Follicular lymphoma (FL) is the most common indolent (slow-growing) form of non-Hodgkin Lymphoma (NHL), accounting for just over 10 percent of all B-cell NHLs.

Common symptoms of FL include enlargement of the lymph nodes in the neck, underarms, abdomen, or groin, as well as fatigue. Typically, patients with FL have no obvious symptoms of the disease at diagnosis and present only with an enlarged lymph node on exam or found incidentally on an imaging study. Most patients with FL are age 50 years and older when they are diagnosed.

Some patients with FL may eventually develop a transformed lymphoma, which is often more aggressive and usually requires more intensive types of treatment. For more information on transformed lymphomas, view the Transformed Lymphomas fact sheet on the Lymphoma Research Foundation’s (LRF’s) website at lymphoma.org/publications.

TREATMENT OPTIONS

In some patients, FL may go away without treatment. If treatment is needed and patients show no or very few symptoms, physicians may recommend not to treat the disease right away, an approach referred to as active surveillance (also known as “watchful waiting” or “careful observation”). Studies have shown that patients managed with an active surveillance approach have survival outcomes similar to those treated early in the course of their disease. With this strategy, patients’ overall health and disease are monitored through regular physical exams or periodic imaging tests. Active treatment is started if the patient begins to develop lymphoma-related symptoms or signs that the disease is progressing based on testing during follow-up visits. There are various therapeutic options for FL based on the severity of associated symptoms and the rate of cancer growth.

FL is generally very responsive to radiation and chemotherapy. Radiation alone can provide a long-lasting remission (disappearance of signs and symptoms) in some patients with early-stage disease.

In patients requiring chemotherapy, physicians may use one or more chemotherapy drugs such as the monoclonal antibodies obinutuzumab (Gazyva) or rituximab (Rituxan). Rituximab hyaluronidase human (Rituxan Hycela) can be administered as a subcutaneous (under the skin) injection.

Monoclonal antibodies are a type of immunotherapy drug that targets particular markers found on tumor cells and recruit immune cells to promote tumor destruction, which can increase response to chemotherapy drugs. Rituximab (Rituxan) and obinutuzumab (Gazyva) are examples of some of the most frequently used monoclonal antibodies to treat lymphoma, either alone or in combination. Common combination regimens include:

- Bendamustine (Treanda) and obinutuzumab (Gazyva)
- R-Bendamustine (rituximab [Rituxan] and bendamustine)
- R-CHOP (rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisone)
- R-CVP (rituximab, cyclophosphamide, vincristine, and prednisone)
- R-Lenalidomide (rituximab and lenalidomide [Revlimid]), often referred to as R2 (R-squared)

Some monoclonal antibodies such as obinutuzumab, can also be used as maintenance therapy to prolong remission in patients with no signs of lymphoma.

After treatment, many patients can go into a remission that lasts for years; however, this disease should be considered a chronic or lifelong condition. Thus, relapse (disease returns after treatment) and in some cases, refractory (disease no longer responds to treatment) disease can occur. For patients with relapsed FL, the same management choices listed above may be utilized, and additional therapies such as the PI3
kinase inhibitors idelalisib (Zydelig), copanlisib (Aliqopa), and duvelisib (Copiktra), and dual PI3K and casein kinase-1 inhibitor umbralisib (Ukoniq) may be successful in providing another remission. Tazemetostat has also been recently approved for relapsed/refractory FL with an EZH2 mutation or for patients with FL who have no satisfactory alternative treatment option. Chimeric antigen receptor (CAR) T cell therapy with axicabtagene ciloleucel (Yescarta) is also approved to treat relapsed or refractory FL. For more information on relapsed and refractory FL, view the Follicular Lymphoma Relapsed/Refractory fact sheet on LRF’s website (click here).

For some patients with multiple relapsed FL, high-dose chemotherapy followed by stem cell transplantation may be an option. For more information on transplantation, view the Understanding the Stem Cell Transplantation Process publication on LRF’s website (click here).

TREATMENTS UNDER INVESTIGATION

Many treatments are currently being tested in clinical trials in patients who are newly diagnosed or have relapsed/refractory FL. These trials help determine the best treatment for patients with newly diagnosed FL and discover new treatments for recurrent FL. Examples of treatments under investigation include:

- Monoclonal antibodies (Ublituximab)
- Phosphoinositide 3-kinase (PI3K) inhibitors such as parsaclisib and zandelisib
- Bruton’s tyrosine kinase (BTK) inhibitors like ibrutinib (Imbruvica), acalabrutinib (Calquence)
- Immune checkpoint inhibitors like durvalumab (Imfinzi), nivolumab (Opdivo), pembrolizumab (Keytruda)
- B-cell lymphoma-2 (Bcl-2) inhibitors like venetoclax (Venclexta)
- Chimeric antigen receptor (CAR) T cell therapies like tisagenlecleucel (Kymriah) and relmacabtagene autoleucel

It is critical to remember that scientific research is continuously 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 emerged.

CLINICAL TRIALS

Clinical trials are crucial in identifying effective drugs and determining optimal doses for patients with lymphoma. Patients interested in participating in a clinical trial should view the Understanding Clinical Trials fact sheet on LRF’s website (click here), and the Clinical Trials Search Request Form at 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.

FOLLOW-UP

Since FL is generally characterized by multiple disease relapses after responses to a variety of treatments, patients should have regular visits with a physician who is familiar with their medical history and the treatments they have received. Medical tests (such as blood tests, computed tomography [CT] scans, positron emission tomography [PET] scans, and biopsies of suspicious masses or the bone marrow) may be required at various times during remission to evaluate the need for additional treatment. Some treatments can cause long-term side effects or late side effects, which can vary based on the duration and frequency of treatments, age, gender, and overall health of each patient 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 disease remains in remission.

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 recurrence. LRF’s award-winning Focus On Lymphoma mobile app (lymphoma.org/mobileapp) and Lymphoma Care Plan (lymphoma.org/publications) can help patients manage this documentation.

LRF’S HELPLINE AND LYMPHOMA SUPPORT NETWORK

A lymphoma diagnosis often triggers a range of feelings and concerns. In addition, cancer treatment can cause physical discomfort. The LRF Helpline staff members are available to answer your general questions about a lymphoma diagnosis 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.

A part of the Helpline is LRF’s one-to-one peer support programs, Lymphoma Support Network. This program connects patients and caregivers with volunteers who have experience with FL, similar treatments, or challenges, for mutual emotional support and encouragement. Patients and loved ones may find this useful whether the patient is newly diagnosed, in treatment, or in remission.
Focus On Lymphoma is the first mobile application (app) that provides patients and caregivers comprehensive content based on their lymphoma subtype, including FL, and tools to help manage their lymphoma such as, keep track of medications and blood work, track symptoms, and document treatment side effects. The Focus On Lymphoma mobile app is available for download for iOS and Android devices in the Apple App Store and Google Play. For additional information on the mobile app, visit FocusOnLymphoma.org. To learn more about any of these resources, visit our website at lymphoma.org, or contact the LRF Helpline at 800-500-9976 or helpline@lymphoma.org.