overall health and disease are monitored through regular checkup visits that can include laboratory and imaging tests. For more information on active surveillance, view the *Active Surveillance* fact sheet on Lymphoma Research Foundation’s website ([lymphoma.org/publications](http://lymphoma.org/publications)).

Treatments for this type of CBCL include:

- Intralesional corticosteroids (applied directly into the lesion)
- Topical therapies (treatment applied to the skin), such as chemotherapy, bexarotene (Targretin), and imiquimod (Zyclara)
- Surgical removal of lesions
- Radiation therapy (applied directly to the lesions)

If lesions are very widespread and symptomatic, systemic therapies (treatment with drugs that travel through the bloodstream and reach all parts of the body) may be appropriate. This includes monoclonal antibodies (proteins made in the lab that recognize substances at the surface of cancer cells) like rituximab (Rituxan), with or without chemotherapy.

Regular skin examinations are very important, especially for indolent CBCLs, as the skin is the most common site of new lesions. General laboratory tests may also be done, but imaging is not needed unless there is a concern of systemic (widespread) disease.

For aggressive CBCLs, the patient’s overall health is taken into account to select the best treatment option. In CDLBCL,

Leg-Type, systemic chemotherapy (usually cyclophosphamide, doxorubicin, vincristine, and prednisone [CHOP]) with or without rituximab (Rituxan) is often more appropriate for initial treatment, with or without radiation therapy. Regular imaging studies are usually done to evaluate treatment response or disease status.

Treatment for relapse (disease returns after treatment) of indolent CBCL can include observation, surgery, topical treatments, injected steroids, or radiation (low-dose). Indolent CBCLs usually remain indolent and relapse in the skin. Very rarely, indolent CBCLs relapse as systemic disease, most commonly in regional lymph nodes. In extremely rare cases, indolent CBCLs can transform into more aggressive types of lymphoma.

Relapsed aggressive CBCLs may be treated with chemotherapy (with or without rituximab), targeted therapies such as ibrutinib (Imbruvica), lenalidomide (Revlimid), radiation therapy, and/or radioimmunotherapy.



## TREATMENTS UNDER INVESTIGATION

Many new treatments (also referred to as investigational drugs) and combination therapies are currently being studied for the treatment of patients with CBCL. Results from these clinical trials may improve or change the current standard of care (the proper treatment that is widely used by health care professionals and accepted by medical experts). The table below lists some of these investigational drugs that can be accessed through a clinical trial. For more information on clinical trials, view the *Understanding Clinical Trials* publication on LRF’s website ([lymphoma.org/publications](http://lymphoma.org/publications)).

**Table 1. Treatments Under Investigation for CBCL in Phase 2 or 3 Clinical Trials.**

Agent (Drug)	Class (Type of treatment)
<b>Lenalidomide (Revlimid)</b>	Chemotherapy
<b>Ontopacept (TTI-621)</b>	Immunotherapy; fusion protein
<b>Maplirpacept (TTI-622)</b>	Immunotherapy; fusion protein
<b>Pembrolizumab (Keytruda)</b>	Immunotherapy; immune checkpoint inhibitor, anti-PD-1
<b>Nivolumab (Opdivo)</b>	Immunotherapy; immune checkpoint inhibitor, anti-PD-1
<b>Varlilumab (CDX-1127)</b>	Immunotherapy; monoclonal antibody, anti-CD27
<b>Zanubrutinib (Brukinsa)</b>	Targeted therapy; BTK inhibitor

BTK, Bruton’s tyrosine kinase; CBCL, cutaneous B-cell lymphoma; PD-1, programmed cell death protein 1.

It is important to remember that scientific research is always evolving. Treatment options may change as new treatments are discovered and current treatments are improved. Therefore, it is important that patients check with their physician or with LRF for any treatment updates that may have recently appeared.

## CLINICAL TRIALS

Clinical trials are crucial in identifying effective drugs and the best treatment doses for patients with lymphoma. Patients interested in participating in a clinical trial should view the *Understanding Clinical Trials* fact sheet ([lymphoma.org/publications](https://lymphoma.org/publications)) and the *Clinical Trials Search Request Form* ([lymphoma.org](https://lymphoma.org)), talk to their physician, or contact the LRF 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 lymphoma should have regular visits with their physician. During these visits, medical tests (such as blood tests, computed tomography [CT] scans, and positron emission tomography [PET] scans) may be required to evaluate the need for additional treatment.

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

## LRF CARE PLAN AND PATIENT EDUCATION PROGRAM

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. LRF'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](https://lymphoma.org/publications). LRF also

offers a variety of educational activities, including live meetings and webinars, for individuals looking to learn directly from lymphoma experts. To view our schedule of upcoming programs, please visit [lymphoma.org/programs](https://lymphoma.org/programs).

### LRF Helpline

The LRF 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. LRF 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](https://lymphoma.org), or contact the LRF Helpline at **(800) 500-9976** or [helpline@lymphoma.org](mailto:helpline@lymphoma.org).

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

## LRF FOCUS ON LYMPHOMA MOBILE APP

Focus on Lymphoma is the first app to provide patients and their caregivers with tailored content based on lymphoma subtype and actionable tools to better manage diagnosis and treatment. It provides convenient and comprehensive lymphoma management 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](https://lymphoma.org/mobileapp), or contact the LRF Helpline at **800-500-9976** or [helpline@lymphoma.org](mailto:helpline@lymphoma.org).

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