LYMPHOMA
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Getting the Facts

Helpline: (800) 500-9976
helpline@lymphoma.org

Follicular Lymphoma: Relapsed/Refractory

Overview

Lymphoma is the most common blood cancer. The two main forms of lymphoma are Hodgkin lymphoma (HL) and non-Hodgkin lymphoma (NHL). Lymphoma occurs when cells of the immune system called lymphocytes, a type of white blood cell, grow and multiply uncontrollably. Cancerous lymphocytes can travel to many parts of the body, including the lymph nodes, spleen, bone marrow, blood, or other organs, and form a mass called a tumor. The body has two main types of lymphocytes that can develop into lymphomas: B lymphocytes (B cells) and T lymphocytes (T cells).

Follicular lymphoma (FL) is the most common *indolent* (slow-growing) form of NHL, accounting for approximately 20 percent of all B-cell NHLs. Common symptoms of FL include swelling of the lymph nodes in the neck, underarms, abdomen, or groin, and fatigue, shortness of breath, and much less commonly fevers, night sweats, and weight loss. Often, patients with FL have no obvious symptoms of the disease at diagnosis.

Although many patients go into a remission that lasts for years after their initial treatment, the disease often returns. For patients who *relapse* (disease returns after treatment) or become *refractory* (disease does not respond to treatment), *second-line therapies* (treatment given when initial therapy does not work or stops working) are often successful in providing another remission. Some patients who relapse do not need treatment right away, and a "watch and wait" or "watchful waiting" approach might be used. With this strategy, patients' overall health and disease are monitored through regular checkup visits and various evaluating procedures, such as laboratory and 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. For those who need treatment, the same therapies used for newly diagnosed patients can often be used in patients with relapsed/refractory FL, but additional treatments are also available.

Treatment Options

Treatment for relapsed/refractory FL is based on a patient's age, overall health, symptoms, and the duration of remission from the last treatment they received. Chemotherapy, radiation, and monoclonal antibodies such as rituximab (Rituxan) and obinutuzumab (Gazyva) may be used to treat relapsed/refractory FL. Common second-line regimens include:

- Bendamustine (Treanda) with or without rituximab
- Fludarabine (Fludara) and rituximab
- Idelalisib (Zydelig)
- Lenalidomide (Revlimid) with or without rituximab
- R-CHOP (rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisone)
- R-CVP (rituximab, cyclophosphamide, vincristine, and prednisone)
- R-FND (rituximab, fludarabine, mitoxantrone, and dexamethasone)
- Rituximab alone

Although uncommon, radioimmunotherapy (RIT) using an agent such as yttrium-90 ibritumomab tiuxetan (Zevalin), which is a radioactive particle connected to an antibody that targets cancer cells, may also be used alone or in combination with chemotherapy to treat relapsed/refractory FL. To learn more about RIT, view the *Radioimmunotherapy* fact sheet on the Lymphoma Research Foundation's (LRF's) website at www.lymphoma.org.

Bendamustine is approved for patients with indolent B-cell NHLs, like FL, whose disease is refractory to rituximab.

Radiation therapy can be effective in some patients with relapsed/refractory FL who have large tumors or disease symptoms. Often very low doses of radiation can be quite beneficial.

For some patients with relapsed/refractory 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* booklet on LRF's website at www.lymphoma.org.

Response to Retreatment

Generally, the length of remission is shorter after treatment for relapsed/refractory disease. However, this is changing. Newer therapies for patients with FL can lead to remissions after second- or third-line treatments that are longer than the patient's previous remission(s).

Transformed FL

Over time, 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 LRF's website at www.lymphoma.org.

Contact the
Lymphoma Research Foundation

Helpline: (800) 500-9976

National
Headquarters: (212) 349-2910

Email: LRF@lymphoma.org

Website: www.lymphoma.org

Medical reviewer:
Arnold S. Freedman, MD
Dana-Farber Cancer Institute

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Treatments Under Investigation

Many treatments are currently being tested in clinical trials alone or as part of a combination therapy regimen in patients with relapsed/refractory FL. Some of these treatments include:

- Bortezomib (Velcade)
- Buparlisib
- Copanlisib
- Everolimus (Afinitor)
- Ibrutinib (Imbruvica)
- Lenalidomide (Revlimid)
- Nivolumab (Opdivo)
- Ofatumumab (Arzerra)
- Panobinostat (Farydak)
- Pembrolizumab (Keytruda)
- Pinatuzumab vedotin
- Polatuzumab vedotin
- 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 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

Because FL is generally characterized by multiple disease relapses after responses to a variety of treatments, patients in remission 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 and computed tomography [CT] scans) may be required at various times during remission to evaluate the need for additional treatment.

Some treatments can cause long-term effects or late effects, which can vary based on 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 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 effects resulting from treatment or potential disease recurrences.

Support

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, connects patients and caregivers with volunteers that have experience with FL, similar treatments, or challenges, for mutual emotional support and encouragement. You may find this useful whether you or a loved one 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 teleconferences and webcasts for people with FL, as well as follicular lymphoma e-Updates that provide the latest disease-specific news and treatment options. For more information about any of these resources, visit our websites at www.FocusOnFL.org or www.lymphoma.org, or contact the LRF Helpline at (800) 500-9976 or helpline@lymphoma.org.