

## Indolent Follicular Lymphoma

*Expert review by:*

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### Non-Hodgkin Lymphoma Overview

Lymphoma is a cancer of the white blood cells, namely lymphocytes, that happen to constitute the lymphatic system. Of the more than 67 types of lymphoma, more than 61 are classified as non-Hodgkin lymphoma (NHL). Nearly all non-Hodgkin lymphoma cases occur in adults, with the average age of diagnosis in the 60's. While scientists do not know the exact causes of non-Hodgkin lymphoma, they do know that it is not caused by injury or by coming into contact with someone else with the disease. Most people diagnosed with non-Hodgkin lymphoma have no known risk factors, though increasingly many scientists believe infections may play an important role in causing select types of non-Hodgkin lymphoma.

### Follicular Lymphoma Overview

Follicular lymphoma is typically a slow-growing, or indolent, form of non-Hodgkin lymphoma. This cancer, which accounts for roughly 20 to 30 percent of all non-Hodgkin lymphomas, usually takes several years to develop. It usually appears in a lumpy, or nodular pattern, within lymph nodes throughout the body. Often, the first sign of follicular lymphoma is a painless swelling in the neck, armpit or groin caused by enlarged lymph nodes. Some people also report loss of appetite and fatigue.

### Diagnosing Follicular Lymphoma

Doctors usually diagnose follicular lymphoma by taking a small sample of the tumor, called a biopsy, and looking at the cells under a microscope. In addition, follicular lymphoma cells often carry abundant amounts of a protein called bcl-2, which protects cells from dying. Additional

tests, such as blood tests, x-rays, and scans may be used to help determine how far the cancer has spread, indicating its "stage." In Stage I, lymphoma appears only in one group of lymph nodes in a particular body region, while in patients with Stage II, disease in more than one lymph node group is involved. Patients with Stage II disease have disease limited to one side of the diaphragm (midline of the chest or abdomen). In contrast, patients with Stage III or IV disease have lymphoma on both sides of the diaphragm or involving other organ systems including the bone marrow. Most patients with follicular lymphoma are diagnosed with Stage III or IV disease.

### Treatment Options

Treatment of lymphoma is based on the severity of associated symptoms and the rate of growth. Since follicular lymphoma grows very slowly, doctors may decide not to treat it right away, an approach often referred to as "watch and wait." Many studies have shown that patients treated earlier in their disease course, compared to those followed with a "watch and wait" approach, exhibit similar overall survival. Radiation treatment is often used to treat early-stage (I and II) follicular lymphoma. High-energy x-rays targeted at specific groups of involved lymph nodes can provide cure in some patients with limited disease. In addition to radiation, doctors may use chemotherapy to control this disease. Unlike many cancers, the follicular lymphomas tend to be very sensitive to both radiation and chemotherapy. There are many drugs or combinations of drugs that can be used to manage this disease, including those listed in Table 1.

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Table 1.

## Treatments Used in Follicular Lymphoma

- Cyclophosphamide, vincristine, prednisone (CVP)
- Cyclophosphamide, doxorubicin, vincristine, prednisone (CHOP)
- Fludarabine (+/- mitoxantrone, +/- cyclophosphamide)
- 2-chlorodeoxyadenosine (2-CdA)
- Chlorambucil (+/- prednisone)
- Rituximab (Rituxan)
- Iodine 131 tositumomab (Bexxar)
- Y90 ibritumomab tiuxetan (Zevalin)

While there are many treatments available, the data to date have not shown that any one treatment is better than any other. For this reason, patients should consider participating in a clinical trial as part of their therapy whenever possible. Many of the improvements in managing these diseases have been made using investigational therapies aiming to improve on the conventional treatments. For patients with relapsed follicular lymphoma, high dose chemotherapy and an autologous stem cell transplant or an allogeneic (or "mini"-allogeneic) transplant may be an option that provides a prolonged disease-free interval in some patients.

## Treatment Resistance

Although initial responses to treatment with chemotherapy are often quite good, over time lymphoma cells will learn how to become resistant to treatment, meaning the drugs no longer work. This is called refractory lymphoma. In these cases, drugs like Iodine 131 tositumomab (Bexxar) or Y90 ibritumomab tiuxetan (Zevalin), which can target the tumor with a monoclonal antibody armed with a dose of radiation, have been found to be particularly useful. These drugs are approved for the treatment of follicular lymphoma that has relapsed after chemotherapy. Some

physicians are also currently testing this approach in newly diagnosed follicular lymphoma patients in combination with chemotherapy.

## Side Effects

Some chemotherapy drugs can damage healthy cells and cause side effects such as nausea and vomiting, reduced appetite, hair loss and mouth sores. Damage to healthy immune cells may also put lymphoma patients undergoing treatment at risk for infection. Doctors can prescribe medicines to offset these effects.

## Relapse or Recurrence

If lymphoma returns after a complete remission, it is called relapse or recurrence. Chemotherapy, monoclonal antibodies, and radiation may be used alone or in combination to treat relapsed follicular lymphoma. The duration of remission from the last chemotherapy, along with the symptoms produced by the cancer, will often influence what treatments your doctor may recommend. High dose chemotherapy and either autologous stem cell or allogeneic stem cell transplantation may also be an option in selected patients at the time of relapse. These are often the most common settings for patients to discuss new drugs and the availability of clinical trials for the management of their disease.

## Transformation

About half of all patients with follicular lymphoma will eventually develop a transformed lymphoma, often referred to as histologic transformation. These lymphomas are often more aggressive in their behavior and are usually treated with combination chemotherapy.