Waldenstrom's Macroglobulinemia

Essential Information: A Patient's Guide

IWMF
International Waldenstrom's Macroglobulinemia Foundation

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Medical Disclaimer: The information presented here is intended for educational purposes only. It is not meant to be a substitute for professional medical advice. Patients should use the information provided in full consultation with, and under the care of a physician with experience in the treatment of WM. We discourage the use by a patient of any information contained herein without disclosure to his or her medical specialist.

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What is Waldenstrom's macroglobulinemia (WM)?

WM is a type of blood cancer where too much of a specific abnormal protein – an antibody (or immunoglobulin) called IgM – is produced. IgM is the largest of all the antibodies, called a macroglobulin. Generally, IgM is a "first responder" to infections. The abnormal IgM protein is normally not present in healthy people and is also called an M-protein or paraprotein.

In the case of WM, the abnormal WM cells do not undergo programmed cell death. Instead, they accumulate in the bone marrow. This can crowd out normal bone marrow cells that make new red blood cells, leading to anemia, and crowd out production of other cells that protect us from infection.

These abnormal WM cells can also grow outside the bone marrow and cause enlargement of the lymph nodes and spleen, or proliferate in the lung space, brain, or spine.

The WM cells and the excess IgM can damage cells and organs in the body causing symptoms, such as fatigue, numbness, tingling, and weakness.

The excess IgM also circulates in the blood. Because of IgM's large size, the blood can become very thick, a condition known as hyperviscosity. This can lead to blood vessels bursting, causing bleeding in the retina or brain. IgM can also deposit in organs like the kidney and affect its function.

Some patients with WM can have symptoms that are directly related to the IgM protein itself such as amyloidosis, cryoglobulinemia, cold agglutinin hemolytic anemia, and demyelinating peripheral neuropathy. These are rare. More information about these complications can be found on the IWMF website: **iwmf.com.**

WM is a rare, currently incurable, but treatable blood cancer.

WM is usually an indolent or slow-growing cancer and many patients do not require treatment, only periodic blood tests. Most people with WM requiring treatment have time to consider their treatment options.

How rare is WM? What is the incidence of WM?

There are about 1,500-3,000 new cases of WM per year in the US and 1,500-3,000 per year in Europe. Overall, WM comprises only 1-2% of all blood cancers.

This rarity means that most community oncologists see few, if any, WM cases in their career.

How is WM diagnosed?

In addition to blood tests, a bone marrow biopsy is essential for diagnosis.

About 90-95% of people with WM have the same genetic mutation in a gene that encodes a protein called MYD88, while 30-40% have a genetic mutation in the CXCR4 gene. Some CXCR4 mutations affect the effectiveness of certain treatments.

Why did I get WM? Will my kids get it?

The cause of WM is unknown. However, the genetic mutations associated with WM (MYD88 and CXCR4) are acquired during your lifetime and are not passed down from your parents to you, or from you to your children.

Up to 25% of people with WM do have a first-degree (parent, sibling, or child) or second-degree relative (grandparent, aunt, uncle, cousin) with WM or another B-cell lymphoma. A small number

of WM families exist where both parents and children, as well as siblings have WM.

In cases of "familial" WM, a reasonable step would be to perform blood tests to check blood cell numbers and test for an abnormal protein by doing serum protein electrophoresis. Your primary care physician can consider ordering these blood tests for offspring who are 40 years of age or older, given the late onset of WM.

WM usually occurs in stages. Will I go through all the stages?

It often starts with a diagnosis of MGUS (monoclonal gammopathy of undetermined significance) which, most commonly, is a precursor to WM. From there, some people progress to asymptomatic (or smoldering) WM. It is only when someone progresses to symptomatic WM that treatment is needed.

Not everyone progresses through these stages. In fact, most patients with MGUS do not progress to symptomatic WM. One could remain in the MGUS or the asymptomatic stage forever.

When do I need treatment?

Usually, treatment is needed when a person has symptoms related to either low blood counts and high tumor load – like fatigue or bleeding – or when elevated IgM levels cause symptomatic hyperviscosity, or damage cells or organs.

The course of WM can vary significantly from person to person. For example, some people are symptomatic with a low level of IgM while others do fine with a high level. Therefore, physicians generally treat people based on their symptoms. Only when IgM levels are becoming very high, might your physician decide to start treatment to reduce the risk of developing hyperviscosity.

Should I get a second opinion?

Since WM is a rare disease, it's recommended that you try to get a second opinion from a physician listed in the IWMF International Physician's Directory. Discuss getting a second opinion with your medical team.

What are my treatment options?

The good news is these days there are many treatment options. In the past there were only a few, often with significant side effects.

Treatment roughly falls into two categories: Oral medication(s) that you may take indefinitely, or an infusion treatment you take for a limited time. Your medical team will help you decide the best option for you.

Rituximab is a medication used to treat many blood cancers, including WM. Unfortunately, it sometimes causes a short-term rise in IgM levels – called an IgM flare – that could be dangerous. Some people require a medical procedure called plasmapheresis to reduce their IgM level on a short-term basis before starting therapy with rituximab. Alternatively, rituximab may be started later in the treatment regimen.

Make sure you tell your medical team about any side effects that you experience following treatment. There are often strategies that can be employed to reduce their impact.

What if my WM comes back?

WM may come back or progress after an initial treatment, despite a long period of remission after chemotherapy treatment or being on continuous therapy. If the initial treatment was successful for several years, your doctor may repeat it or recommend a new treatment. In many patients, direct treatment is not needed immediately because the

relapse is asymptomatic, and the patient can be followed with regular controls. Discuss options with your medical team.

How long am I going to live?

The life span of people with WM has increased dramatically in recent years. In the past, many patients were told they had 3-5 years to live after diagnosis.

It is now much longer, with some WM thought leaders saying 15-20 years on average from the date of diagnosis. In fact, many patients' cause of death is unrelated to their WM. What's most important is that the time frame has increased dramatically and is continuing to increase with newer, safer, and more effective drugs.

International Waldenstrom's Macroglobulinemia Foundation

Website: **iwmf.com**
Email: **info@iwmf.com**
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The IWMF, the only international organization dedicated solely to Waldenstrom's macroglobulinemia, is a patient-founded and patient-driven nonprofit with a simple but compelling vision and mission.

VISION: A world without Waldenstrom's macroglobulinemia.

MISSION: Support and educate everyone affected by Waldenstrom's macroglobulinemia to improve patient outcomes while advancing the search for a cure.

The IWMF is committed to creating a world without WM by finding a cure. Since 1999, the IWMF has invested over $23 million in WM research projects throughout the world. Thanks to this research, WM patients are living longer and have better treatment options that can lead to longer-lasting remissions with fewer side effects.

Visit the IWMF website to:

- Download a free Newly Diagnosed Info Pak.
- Learn about WM and download free publications available in multiple languages.
- Find curated resources to help support your mental, physical, and financial health.
- Join a local IWMF Support Group or IWMF International Affiliate.
- Refer to the IWMF Directory of Physicians available for consultations or second opinions.
- Subscribe to the IWMF Torch, our free quarterly newsletter.
- Participate in the annual IWMF Educational Forum or our online webinars.
- Join IWMF Connect, an online community offering a wide variety of moderated WM-related email discussions, or the IWMF Facebook Discussion Group.
- Find contact information for our partner organizations.

The IWMF relies on donor contributions to fulfill its mission, and we welcome your support. You can contribute to the organization by visiting our website or by mailing a check to:

International Waldenstrom's Macroglobulinemia Foundation
1449 S Michigan Ave Ste 13329
Chicago, IL 60605

CancerCare

cancercare.org

Phone: 800 813 HOPE (4673)

Founded in 1944, CancerCare is the leading national organization providing free, professional support services and information to help people manage the emotional, practical and financial challenges of cancer. Our comprehensive services include case management, counseling and support groups over the phone, online and in-person, educational workshops, publications and financial and co-payment assistance. All CancerCare services are provided by master's-prepared oncology social workers and world-leading cancer experts.

Cancer Support Community (CSC)

CancerSupportCommunity.org

Phone: 888-793-9355

As the largest professionally led nonprofit network of cancer support worldwide, the Cancer Support Community (CSC), including its Gilda's Club affiliates, is dedicated to ensuring that all people impacted by cancer are empowered by knowledge, strengthened by action, and sustained by community. CSC achieves its mission through three areas: direct service delivery, research, and advocacy. The organization's Institute for Excellence in Psychosocial Care includes an international network of affiliates that offer the highest quality social and emotional support for people impacted by cancer, as well as a community of support available online and over the phone. The Research and Training Institute conducts cutting-edge psychosocial, behavioral, and survivorship research. CSC furthers its focus on patient advocacy through its Cancer Policy Institute, informing public policy in Washington, D.C. and across the nation.

Leukemia & Lymphoma Society® (LLS)

lls.org

Phone: 800-955-4572

The Leukemia & Lymphoma Society® (LLS) is the global leader in the fight against blood cancer. The LLS mission: Cure leukemia, lymphoma, Hodgkin's disease and myeloma, and improve the quality of life of patients and their families. LLS funds lifesaving blood cancer research around the world, provides free information and support services, and is the voice for all blood cancer patients seeking access to quality, affordable, coordinated care.

Founded in 1949 and headquartered in Rye Brook, NY, LLS has regions throughout the United States and Canada. To learn more, visit **lls.org**. Patients should contact the Information Resource Center at (800) 955-4572, Monday through Friday, 9 a.m. to 9 p.m. ET.

For additional information visit **lls.org/lls-newsnetwork.**

Lymphoma Coalition

lymphomacoalition.org

Lymphoma Coalition is a worldwide network of patient organisations that support those affected by lymphoma. LC acts as a central hub for reliable and current information, as well as advocating for equitable care globally. Its mission is to enable global impact by fostering a lymphoma ecosystem that ensures local change and evidence-based action. Today, there are more than 80 member organisations from over 50 countries.

Lymphoma Research Foundation (LRF)

lymphoma.org

LRF Helpline: 800-500-9976

The Lymphoma Research Foundation (LRF) is the nation's largest non-profit organization devoted exclusively to funding lymphoma research and supporting the lymphoma community through evidence-based education, support services, and resources.

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