

Waldenström Macroglobulinemia

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).

Waldenström macroglobulinemia, which is an *indolent* (slow-growing) B-cell lymphoma, is a type of lymphoplasmacytic lymphoma. It is rare, representing only approximately one percent of all NHLs. There are about 3,000 new cases of Waldenström macroglobulinemia diagnosed each year in the United States. The disease usually affects older adults and is primarily found in the bone marrow, although lymph nodes and the spleen may be involved. Lymphoma cells in the bone marrow can outgrow the normal cells, making it difficult for the bone marrow to produce normal amounts of red and white blood cells. This can result in *anemia* (low levels of red blood cells), *neutropenia* (low levels of white blood cells called neutrophils), and *thrombocytopenia* (low levels of platelets).

Patients with Waldenström macroglobulinemia have a high level of a protein called immunoglobulin M (IgM) in their blood. High levels of IgM can cause *hyperviscosity* (thickening of the blood). Although some patients with hyperviscosity experience no symptoms, when present, symptoms may include bleeding (particularly of the nose and gums), headaches, dizziness, double vision, *fatigue* (extreme tiredness), night sweats, pain or numbness in the extremities, and increased size of the liver, spleen, and lymph nodes.

To diagnose Waldenström macroglobulinemia, blood tests are usually performed, as well as a bone marrow biopsy. During the biopsy, a needle is inserted into a bone (usually the pelvic bone), and a small sample of bone marrow is extracted for examination.

Treatment Options

Although Waldenström macroglobulinemia is an incurable disease, it is treatable, and many patients have a long-term response to treatment. For patients with stable disease and no symptoms, physicians may decide not to treat the disease right away, an approach referred to as *active surveillance* (also known as “watchful waiting” or “careful observation”). With this strategy, patients’ overall health and disease

are monitored through regular checkup visits and various evaluation procedures, such as laboratory and imaging tests. Active surveillance can last for many years for some patients. For patients who have symptoms, the type and severity of the symptoms, such as the degree of hyperviscosity and the patient’s age and overall health, help determine the type of treatment selected. Once treatment is deemed necessary, the choice of treatment is based on individual patient’s needs, as well as considerations for short-term and long-term side effects.

Some patients undergo a procedure called plasmapheresis to temporarily reverse or prevent the symptoms associated with hyperviscosity. This procedure involves removing the patient’s blood, passing it through a machine that removes the part of the blood containing the IgM antibody, and returning the remaining blood to the patient. Physicians often combine plasmapheresis with other more definitive treatments, such as chemotherapy.

In 2015, ibrutinib (Imbruvica) was the first therapy approved by the U.S. Food and Drug Administration (FDA) specifically for patients with Waldenström macroglobulinemia. There are many other drugs that can be used to manage this disease, alone and/or in various combinations, including the following:

- Bendamustine (Treanda)
- Bortezomib (Velcade)
- Carfilzomib (Kyprolis)
- Chlorambucil (Leukeran)
- CHOP (cyclophosphamide, doxorubicin, vincristine, prednisone)
- Cladribine (Leustatin)
- Cyclophosphamide (Cytoxan)
- Fludarabine (Fludara)
- Rituximab (Rituxan)

For patients whose disease *relapses* (returns after treatment) or becomes *refractory* (does not respond to treatment), secondary therapies may be successful in providing additional *remissions* (disappearance of signs and symptoms). Some of the previous therapies discussed can be used or reused depending on a patient’s age, length of remission, stem cell transplant eligibility, and previous toxicities encountered. Additional therapies to treat relapsed/refractory Waldenström macroglobulinemia include:

- Everolimus (Afinitor)
- Ofatumumab (Arzerra) for patients who are intolerant to rituximab (Rituxan)
- High-dose chemotherapy followed by an *autologous* (patients receive their own stem cells) or *allogeneic* (patients receive stem cells from a donor) stem cell transplant in select patients

Treatments Under Investigation

Several promising new drugs and drug combinations are being studied in clinical trials for the treatment of patients with Waldenström macroglobulinemia (some for relapsed/refractory disease), including:

- Acalabrutinib (Calquence)
- Ixazomib (Ninlaro)
- BGB-3111
- Ulocuplumab
- Daratumumab (Darzalex)
- Venetoclax (Venclexta)

Chimeric antigen receptor (CAR) T-cell therapy targeting CD19 is another promising therapy for patients with Waldenström macroglobulinemia. In this technique, a patient's own T cells are removed and genetically reprogrammed to attack lymphoma cells. These clinical trials are in various phases of development. 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 the Lymphoma Research Foundation (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, 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

Patients with lymphoma 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, and positron emission tomography [PET] scans) 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 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) and the *Lymphoma Care Plan* (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 Waldenström macroglobulinemia, 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 Waldenström macroglobulinemia, including our award-winning mobile app. LRF also provides many educational activities, from in-person meetings to teleconferences and webcasts for people with Waldenström macroglobulinemia, as well as patient guides and e-Updates that provide the latest disease-specific news and treatment options. For more information about any of these resources, visit our website lymphoma.org, or contact the LRF Helpline at (800) 500-9976 or helpline@lymphoma.org.

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