

Understanding Waldenström Macroglobulinemia Lymphoma

Waldenström macroglobulinemia, which is an *indolent* (slow-growing) B-cell lymphoma, is a type of lymphoplasmacytic lymphoma. It is rare, representing approximately one percent of all non-Hodgkin lymphomas (NHLs).

There are about 5,000 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 normal cells, making it difficult for the bone marrow to produce normal amounts of red and white blood cells and platelets. 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* (observation with no treatment [drug therapy, radiation therapy, or stem cell transplantation] given). With this strategy, patients' overall health and disease are monitored through regular checkups and 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 an 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. The combination of ibrutinib and rituximab (Rituxan) was recently approved by the FDA. 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) CVP (cyclophosphamide, vincristine, prednisone)
- CVP (cyclophosphamide, vincristine, prednisone)
- Cyclophosphamide (Cytoxan)
- Fludarabine (Fludara)
- Ixazomib (Ninlaro)
- Rituximab (Rituxan)

For patients whose disease *relapses* (disease 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 (self) or allogeneic (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:

- 19(T2)28z1XX (Chimeric antigen receptor [CAR] T-cell therapy targeting CD19)
- Acalabrutinib (Calquence)
- Daratumumab (Darzalex)
- Tirabrutinib (Velexbro)
- Ulocuplumab
- Venetoclax (Venclexta)
- Zanubrutinib (Brukinsa)

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 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.

Contact LRF:
Helpline: (800) 500-9976
Email: helpline@lymphoma.org
www.lymphoma.org

Medical reviewers:
Jorge J. Castillo, MD
Dana-Farber Cancer Institute
M. Lia Palomba, MD
Memorial Sloan Kettering Cancer Center

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-on-one peer support programs, such as LRF's *Lymphoma Support Network*, connect patients and caregivers with volunteers who have experience with Waldenström macroglobulinemia 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 Waldenström macroglobulinemia, including our award-winning mobile app. LRF also provides many educational activities, from in-person meetings to webinars, 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.

Contact LRF:

Helpline: (800) 500-9976

Email: helpline@lymphoma.org

www.lymphoma.org

Medical reviewers:

Jorge J. Castillo, MD

Dana-Farber Cancer Institute

M. Lia Palomba, MD

Memorial Sloan Kettering Cancer Center

Supported through grants from:

 Genentech

 Biogen

 Bristol Myers Squibb

 pharmacyclics

The *Understanding Lymphoma* series is published by the Lymphoma Research Foundation (LRF) for the purpose of informing and educating readers. Facts and statistics were obtained using published information, including data from the Surveillance, Epidemiology, and End Results (SEER) Program. Because each person's body and response to treatment is different, no individual should self-diagnose or embark upon any course of medical treatment without first consulting with his or her physician. The medical reviewer, the medical reviewer's institution, and LRF are not responsible for the medical care or treatment of any individual.

© 2020 Lymphoma Research Foundation

Last updated 2020