

# Understanding Follicular Lymphoma

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.

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](http://lymphoma.org/publications).



## TREATMENT OPTIONS

There are various treatment options for FL based on the severity of associated symptoms and the rate of cancer growth. If 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 who are managed with an active surveillance approach have survival outcomes similar to those who are 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 there are signs that the disease is progressing based on testing during follow-up visits.

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, often adding the monoclonal antibodies obinutuzumab (Gazyva) or rituximab (Rituxan). Rituximab hyaluronidase human (Rituxan Hycela) can be given as a *subcutaneous* (under the skin) injection instead of *IV* (intravenous) rituximab after the first IV infusion of rituximab.

Monoclonal antibodies are a type of immunotherapy that targets particular markers found on tumor cells and recruits immune cells to promote tumor destruction, which can increase response to chemotherapy drugs. Rituximab and obinutuzumab 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 for 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* (returns after treatment) and in some cases *refractory* (no longer responds to treatment) disease can occur. For patients with relapsed FL, the same management choices as listed above may be utilized, or additional therapies may be successful in providing another remission, such as the PI3 kinase inhibitors idelalisib (Zydelig), copanlisib (Aliqopa), and duvelisib (Copiktra). Tazemetostat has also been recently approved for relapsed/refractory FL with an EZH2 mutation or for patients with relapsed/refractory FL who have no satisfactory alternative treatment option. For more information on relapsed and refractory FL, view the *Understanding Follicular Lymphoma: Relapsed/Refractory* fact sheet on LRF's website at [lymphoma.org/publications](http://lymphoma.org/publications).

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 at [lymphoma.org/publications](http://lymphoma.org/publications).

## TREATMENTS UNDER INVESTIGATION

Many treatments are currently being tested in clinical trials for patients who are newly diagnosed or have relapsed/refractory FL. These trials help determine what is the best treatment for patients with newly diagnosed FL and also help discover new treatments for FL that has recurred. Examples of therapies under investigation include new monoclonal antibodies such as Ublituximab (TG-1101); PI3 kinase inhibitors; ibrutinib (Imbruvica), acalabrutinib (Calquence), and other BTK inhibitors; durvalumab (Imfinzi), nivolumab (Opdivo), pembrolizumab (Keytruda), and other checkpoint inhibitors; and new immunotherapies including chimeric antigen receptor (CAR) T-cell therapies. Other classes of therapy include dual inhibitors such as umbralisib, which inhibits both PI3K delta and CK1 epsilon; B-cell lymphoma-2 (BCL-2) inhibitors; and venetoclax (Venclexta).

It is critical to remember that today's 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 at [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 LRF Helpline for an individualized clinical trial search by calling (800) 500-9976 or emailing [helpline@lymphoma.org](mailto: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 the 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 recurrences. LRF's award-winning *Focus On Lymphoma* mobile app ([lymphoma.org/mobileapp](http://lymphoma.org/mobileapp)) and *Lymphoma Care Plan* ([lymphoma.org/publications](http://lymphoma.org/publications)) can help patients manage this documentation.

## PATIENT AND CAREGIVER SUPPORT SERVICES

A lymphoma diagnosis often triggers a range of feelings and concerns. In addition, cancer treatment can cause physical discomfort. One-to-one peer support programs, such as LRF's *Lymphoma Support Network*, connect patients and caregivers with volunteers who have experience with lymphoma or FL and similar treatments or challenges, for mutual emotional support and encouragement. Patients and loved ones may find this information useful whether the patient is newly diagnosed, in treatment, or in remission.

### Resources

LRF offers a wide range of resources that address treatment options, the latest research advances, and ways to cope with all aspects of lymphoma and FL, including our award-winning mobile app. LRF also provides many educational activities, from in-person meetings to webinars, for people with lymphoma, as well as FL e-Updates that provide the latest disease-specific news and treatment options. To learn more about any of these resources, visit our websites at [lymphoma.org/FL](http://lymphoma.org/FL) or [lymphoma.org](http://lymphoma.org), or contact the LRF Helpline at (800) 500-9976 or [helpline@lymphoma.org](mailto:helpline@lymphoma.org).

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