IWMF Vision Statement
A world without WM (Waldenstrom's macroglobulinemia).

IWMF Mission Statement
Support and educate everyone affected by Waldenstrom's macroglobulinemia (WM) while advancing the search for a cure.

Published by the International Waldenstrom's Macroglobulinemia Foundation (IWMF)

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Waldenstrom's Macroglobulinemia

Glossary and Abbreviations

IWMF
International Waldenstrom's Macroglobulinemia Foundation

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The International Waldenstrom's Macroglobulinemia Foundation (IWMF) is a patient-founded and patient-led, nonprofit organization that is dedicated to a simple but compelling vision and mission:

Vision: A World Without WM (Waldenstrom's macroglobulinemia).
Mission: Support and educate everyone affected by Waldenstrom's macroglobulinemia (WM) while advancing the search for a cure.

To accomplish this vision, the IWMF offers WM patients, caregivers, family members, and friends six invaluable services:

- **Information** from our website and our **publications** written in a patient-friendly way to promote understanding of our rare disease
- **Education** at our annual Educational Forum to help patients and caregivers learn about our disease from WM researchers and clinicians
- **On-going updates** about WM and the IWMF sent through our quarterly ***IWMF Torch*** magazine and our **NEWS releases**
- Peer **support** from others who've been where you are
- **Information** for medical professionals who may have limited experience with our rare disease
- **Research** directed to better treatments while we search for a cure

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Preface

This glossary is designed to help patients with Waldenstrom's macroglobulinemia to learn and understand pertinent medical terms that relate to our disease. These terms are no doubt unfamiliar to the majority of patients. However, for those who wish to build their medical vocabulary to better understand medical publications, we hope this will be a helpful guide.

Medical terminology is expanding rapidly in today's world, and from time to time this Glossary will be updated and re-published.

The IWMF community has been extremely fortunate to have had Guy Sherwood, MD, CCFP, ABHM, Sue Herms, Pete DeNardis, and Bret Blakeslee develop the first editions of this Glossary and Abbreviations booklet. More recently, Sue Herms, Glenn Cantor, and Linda Nelson have diligently researched medical terms related to Waldenstrom's macroglobulinemia and patiently developed this current aid.

Fall 2020

GLOSSARY and Abbreviations

Acalabrutinib (Calquence): An oral drug that targets and inhibits Bruton's tyrosine kinase (BTK), an enzyme which is important in the development and activation of B-cells and is over-expressed in WM. It is in the same drug class as ibrutinib (Imbruvica) but is a second-generation drug that is more selective for BTK and reportedly has fewer side effects. Acalabrutinib has been approved by the FDA for mantle cell lymphoma and has been studied in clinical trials for WM.

Adverse events: Any undesired medical occurrence associated with the use of a drug in humans. For example, an adverse event might be development of skin rash in a patient taking a drug for WM. Adverse events are not necessarily caused by the drug. For example, a patient taking a drug may just happen to develop a rash for other reasons. In clinical trials, all adverse events are recorded and reported. In that way, the adverse events can be compared between patients taking different drugs. Adverse events are categorized by grade. Grade 1 adverse events are mild, Grade 2 moderate, Grade 3 severe, Grade 4 life-threatening or disabling, and Grade 5 results in death.

Albumin: The main protein found in blood plasma. It is produced in the liver and is important in regulating blood volume and carrying such molecules as hormones, fatty acids, calcium, and certain drugs.

Alkylating agent: A chemotherapy agent, such as chlorambucil (Leukeran), cyclophosphamide (Cytoxan), or bendamustine (Treanda or Bendeka), which blocks cell division by attaching to and altering DNA. Alkylating agents are used to treat some cancers, including WM.

Amino Acid: The basic chemical building block of proteins. Proteins are composed of strings of amino acids. Changes in DNA (see "Mutation") can sometimes cause a protein to have different amino acids. In some cases, a switch in amino acids can cause a protein to become excessively active and lead to cancerous cell growth and proliferation (see "MYD88 L265P"). Amino acids are often abbreviated with single letters (such as L for Leucine or P for Proline).

Amyloidosis: A group of conditions characterized by the accumulation of insoluble fine protein fibers (amyloid) in various organs and tissues of the body so that their function is compromised. The protein accumulation can be local or systemic. Amyloidosis in WM is usually caused by fragments of light chains from the monoclonal IgM molecule and affects predominantly the kidneys and heart.

Anemia: A condition in which the number of red cells or the amount of hemoglobin in the red blood cells is abnormally low. Signs and symptoms include fatigue, feeling cold, light-headedness, pale skin, low energy level, shortness of breath. There are numerous causes for anemia, among them blood loss, hereditary conditions, iron deficiency, vitamin deficiency, bone marrow problems, certain chronic conditions, toxins, red blood cell hemolysis, and enlarged spleen. Anemia is the most common indication for treatment in WM patients.

Anoikis: Death of tumor cells when they are dislodged into the bloodstream from their preferred environment in the bone marrow. WM drugs directed at CXCR4 such as mavorixafor or ulocuplumab may act by this mechanism.

Antibody: Also called immunoglobulin, this Y-shaped protein is produced by B-cells and plasma cells in response to a foreign substance (antigen). The most common antigens that are harmful to the body are

bacteria, viruses, and parasites. Each antibody binds only to one specific antigen, and its purpose is to help neutralize the antigen or enlist other immune cells or complement proteins to attack the antigen. Antibodies are divided into five classes (IgA, IgD, IgE, IgG, and IgM) based on structure and activity. For a description of each class, see **Immunoglobulin**.

Antibody-drug conjugate: A cancer drug in which the drug itself is attached to an antibody directed to a molecule on the surface of cancer cells. After the antibody binds to the cancer cell, the drug is released, either inside or in the close vicinity of the cancer cell. This approach enables localized delivery of drugs that would be toxic if they were distributed throughout the body. A drug currently in early trials for WM patients, CLR 131, is like antibody-drug conjugates, although it uses a phospholipid ether to target to the WM cells instead of an antibody. The active drug of CLR 131 is a radioactive isotype of iodine, called iodine-131.

Antigen: Any molecule that reacts with antibody and specific receptors on T- and B-cells, which are cells of the immune system, to provoke an immune response.

Antigen-antibody complex: A compound formed by the attachment of an antibody to an antigen; most such complexes are harmless, but some may cause tissue damage by activation of the immune system or by inciting an inflammatory reaction.

Apoptosis: A normal process of programmed cell death. Defective apoptosis helps cancer cells evade death and has been implicated in many types of cancer.

ARQ-531: An investigational Bruton's tyrosine kinase (BTK) inhibitor that binds differently to BTK than ibrutinib (Imbruvica), in theory preventing resistance caused by the BTK-C481S mutation.

AS-PCR (allele specific-polymerase chain reaction): A genetic technique that uses polymerase chain reaction testing to detect whether there is a variation in one gene, called an allele, located at a given site on a chromosome. AS-PCR is recommended to detect the MYD88 mutation common in WM patients. For a description of the technique, see **Polymerase chain reaction (PCR)**.

Asymptomatic: Without symptoms.

Atrial fibrillation (Afib): An irregular and often rapid heart rate that can increase the risk of strokes, heart failure, and other heart-related complications. During atrial fibrillation, the heart's two upper chambers (the atria) beat irregularly and out of coordination with the two lower chambers (the ventricles). Symptoms often include heart palpitations, shortness of breath, and weakness. Atrial fibrillation is a side effect associated with the use of BTK inhibitors such as ibrutinib (Imbruvica).

Autoantibody: An antibody directed against a self-antigen, i.e., against a normal tissue component.

Autoimmune: Relating to a disease caused by autoantibodies. Examples include rheumatoid arthritis, lupus, multiple sclerosis, and psoriasis.

B cells/B lymphocyte (sometimes hyphenated, B-cells/B-lymphocyte): A white blood cell formed in the bone marrow that is the precursor of a plasma cell. The B-cell carries antibodies (immunoglobulins) on its surface.

Basophil: A white blood cell that is involved in triggering allergic reactions.

BCL-2 (B-cell lymphoma 2): One protein in a family of proteins that regulate apoptosis (programmed cell death). BCL-2 is an anti-apoptotic protein, which enables cells to avoid regulatory signals that cause them to die. Over-expression of BCL-2 in several cancers allows the cancer cells to survive; drugs that inhibit BCL-2 cause the over-expressing cancer cells to die. BCL-2 is the target of the cancer drug venetoclax (Venclexta or Venclyxto), which is FDA-approved for chronic lymphocytic leukemia and is being studied in WM patients.

BDR: An abbreviation for a treatment combination consisting of bortezomib (Velcade), dexamethasone (Decadron), and rituximab (Rituxan). It is used for multiple myeloma and certain types of lymphoma, including WM.

Bence Jones protein: The immunoglobulin light chain protein detected in the urine of patients with multiple myeloma or WM.

Bendamustine (Treanda or Bendeka): A drug that is used to treat slow-growing B-cell non-Hodgkin's lymphomas (NHL) such as WM. Bendamustine attaches to and alters the DNA in cancer cells, thereby blocking cell division. It is primarily a type of alkylating agent. Treanda and Bendeka are slightly different formulations of bendamustine.

Benda-R: Sometimes referred to as B-R. An abbreviation for a chemoimmunotherapy treatment combination consisting of bendamustine (Treanda or Bendeka) and rituximab (Rituxan). It is used for WM.

Beta-2 microglobulin (B2M): A protein found in all cells with a nucleus; levels of B2M are elevated in multiple myeloma and WM.

Bing-Neel syndrome (BNS): A rare condition that involves infiltration of the central nervous system (brain and spinal cord) by WM cells, causing a variety of neurological symptoms.

Biosimilar: An almost identical copy of an original biologic drug, such as a monoclonal antibody, which can be manufactured when the original biologic drug's patent has expired. If a biosimilar drug is approved by a regulatory agency, it is considered as safe and effective as the original drug that was copied. Biosimilars for rituximab (Rituxan) that have been approved in Europe, the US, and/or Canada include Truxima, Rixathon, and Ruxience, with additional biosimilars under consideration.

Bone marrow: The **s**pongy tissue occupying the hollow central cavity of bones that is the site of hematopoiesis (blood cell formation). In adults, the marrow is most active in the spine, ribs, breastbone, hips, shoulders, and skull.

Bone marrow aspiration: The removal by needle of fluid and cells from the bone marrow to look for abnormalities of the bone marrow. The sample is usually taken from the back of the hip bone.

Bone marrow biopsy (BMB): The removal of solid tissue from the bone marrow to look for abnormalities of the bone marrow. The sample is usually taken from the back of the hip bone. Typically, an aspiration and a biopsy are performed together.

Bone marrow microenvironment: The immediate neighborhood of the blood cells in the bone marrow; it is composed of support cells (see “Stroma”) and the signaling proteins they produce to facilitate the survival, differentiation, and proliferation of different kinds of blood cells.

Bone marrow transplant: A bone marrow transplant (also referred to as a bone marrow stem cell transplant) is a procedure to replace damaged or diseased bone marrow with healthy bone marrow stem cells. These stem cells can be collected directly from the bone marrow, or more commonly, from the bloodstream by apheresis (a process similar to plasmapheresis). There are three types of bone marrow transplants:

> **Allogeneic bone marrow transplant ("allo" means "other"):** A procedure that occurs when stem cells are removed from another person, called a donor, and given to the patient after the patient has received high-dose chemotherapy and/or radiation to destroy his own bone marrow. These donated stem cells re-establish the bone marrow. The donor must have the same or similar genetic makeup as the patient, so that he or she is a "match." Special blood tests are done to determine if a donor is a good match, and a brother or sister is most likely to be a good match. However, sometimes parents, children, and other relatives may be good matches. Donors who are not related to the patient but who have closely matching marrow may be found through national bone marrow registries.
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> **Autologous bone marrow transplant ("auto" means "self"):** A procedure that occurs when stem cells are removed from the patient before he or she receives high-dose chemotherapy and/or radiation treatment to destroy the bone marrow. After the chemotherapy and/or radiation treatments are completed, the patient’s own stem cells that were collected earlier are given back in order to re-establish the bone marrow.
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> **Reduced-intensity conditioning allogeneic bone marrow transplant:** A type of allogeneic transplant that uses smaller doses of chemotherapy and/or radiation for patients who may not be able to tolerate a full-intensity allogeneic transplant, for example, older patients or those with multiple medical issues. Sometimes referred to as a “mini-allo” transplant.

Bortezomib (Velcade): A drug used for the treatment of multiple myeloma and certain types of lymphoma, including WM. It is in the drug class called proteasome inhibitors. It can be administered intravenously or subcutaneously.

Bruton’s tyrosine kinase (BTK): An enzyme important in the development and activation of B-cells; it is often excessively activated in patients with WM and is targeted by inhibitors of BTK such as ibrutinib (Imbruvica), acalabrutinib (Calquence), and zanubrutinib (Brukinsa).

CaRD: An abbreviation for a treatment combination consisting of carfilzomib (Kyprolis), rituximab (Rituxan), and dexamethasone (Decadron). It is used for multiple myeloma and WM.

Carfilzomib (Kyprolis): A newer member in the family of drugs called proteasome inhibitors that are used for the treatment of multiple myeloma and certain lymphomas, including WM.

CAR T-cell therapy: A promising new type of immunotherapy that is being used with some success against certain solid tumors such as melanoma and blood cancers such as leukemia, lymphoma, and multiple myeloma. T-cells are collected from a patient via apheresis (a process similar to

plasmapheresis). They are sent to a laboratory where they are genetically engineered to produce chimeric antigen receptors (CARs) on their surface. The CARs are proteins that allow the T-cells to recognize an antigen on the patient's tumor cells. The engineered T-cells are known as CAR T-cells. The number of CAR T-cells is expanded by growing them in the laboratory in the millions, following which they are re-introduced into the patient's bloodstream, usually after a brief course of chemotherapy. The CARs on the T-cell surface recognize tumor cells in the patient's body and attack them; they may remain in the body long after the infusion has been completed and can guard against cancer recurrence, frequently resulting in long-term remissions.

Cell line: A culture of continuously growing cells used in laboratory research. Cell lines are originally derived from patients' cancer cells. Normally, cancer cells taken directly from patients (called "primary cells") do not grow well in laboratory conditions; cell lines are derived from cancer cells that have changed in ways that enable them to grow in the laboratory. WM cell lines are useful because they allow researchers to efficiently test new drugs. However, because cell lines differ from cancer cells in patients' bodies, results from cell lines do not necessarily predict results of drugs in patients.

Centipoise (cp): A unit of viscosity, used to measure if serum is excessively thick or sticky. Water has a viscosity of 1.0 centipoise (cp). Normal serum viscosity is 1.4 to 1.8 cp. In WM patients, excessive IgM can cause high serum viscosity. High serum viscosity in WM patients, such as more than 4 cp, can cause many disorders, including damage to the retina (the back of the eye).

Checkpoint Inhibitor: See "Immune Checkpoint Inhibitor"

Chemoimmunotherapy: The use of chemotherapy combined with immunotherapy. Chemotherapy uses drugs to kill or slow the growth of cancer cells; immunotherapy uses treatments such as monoclonal antibodies to recognize, stimulate, or assist the ability of one's own immune system to fight cancer.

Chemotherapy: Often just called chemo, this is a treatment with one or more of a specific group of anti-cancer drugs that are cytotoxic and damage or kill cells that divide rapidly, one of the main properties of most cancer cells. They can also harm normal cells that divide rapidly, including cells of the bone marrow, digestive tract, and hair follicles. They are frequently given in combination with other drugs.

Chlorambucil (Leukeran): A drug used to treat several types of leukemia and lymphoma, including WM. It blocks cell growth by attaching to and altering the cell's DNA and is a type of alkylating agent.

CHOP: An abbreviation for a chemotherapy combination that is used to treat lymphoma. It includes the drugs Cytoxan, hydroxydoxorubicin (also known as Doxorubicin or Adriamycin), Oncovin (also known as vincristine), and prednisone or prednisolone.

Chromosome: A tightly coiled rod-shaped structure inside the nucleus of the cell that contains DNA. Humans typically have 46 chromosomes in most of their cells, arranged in 23 pairs.

Chronic lymphocytic leukemia (CLL): A type of blood cancer in which the bone marrow produces too many B-lymphocytes. It usually occurs in older people, is typically indolent, and causes the lymph nodes to become enlarged. Because CLL and WM share some characteristics, several drugs used to treat CLL can also be used to treat WM.

Clinical trial: A type of research study that tests how well new medical approaches work in people, including new methods of screening, prevention, diagnosis, or treatment of a disease. Clinical trials can vary in size and cost and can involve a single research center or multiple centers, in one country or in multiple countries. Clinical trials for new treatments or devices are conducted to determine their safety and effectiveness, and they are carried out in a series of steps called phases:

> **Phase 1:** This first stage of a clinical trial must assess the safety of the study treatment. Only a small number of people, usually 20 to 80, participate at this stage. Phase 1 studies aim to find a safe dosing range, decide how the treatment should be given and see how the treatment affects the human body. Some information may be gathered on the effectiveness of the treatment.
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> **Phase 2:** As soon as the initial safety of the treatment is ensured in Phase 1, Phase 2 trials are initiated. At this stage, a slightly larger group of individuals are enrolled to receive the study treatment. Phase 2 trials seek to determine if the treatment has an effect on a certain disease and continue to monitor how the treatment affects the individual.
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> **Phase 3:** As opposed to earlier stages, Phase 3 trials involve a very large group of participants and are conducted in more than one clinical setting. Multicenter trials include more participants and a wider range of participant groups from different geographic locations, which enhances the ability to compare results among centers. This phase assesses the effectiveness of the study treatment by comparing the new treatment (or new use of a treatment) with the current standard of treatment (see "Head-to-Head"). Typically, after a successful Phase 3 trial, a treatment is eligible for review by the FDA to be marketed to the public.
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> **Phase 4:** This phase of "post-marketing surveillance" begins after the treatment is made available for the general public. These trials can be carried out for many reasons, such as to find a new market for the treatment, to study its interactions with any other treatments, and to further assess the long-term safety and effectiveness of the treatment.

Clone: One or more of a group of genetically identical cells derived by reproduction from a single parent cell.

CLR 131: A drug currently in clinical trials for WM, as well as other malignancies such as multiple myeloma. The drug, a radioactive isotype of iodine, is targeted to the tumor cells by a phospholipid ether. See "Antibody-drug Conjugate."

Cluster of differentiation (CD): A system used for the identification and investigation of surface molecules present on almost any kind of cell of the body, providing a way to help identify the type of cell. The surface molecules can also be used as a target for monoclonal antibody therapy. A few of interest to WM are described below:

> **CD19:** Cluster of differentiation B-lymphocyte antigen CD19 is present on B-cells from their earliest development but is lost upon maturation to plasma cells. Certain treatments for leukemia and lymphoma target CD19.
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> **CD20:** Cluster of differentiation B-lymphocyte antigen CD20 is present on the surface of B-cells from early in their development but is lost upon maturation to plasma cells. CD20 is the target of

the monoclonal antibodies rituximab (Rituxan), ofatumumab (Arzerra), and obinutuzumab (Gazyva), which are all active agents in the treatment of B-cell lymphomas such as WM.

CD34: Cluster of differentiation hematopoietic progenitor cell antigen CD34 is present on stem cells in the bone marrow. It is a useful marker for determining the success of stem cell collection in preparation for a bone marrow transplant.

CD38: Cluster of differentiation 38 is expressed on plasma cells. Certain monoclonal antibody treatments for multiple myeloma target CD38 and are being tested in clinical trials for WM.

Cold agglutinin disease (CAD): An autoimmune condition caused by one's own antibodies that bind to red blood cells at the cooler temperatures reached in the capillaries of the skin and subcutaneous tissues. This can cause red blood cell destruction (hemolysis), possibly leading to anemia. The condition can be seen in WM patients.

Colony-stimulating factor: One of a group of cytokines which control the differentiation of stem cells into mature blood cells, usually red or white blood cells. They can be manufactured and administered to patients undergoing chemotherapy to help stimulate their bone marrow's production of red or white blood cells if abnormally low blood cell counts occur. Common examples include Neupogen, Neulasta, Procrit, Epogen, and Aranesp.

Combination therapy: Treatment that uses more than one drug.

Comorbidity: Having two or more diseases at the same time, usually chronic diseases such as diabetes or cardiovascular diseases.

Complement: A system of small proteins, synthesized primarily in the liver and circulating in the blood that, when stimulated, are involved in the inflammatory process and aid in neutralizing pathogens. Complement is part of the innate immune system.

Complete blood count (CBC): A complete blood count is a test panel requested by a doctor or other medical professional that gives information about the cells in a patient's blood. The cells that circulate in the bloodstream are generally divided into three types: white blood cells (leukocytes), red blood cells (erythrocytes), and platelets (thrombocytes). Abnormally high or low counts may indicate the presence of many forms of disease, and hence blood counts are among the most commonly performed blood tests in medicine, as they can provide an overview of a patient's general health status. The components of a CBC include the following:

Platelet count and mean platelet volume: A platelet (Plt) count provides information about how many platelets are in a given amount of blood, and mean platelet volume (MPV) provides information about their volume or size.

Red blood cell count, hemoglobin, and hematocrit: A red blood cell (RBC) count provides information about how many red blood cells are in a given amount of blood, as well as the amount of hemoglobin (Hgb or Hb) and the percentage of red blood cells (hematocrit or Hct) in the sample.

Red blood cell indices: These provide important information about the volume or size (MCV), hemoglobin weight (MCH), and hemoglobin percentage (MCHC) of the red cells. The red cell distribution width (RDW) is a quantitative measure of variation in the size of the red blood cells.

White blood cell count and differential: Also known as the leukocyte count, the white blood cell count (WBC) determines how many white blood cells are in a given amount of blood. The white blood cell differential is used to evaluate the distribution of the five major types of white blood cells in the blood: neutrophils, lymphocytes, monocytes, eosinophils, and basophils. Some laboratories combine neutrophils, eosinophils, and basophils into one category called granulocytes because these cells all have granules in their cytoplasm. A white blood cell count screens for a wide range of diseases and conditions; can help diagnose an infection or inflammatory process; can determine the presence of other diseases that affect white blood cell counts such as allergies, leukemia, lymphoma, or immune disorders; can monitor the progression of conditions such as those named above; and can monitor the bone marrow's response to various treatments.

Complete response (CR): In WM, a complete response following treatment is defined as the absence of serum monoclonal IgM by immunofixation; normal serum IgM level; complete resolution of enlarged lymph nodes and enlarged spleen if present at baseline; and normal bone marrow aspiration and biopsy. It must be confirmed by repeat testing.

Comprehensive metabolic panel (CMP): A panel of 14 or so blood tests that is an initial screening tool. Because it is often ordered as a routine part of an annual physical examination or check-up, over time the CMP provides an important baseline of a patient's basic physiology, including kidney function, liver function, and electrolyte and fluid balance. Any changes or abnormal results, and particularly, combinations of abnormal results, thus provide important initial data for diagnosis, in which case more specialized tests may be indicated. In addition to being used as part of routine physicals for healthy patients, the CMP may be administered to monitor the status of a patient with a chronic disease.

Constant region: The portion of an antibody that determines its class (IgA, IgD, IgE, IgG, or IgM) and binds to the cells and complement proteins of the immune system in order to elicit an immune response to an antigen.

Constitutional symptom: One of a group of symptoms that can affect many different parts of the body. Examples include weight loss, fevers, fatigue, chills, night sweats, and decreased appetite. Generally, they are very nonspecific, with a vast number of diseases and conditions as potential causes, thereby requiring further evaluation for any diagnosis. Sometimes referred to as B-cell symptoms because they are common in B-cell lymphomas.

Copanlisib (Aliqopa): An intravenous drug that targets and inhibits phosphoinositide 3-kinase (PI3K). It has been approved for the treatment of follicular lymphoma and has been used in clinical trials for WM.

COVID-19: A novel virus, also referred to as coronavirus or SARS-CoV-2, which is currently causing a worldwide epidemic, called a pandemic. It is primarily a respiratory virus, generally causing symptoms of cough, high fever, shortness of breath, fatigue, and loss of taste and smell. However, it also affects other body systems, including endothelial cells (the inner lining of blood vessels), the brain, kidneys, heart,

pancreas, and other organs. While the majority of cases result in mild symptoms, some progress to acute respiratory distress syndrome, multi-organ failure, septic shock, blood clots, and stroke.

CRISPR-Cas9: A technology that enables geneticists and medical researchers to edit parts of the genome by removing, adding, or altering sections of the DNA sequence.

Cryoglobulinemia (Cryo): A condition caused by abnormal antibody proteins that precipitate at cooler temperatures than normal body temperature. When this happens at the cooler temperatures reached in the capillaries of the skin and subcutaneous tissue, the precipitated antibodies can block the smaller blood vessels and/or deposit in the kidneys and other tissues, causing damage.

CT or CAT (computerized axial tomography) scan: An imaging procedure that uses narrow X-ray beams to examine a body section from different angles and produces a precise image of the area. It can be performed with or without contrast medium (X-ray dye).

CVP: An abbreviation for a chemotherapy combination used to treat some types of lymphoma. It includes the drugs cyclophosphamide (Cytoxan), vincristine (Oncovin), and prednisone or prednisolone.

CXCR4 (C-X-C chemokine receptor type 4): A chemical messenger that is important in the homing of stem cells to the bone marrow. Mutations in CXCR4 have recently been identified in approximately 35-40% of patients with WM and may impact clinical presentation and response to certain treatments, such as ibrutinib (Imbruvica). Inhibitors of CXCR4, such as ulocuplumab and mavorixafor, are currently under development and are being tested in WM patients.

Cyclophosphamide (Cytoxan): A drug used to treat many types of cancer; it alters the DNA in cells and blocks cell division. It is a type of alkylating agent.

Cytokine: The broad category of small proteins that are important in cell signaling. They are released by cells and affect the behavior of other cells.

Cytopenia: An **a**bnormally low number of blood cells. See **Anemia**, **Leukopenia**, **Neutropenia**, and **Thrombocytopenia**.

Cytotoxic: Toxic to cells.

Daratumumab (Darzalex): A drug that targets the CD38 antigen found on the surface of plasma cells. It is a type of monoclonal antibody therapy approved for multiple myeloma and is being tested in clinical trials for WM. It can be administered intravenously or subcutaneously.

Dexamethasone (Decadron): A synthetic corticosteroid similar to steroid hormones produced naturally in the adrenal gland. It suppresses the immune system and reduces inflammation. It can be used to treat a variety of conditions, including autoimmune diseases and certain cancers.

DLBCL (diffuse large B cell lymphoma): A form of lymphoma that is more aggressive than WM. Sometimes, WM cells transform (change) and the patient develops DLBCL. This requires different types of therapy.

DNA (deoxyribonucleic acid): A molecule composed of two chains that coil around each other to form a double helix carrying genetic instructions for the development, functioning, growth, and reproduction of all known organisms and many viruses.

DRC: An abbreviation for a chemoimmunotherapy treatment combination consisting of dexamethasone (Decadron), rituximab (Rituxan), and cyclophosphamide (Cytoxan). This combination is sometimes also referred to as RCD and is used for WM.

Duvelisib (Copiktra): An oral drug that targets and inhibits phosphoinositide 3-kinase (PI3K). It has been approved for the treatment of chronic lymphocytic leukemia and follicular lymphoma.

Efficacy: Effectiveness; the ability of a treatment to produce the desired result.

Eosinophil: A white blood cell that is involved in reactions against parasitic worms and in some allergic reactions.

Epigenetics: The study of structural changes that regulate how genes are expressed. Most cells in the body share the same DNA (called the genome). However, different cell types must use their DNA differently, so that one cell becomes a liver cell while another becomes a skin cell. This is accomplished by regulating how DNA is folded and compacted, resulting in some stretches of DNA being "open" or exposed while other stretches are "closed" and inaccessible. Epigenetic changes govern the appropriate development and fate of cell types throughout the body. Epigenetic abnormalities are common in cancer cells, resulting in inappropriate or dysregulated growth.

Epigenome: The complete set of chemical compounds that modify, or mark, the genome (DNA) in a way that tell it the DNA what to do, where to do it, and when to do it. The epigenome includes not only the chemicals that modify the genome but also exactly where in the genome these modifications are located. Cancer cells, including WM cells, can have altered epigenomes.

Epistaxis: Bleeding from the nose.

Erythrocyte (red blood cell/RBC): See **Red blood cell**.

Event free survival (EFS): The percentage of patients who remain free of complications after a treatment intended to prevent or delay such complications.

Everolimus (RAD001 or Afinitor): A drug that inhibits mammalian target of rapamycin (mTOR), which is a member of the phosphatidylinositol 3-kinase (PI3K) family of proteins and has been used for the treatment of relapsed WM.

Extramedullary disease: In the case of lymphoma, this refers to mass(es) of cancerous lymphoid cells outside of the bone marrow.

Flow cytometry: A process in which an instrument uses a laser beam to scatter light from cells as they pass through a liquid in the instrument's chamber; the laser beam light bounces off each cell, is picked up by detectors, and provides information about the cell's characteristics, such as size and inner structure. Flow cytometry can also use antibodies tagged with fluorescent stains that bind to specific antigens on the cell surfaces, such as CD antigens, to help identify the type of cells present.

Fludarabine (Fludara): A drug used to treat chronic lymphocytic leukemia (CLL) and non-Hodgkin's lymphomas, including WM. Fludarabine blocks cell division and is a type of nucleoside analog.

Follicular lymphoma (FL): The most common indolent B-cell non-Hodgkin's lymphoma, typically causing enlarged lymph nodes.

Free light chain (FLC): The light chain (kappa or lambda) of the immunoglobulin (antibody) molecule that is circulating in serum or urine in a free (unbound) state. Measurement of the serum level of FLCs is used as an aid in the diagnosis and monitoring of multiple myeloma and related disorders. The usefulness of this test in WM is not well defined.

Frontline therapy: The first treatment for a disease. Also called first-line (sometimes abbreviated 1L) or initial therapy.

Funduscopic exam: The examination of the back of the eye (fundus) with an ophthalmoscope; it allows a magnified evaluation of the blood vessels, nerves, and retina. This examination is especially important in WM patients at risk of developing hyperviscosity syndrome (a condition due to excessive blood thickness caused by high IgM).

Gene: A region of DNA on a chromosome that controls a hereditary trait in an individual.

Genome sequencing: Any method or technology for determining the order of DNA found in the genes of an individual. Specific methods include Sanger sequencing, next generation sequencing (NGS), whole exome sequencing (WES), and whole genome sequencing (WGS).

Genomics: The study of the complete set of DNA within a single cell of an organism.

Graft vs. host disease (GVHD): A complication that can occur following allogeneic stem cell transplant, in which the donor's immune cells see the recipient's cells as foreign and attack them, causing a variety of symptoms.

Granulocyte: A white blood cell that attacks and destroys bacteria. It has granules in its cytoplasm, hence the name, and includes neutrophils, eosinophils, and basophils. Normally, neutrophils are by far the most common granulocytes.

HCK (Hematopoietic cell kinase): A signaling molecule in the kinase class, located inside cells. Some investigators hypothesize that HCK activity is excessive in WM cells and are attempting to discover a drug to inhibit HCK.

Head-to-head: A clinical trial that is designed to compare two drugs. Usually, a head-to-head trial compares a new, investigational drug to the existing standard-of-care drug. To avoid bias, patients usually are randomly assigned to receive either the investigational drug or the standard-of-care drug. Groups are additionally sorted or "stratified" so that key parameters (such as age or severity of disease) are similar between the two groups.

Heavy chain: The large polypeptide subunit of an immunoglobulin molecule. There are five types of heavy chains in mammals: γ, δ, α, μ and ε that define the classes of immunoglobulins as IgG, IgD, IgA, IgM, and IgE, respectively.

Hematocrit (Hct): A measure of red blood cells as a percentage of whole blood.

Hematologist-oncologist: A doctor with special training in the diagnosis and treatment of blood diseases, especially blood cell cancers. This doctor is trained in hematology (the study of blood) and oncology (the study of cancer).

Hematopoiesis: The process of blood cell formation.

Hematopoietic stem cell (HSC): Residing in the bone marrow, this is the common ancestor to all the functional cells found in the blood. Stem cells represent less than 0.01% of bone marrow cells in adults and give rise to a population of precursor cells. These precursor cells in turn divide and differentiate further through several stages into mature cells responsible for specific tasks. The stem cells are also able to re-create themselves through self-renewal.

Hemoglobin (Hb or Hgb): The iron-containing oxygen-transport protein in red blood cells that carries oxygen from the lungs to the rest of the body where it releases oxygen to the cells for metabolism; it also collects the resultant carbon dioxide to bring it back to the lungs to be exhaled.

Hemolysis: The rupture or destruction of red blood cells.

Hepatosplenomegaly: Enlargement of both the liver (hepatomegaly) and the spleen (splenomegaly). Hepatosplenomegaly can occur as the result of infectious diseases and blood disorders.

Hepcidin: A protein that is a key regulator of the entry of iron into the circulation. During conditions in which the hepcidin level is abnormally high, serum iron falls due to iron trapping within macrophages and liver cells and decreased gut iron absorption. This typically leads to anemia due to an inadequate amount of serum iron being available for developing red blood cells. High hepcidin levels have been noted in WM patients.

Hyaluronidase: An enzyme added to some biological drugs, which are normally given as slow intravenous infusions, to enable more rapid subcutaneous injection. Hyaluronidase is an enzyme which temporarily degrades hyaluronic acid in the subcutaneous tissue, allowing injection of a larger volume of drug than would normally be possible. The drug is then slowly absorbed into the body. Rituximab is now available in combination with hyaluronidase for subcutaneous injection.

Hycela: The brand name of hyaluronidase (see “hyaluronidase”)

Hypertension: High blood pressure.

Hyperviscosity: Excessive blood thickness.

Hyperviscosity syndrome (HVS): A group of symptoms triggered by an increase in the viscosity of the blood. These include spontaneous bleeding from mucous membranes, visual disturbances, and neurologic symptoms ranging from headache, dizziness, and vertigo to seizures and coma.

Hypogammaglobulinemia: A type of immune deficiency characterized by a reduction in normal immunoglobulins (antibodies) such as IgA, IgG, or IgM. If warranted, it can be treated with infusions of intravenous immunoglobulin (IVIg).

Hypotension: Low blood pressure.

Ibrutinib (Imbruvica): An oral drug that targets and inhibits Bruton's tyrosine kinase (BTK), an enzyme which is important in the development and activation of B-cells and which is often over-activated in WM. It is the first, FDA-approved drug for the treatment of WM. Recently, the combination of ibrutinib with rituximab (Rituxan) was also approved for WM.

Idiotype vaccine: A cancer vaccine manufactured from antibodies directed against the unique part of each patient's cancer cells. The procedure typically consists of a monthly, subcutaneous injection of the vaccine; after 5 or 6 monthly doses, further boosts every 2-3 months are becoming increasingly popular and recommended. This type of treatment has been used to treat a type of B-cell lymphoma called follicular lymphoma and is being studied in WM. Note: Unlike vaccines for infectious diseases, cancer vaccines are not administered to the general population to prevent cancer; they are used to treat patients who are already diagnosed with cancer. This is not an "off-the-shelf" vaccine; it must be customized for each individual cancer patient.

Immune checkpoint inhibitor: A drug that overcomes some of a cancer cell's main defenses against an immune system attack. Immune checkpoints are specific molecular signals that turn down or deactivate an immune response when it is no longer necessary. Some cancer cells have exploited this normal body mechanism by expressing proteins that activate checkpoints on immune cells. This deactivates the immune cells, prevents them from attacking the cancer cells, and allows the cancer cells to go unharmed. Drugs called checkpoint inhibitors reactivate immune cells so that they can attack cancer cells. Examples of immune checkpoint inhibitors include nivolumab (Opdivo), pembrolizumab (Keytruda), and ipilimumab (Yervoy). See "PD-1" and "PD-L1."

Immune system: The system that protects an organism against a wide variety of injuries or infectious agents (pathogens), including viruses, bacteria, and parasites, and can distinguish them from the organism's own healthy tissue and processes. There are two major subsystems of the immune system, called the innate and the adaptive. The innate immune system provides an immediate, but non-specific response. This consists of physical and chemical barriers, such as skin, mucus, and tears; specialized white blood cells such neutrophils, basophils, eosinophils, macrophages, and natural killer cells; and the complement system of proteins that neutralize pathogens. The adaptive immune system comes into play if pathogens successfully evade the innate response. The adaptive immune system consists primarily of the B- and T-lymphocytes and the immunoglobulins (antibodies), which are very specific and targeted to the pathogen causing disease. The adaptive immune system can "remember" the pathogens it has previously been exposed to and can mount a strong immune response if it is exposed again.

Immunofixation: A laboratory test used to identify the immunoglobulins (antibodies) present in a serum or urine sample.

Immunoglobulin (Ig): See **Antibody**. Immunoglobulins are divided into five basic classes (IgA, IgD, IgE, IgG, IgM) based on structure and activity:

Immunoglobulin A (IgA): Plays a critical role in mucosal immunity. More IgA is produced in mucosal linings than all other types of antibody combined and is found in tears, saliva, breast milk, and secretions from the genitourinary tract, gastrointestinal tract, prostate, and respiratory system.

Immunoglobulin D (IgD): Found in very small amounts in the blood, its function has been somewhat of a puzzle since its discovery. IgD signals B-cells to become activated, at which point they are ready to take part in the defense of the body. During B-cell development, IgM is exclusively expressed by immature B-cells. As the B-cell matures, IgD is co-expressed with IgM.

Immunoglobulin E (IgE): Mainly functions to provide immunity to parasites. It also plays an essential role in hypersensitivity responses such as allergies. It is the least abundant immunoglobulin in the blood.

Immunoglobulin G (IgG): Constitutes 75% of serum immunoglobulins in humans. IgG antibodies generally appear later in response to initial exposure to an antigen but, upon re-exposure to the same antigen, are important in determining the strength of the subsequent immune response.

Immunoglobulin M (IgM): By far, this is physically the largest antibody in the human circulatory system. Its size can cause increased blood viscosity if it is produced in large amounts. It is the first antibody to appear in response to initial exposure to antigen and usually reappears, to a lesser extent, after subsequent exposure.

Immunohistochemistry: Refers to the use of special stains to identify antigens in the cells of a tissue section for purposes of identification; this procedure is widely used in the diagnosis of abnormal cells such as those found in cancer.

Immunomodulatory drug (IMiD): A class of drugs that constitute thalidomide, lenalidomide, and pomalidomide, used in the treatment of multiple myeloma and, less commonly, WM. These drugs are not traditional chemotherapy drugs; their mechanism of action is not completely understood, but they are anti-angiogenic (inhibit growth of new blood vessels) and help stimulate T-cell and natural killer cell production.

Immunosuppression: A weakening of the immune response.

Immunotherapy: A treatment to boost or restore the ability of one's own immune system to fight cancer, infections, and other diseases. Agents used in immunotherapy include monoclonal antibodies, idiotype vaccines, CAR T-cells, and immune checkpoint inhibitors.

Indolent: Slow growing.

Informed consent: A document that must be signed by a patient or patient's representative before participation in a clinical trial. The informed consent document explains possible risks and side effects and ensures that the patient is participating in a clinical trial willingly and with full knowledge.

Infusion: The introduction of fluid into a vein.

Inhibitor: A drug to block or inactivate a specific molecule.

Injection: Use of a syringe and needle to push fluids or drugs into the body; often called a "shot."

Institutional Review Board (IRB): Each hospital where a clinical trial is conducted is required to have an institutional review board (IRB). The IRB is an oversight group which evaluates the study protocol to ensure the rights and welfare of the human research subjects are protected and that the study is ethical and scientifically valid. All clinical studies are required to have IRB approval before they can start.

Interleukin (IL): One of a family of factors produced by lymphocytes, monocytes, and other cells that induce growth and differentiation of lymphoid cells and hematopoietic stem cells. Each distinct interleukin is designated by a number (such as "IL-2" or "IL-6").

Intravenous (IV): Into the vein.

Intravenous immunoglobulin G (IVIg): A blood product administered into the vein in order to boost immunity. It contains the pooled IgG extracted from the plasma of many donors. Intravenous IgG's effects last between 2 weeks and 3 months. This product is also available for subcutaneous administration.

In vitro: Literally "in glass". A term used to describe experiments performed in cells or molecules outside the body ("in test tubes").

In vivo: Literally "in life". A term used to describe experiments in living organisms

IRAK (interleukin receptor-associated kinase): A family of signaling proteins that play a vital role in immunity, particularly involving autoimmune and inflammatory diseases. Several members of this family are thought to be important in the pathogenesis of WM and may be targets for future therapy.

Ixazomib (Ninlaro): A drug used for the treatment of multiple myeloma and certain types of lymphoma, including WM. It is in the drug class called proteasome inhibitors.

Kappa light chain: One of the two types of light chains present in all individuals.

Kinase: A protein inside cells that often sends signals from one part of the cell to another. Kinases do this by adding a phosphate group to another protein. The addition of a phosphate group either activates or inactivates the receiving protein. An example of a kinase is BTK. In WM cells, BTK sends signals from MYD88 to other parts of the cell. BTK inhibitors, such as ibrutinib, are called kinase inhibitors, because they block the ability of kinases such as BTK from sending signals.

Knockout mouse: A genetically-engineered mouse, used in research, in which one or more specific genes have been deleted. Study of knockout mice enables scientists to determine the roles of specific genes in the body.

Lactate dehydrogenase (LDH): An enzyme found extensively in tissues such as blood cells and heart muscle; it is released during tissue damage and thus can be a marker of common injuries and disease. LDH can be elevated in certain cancers, including WM, especially during disease progression.
Lambda light chain: One of the two types of light chains present in all individuals.
Leukocyte: See **White blood cell**.

Leukopenia: An abnormally low number of white blood cells.

Light chain: The small polypeptide subunit of an immunoglobulin molecule. There are two types of light chains: kappa (κ) and lambda (λ). Both types of light chains are present in all individuals, and either of the light chain types may combine with any of the heavy chain types.

LOXO-305: An investigational Bruton's tyrosine kinase (BTK) inhibitor that binds differently to BTK than ibrutinib (Imbruvica), in theory avoiding resistance caused by the BTK-C481S mutation.

Lymph: A colorless fluid containing white blood cells that bathes the tissues and drains through the lymphatic system into the bloodstream.

Lymph node: A bean-shaped organ found in the underarm, groin, neck, and abdomen that acts as a filter for the lymph fluid as it passes through. The lymph nodes are major sites of antigen exposure to lymphocytes, thereby activating an immune response.

Lymphadenopathy: Enlargement of the lymph nodes.

Lymphatic system: An organ system that Includes the bone marrow, spleen, thymus, lymph nodes, and the vessels that carry lymph.

Lymphocyte: The white blood cell known as a B-cell or T-cell.

Lymphoma: A cancer of the lymphatic system. The lymphomas are classified generally in two broad categories: Hodgkin's lymphoma and non-Hodgkin's lymphoma (also called Hodgkin lymphoma and non-Hodgkin lymphoma [with no apostrophe]).

Lymphoplasmacytic lymphoma (LPL): The type of non-Hodgkin's B-cell lymphoma that includes WM. It refers to the morphology of the cells, which are typically intermediate in appearance between lymphocytes and plasma cells. WM is the most common type of LPL, with its other defining characteristic being the production of monoclonal IgM. Other types of LPL do not secrete monoclonal IgM.

M-spike: Also called monoclonal spike, monoclonal protein, or paraprotein. An IgM M-spike is so characteristic of WM that its presence is important for diagnosis of the disease and follow-up monitoring of patients. An M-spike can be detected by serum protein electrophoresis, which separates the blood proteins into groups based on electrical charge and size. There is a predictable protein pattern in normal serum, with each protein migrating to a certain point on an electrophoretic gel plate. Immunoglobulins migrate to a unique place called the gamma region, and because they are all different in normal patients, they migrate to slightly different places within that region, giving a gentle bell-shaped curve or smear (depending on whether you're looking at a tracing or the actual bands on the gel). In WM, the M-spike is all the same, so that all of it migrates to the same spot on the gel. This results in a big, sharp spike (if you're looking at a tracing) or a very distinct, crisp, strong band (if you're looking at the gel itself).

Macrophage: A white blood cell that arises from a monocyte, becomes mobile, and enters the tissues to participate in the immune response. There are many types of macrophages, including ones that kill tumors and others that promote tumor growth. Some newer immuno-oncology therapies are directed

at activating tumor-killing macrophages. Other newer therapies convert tumor-promoting macrophages into tumor-killing macrophages.

MAG (myelin-associated glycoprotein): A cell membrane protein found in Schwann cells, which use it to produce a myelin sheath that surrounds and insulates many nerves. Autoimmune attack against this protein by a monoclonal IgM antibody can result in a type of peripheral neuropathy called anti-MAG neuropathy, which can be seen in IgM MGUS and WM patients.

Maintenance rituximab: A series of regular infusions of rituximab given over a time period (usually two years) to help prolong the response a patient has had to a just-completed therapy containing rituximab (Rituxan). Maintenance rituximab therapy is used in several types of B-cell non-Hodgkin's lymphomas, and a clinical trial is underway to prove or disprove whether maintenance for WM patients is indicated for this purpose.

Major response: In WM, a term referring to the cumulative number of partial responses, very good partial responses, and complete responses to a treatment.

Marginal zone lymphoma (MZL): A group of indolent B-cell non-Hodgkin's lymphomas that can be found in the spleen, lymph nodes, salivary glands, stomach, small intestine, eyes, and lungs. Marginal zone lymphomas can share certain characteristics with WM and other indolent lymphomas, making the differential diagnosis of WM sometimes challenging.

Mast cell: A cell distributed near blood vessels in most tissues, including the bone marrow. Mast cells are often associated with allergic reactions and are believed to offer support to the malignant cells of WM.

Mavorixafor : An oral drug used to inhibit CXCR4 (C-X-C chemokine receptor type 4). It is being used in clinical trials for WM.

Memory B cell: A long-lived B-cell which has already been primed to respond to an antigen but has not undergone differentiation into a plasma cell. It reacts more readily than a naïve B-cell when re-stimulated with the same antigen.

Metabolomics: The study of large numbers of metabolites, the small molecule intermediates and products of metabolism. Metabolomics research is being used to discover diagnostic cancer markers, to determine metabolic pathways involved in cancer that could be used for new treatment targets, and to find markers that monitor the success of treatment.

Minor response: In WM, a minor response following treatment is characterized by a detectable monoclonal IgM protein, a reduction in serum IgM level of equal to or greater than 25% but less than 50% from baseline, and no new signs or symptoms of active disease.

mg: Abbreviation for milligrams. Most drug dosages are measured in milligrams.

MGUS: See "Monoclonal gammopathy of undetermined significance"

Monoclonal: Produced by or composed of cells derived from a single cell.

Monoclonal antibody therapy (MAB therapy): The use of laboratory-developed antibodies that can locate and bind to a targeted antigen in the body, including a tumor cell. Each monoclonal antibody is made to bind to one specific antigen. Monoclonal antibodies can be used alone or to carry drugs, toxins, or radioactive materials directly to a tumor.

Monoclonal gammopathy of undetermined significance (MGUS): A benign condition in which a monoclonal protein (immunoglobulin or immunoglobulin light chain that is produced in excess) is found in the blood during standard laboratory tests. It usually produces no symptoms or problems and no treatment is indicated, although there are some exceptions, such as anti-MAG neuropathy caused by IgM MGUS. Patients with MGUS are at increased risk of developing blood cancers such as multiple myeloma and lymphomas, including WM.

Monocyte: A white blood cell that is present in the blood, comprising 2-5% of the circulating white blood cells. Monocytes can differentiate into macrophages, which participate in the immune response.

Monotherapy: Treatment of a condition by means of a single drug.

Mucositis: A complication of some cancer therapies in which the lining of the digestive system becomes inflamed; often seen as sores in the mouth.

Multiple myeloma (MM): A cancer of the plasma cells. The plasma cells of multiple myeloma most commonly secrete monoclonal IgG and less commonly IgA or IgM. Because multiple myeloma and WM share some characteristics, several drugs used to treat multiple myeloma can also be used to treat WM.

Mutation: Any change in the DNA of a cell.

MYD88 (myeloid differential primary response gene 88) gene: A gene that codes for the MYD88 protein, which plays a central role in the innate and adaptive immune response. This protein is an essential one in the Interleukin-1 and Toll-like receptor signaling pathways of B-cells. In most WM patients, MYD88 is mutated (changed), which makes it excessively active. This causes too much signaling inside the WM cells, resulting in cancerous cell growth and proliferation (See “MYD88 L265P”)

MYD88 L265P: A single mutation in the MYD88 gene that changes the amino acid leucine to proline at amino acid position 265. This mutation is found in 90-95% of Waldenstrom’s macroglobulinemia patients and is important to the continued growth and proliferation of WM cells. The presence of this mutation assists in the diagnosis of WM and may impact response to certain treatments.

Myelodysplasia (MDS): A condition characterized by the production of abnormal blood cells in the bone marrow that can lead to leukemia. Treatment with certain chemotherapy drugs can increase the risk of developing myelodysplasia.

Myelosuppression: A condition in which bone marrow activity is decreased, resulting in decreased platelets, red blood cells, and white blood cells. Myelosuppression can be a side effect of some cancer treatments.

n: The number of people or animals included in an experiment or clinical trial, or the number in each group within the experiment or trial. A large trial has a higher n.

Natural killer (NK) cell: A specialized white blood cell of the immune system that can recognize cancer cells or cells infected with viruses or other pathogens and can trigger a process to kill them.

Neoplasm: Synonym for tumor or cancer. “Neoplasm” is a noun. “Neoplastic” is the corresponding adjective (as in “neoplastic cell”).

Neutropenia: An abnormally low number of neutrophils.

Neutrophil: Also known as a polymorphonuclear (PMN) white blood cell, this is a white blood cell that has a variably shaped nucleus. Neutrophils are an abundant type of white blood cells and form an essential part of the innate immune system, responding quickly to invading bacteria or foreign objects. Pus is composed of huge numbers of neutrophils.

NF kappa B (often written as NF-κB): A protein complex that controls transcription of DNA and plays a key role in regulating the immune response to infection. Incorrect regulation (generally excessive activation) of NF kappa B has been linked to cancer, inflammatory, and autoimmune diseases. It plays an important role in the growth and proliferation of WM cells.

Night sweats: The occurrence of excessive sweating during sleep.

Nonclinical: Experiments performed in animals other than humans. Synonym “Preclinical”

Non-Hodgkin’s lymphoma (NHL) (or non-Hodgkin lymphoma): A diverse group of blood cancers that include any kind of lymphoma except Hodgkin’s lymphoma. Non-Hodgkin’s lymphomas can occur at any age and are often marked by lymph nodes that are larger than normal, fever, and weight loss. These various lymphomas can be divided into high grade (aggressive), intermediate grade, and low grade (indolent) and can originate from B-cells or T-cells. WM is one type of non-Hodgkin’s lymphoma.

Nucleoside analog (NA): Part of a larger class of anti-cancer drugs termed antimetabolites, which act specifically on proliferating cells by blocking cell division. Fludarabine (Fludara) is a nucleoside analog used to treat WM.

Obinutuzumab (Gazyva): A humanized monoclonal antibody therapy that has been approved for the treatment of chronic lymphocytic leukemia (CLL). It targets the same CD20 protein on B-cells as rituximab (Rituxan).

Ofatumumab (Arzerra): A fully human monoclonal antibody therapy drug that binds to CD20, a protein on the surface of normal B-cells and most B-cell tumors. In WM, it is primarily used in cases where patients are intolerant to rituximab (Rituxan).

Omics: Analysis of large sets of biological molecules. Metabolomics refers to the analysis of body metabolites, genomics is the analysis of genes, and transcriptomics is the analysis of RNA transcripts (see “Metabolomics”, “Genomics,” or “Transcriptomics”). Omics is the general term for this type of analysis, regardless of the type of biological molecule.

Overall survival (OS): The percentage of people in a study or treatment group who are still alive for a certain period of time after they were diagnosed with or started treatment for a disease, such as cancer. In a clinical trial, measuring the overall survival is one way to see how well a treatment works.

p (or p-value): One measure of the statistical significance of an experiment. Statistics are used to evaluate the likelihood that the results of an experiment or a clinical trial were due to random chance or due to the experimental treatment (such as a drug). P values can vary from 1 to very small numbers. By convention, most researchers use p less than 0.05 ($p<0.05$) to indicate that the results were likely due to the drug rather than to random chance.

Paraprotein: An abnormal plasma protein of one type, such as the monoclonal IgM of WM. Also called an M-spike or a monoclonal protein.

Partial response (PR): In WM, a partial response to treatment is characterized by a detectable monoclonal IgM, a reduction in serum IgM equal to or greater than 50% but less than 90% from baseline, a reduction in the size of enlarged lymph nodes and enlarged spleen if present at baseline, and no new symptoms or signs of active disease.

PD-1 (Programmed Death-1): PD-1 is a protein on T cells called a "checkpoint." When activated, the PD-1 checkpoint suppresses T cell immune responses. Normally, PD-1 is activated following resolution of infections to prevent an excessive immune response or autoimmune diseases. Some cancer cells have evolved a way to exploit this. Some cancer cells express PD-L1, a protein which binds to PD-1. This interaction between PD-L1 and PD-1 activates PD-1, which prevents T cells from attacking the cancer cells. This shuts down some of the body's anti-cancer immune responses. Drugs such as Opdivo (nivolumab) and Keytruda (pembrolizumab) have been developed to block activation of PD-1. Because PD-1 is an immune system "checkpoint", these drugs are called "checkpoint inhibitors". These drugs are now in clinical trials for WM (see "Immune Checkpoint Inhibitors").

PD-L1 (Programmed Death-Ligand 1): PD-L1 is a protein that binds to and activates PD-1 (see above). When PD-1 is activated on T cells, it suppresses T cell immune responses. Some cancer cells express PD-L1, and the resulting interaction between PD-L1 on the cancer cells and PD-1 on the body's T cells prevents T cells from attacking the cancer cells. Drugs such as Tecentriq (atezolizumab), Imfinzi (durvalumab), and Bavencio (avelumab) bind to PD-L1 and prevent it from interacting with PD-1. Like Opdivo and Keytruda, which bind directly to PD-1 (see above), these PD-L1-binding drugs are also called "checkpoint inhibitors."

Peripheral neuropathy (PN): A condition characterized by a permanent or temporary problem with the functioning of the nerves outside the brain and spinal cord. The symptoms of a peripheral neuropathy may include numbness, weakness, tingling, burning pain, and loss of reflexes (usually in feet and/or hands). The pain may be mild or severe and disabling. Peripheral neuropathy can be caused by several conditions.

PET (positron emission tomography) scan: A nuclear medicine procedure that uses gamma rays to produce three dimensional images of functional processes in the body.

Pharmacokinetics: The study of drug concentration in blood and body tissues at different times. Some drugs quickly reach a high concentration in the blood and then are eliminated from the body. Other drugs stay around in the blood for a longer period of time.

PI3K (phosphoinositide 3-kinase): This group of proteins plays an important role in moving signals from the outside of cells into various intracellular pathways involved in cell cycle regulation, apoptosis

(programmed cell death), DNA repair, senescence (cell aging), angiogenesis (blood vessel formation) and cell metabolism. In some cancers, these proteins are overactive, thereby allowing cancer cells to grow and proliferate. Various inhibitors to target PI3K are in development, and several are being tested in WM; these include copanlisib (Aliqopa), duvelisib (Copiktra), and umbralisib.

Plasma: The fluid component of blood containing water, electrolytes, and various proteins.

Plasma cell: A fully mature white blood cell of the B-cell lineage that produce antibodies. In multiple myeloma, the plasma cell becomes malignant and produces in most cases large amounts of IgG antibodies, although rarely the malignant plasma cell produces IgM or IgA instead of IgG.

Plasmapheresis (PP): In WM, this process is used to remove excess IgM, which is primarily in the plasma. Blood is continuously withdrawn and circulated through an apparatus that removes the plasma, and the remaining blood is returned along with a plasma substitute. A central venous catheter or large-bore needles inserted in the veins (typically the arm veins) are used to withdraw and return the blood.

Platelet (Plt): A fragment produced from a cell called a megakaryocyte, which is in turn produced from stem cells in the bone marrow; platelets circulate in the blood and are necessary to help the blood clot and control bleeding.

Pleural effusion: The accumulation of fluid in the pleural space (the space between the two layers of the pleural membrane that surrounds each lung). The condition is characterized by shortness of breath, chest pain, gastric discomfort, and cough. A wide range of conditions may cause a pleural effusion, including congestive heart failure, pulmonary infection, tumor, connective tissue disorder, or blood clot.

Polyclonal: Produced by or composed of cells derived from different cells. Normal immunoglobulin M is polyclonal since it is derived from many different B-cells, each producing a different kind of IgM, as opposed to monoclonal IgM produced by the WM malignant clone, which is all of one kind.

Polymerase chain reaction (PCR): A genetic technique used to increase selected sections of DNA or RNA for analysis. PCR is done in a test tube and relies on cycles of repeated heating and cooling of the reaction for DNA or RNA melting and replication. Primers (short DNA or RNA fragments) containing sequences complementary to the target region, along with an enzyme, are key components to enable selective and repeated increase (amplification). As PCR progresses, the DNA or RNA generated is itself used as a template for replication, setting in motion a chain reaction in which the DNA or RNA template is exponentially increased. The amplified segments are then compared to nucleotide segments from a known source to see if that DNA or RNA segment in the patient sample is present. This test can be used to detect the MYD88 mutation in WM patients.

Port: In medicine, a port is a small medical appliance that is installed beneath the skin. A catheter connects the port to a vein. Under the skin, the port has a septum through which drugs can be injected and blood samples can be drawn many times, usually with less discomfort for the patient than a more typical “needle stick.”

Post-translational: Changes to proteins after they are synthesized or made.

Potency: A measure of drug activity. A cancer drug that is more potent kills cancer cells at a lower concentration than one that is less potent.

Precision medicine: A philosophy of cancer treatment that aims to leverage new genetic information about a specific cancer to more precisely target treatment. It seeks to define the genetic alterations that are driving a specific cancer, rather than relying on a simple broad classification of cancer based only on its site of origin.

Prednisolone: A synthetic corticosteroid similar to steroid hormones produced naturally in the adrenal gland. It suppresses the immune system and reduces inflammation. It can be used to treat a variety of conditions, including autoimmune diseases and certain cancers, and may be indicated instead of prednisone if a patient has liver disease.

Prednisone: A synthetic corticosteroid similar to steroid hormones produced naturally in the adrenal gland. It suppresses the immune system and reduces inflammation. It can be used to treat a variety of conditions, including autoimmune diseases and certain cancers.

Prognosis: A prediction of the course of a disease and its outcome.

Progression-free survival (PFS): The length of time during and after the treatment of a disease, such as cancer, that a patient lives with the disease but it does not get worse. In a clinical trial, measuring the progression-free survival is one way to see how well a treatment works.

Prophylaxis: A treatment to prevent disease.

Prospective: A prospective study (sometimes called a prospective cohort study) is a type of cohort study, or group study, where participants are enrolled into the study before they develop the disease **or** outcome in question. The opposite is a retrospective study, where researchers enroll people who already have the disease/condition. Prospective studies typically last a few years, with some (like the Framingham Heart Study) lasting for decades.

Proteasome inhibitor: A drug that blocks the action of proteasomes. A proteasome is a large protein complex that helps destroy other cellular proteins when they are no longer needed. When the action of the proteasome is blocked, this cellular protein "garbage" backs up in the cell and eventually kills it. Proteasome inhibitors are used in the treatment of multiple myeloma and WM. Examples of proteasome inhibitors include bortezomib (Velcade), carfilzomib (Kyprolis), and ixazomib (Ninlaro).

Proteomics: The study of the structure and function of proteins, including the way they work and interact with each other inside cells.

Protocol: A detailed plan of a medical experiment, treatment, or procedure.

Pyrexia: A fever.

R-CHOP: An abbreviation for a chemoimmunotherapy combination that is used to treat lymphoma. It includes the drugs rituximab (Rituxan), cyclophosphamide (Cytoxan), hydroxydoxorubicin (also known as Doxorubicin or Adriamycin), Oncovin (vincristine), and prednisone or prednisolone. This therapy is also referred to as CHOP-R.

Radioimmunotherapy (RIT): A class of drugs which uses an antibody labeled with a radioactive particle to target and kill a cancer cell.

Raynaud's phenomenon: A medical condition in which spasm of small blood vessels, typically triggered by cold, causes episodes of reduced blood flow to the fingers, and less commonly, the toes, nose, ears, or lips. The episodes result in the affected part turning white and then blue. Often, numbness or pain occurs. As blood flow returns, the area turns red and burns. Also known as Raynaud's syndrome.

Red blood cell (RBC): Also called an erythrocyte. A blood cell that contains hemoglobin, which is the transport protein carrying oxygen from the lungs to the cells for metabolism and returning carbon dioxide from the cells back to the lungs to be exhaled. Red blood cells make up a little less than half the volume of blood in healthy individuals.

Reference range: In medicine, this is a set of values that a doctor uses to interpret a patient's test results. The reference range for a given test is based on test results for 95% of the healthy population. Sometimes patients whose test results are outside of the reference range values may be healthy, and some patients whose test results are within the reference range values may have a health problem. The reference range for a test may be different for different groups of people (for example, men and women or young and old).

Refractory: Not responding to treatment.

Regimen: A treatment plan that specifies the dosage, schedule, and duration of treatment.

Relapse: The return of disease after it has been treated and the patient has been in remission.

Resistance: In the context of cancer, resistance is the ability of cancer cells to overcome the effects of drug therapy so that the drug no longer works as well, and the cancer cells grow.

Response: A description of how and to what extent a cancer has responded to treatment. Sometimes also referred to as remission.

Response categories: For the purposes of comparing one clinical trial with another, WM researchers have established a uniform set of definitions of responses to therapy:

Complete response (CR): Absence of serum monoclonal IgM protein by immunofixation
Normal serum IgM level
Complete resolution of extramedullary disease,
i.e., lymphadenopathy and splenomegaly if present at baseline
Morphologically normal bone marrow aspirate and trephine biopsy

Very good partial response (VGPR): Monoclonal IgM protein is detectable
$\geq$ 90% reduction in serum IgM level from baseline
Complete resolution of extramedullary disease,
i.e., lymphadenopathy/splenomegaly if present at baseline
No new signs or symptoms of active disease

Partial response (PR): Monoclonal IgM protein is detectable
$\geq$ 50% but <90% reduction in serum IgM level from baseline

	Reduction in extramedullary disease, I.e., lymphadenopathy/splenomegaly if present at baseline No new signs or symptoms of active disease
Minor response (MR):	Monoclonal IgM protein is detectable ≥ 25% but <50% reduction in serum IgM Level from baseline No new signs or symptoms of active disease
Stable disease (SD):	Monoclonal IgM protein is detectable <25% reduction and <25% increase in serum IgM from baseline No progression in extramedullary disease, i.e., lymphadenopathy/splenomegaly No new signs or symptoms of active disease
Progressive disease (PD):	≥25% increase in serum IGM level from lowest nadir (requires confirmation) and/or progression in clinical features attributable to the disease

Retina: The back part of the eye, which receives light and transmits visual signals to the brain. Blood vessels in the retina can be damaged in WM patients.

Retinopathy: A disease of the retina which results in impairment or loss of vision.

Retrospective: A retrospective study looks backwards and examines exposures to suspected risk or protection factors in relation to an outcome that is established at the start of the study. The opposite is a prospective study where the researchers watch for outcomes, such as the development of a disease, during the study period and relate this to other factors such as suspected risk or protection factor(s). The study usually involves taking a cohort (group) of subjects and watching them over a long period.

Rituximab (Rituxan or Mabthera): A drug used to treat certain types of B-cell non-Hodgkin's lymphoma. It can be used alone or in combination with other drugs. Rituximab binds to a protein called CD20, which is found on B-cells, and it kills cancer cells by utilizing one's own immune system. It is a type of monoclonal antibody therapy and can be administered by IV infusion or subcutaneously. The subcutaneous formulation is called Rituxan Hycela (see above, "Hycela" and "hyaluronidase".

RNA (ribonucleic acid): A molecule essential in coding, decoding, regulation, and expression of genes and the translation of DNA into proteins. Unlike DNA, RNA is found in nature as a single strand folded onto itself, rather than a paired double strand. Many viruses encode their genetic information using RNA rather than DNA.

Salvage therapy: Any therapy administered after frontline treatment has failed.

Selectivity: The ability of a drug to inhibit its intended target but not inhibit other molecules in the body (referred to as "off-target"). For example, ibrutinib has not-so-good selectivity because it inhibits not only its target, BTK, but also other molecules such as the epidermal growth factor receptor, EGFR. Unintended inhibition of EGFR results in toxicities such as skin rash and diarrhea in some patients. Often, second-generation drugs are developed to improve the selectivity of the original drug.

Sepsis: A potentially life-threatening condition caused by the body's response to an infection. The body normally releases chemicals into the bloodstream to fight an infection. Sepsis occurs when the body's

response to these chemicals is out of balance, triggering changes that can damage multiple organ systems. If sepsis progresses to septic shock, blood pressure drops dramatically, possibly leading to death.

Serum: The fluid component of blood minus the clotting factors.

Serum protein electrophoresis (SPEP): A laboratory test that examines proteins in the blood by exposing the collected serum to an electric current to separate the protein components into five classifications by size and electrical charge (serum albumin, alpha-1 globulins, alpha-2 globulins, beta globulins, and gamma globulins). In WM and related disorders, this technique is used to detect monoclonal immunoglobulin proteins, which are typically found within the gamma globulin fraction.

Serum viscosity (SV): The physical property of serum as it relates to its "thickness." The serum viscosity is affected by the concentration of constituents in the serum. The greater the number of soluble molecules in the serum, the higher will be the viscosity. In WM, the presence of a large amount of IgM can cause high serum viscosity.

Shingles (herpes zoster): The disease caused when varicella zoster virus is reactivated later in life in a person who has had chickenpox. Shingles usually affects a small section or one side of the body. Its symptoms include pain, burning, or tingling; sensitivity to touch; a red rash that begins a few days after the pain; itching; and fluid-filled blisters that break open and crust over. Until recently, the vaccine used to protect against shingles was not indicated for WM patients because it is a live virus vaccine; however, a new vaccine called Shingrix is a non-live virus vaccine, has recently been approved by the FDA for people over 50, and is considered safe for WM patients.

Sign: In medicine, an objective indication of a medical condition or disease. Examples might include fever, high blood pressure, and rapid pulse.

Smoldering Waldenstrom's macroglobulinemia (SWM): This has been defined clinically with the following characteristics: a serum monoclonal immunoglobulin M protein equal to or greater than 3 g/dL and/or bone marrow lymphoplasmacytic infiltration equal to or greater than 10%, but with no evidence of end-organ damage, anemia, constitutional symptoms, hyperviscosity, lymphadenopathy (enlarged lymph nodes), or hepatosplenomegaly (enlarged liver and spleen). Patients with smoldering WM are not treated but are instead considered to be on "watch and wait" and are monitored until symptoms develop that require treatment.

Spleen: The largest structure in the lymphoid system, this is a gland-like organ situated in the left upper abdomen. It serves as a reservoir of blood, produces lymphocytes and plasma cells, and functions as a filter for the blood by removing damaged red blood cells from the circulation.

Splenectomy: Surgical removal of the spleen.

Splenomegaly: Enlargement of the spleen.

Stroma: The non-neoplastic ("normal") cells within a tumor that help to sustain a tumor and permit it to grow. In bone marrow tumors such as WM, the stroma includes blood vessels, fibroblasts, nerves, and other cell types. Some scientists are investigating drug treatments to prevent stromal cells from supporting tumor growth.

Subclinical: Abnormalities or disease processes that are low-grade and do not cause clinical signs or symptoms. See also "Asymptomatic"

Subcutaneous (sub-Q or sc): Under the skin.

Symptom: A subjective indication of a condition or disease, usually experienced by the patient. Examples might include fatigue, pain, and dizziness.

Syncope: Fainting, usually related to decreased blood flow to the brain. It occurs most often when blood pressure is too low (hypotension).

T cell/T lymphocyte (sometimes hyphenated, T-cell/T-lymphocyte): T cells are a broad type of lymphocyte with diverse subtypes. Naïve T cells are in a resting state, activated T cells can secrete a wide range of cytokines, growth factors and immune modulators, and memory T cells can be re-activated quickly. T cells which express CD8 (called CD8 T cells) often directly kill virus-infected or cancer cells ("cytotoxic T cells"), while T cells which express CD4 (called CD4 T cells) often secrete chemicals called cytokines which increase overall inflammation, contributing indirectly to tumor killing. Regulatory T cells (called Tregs) act in the opposite way and down-regulate immune responses. Some immuno-oncology therapies are directed at increasing the activity of CD8 T cells, while other therapies are directed at inhibiting Tregs.

Targeted therapy: A type of treatment that uses drugs or other substances designed to identify and attack specific molecules ("targets") on cancer cells and reduce collateral damage to normal cells. For this reason, targeted therapy may have fewer side effects than other types of cancer treatments.

Thrombocyte: See **Platelet**.

Thrombocytopenia: An abnormally low number of platelets.

Tirabrutinib: An oral investigational drug that targets and inhibits Bruton's tyrosine kinase (BTK), an enzyme which is important in the development and activation of B-cells and which is often over-activated in WM. It is in the same drug class as ibrutinib (Imbruvica) but is a second-generation drug. It is being studied in clinical trials for WM.

Toxicity: Having to do with something harmful to the body. Toxicity often refers to undesired and harmful side effects of a drug.

Transcription: The first step of gene expression, in which a particular segment of DNA is copied to messenger RNA by the enzyme RNA polymerase.

Transcriptomics: The study of all the RNA transcripts (collectively referred to as the transcriptome) present in a cell. Unlike the genome of a cell, which does not typically vary unless it is mutated, the transcriptome can vary with environmental conditions and thus can be studied to provide a snapshot of the inner workings of a cell at a particular moment in time.

Transformation: The process by which an indolent lymphoma develops into a more aggressive lymphoma. Indolent lymphomas generally grow slowly and can remain stable for a long while. However,

because of additional acquired mutations, a more aggressive type of cell can emerge from the population of indolent cells (and soon outnumbers the indolent cells), leading to symptoms and the need to treat. When an indolent lymphoma transforms, there will be a mix of indolent and aggressive cells, and the goal of therapy is to cure the aggressive component. Following successful therapy, the indolent lymphoma may remain. In WM, one concern is transformation of WM cells to a more aggressive cancer called diffuse large B cell lymphoma (DLBCL).

Transgenic mouse: A genetically-engineered mouse, in which specific genes have been altered (either removed ("knock-out") or added ("knock-in") to enable study of the role of specific genes.

Translation: The process by which a cell synthesizes proteins after the process of transcription of DNA to messenger RNA.

Ubiquitin: A type of small protein that is affixed to other proteins after they are made (see "Post-translational"). Some ubiquitins mark their target protein for degradation. This regulates the lifespan of proteins. Some cancer drugs use this mechanism to direct cancer drugs to specific targets. On the other hand, other types of ubiquitins may increase cancer. Scientists are attempting to discover drugs to block that type of ubiquitin.

Ulocuplumab: A monoclonal antibody that targets CXCR4 (C-X-C chemokine receptor type 4). It is being used in clinical trials for WM.

Umbralisib: An investigational oral drug that targets and inhibits phosphoinositide 3-kinase (PI3K). It has been used in clinical trials for WM.

Variable region: The portion of an antibody's light and heavy chains that is primarily responsible for binding to an antigen. An antibody is Y-shaped, and each tip of the "Y" is composed of the portions of the antibody's light and heavy chains that are specific for one particular antigen, allowing the antibody and antigen to bind together with precision. Using this binding mechanism, an antibody can tag a microbe or an infected cell for attack by other parts of the immune system or can neutralize its target directly. During B-cell development, this region of an antibody is subject to frequent genetic mutation in order to make the antigen binding more specific.

Venetoclax (Venclexta or Venclyxto): An oral drug that targets and inhibits BCL2 (B-cell lymphoma 2), a protein important in cell survival and over-expressed in several types of cancer. It is used to treat a B-cell malignancy called chronic lymphocytic leukemia (CLL) and is being studied in clinical trials for WM.

Very good partial response (VGPR): In WM, a very good partial response following treatment is characterized by a detectable monoclonal IgM protein, a reduction in serum IgM level equal to or greater than 90% from baseline, complete resolution of enlarged lymph nodes and enlarged spleen if present at baseline, and no new signs or symptoms of active disease.

Waldenstrom's macroglobulinemia (WM): A type of B-cell non-Hodgkin's lymphoma. A cancer of the lymphatic system, it is sometimes referred to as a lymphoplasmacytic lymphoma (LPL) with an associated monoclonal IgM paraprotein. The disease occurs in a type of white blood cell called a B-lymphocyte or B-cell, which normally matures into a plasma cell whose function is to manufacture immunoglobulins (antibodies) to help the body fight infection. In WM, there is a malignant change to the B-cell in the late stages of maturing, and it continues to proliferate into a clone of identical cells, primarily in the bone marrow but also in the lymph nodes and other organs of the lymphatic system.

These clonal cells over-produce an antibody of a specific class called IgM. Under the microscope, WM cells have characteristics of both B-lymphocytes and plasma cells, and they are called lymphoplasmacytic cells, hence the classification of WM as a lymphoplasmacytic lymphoma. The variety of symptoms that arise from WM are a result of the presence of the lymphoplasmacytic cells and/or the monoclonal IgM.

Watch and wait (W&W): A term often used in indolent cancers to mean that a doctor does not actively treat a patient, but rather monitors the disease. This is desirable because treating asymptomatic patients does not cure the disease, improve quality of life, or change the outcome, plus many treatments have adverse side effects. The watch and wait method is used to ensure that treatment occurs when it is necessary to alleviate symptoms and improve quality of life. During the period of watch and wait, the patient will undergo regular medical testing to determine the current status of his or her disease.

White blood cell (WBC): Also called a leukocyte. Any cell of the immune system that protects the body against both infectious disease and foreign invaders. See **Lymphocyte**, **Neutrophil**, **Eosinophil**, **Monocyte**, **Macrophage**, and **Natural killer cell**.

Wild type gene: A gene in its typical form that predominates in a population, as opposed to a mutated (altered) gene. Sometimes abbreviated as "WT".

Xenograft: An experimental procedure in which tumor cells, typically from a human, are placed under the skin of a mouse and allowed to grow. The mice are then treated with drugs to evaluate the ability of the drugs to control the tumor.

Zanubrutinib (Brukinsa): An oral drug that targets and inhibits Bruton's tyrosine kinase (BTK), an enzyme which is important in the development and activation of B-cells and which is often over-activated in WM. It is in the same drug class as ibrutinib (Imbruvica) but is a second-generation drug that reportedly is more selective for its target, BTK, and has fewer side effects. It is FDA-approved for mantle cell lymphoma and has been studied in clinical trials for WM.