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INSIDE THIS ISSUE

OVERVIEW OF COLD AGGLUTININ HEMOLYTIC ANEMIA AND CRYOGLOBULINEMIA

BY MORIE A. GERTZ, MD, MACP
MAYO CLINIC, ROCHESTER, MN, USA

Dr. Morie A. Gertz

Morie A, Gertz, MD, MACP, received his medical degree from Loyola University Chicago Stritch School of Medicine and completed his residency in internal medicine at Rush Presbyterian St. Luke's Medical Center. He obtained a Fellowship in Hematology and Oncology at Mayo Graduate School of Medicine. Dr. Gertz is a Professor of Medicine at the Mayo Clinic in Rochester, MN, and his areas of interest are multiple myeloma, Waldenstrom's macroglobulinemia, and amyloidosis. He has authored numerous articles on these subjects in scientific journals and is a popular speaker at IWMF Educational Forums.

In Waldenstrom's macroglobulinemia, the principal problems are typically related to the progressive growth in the bone marrow of the malignant lymphoplasmacytic lymphoma cells, the so-called Waldenstrom's cells. This progressive growth of the malignant cells (the "weeds" in the bone marrow "garden") results in the loss of properly functioning bone marrow and the well-known symptoms associated with that loss, such as anemia with fatigue, loss of energy, and breathlessness. In this most common circumstance, the IgM protein in the blood, also known as the M spike or the IgM level, is merely a way in which we can measure the disease activity. A rising IgM protein would suggest that the marrow activity of the malignant cells is increasing, a falling level would usually reflect effective treatment of the Waldenstrom's, and a stable level would be what we would expect for most patients on watch-and-wait. In this situation, the IgM protein is not a significant component of the disease but is simply the measure we use, along with clinical signs and symptoms, to understand whether treatment is effective or whether treatment is required. It is important to remember that in most cases of Waldenstrom's, the problem is the bone marrow and not the blood protein.

As in most medical situations, there are exceptions. These exceptions are circumstances where the problem is not the bone marrow but rather the IgM protein in the bloodstream that misbehaves and causes illness due to unusual chemical properties of the IgM. The most common of these is neuropathy, and the next most common is hyperviscosity, neither of which will be covered in this article. Instead, this discussion will focus on two of the rare complications of IgM proteins with unusual properties: cold agglutinin hemolytic anemia and type 2 mixed cryoglobulinemia.

Cold agglutinin hemolytic anemia

Rarely, the monoclonal IgM protein develops the unusual ability to bind to the surface of the red blood cell. The red blood cell is the packet that carries hemoglobin through the circulation and delivers oxygen to all the tissues. On a routine blood count, you will notice that both the hemoglobin level and the red blood cell count are reported—these two measurements go hand-in-hand. In individuals who develop cold agglutinin hemolytic anemia, the IgM protein, which is usually at a very small level (often under 1,000 mg/dL), will bind to the red blood cell surface, and the protein changes the red blood cell so that it becomes recognized by the body's immune

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system as being "different." Because it is "different," the red blood cell is subsequently removed from the circulation and destroyed, resulting in lowering of the red blood cell count and consequent anemia.

The term "cold" in cold agglutinin is derived from the testing for this condition, which takes place on blood placed in the refrigerator at 38 degrees Fahrenheit (see **Figures 1 and 2**). "Agglutinin" or "agglutination" means that the red blood cells stick together and are seen as clumps in a refrigerated tube of blood. Cold agglutinins were identified over 100 years ago, and the very first monoclonal antibody ever identified was a cold agglutinin.

Figure 1. *This test tube contains a sample of refrigerated whole blood from a person with cold agglutinin disease. Note the clumping or agglutination that has occurred.*

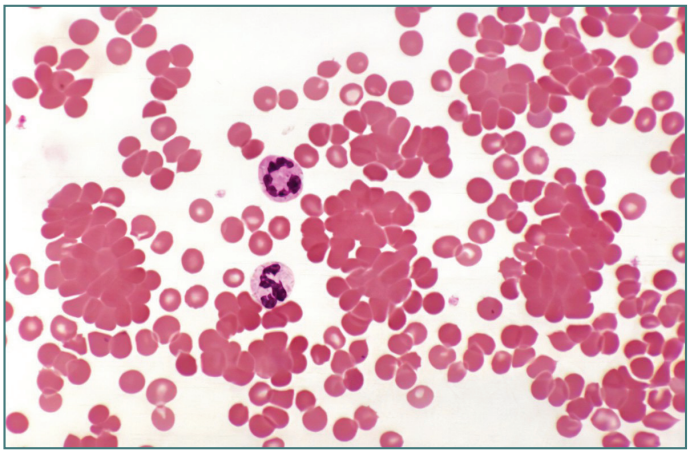

Figure 2. *Another view of red blood cells affected by cold agglutinin disease, this one showing how the red blood cells look under a microscope. Instead of being spread evenly on the slide, many of the red blood cells are in agglutinated clumps.*

Confusion may arise in an anemic patient with an IgM protein. Both active Waldenstrom's cells in the bone marrow as well as cold agglutinin disease from IgM in the blood can cause a person to be anemic. Specialized testing is required to determine which disorder is causing the anemia. When severe, the anemia of cold agglutinin disease can cause profound symptoms of weakness, shortness of breath, and fatigue. Occasionally, patients with cold agglutinin disease require blood transfusions. This can be a complicated process because the cold agglutinin IgM protein interferes with blood cross-matching required to provide safe blood for transfusion. Often specialized blood banking facilities are necessary to find compatible blood.

Although the most common symptoms of cold agglutinin disease relate to anemia, some patients will develop discoloration in their hands or feet upon exposure to cold temperature and may develop pain and redness in their fingertips, referred to as Raynaud's phenomenon. The bone marrow in cold agglutinin disease frequently will show Waldenstrom's macroglobulinemia with the widely recognized MYD88 genetic change. The average age at diagnosis is 71 years. Ninety-one percent of patients will have a monoclonal IgM protein. Some patients have an increased risk of developing blood clots. The severity of anemia is quite variable, and there are many patients with this disorder who are candidates for watch-and-wait. However, when the anemia is severe and interferes with quality of life, treatment is appropriate.

Previously, the most common treatments were identical to those used for Waldenstrom's. These include rituximab, rituximab combined with bendamustine, bortezomib, and ibrutinib. Recently, a new medication has been introduced—it acts by blocking the protein from sticking to the red blood cell surface and therefore prevents the red blood cell from being removed from the circulation and destroyed. This medication is called sutimlimab (Enjaymo) and is given as an injection under the skin that can be self-administered at home.

Type 2 mixed cryoglobulinemia

Rarely, an IgM protein can combine with other proteins and form a single unit that can gel in the bloodstream (think JELL-O). These gel complexes, called cryoglobulins, can deposit in the lining of blood vessels and cause them to be inflamed; the complexes will develop on exposure to cold temperatures and then will redissolve when warming occurs. The most common sites of inflammation are the blood vessels of the skin of the lower extremities. When this occurs, easy bruising and bleeding under the skin can be seen. The designation of type 2 cryoglobulinemia usually indicates that there is in IgM protein combined with an IgG protein that leads to the damage to the lining of blood vessels. There is also a type 1 cryoglobulin, but many of these are solely IgG-related and are not connected with Waldenstrom's. Type 2, commonly associated with Waldenstrom's, can occasionally cause kidney damage.

The skin lesions of cryoglobulinemia are quite harmless, painless, and generally do not require treatment if the skin

Overview, cont. on page 4

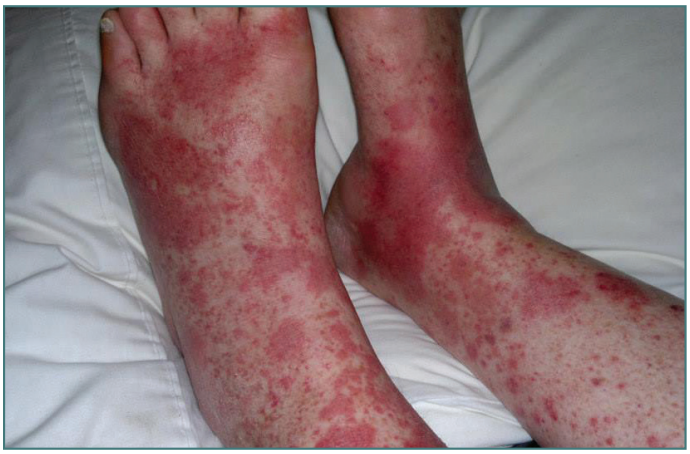

Figure 3. *Skin lesions, called purpura, on the legs of a person with cryoglobulinemia exposed to cold temperature.*

surface remains intact (see **Figure 3**). If the skin breaks, however, ulceration may occur and require intervention. Other organs can be affected by the deposit of this gel. The kidneys can be damaged by the gel, causing them to leak protein into the urine. Cryoglobulinemia is always a consideration in a Waldenstrom's patient who has protein in the urine, and kidney disease is seen in 35% of people with cryoglobulinemia. As stated above, this is particularly the case with type 2 cryoglobulinemia.

People with cryoglobulinemia often have a history of viral hepatitis that interacts with the IgM monoclonal protein to cause symptoms. Liver function is frequently abnormal. People with type 2 cryoglobulinemia usually have a positive rheumatoid arthritis blood test, and many of them can be misdiagnosed with rheumatoid arthritis if cryoglobulinemia is not considered as a possible cause.

Testing is simple and requires placing a sample of serum in the refrigerator for seven days to observe the formation of a gel (see **Figure 4**). Treatment of the underlying disorder can be quite complicated and may focus on treating the underlying hepatitis if present, treating the underlying Waldenstrom's, or treating the inflamed blood vessels that cause damage of the kidney and skin. Migratory joint pain (pain that spreads from one joint to another) and loss of feeling in the hands and feet may accompany cryoglobulinemia if the gel deposits in joint or nerves. Treatment generally requires referral to a specialized center.

Conclusion

Both cold agglutinin hemolytic anemia and cryoglobulinemia are IgM-related disorders that have uncommon activation at temperatures below normal body temperature. The two disorders, however, have very different clinical manifestations. The former causes serious degrees of anemia. The latter causes blood vessel inflammation, resulting in bruising on the lower legs and often kidney problems. However, in both instances, treatment may be directed at the bone marrow cells responsible for the production of the IgM monoclonal protein. All patients with an IgM protein should be aware of these rare manifestations of "misbehaving" IgM proteins.

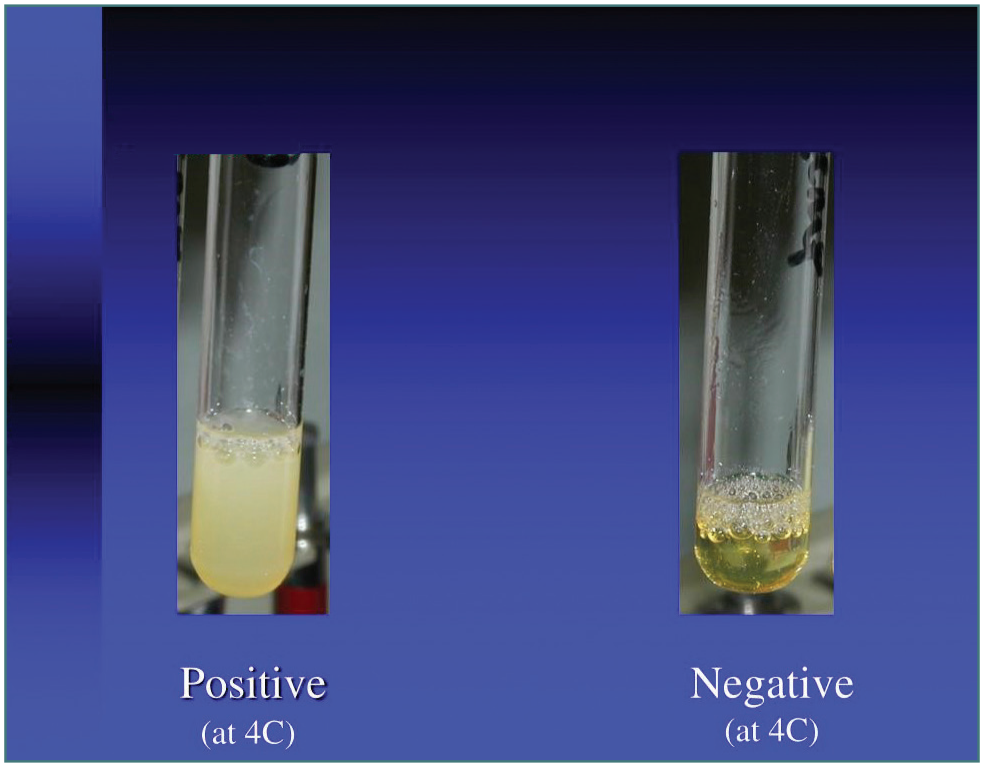

Figure 4. *Results of testing for cryoglobulins at cold temperature. The test tube of serum on the left with a white gel-like precipitate is a positive test, while the clear serum on the right is a negative test.*

Lisa in her "Medusa" hat, Shelly in her antique cloche

THE MANY HATS WE WEAR:

AN INTERVIEW WITH MICHELLE POSTEK AND LISA WISE

Michelle Postek (aka "Shelly") and Lisa Wise collaborate every day and wear many different hats for their IWMF work. They sat down over Zoom to chat about what's in the "special sauce" of their powerful partnership. To watch the recording of this interview—with exclusive questions and lots of fun hats—click on this link and prepare for a good laugh! *https://youtu.be/XcjNloNUrAE*.

FUN FACTS:
City Born In:
Shelly: Cambridge, Massachusetts, US
Lisa: Montreal, Canada (*Go Habs!*)

Decade Born In:
Shelly: 1980s (crimped hair, neon clothing, and legwarmers!)
Lisa: 1960s (song of the year: "California Dreamin'")

Favorite Sunday activity:
Shelly: Going shelling with my cousin at our favorite beach (Pass-A-Grille, St. Petersburg, FL)
Lisa: The beach! But with sunscreen—safety first!

NINE QUESTIONS:

Q: When did you start working with the IWMF? Please describe your title and responsibilities.

Shelly: I am the Manager of Information & Support and have worked at the IWMF for over three years. My responsibilities include: partnering with Lisa to coordinate IWMF regional and specialty topic support groups for US/International Affiliates and LIFELINE; acting as a first point of contact for new community members; creating the *The Waldenstrom's Weekly* newsletter; minor website editing; assisting with Stories of Hope on the IWMF website; entering information into our database and generating reports; serving on the Ed Forum and International Committees; facilitating publication translations; and more!

Lisa: I started volunteering with the IWMF after meeting then IWMF President Carl Harrington at my very first WM support group meeting in Philadelphia in 2014—he totally roped me in! On the Board since 2016, I am the Vice Chair for Information and Support, helping to coordinate our amazing support groups and LIFELINE. I also co-lead the Eastern PA and Southern NJ Support Group with Andrea Bensusan.

Q: What work did you do before you joined the IWMF?

Shelly: I have a background in social work and held multiple jobs in the field. I was a case manager for the homeless, foster care treatment coordinator, 1:1 student helper at a school, and care manager for seniors. I've worked in two senior retirement communities as an independent living social worker and in a sub-acute rehabilitation unit.

Lisa: For 16 years I worked as a family and patient centered healthcare specialist at Packard Children's Hospital at Stanford in Palo Alto, CA. I worked with senior administration to improve the patient experience in navigating the medical maze and chaired their Family Advisory Counsel. I'm also a trained mediator. My favorite job? Art teacher at summer camp!

The Many Hats We Wear, cont. on page 6

Lisa and Shelly at the IWMF Board meeting in Tampa, FL, 2019

Q: What drew you to work/volunteer with the WM community?

Shelly: I was excited that the IWMF is an international organization, offering the opportunity to connect with people all over the world. Before my interview, I perused the IWMF website and was inspired watching videos from Peter DeNardis, current Board Chair, and from Lu Kleppinger, former support group leader.

Lisa: A series of priceless connections. First, I met the WM global community on IWMF Connect. Then I made my first local friend, Carl Harrington, who modeled truly inspirational leadership. Then I needed treatment and reached out to LIFELINE volunteers for help. After experiencing the IWMF's invaluable free services, I just had to give back to others.

Q: Is there a WM moment that will stick with you forever?

Shelly: My first day at the IWMF, I attended a Board Meeting in Tampa, FL! I was very nervous, and when I arrived and was being greeted by folks, LISA WISE walked across the room with a big smile on her face and gave me a HUGE hug. It was such a warm welcome and took away my new work jitters! Carl Harrington invited me to sit beside him at dinner, and I sat across from Dr. Robert Kyle, who is a WM rockstar!

Lisa: Many WM patients share: "You are the first person I've ever spoken to who shares this weird diagnosis. You have no idea how comforting it is to meet someone with the same disease." Brings me to tears every time.

Q: What are the greatest WM challenges you hear about from patients and caregivers living with WM?

Shelly: Three greatest challenges: finding a doctor knowledgeable in WM, securing financial support for the cost of WM medications, and finding support to best meet their needs. We now have "specialty" groups and I'm helping create one to support patients facing the challenges of peripheral neuropathy (PN), which is extremely rewarding.

Lisa: How to hold two truths simultaneously: 1) I have cancer, which changes everything, and 2) I have a chronic, slow growing disease that I will probably die WITH not FROM, so I will live fully! How do you walk between those two realities, learning to live with chronicity *and* gratitude?

Q: When speaking with patients and caregivers around the world, what are the IWMF services and resources that they're most grateful for?

Shelly: I've heard that the IWMF information packet is an invaluable resource for getting acquainted with WM and learning about the community resources available. Connecting with a support group or LIFELINE volunteer is very meaningful, and our patient forums are buzzing all day with folks around the world supporting one another. A patient told me she "devours every issue of the *IWMF Torch!"*

Lisa: IWMF Physician's Directory. People, get that second consult from a WM expert, please!!!

Q: You have been working together in partnership for the past three years and three months. How does that collaboration impact the nature of your IWMF work?

Shelly: Our collaboration is truly a highlight of my job at the IWMF. Having a partner in WM crime who is on the same page to expand our programs and support patients and caregivers around the world is what keeps me motivated and excited for what's next on the horizon!

Lisa: It completely changed my life! Before Shelly arrived, my volunteering was unsustainable. Then the IWMF moved from a model of lay leadership managing programs to an

The Many Hats We Wear, cont. on page 7

outstanding, professional office team in charge…what a difference! The whole team is exceptional—ALL superstars! Shelly's specific expertise—her extensive background in social work, her heartfelt passion, and her ability to connect so deeply—makes her beloved by every person she touches. She makes you feel like you're the only person in the world and meets you where you are! She's invaluable.

Q: When creating new support groups, mentoring volunteer leaders, or interacting with WM patients globally, do you each have a specific, designated role?

Shelly: We work in partnership to interview new support group leaders and LIFELINE volunteers. At times we divide and conquer to address patient/caregiver or support group leader concerns. During our support group leader meetings, I am mostly working behind the scenes managing the meeting while Lisa does an amazing job moderating!

Lisa: Shelly has deep intuition and the most sensitive way of inquiring and making profound connections. We figure out organically what is needed in any situation and how to fill it. It's like doing a dance, and it just feels very natural and stress-free. Also, she's better at US geography (since I'm Canadian) and knows exactly where every state is—super helpful!

Q: What is the most important life lesson/shared wisdom you've learned from each other?

Shelly: One of my first days working at the IWMF, I attended a Sarasota Support Group meeting that Lisa facilitated in-person and observed her in action. The way she set the tone for the meeting, held a safe space for people to share, and then demonstrated care and compassion to attendees was inspirational! I continue being inspired by the way she holds the reins while moderating meetings. She is poised, professional, and always conveys her messages so beautifully. She is truly a role model for me!

Lisa: Shelly teaches us all how to lead with compassion—to never forget our core value of helping WM patients, first and foremost, and to put our whole heart into everything we do. Shelly can do ANYTHING! I can't ever take that magic for granted! She's like a swan, gracefully gliding along the water's surface effortlessly, but she must be paddling like mad underneath, sweating out every detail to ensure perfection! We just see her warm smile. How lucky are we?

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DRUG NAMES: WHY ARE THEY SO COMPLICATED?

By Glenn Cantor, Science Editor and IWMF Trustee

I received the following question recently from my support group leader:

"When you have a minute, would you explain for me why zanubrutinib is also called Brukinsa when it is manufactured by BeiGene?

"And so many meds end in either "-nib" or "-mab." There must be some reason for that.

"Thanks."

Here was my response, expanded slightly for this *Torch* article.

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Ah, the complicated world of drug names!

Drugs that make it to commercialization go through three major name stages:

First, the company that invents it gives it a prefix that indicates the company and a number. For example, ibrutinib used to be called PCI-32765. A number of old scientific papers talk about PCI-32765. PCI meant the company Pharmacyclics, and the number probably meant it was the 32,765th molecule that they had invented. (That's a lot of molecules on the shelf—of that large number, very few of them ever become commercial drugs.)

Once a potential drug undergoes preliminary testing, it is given a generic name, such as ibrutinib. In the US, this is done by a committee called the United States Adopted Name Council (USAN), which was established in 1961. Other countries have similar bodies, such as British Approved Names (BAN) in the UK and Dénominations Communes Françaises (DCF) in France. It is most convenient for a company to use the same name in many different countries, so an overarching organization called the World Health Organization International Nonproprietary Names Programme coordinates names among countries. Generic drug names are generally uniform among countries, although there are exceptions, especially with older drugs. (For example, "acetaminophen," the generic name in the US for Tylenol, is called "paracetamol" in other countries.) One important reason for this administrative structure is so that pharmaceutical companies do not inadvertently assign drug names that are the same or similar to other drugs' names, which might confuse doctors and pharmacists and lead to prescribing errors.

As you surmised, there is a rhyme-and-reason to these names. The USAN program has the stated goal of selecting "simple, informative" names. I can't say they succeeded in that goal, but here is how it works. The names are built with a series of roots and suffixes. For example, a drug that is an "inhibitor"—meaning it blocks a biological process—ends in "-nib" (ib = inhibitor). The next-to-last syllable "-ti-" indicates it inhibits a particular class of proteins called tyrosine kinases. So, ibrutinib is an inhibitor ("ib") of a tyrosine kinase ("ti"), in this case, one called BTK. Zanubrutinib (which also ends in "-tinib") is another inhibitor of the tyrosine kinase BTK.

Another suffix that you asked about is "-mab." For example, with rituximab, the "-mab" at the end of the name stands for "monoclonal antibody." The next-to-last syllable, "-xi-" means the monoclonal antibody is chimeric, or a combination protein containing portions derived from mouse antibodies and portions derived from human antibodies. One reason that some people have infusion reactions to rituximab is because the human body reacts to these "foreign" mouse portions. On the other hand, if an antibody is derived purely from human proteins, it contains the next-to-last letter "-u-."

Other syllables refer to the general target of the antibody. For example, "-l-" means that the antibody targets the immune system (the letter "l" stands for lymphocyte, one of the immune cells). For the antibody called nivolumab, "-mab" means it is a monoclonal antibody, "-u-" means it is derived purely from human proteins, and "-l-" means it targets the immune system, in this case to stimulate lymphocytes to attack certain cancers.

Generic drug names** are generally uniform among countries, although there are exceptions, especially with **older drugs.

Similar rules were devised for a great number of drugs, not just those used for WM. Antiviral drugs end in "-vir." The principal drug in the COVID treatment Paxlovid is nirmatrelvir. The blood thinner apixaban ends in "-xaban" because it is a Factor Xa inhibitor. Other endings are much less obvious. Heart medications in the beta-blocker category end in "-olol" and proton-pump inhibitors, used to control stomach acid, end in "-prazole."

There are lots of other rules and suffixes for generic drug names. And every once in a while, to make things more complicated, the rules are changed.

Once a drug is close to being approved for marketing, the company gives it a commercial name. Commercial names are

Drug Names, cont. on page 9

trademarked, meaning that the company owns the name, and it cannot be used by others. There are all sorts of marketing psychologies, which I don't understand, behind choosing a name. The company also does an exhaustive search of hundreds of global languages to make sure the name doesn't mean something crazy, unintended, or embarrassing. Commercial names are not necessarily shared worldwide and can be unique to each country. However, companies often use the same name in different countries. The commercial name for ibrutinib in the US is Imbruvica—it is also the commercial name for ibrutinib in Europe. Sometimes, you will see the names ibrutinib and Imbruvica used interchangeably in articles about WM. BeiGene, the company that developed zanubrutinib, gave it the commercial name Brukinsa. The name Brukinsa is also used in Europe and elsewhere.

When a drug is manufactured in a ***generic form,*** *the copying companies are not allowed to use the original company's* ***commercial name.*** *The drug name must* ***revert*** *back to the generic name.*

Then, to make matters more complicated, drugs are only patented for a certain number of years. When the patent period expires (called "going off patent"), other companies are allowed to copy it. These copies are called generics. When a drug is manufactured in a generic form, the copying companies are not allowed to use the original company's commercial name. The drug name must revert back to the generic name. For example, some day in the future, ibrutinib will be available as a generic drug, which hopefully means it will be cheaper. When that happens, the generic ibrutinib cannot be called Imbruvica. It will have to be called ibrutinib.

There's another twist when protein drugs (called "biologicals"), such as monoclonal antibodies, go off patent, and other companies try to copy them. Unlike small molecules, such as ibrutinib, that are chemically synthesized and can be copied exactly, it is almost impossible to exactly copy an original protein product (see the April 2020 article on biosimilars in the *Torch*, Volume 21.2: *https://iwmf.com/iwmf-torch/*).

That's why they are called biosimilars and not, say, bioidenticals. Without a lot of clinical experience, it is impossible to know if the slight differences between the biosimilar and the original are clinically meaningful or not. Therefore, the medical community and the US Food and Drug Administration (FDA) track differences between biosimilars and the original biologicals. To track them, they have to be given different generic names; otherwise, doctors and even regulators wouldn't know which patient was getting which product. The matter was resolved in a 2017 decision by the FDA, stating that biosimilars should use the generic name of the original drug, plus a hyphen and a four-letter suffix. The suffixes don't have meaning—they are random combinations of letters. The suffixes do, however, need to be approved, so that different companies don't inadvertently create confusion with the same or similar suffix. For example, there's a rituximab biosimilar called "rituximab-arrx." This biosimilar is made by the company Amgen and has been given the commercial name of Riabni. The drug Humira (generic name adalimumab), which is commonly used for autoimmune disorders, now has many biosimilars. These biosimilars all start with the word "adalimumab," but then end in suffixes such as "-atto," "-adbm," "-adaz," "-bwwd," and "-afzb."

Aren't you glad you asked?!

Have Your Say

The *Torch* welcomes letters, articles, or suggestions for articles. If you have something you'd like to share with your fellow WMers, please contact *IWMF Torch* editor Shirley Ganse at *shirleyganse@hotmail.com*

THE IWMF AND DR. TROTMAN TO THE RESCUE IN THE LAND DOWN UNDER

By Joel Rosenblit

Without the help of the IWMF and Dr. Judith Trotman, my recent visit to Australia could have ended with a severe case of COVID. I've lived to tell the tale.

I was diagnosed with WM in 2006 and was on watch-and-wait until I developed peripheral neuropathy in 2014. I was treated in 2015 with cyclophosphamide, rituximab, and dexamethasone and have not needed treatment since then.

Joel Rosenblit and his granddaughter Daisy

In January 2022, my wife and I traveled from our home in the US to visit our daughter, son-in-law, and two grandchildren, Rose and Daisy, in Sydney, Australia. We last visited Rose, now a three-year-old, in January 2020, before the pandemic. Daisy is one, and we had never held or hugged her. We could not be there for Daisy's birth, as we were for Rose's birth, because of COVID.

We planned to stay for two months as our daughter returned to work from her year-long maternity leave. When we left for Sydney, I was a few days short of qualifying for a fourth vaccine shot. I brought a print-out of the IWMF Directory of WM Physicians with me. There were two WM specialists listed in Sydney—I emailed Dr. Judith Trotman and she responded promptly. She offered to write me a prescription for a fourth shot and suggested a friendly pharmacy to use. She also said to contact her again if I contracted COVID because she could help me get sotrovimab, a monoclonal antibody treatment for the virus.

Australia had strict lockdowns to control the spread of COVID during the initial phase with the delta variant. If you were caught outside with an unrelated group or without a good reason, you could incur a large fine. My daughter lived near famous Bondi Beach where mounted police patrolled to prevent its use. The usually crowded beach was deserted. Melbourne endured the longest lockdowns. When Sydney locked down, my daughter and son-in-law had a difficult time. They were both working from home, and the kids could not go to pre-school or day care. One worked while the other looked after the kids for a half a day and then they switched. It was easy to go stir crazy staying at home for weeks. However, like the vast majority of Australians, they accepted the lockdowns as necessary to stop the spread of COVID. Australian culture is not as individualistic as American culture, with less mistrust of the government than in the US, particularly when it comes to public health. Voluntary compliance with lockdowns, contact tracing, masking, testing, and vaccination have kept hospitalizations and deaths low and protected the immunocompromised, such as WM patients. Over 95% of Australians aged 16 and over are fully vaccinated, and 70% have received booster shots.

With the rise of the omicron variant and its increased transmissibility but fewer hospitalizations and deaths, the Australian state government gave up its policy of strict lockdowns and contact tracing, moving to testing and quarantines at home for folks who tested positive. We were allowed to visit as parents of an Australian citizen under a policy of family reunification (my daughter is a dual US and Australian citizen).

View of Sydney Harbor from the zoo, showing the iconic Opera House and Harbor Bridge

The IWMF and Dr. Trotman to the Rescue, cont. on page 11

When we arrived in Australia, people were still masking, but that became less prevalent during our stay. We tried to take precautions while we were there, but with the kids going to pre-school and daycare and our daughter and son-law being less cautious as Australia loosened restrictions, our luck ran out.

The day before we were scheduled to leave, we took a PCR test for COVID, required for reentry into the US. We tested positive and could not fly out the next day. The whole family, all six of us, were positive!

I emailed Dr. Trotman, and she came through again. Two days after my positive test and a day after I exhibited symptoms (mainly a bad cough), I was an outpatient in a hospital getting IV sotrovimab. Despite being immunocompromised, I had a very mild case of COVID, unlike my daughter who was quite sick. The whole family stayed home for a week.

Our return to the US was delayed for three weeks until we were no longer contagious, could rebook our flight, and jump through some bureaucratic hoops placed in our way by Qantas, our airline, and the US Centers for Disease Control and Prevention.

Without the help of Dr. Trotman, I would probably have had a more severe case of COVID. She refused to charge me for her services but asked me to give to the foundation called Great Bloody Cause, which supports her research by funding clinical trials for blood cancer patients. I gladly donated to the foundation (as I do annually to the IWMF). Without the IWMF and its Physicians Directory, I would never have found Dr. Trotman. I am so grateful to the IWMF and to Dr. Trotman.

MEDICAL NEWS ROUNDUP

By Sue Herms, IWMF Research Committee Member

Ibrutinib and Zanubrutinib for WM Treatment Rejected for Authorization in England and Wales – The National Institute for Health and Care Excellence (NICE) in England and Wales has rejected authorization of ibrutinib (Imbruvica) for the treatment of relapsed or refractory WM. The drug had been available as relapsed therapy for the past two years, but authorization was withdrawn upon the second (and final) NICE appraisal of the drug. The rejection was primarily based on NICE's cost vs. benefit analysis for ibrutinib compared to chemoimmunotherapy. WM patients currently on ibrutinib through the Cancer Drugs Fund will be able to continue but with funding provided by Janssen, the drug's manufacturer. Meanwhile, in a separate ruling, a first appraisal by NICE has rejected authorization of zanubrutinib (Brukinsa) for relapsed or refractory treatment of WM or as first-line treatment when chemoimmunotherapy is unsuitable. A final appraisal of zanubrutinib by NICE is planned in the coming months.

Article Discusses Emerging Problem of Acquired Resistance to Ibrutinib in WM – Despite high response rates and durable remissions with ibrutinib (Imbruvica), acquired resistance, or reduced effectiveness over time, to the drug represents an emerging problem in WM patients. An article in the journal *Haematologica* discussed a study of 51 WM patients who had acquired resistance to ibrutinib. The median time between the start of ibrutinib treatment and its discontinuation because of resistance was two years; following discontinuation, a rapid increase in the IgM level was observed in 29 patients, of whom ten developed acute symptomatic hyperviscosity (increased blood thickness). The authors proposed several mechanisms for this rapid disease progression: 1) the BTK substrate STAT5A regulates IgM secretion in WM cells, and its reactivation following ibrutinib withdrawal likely contributes to the rapid increase in IgM; 2) acquired ibrutinib resistance is associated with the expansion of BTK and PLCg2 mutations that trigger other cancer cell survival pathways; 3) deletions in chromosomes 6q and 8p remove genes that regulate BTK, MYD88, NF-kappa B, and programmed cell death signaling. After salvage therapy with other treatments, patients in this study achieved overall and major response rates of 56% and 44% respectively, and the median duration of response was 48 months. The five-year overall survival following discontinuation of ibrutinib was 44%, with TP53 gene mutations associated with shorter survival. These findings indicate that close monitoring of serum IgM levels is necessary in WM patients immediately after stopping ibrutinib. Patients who received salvage therapy within one week of ibrutinib discontinuation had a significantly lower risk of IgM rebound, as well as a higher response rate to salvage therapy. Notably, combining ibrutinib with subsequent salvage therapy for one or two cycles—called "bridging therapy"—achieved a response in all patients and may represent a strategy to maintain disease control. The optimal treatment regimens for WM patients after ibrutinib have yet to be established with prospective clinical trials.

Abstract from EHA 2022 Congress Evaluates Bendamustine and Rituximab Frontline Therapy in Large Group of WM Patients – A multicenter international evaluation of frontline therapy with bendamustine and rituximab (Rituxan) for WM was presented at the recent

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European Hematology Association (EHA) 2022 Congress. Records of patients with newly diagnosed, active WM who received this BR therapy between January 2012 and July 2021 in the US and Europe were reviewed. Mutation status for MYD88 and CXCR4 was captured, if available. Among 248 patients studied, 208 received BR without subsequent rituximab maintenance. The median follow-up was four years. The estimated median progression-free survival was 5.9 years, and the estimated five-year overall survival was 90%. The overall response, major response, and very good partial response rates were 95%, 93%, and 31%, respectively. Patients with disease progression within 24 months of BR therapy had an inferior subsequent survival at five years (71%) compared to those without disease progression within this time period (86%). Among 131 patients with known MYD88 mutation status, 88% had the MYD88 L265P mutation; the four-year progression-free survival was 71% for both MYD88 L265P mutated and wild-type (unmutated) patients. The very good partial response rates were comparable between the two groups (41% for mutated and 50% for wild-type patients). Among 42 patients with known CXCR4 mutation status, 28% harbored a CXCR4 mutation. The very good partial response rate for patients with CXCR4 mutations was lower at 33% vs. 57% for those with wild-type (unmutated) CXCR4. A trend toward shorter progression-free survival among patients with CXCR4 mutations was observed. Among the 40 patients who received rituximab maintenance following BR therapy, the four-year progression-free survival for the maintenance group was 89% vs. 73% for patients who did not receive maintenance; overall survival was comparable for both groups.

AACR Research Presentation Suggests That Mavorixafor Combined with BTK Inhibitors May Be Useful for Treating WM Patients with Unmutated CXCR4 – A report presented during the American Association of Cancer Research (AACR) Annual Meeting 2022 discussed the use of mavorixafor along with BTK inhibitors to overcome the protective effect of the bone marrow on WM tumor cells. Mavorixafor, an antagonist to CXCR4, is currently being investigated in combination with ibrutinib in WM patients with CXCR4 mutations and showing promising interim results; however, the effects of this combination had not yet been investigated in patients with unmutated (wild-type) CXCR4. This study, presented by X4 Pharmaceuticals, used WM cell lines that were MYD88 mutated and CXCR4 unmutated and cultured them with bone marrow stromal cells, mavorixafor, and various BTK inhibitors, including ibrutinib, zanubrutinib, evobrutinib, pirtobrutinib, and nemtabrutinib. The mavorixafor/BTK inhibitor combinations overcame the protective effect of the bone marrow on tumor cells, decreasing their viability and increasing apoptosis (programmed cell death) compared to BTK inhibitors alone. Notably, mavorixafor by itself inhibited the migration of WM cells and disrupted their adhesion to the bone marrow; it also reduced IgM secretion, which was further decreased when combined with BTK inhibitors. The study's authors suggested that these findings may support the greater potential of this combination in WM patients with or without CXCR4 mutations.

Cellectar Biosciences to Proceed with Continuation of Iopofosine (CLR 131) in Phase 2b Study in WM – Cellectar Biosciences announced that an independent Data Monitoring Committee has completed its assessment of the company's Phase 2b study of iopofosine (CLR 131) in WM and has recommended continuation of the trial, which will enroll 50 WM patients. Participants in the continuing trial will receive up to four doses of the drug over two cycles. Iopofosine is a small molecule phospholipid drug conjugate designed to provide targeted delivery of radioisotope iodine-131 to the cancer cells. The trial identifier on *www.clinicaltrials.gov* is NCT02952508.

*A **new bill (HR 2471)** recently signed into law will extend Medicare telehealth coverage for 151 days... after the COVID-19 Public Health Emergency is expected to **officially** end...*

China Accepts Supplemental New Drug Application for Orelabrutinib for Relapsed or Refractory WM Treatment – InnoCare Pharma announced that the China National Medical Products Administration has accepted a supplemental New Drug Application for the BTK inhibitor orelabrutinib for the treatment of patients with relapsed or refractory WM.

Coverage for Telehealth Services Will Be Extended for Medicare Recipients – A new bill (HR 2471) recently signed into law will extend Medicare telehealth coverage for 151 days, or approximately five months, after the COVID-19 Public Health Emergency is expected to officially end sometime in the next few months. Under the provisions of the bill, Medicare beneficiaries can continue to receive the following: 1) coverage for telehealth services from wherever they are located within the US, including their homes; 2) coverage for telehealth services from physical and occupational therapists; 3) coverage for telehealth services from mental health providers without the requirement of an in-person visit within six months of the first telehealth service with that provider or the requirement of an in-person visit every 12 months; 4) coverage for telehealth services using audio-only technology; and 5) coverage for telehealth services from certified Federally Qualified Health Centers and Rural Health Clinics. Some states have restrictions and limitations

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that govern private payer and Medicaid reimbursement for telehealth services, so telehealth users in these plans should check with their private insurer or state Medicaid program to find out which services are covered.

Recent guidance indicates that immunocompromised adults should receive a ***second booster*** *shot of Pfizer or Moderna.*

CDC Posts Latest COVID-19 Vaccination Guidance for the Immunocompromised – The US Centers for Disease Control and Prevention (CDC) has posted the latest COVID-19 vaccination guidance for moderately and severely immunocompromised adults. Recent guidance indicates that **immunocompromised adults should receive a second booster shot** of Pfizer or Moderna. To view the complete guidelines, go to *https://www.cdc.gov/vaccines/covid-19/clinical-considerations/covid-19-vaccines-us.html#considerations-covid19-vax*, scroll down to the section "COVID-19 Vaccines, Recommendations, and Schedule," and click on the heading "People who are immunocompromised." To briefly summarize the guidelines:

- For those who receive the initial two Pfizer or Moderna vaccines, a third primary shot of Pfizer or Moderna should be received at least four weeks afterward, with Moderna dosing at full strength (100 µg in 0.5 mL). A booster (fourth) shot of Pfizer or Moderna should be received at least three months after the third primary shot. A second booster (fifth) shot of Pfizer or Moderna should follow if it has been at least four months after the first booster. For all Moderna booster shots, dosing is at half strength (50 µg in 0.25 mL).
- For those who receive the initial J&J vaccine, a second primary shot of Pfizer or Moderna should be received at least four weeks afterward, with Moderna dosing at full strength (100 µg in 0.5 mL). A booster (third) shot of Pfizer or Moderna should be received at least two months after the second primary shot. A second booster (fourth) shot of Pfizer or Moderna should follow if it has been at least four months after the first booster. For all Moderna booster shots, dosing is at half strength (50 µg in 0.25 mL). However, the CDC notes that, because the second primary shot following the J&J vaccine is a newer recommendation, many recipients of the initial J&J shot may have received a booster shot without having had the second primary shot. In this special situation, regardless of the type and timing of the second shot, a third Pfizer or Moderna shot should be received at least two months after the second shot, with Moderna dosing at full strength (100 µg in 0.5 mL). Recently, the US Food and Drug Administration strictly limited the use of the J&J vaccine because of a rare but serious risk of blood clots. The J&J vaccine is now available only to adults who specifically request it and will not otherwise accept vaccination or who are unable to receive other COVID-19 vaccines because of allergic reactions or other conditions.

US FDA Withdraws Sotrovimab from Emergency Use Authorization for COVID-19 Treatment – The US Food and Drug Administration (FDA) has withdrawn emergency use authorization for the monoclonal antibody therapy called sotrovimab, which was being used to treat patients infected with COVID-19 who are at increased risk of developing severe disease, hospitalization, and death. The FDA determined that sotrovimab is unlikely to be effective against the coronavirus BA.2 variant, which at press time is still the dominant variant in the US (although it is being rapidly overtaken by a subvariant of BA.2 called BA.2.12.1).

The FDA determined that ***sotrovimab*** *is unlikely to be effective against the coronavirus* ***BA.2 variant...***

Health Canada Approves Evusheld to Help Prevent COVID-19 in Immunocompromised Canadians – Health Canada has approved AstraZeneca's Evusheld, an injectable two-drug combination used for the prevention of COVID-19, in individuals aged 12 years and older who are immunocompromised and unlikely to mount an adequate immune response to vaccination or for whom vaccination is not recommended. Evusheld has already received emergency use authorization by the US Food and Drug Administration and is recommended by the European Medicines Agency. AstraZeneca has an arrangement with Canada to supply 100,000 doses of Evusheld to be delivered in 2022.

New Oral Drug Cuts Mortality Rate from COVID-19 in Phase 3 Trial – A new oral drug called sabizabulin has the potential to cut the mortality rate in half for moderate and severe cases of COVID-19 disease, according to the manufacturer Veru Inc. Data reported from a Phase 3 trial of 150 patients at high risk of acute respiratory distress syndrome from COVID indicated that the drug significantly reduced

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the mortality rate to 20%, compared to a 45% mortality rate for those on placebo. Sabizabulin has received Fast Track designation by the US Food and Drug Administration, and emergency use authorization is being sought by the manufacturer. Sabizabulin functions as both an anti-viral and an anti-inflammatory drug that targets cellular structures called microtubules, which the coronavirus uses to travel into cells to infect them.

...news media are reporting that doctors are observing apparent ***relapses*** *after the prescribed five-day course of* ***oral Paxlovid*** *to treat mild or moderate COVID-19 infections.*

Experimental COVID-19 Vaccine Leads to T Cell Immune Responses in Patients with B Cell Deficiencies – An experimental COVID-19 vaccine, called CoVac-1, produced T cell immune responses in 93% of patients with B cell deficiencies (including patients with leukemia and lymphoma), according to results presented at the American Association for Cancer Research Annual Meeting 2022. The study, presented by German researchers, noted that currently approved COVID-19 vaccines rely heavily on antibody responses, which may be impaired in people with a B cell deficiency. One way to compensate for this is to enhance the body's response from T cells, another type of immune cell. The researchers chose six specific antigens from different parts of the COVID-19 virus, not just the spike protein, to make up their vaccine. Also, CoVac-1 is a peptide vaccine, meaning that the protein pieces are injected directly, rather than being encoded via messenger RNA. A Phase 1 trial of the vaccine included patients with leukemia or lymphoma, and T cell immune responses were observed in 71% of patients 14 days following vaccination, increasing to 93% after 28 days. A Phase 3 trial to evaluate CoVac-1 in a larger population of immunocompromised individuals is being planned.

Some Patients Are Experiencing COVID-19 Symptom Recurrence After Completing Paxlovid Treatment – Several articles in the popular news media are reporting that doctors are observing apparent relapses after the prescribed five-day course of oral Paxlovid to treat mild or moderate COVID-19 infections. Clinical trial data submitted by Pfizer to the US Food and Drug Administration indicated that about 2% of participants appeared to have a rebound in viral RNA levels around day 10 to day 14, and real-world reports appear to be confirming rebound increases in viral loads and usually mild symptoms that recur several days after some people have completed their course of Paxlovid treatment. Not much is understood about this phenomenon, including whether a repeat course of Paxlovid may be necessary in these cases.

Pirtobrutinib Is Now Available Under FDA Expanded Access Program – Pirtobrutinib, a BTK inhibitor currently in clinical trials for participants with B cell cancers (including WM), is being made available under the US Food and Drug Administration (FDA) Expanded Access Program for relapsed or refractory patients with an urgent life-threatening situation who have no satisfactory therapy options available and are not eligible for clinical trials. Expanded access is also commonly referred to as "compassionate use." Under this program, a treating physician should contact the manufacturer, Eli Lilly and Company, if a patient meets the criteria for inclusion in the expanded access program for pirtobrutinib.

TG Therapeutics Withdraws Umbralisib from Treatment for Several B Cell Cancers – TG Therapeutics announced that it is voluntarily withdrawing the PI3K inhibitor umbralisib (Ukoniq) from use in the clinical trial combination of umbralisib plus the monoclonal antibody ublituximab to treat chronic lymphocytic leukemia and small lymphocytic lymphoma. The company is also withdrawing the drug for sale in already-approved treatment indications for marginal zone lymphoma and follicular lymphoma. Updated data from the Phase 3 UNITY-CLL trial showed a reduction in overall survival in the umbralisib/ublituximab arm when compared to the control arm of the trial. The US Food and Drug Administration has expressed concerns about the serious toxicities of PI3K inhibitors (idelalisib, copanlisib, duvelisib, and umbralisib) currently used in blood cancer patients and plans to discuss the appropriate approach for their use.

Mustang Bio Updates Interim Phase 1/2 Trial Data for CAR T Cell Therapy in Relapsed or Refractory B Cell NHL and CLL – Mustang Bio updated interim Phase 1/2 clinical trial data for its CAR T cell therapy targeted to CD20 in patients with relapsed or refractory B cell non-Hodgkin's lymphoma (NHL) and chronic lymphocytic leukemia (CLL). The therapy, called MB-106, was used at five dose levels in 25 patients (including some with WM). An overall response rate of 96% and a complete response rate of 72% were observed, with the WM patients in the trial achieving a response rate of 100%. Two NHL patients who had relapsed from previous CD19-directed CART T cell therapy responded to MB-106. No patients experienced severe cytokine release syndrome or neurotoxicity. The trial is being conducted at Fred Hutchinson Cancer Center in Seattle, which developed the therapy along with Mustang Bio. The company is also collaborating with the National Cancer Institute (NCI) to open another Phase 1/2 trial of MB-106 at multiple centers for patients with relapsed or refractory B cell NHL (to include WM) and CLL. The trial expects to enroll 287 participants and is identified as NCT05360238 on *www.clinicaltrials.gov*.

Phase 1 Study Results Discussed for Bispecific Antibody Odronextamab in Relapsed or Refractory B Cell NHL – An article in the journal *The Lancet Haematology* reported Phase

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1 study results of a bispecific antibody called odronextamab used for the treatment of relapsed or refractory B cell non-Hodgkin's lymphoma (NHL). The study, designated ELM-1, was conducted at ten sites across the US and Germany. Odronextamab is a fully human antibody and binds both the CD3 surface antigen on T cells and the CD20 surface antigen on B cells, thereby recruiting the body's own T cells to help destroy CD20 positive cancer cells. During dose escalation, the therapy was administered intravenously up to the maximum dose of 320 mg once per week, and no dose-limiting toxicities were observed. The objective response rate was 51%; the most common serious adverse events were anemia, low lymphocyte count, low phosphorous level, low neutrophil count, and low platelet count.

Investigational New Drug Applications Accepted in US and China for Non-Covalent, Reversible BTK Inhibitor – The US Food and Drug Administration and the China National Medical Products Administration have accepted Investigational New Drug applications from TransThera Sciences for its drug candidate TT-01488 to treat B cell lymphomas. TT-01488 is a non-covalent, reversible BTK inhibitor; this type of BTK inhibitor is not affected by the C481S mutation in BTK that can cause resistance to covalent BTK inhibitors such as ibrutinib (Imbruvica). The company stated that it intends to launch Phase 1 clinical trials in the US soon.

The author gratefully acknowledges the efforts of Glenn Cantor, Grete Cooper, Steven De Cenzo, Peter DeNardis, Julianne Flora-Tostado, Tom Hoffmann, Pavel Illner, Meg Mangin, Colin Perrott, Howard Prestwich, Richard Savoy, Charles Schafer, Ron Ternoway, and others in disseminating research news of interest to the WM community. The author can be contacted at suenchas@bellsouth.net *for questions or additional information.*

LIVING A FULL LIFE WITH WM

By Arthur Brewer

Art Brewer

I am a 58-year-old Black man who was diagnosed with Waldenstrom macroglobulinemia (WM) in 2019. My WM story began in September of that year when I visited my primary care physician for a routine annual physical examination, shortly after a family vacation to Jamaica to celebrate my daughter's high school graduation. I was in a good place emotionally, having just accepted a new job offer and—travel enthusiast and history buff that I am—looking forward to a long-awaited trip to Israel in the spring.

In the past, I had received my bloodwork results within a few days, but this time there was an unusual and disturbing delay. When I finally received the results over a week later, I was shocked to discover my blood counts were abnormal. Specifically, I had anemia, a high white blood cell count and an elevated IgM level of 2,800 mg/dL. Aside from mild but persistent shortness of breath and weight loss (which I attributed to a lingering cold and work stress, respectively), I felt fine and was largely asymptomatic. The official diagnosis was "monoclonal gammopathy of undetermined significance (MGUS)," meaning I had an abnormal monoclonal protein in my blood that is often a precursor to multiple myeloma, another blood cancer. I asked myself, "How could this be cancer when I feel fine, and why now, when I have so much to look forward to?"

My doctor referred me to a hematologist for further evaluation. After a PET scan, a bone marrow biopsy and additional blood tests, the hematologist pinpointed my condition as WM in October 2019. It was distressing, to say the least, to find out I had a rare and incurable subtype of non-Hodgkin's lymphoma, especially since I had been in very good health prior to this diagnosis. My father died from complications related to non-Hodgkin's lymphoma in 1991 at the age of 82, so I assumed the worst. However, the hematologist assured me that although incurable, the disease was manageable, and I could live for decades with treatment.

In short order, I went through four of the stages of grief—denial, anger, bargaining, and depression—but quickly arrived at acceptance without looking back. I was grateful

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that the disease was detected early and that I was in the care of a specialist I trusted and liked, one who worked at a highly regarded cancer treatment facility.

Since I was largely asymptomatic, my hematologist advised me to adopt a watch-and-wait approach and to begin treatment when symptoms had sufficiently worsened. The stress of the disease was compounded by the start of the COVID pandemic and a toxic work environment at my new job.

As my blood counts steadily deteriorated over the course of the next year (my hemoglobin dropped to 10 g/dL, my platelet level rose to 646,000, and my IgM level climbed to 3,430 mg/dL), my hematologist advised me to begin treatment in October 2020. She gave me the option of treating the disease with a chemotherapy combination of bendamustine and rituximab, or with rituximab accompanied by a daily oral dose of ibrutinib for an indefinite period. I chose the latter option because recent studies had shown it to be highly effective with fewer side effects.

During my first infusion of rituximab, I developed chills and uncontrollable tremors that required the infusion to be temporarily suspended. After a short hiatus, the infusion resumed, and I never experienced any more side effects during subsequent treatments. The ibrutinib has caused only minimal side effects, including mild hypertension and arrhythmia, which I have under control with medication, as well as minor bruising. My IgM level has consistently been below 1,000 mg/dL since January 2021, a significant reduction since treatment began, and all of my blood counts are well within normal range. In short, I feel great and live a full life largely unhindered by symptoms of the disease.

That doesn't mean I haven't had bumps in the road. One particularly distressing experience was my bout with COVID in December 2021 right before the holidays, despite being fully vaccinated and boosted. I first noticed a sore throat the Sunday before Christmas that got progressively worse throughout the day. That evening, my wife and I took my daughter out to dinner to celebrate her 21st birthday, and when I returned home, I had a fever, chills, and a headache in addition to the sore throat. Several of my family members have died from COVID, and as an immunocompromised person, I knew this could be serious indeed, if I had contracted this dreaded disease as suspected.

The next morning, I drove myself to a COVID testing center and waited in line for about an hour in 20-degree weather, just to put my name on the list to be tested. Then I returned home and waited to be notified to come back for the test later that day. I was not surprised when the results were positive. I promptly notified my hematologist, got in bed, and stayed there in isolation for the next few days.

By Christmas Day, I was out of bed, but still under quarantine, and felt well enough to work from home the next week. Fortunately, my case was not severe, with no breathing difficulties or loss of taste or smell, nor do I have any lasting side effects from the disease. I am also fortunate that neither my wife nor my daughter, both fully vaccinated and boosted, contracted COVID.

Art with his wife Iris and daughter Kristen at SHI Stadium at Rutgers University in Piscataway, NJ

As a Black WM patient, I am aware that this rare disease is even less prevalent among people of color, and that there are ethnic disparities in cancer treatment and outcomes. Given this reality, I try to stay abreast of the latest developments in WM and tap into available educational resources. I subscribe to the *IWMF Torch* and have joined the WM People of Color Support Group, as well as the WM support group for the New York metro area and the WM Facebook group. For such a rare disease, it is important to connect with fellow patients to reduce the feeling of isolation, share information with them, and benefit from their collective wisdom. Knowledge is power, and forums like these are valuable resources.

Since April 2021, I have been under the care of a different hematologist who is one of the top specialists in the field of lymphoid malignancies, including WM, after my former hematologist accepted a new position. So far, I have been spared the debilitating health challenges faced by many other WM patients, who tend to be older than I am. My quality of life has not been significantly diminished, and while the disease is always in the back of my mind, it has not become an overwhelming concern. I take reasonable precautions to prevent contracting COVID without isolating myself. I now have a very satisfying job with a flexible work schedule, and I have never missed a day from work because of WM, except for doctor's appointments. I work out and exercise every day and try to eat healthy meals (though I have so far been unable to shed the excess weight I gained during the pandemic and since my recovery!). I am surrounded by loving and supportive family and friends and am determined to enjoy life to the fullest for as long as I can.

When I was initially diagnosed, my primary desire was to live long enough to see my daughter graduate from college. Now, encouraged by my prognosis and the new and effective treatments on the horizon, I look forward to walking her down the aisle someday and doting on my grandchildren to come.

FROM THE FACEBOOK WM SUPPORT GROUP: SUMMER 2022

By Betty Ann Morton

Our Facebook WM Support Group continues to grow, currently numbering approximately 5,000 WMers and support people. People post from Lebanon, South Africa, Belgium, the UK, Taiwan, the US, and Canada, among other countries. This group understands the "I for International" in IWMF.

Although we all hoped that COVID-19 would be just a bad memory by now, the Facebook WM Support Group has continued discussing many issues related to it: what precautions are needed and how to balance those with the desire to live a more normal life; the effectiveness of vaccines for immunocompromised people; and the availability of the preventative Evusheld and of various treatments such as Paxlovid.

DW wrote, "So my hematologist said I could go out masked and distanced. No stores or restaurants. What is everyone else doing? Are you going to stores? Are you masked? Restaurants?"

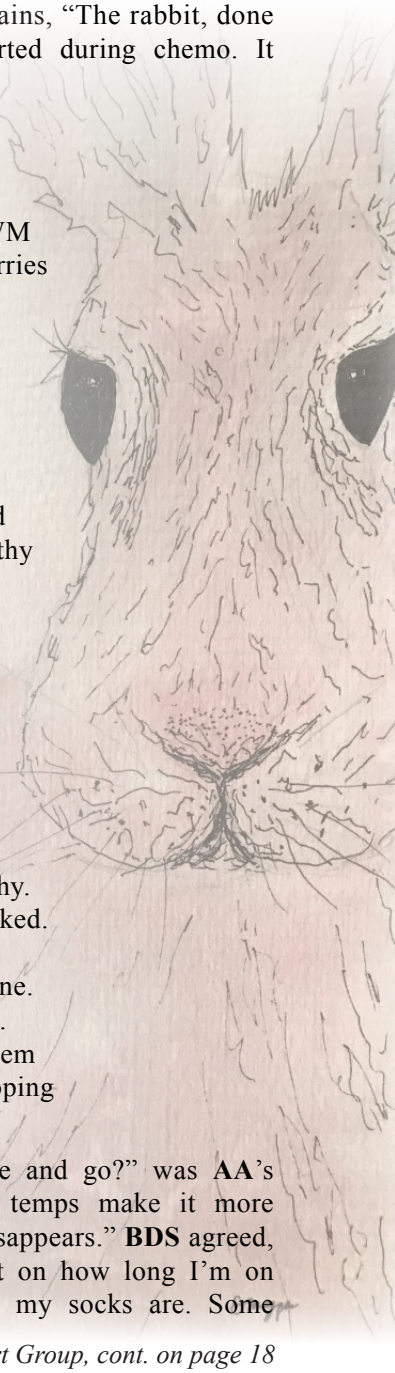
SDH responded, "I am always masked, as is my husband. We have had our groceries delivered since the start of the pandemic. We will rarely go to the drug store, but not at busy times. We have not been to a restaurant, indoors or out. We have our medications delivered. Our adult children are masked if they come into our house, and they do a rapid test before coming in. We are going to take a chance on Sunday and go to our daughter's house for Mother's Day. We will spend most of the time outdoors. But we will be having dinner, probably inside. Hopefully we can distance ourselves. It's tough. But we want to avoid the virus if we can."

As a group, it appears that WMers continue to be cautious, but many of us feel hesitant, like ***Diane Mazza's rabbit*** *[to the right].*

In another opinion, **FTQ** explained: "I continue to travel extensively. Central California this week, Illinois next week, and Switzerland next month. I wear a mask when indoors in public areas such as airports, airplanes, hotel lobbies, etc. It's all about effectively managing risk."

B-DB added, "I go to outside restaurants when the weather permits. I choose off hours like early bird dinners or late lunch service. I go inside stores occasionally. I double mask for indoor trips, I wear N95 masks and cover that with a fabric gaiter that I tuck in my shirt. But I do that because I have a beard and the masks don't fit securely under my chin and the beard hair sticking out from under the mask isn't a good look on anyone. And don't tell me to shave off my beard—last time I did that even my mother told me to grow it back ASAP."

As a group, it appears that WMers continue to be cautious, but many of us feel hesitant, like Diane Mazza's rabbit [below]. As the artist explains, "The rabbit, done in pen and watercolor, was started during chemo. It represents the upcoming changes in mask wearing and my concern about going out in public. The rabbit is half hiding!"



Many members of the Facebook WM Support Group expressed their worries about various WM symptoms and asked for guidance. Some WMers asked how peripheral neuropathy might be treated and for suggestions about coping with its symptoms.

LNW wrote, "I've seen a lot of chatter about Velcade. My husband received it and developed neuropathy in his feet after the treatment was done. For those of you who developed neuropathy from Velcade, did it go away after a period of time? He saw Dr. Ansell at Mayo after treatment, and he said it could take several months. Blood work is great right now, so the Velcade did its job, but he is paying the price with the neuropathy. Neither gabapentin nor Lyrica worked. Just curious of what other people have experienced as far as a timeline. I know the median is three months. He is about there, and it doesn't seem to be getting a whole lot better. Hoping it isn't permanent."

"Can peripheral neuropathy come and go?" was **AA**'s question. **DR** replied, "Warmer temps make it more tolerable, but mine never really disappears." **BDS** agreed, writing, "Yes. Mine is dependent on how long I'm on my feet, the weather, how tight my socks are. Some

From the Facebook WM Support Group, cont. on page 18

days none (few, far between); some days horrible." **JW** posted, "Because of the increased neuropathy in my feet, I am looking at shoes for specifically for people with foot problems. Does anyone have recommendations?"

Some WMers have found improvement in peripheral neuropathy after treatment for the underlying WM. **MF** wrote (in Italian), "Hi to everyone! Today I saw the hematologist and showed him the last blood tests. He said they were perfect. Anti-MAG neuropathy remains, which has improved a lot but not gone away, and it pains me and creates problems in my everyday life. I hope it gets better. How I would love to race!!!!" We all hope that **MF**'s neuropathy will continue to improve and allow racing again.

Fatigue is another common symptom of WM, much-discussed in our group. **CY** wrote, "Big Venting. I don't think the people surrounding me, including family, understand how tired I am. They consider me lazy. Because I am 42, and I look very young for my age, I shouldn't be tired. Fatigue leads to depression; I just want to lie in the bed sleeping mostly. I struggle even to shower, wash my hair, go to work, face people, and talk. People surrounding me don't understand, because they think I am HEALED. They won't accept the truth."

CY's lament hit a common chord, with almost a hundred responses. **PTC** wrote, "I don't normally respond, but this hit home. I am exhausted ALL the time, which led to the diagnosis. I look great, but some days it's hard to get out of bed. I have begged to be on a clinical trial about the fatigue. Just know there is someone else sharing your struggle." **BM** added, "Fatigue is a factor with WM. I just feel like I could fall asleep walking—hang in there. You're not lazy; you're dealing with WM."

BL's post said, "Girl, you are singing my song. I swear the fatigue is the worst part of the whole thing. I've been in remission for several years but cannot shake the constant drowsiness. I sleep ten hours a night. Then I'm good for about three hours in the morning and have to go back down for an hour or two. Another nap in late afternoon. I've quit making plans with friends, unless they understand I can cancel at the last minute. It's horrible."

RCH posted, "Sounds to me like you have regular depression along with everything else. I've had severe depression for the last eight years. I was diagnosed last November but on watch-and-wait. Talk with your primary care physician about the depression. They should be able to help you with that…When I was first diagnosed I was extremely tired all of the time. I still have to pace myself compared to what I used to do. Blessings to you."

AB wrote, "Take care of yourself. It's hard with WM because nothing shows, and it's difficult to explain. But fatigue is fatigue, and it is the enemy. This group can help a lot." **GG** added, "Take care of you! Do just what you can, when you can. Try to get some sun and fresh air, some short walks, some special time for you. Ask for help. Do not apologize when you need to rest. This cancer fatigue is real."

To take part in the conversation and see other WMers' suggestions, join the Facebook WM Support Group page and search topics of interest. I wish you each a good summer (or winter to our Southern Hemisphere WMers). I'll see you on Facebook.

To join the Facebook WM Support Group, go to *https://facebook.com/groups/wmsupportgroup*. In order to join, people must answer two membership questions. WMers and their support people are welcome. Since the group is private, only group members are able to see the posts. If you need additional help with the process, please contact the IWMF office 941-927-4963 or email to *office@iwmf.com*.

A CAREGIVER'S TIPS

By Bruce Jackson

A little over fifteen years ago, my wife's father, "Dad," was diagnosed with WM. He was otherwise a very healthy and strong 80+ year old. Although we lived over two thousand miles away, my wife, Susan, became Dad's caregiver and eventually found herself spending weeks and months out of state to care for her "dying" Dad.

Three years after Dad's diagnosis, Susan was also diagnosed with WM. In her case, the caregiver became the patient, and I had the honor of becoming a caregiver to two WMers at the same time.

In this short article, I would like to share some of the things we've learned after over 15 years of caring for WM patients and to provide five tips for caregivers from this experience.

TIP 1: As a caregiver, prepare yourself with knowledge by spending time reading the posts on IWMF Connect, watching the archived videos on the IWMF website, and reading the articles and other references there. You will find that you will soon have knowledge enough to ask informed questions of your patient's health team and to help your patient with treatment decisions.

When Dad was diagnosed, I had easy access to most medical journals at the university teaching hospital where I worked. I began to read everything I could on this disease. However, I found the resources on the IWMF website and the original IWMF Talk List (now IWMF Connect) to be everything I needed to be a supporter for my WMers.

As an illustration of how helpful this information might be—here's a personal experience. Less than six months after my wife was diagnosed, I had learned from the IWMF that soft tissue cancers are common in WM and other lymphomas. Therefore, when Susan developed a suspicious lump in her neck, we immediately engaged with an endocrinologist. Upon examination, he thought it was merely a cyst and recommended that we wait six months to see if it improved. Armed with the knowledge from the IWMF, I urged the doctor to do a biopsy and not delay. He reluctantly agreed, and it turned out she had aggressive thyroid cancer in both thyroid lobes. Her medical team observed that if we had waited six months, the prognosis would not have been positive. The knowledge I had gained from the IWMF helped us make the best medical decision in that case.

TIP 2: As caregiver, Susan had to create boundaries with her dad, since she could not continue to meet the demands he was placing on her. Caregivers MUST maintain some boundaries in order to continue to provide care and to remain emotionally healthy themselves.

After almost two years of spending more time in Dallas caring for Dad than being home in Seattle, Susan told Dad that if he did not move into a retirement center, she would not be able to come to Dallas to care for him. It was clear she could not continue to be his primary caregiver while living 2,000 miles away—and that she herself needed help.

Editor's Note: Torch *cartoonist Linda Pochmerski passed away in March of 2021of WM complications. I recently remembered this cartoon that was tucked away in my files, and since we never used it, I felt this would be a most appropriate place for it. We certainly miss Linda and her cartoons.*

We subsequently helped Dad relocate into a wonderful retirement center. Dad later said it was the best decision "he" had ever made. On one of our visits he observed, "This Waldenstrom is not that bad, especially when compared to what I see with all these 'old people' who live here." He was about 90 years old at the time.

TIP 3: We all need community. Anyone dealing with a long-term disease needs to get out and spend time with people. As caregivers, we should help encourage and support that. It was amazing how much better Dad felt after he moved into a retirement home with his peers.

TIP 4: As caregivers, we need to understand the goals of the patient. With that knowledge, we can help the medical team focus on the desired plan, which is often no treatment (watch-and-wait). We can do this by simply asking questions. For example, in Dad's case, we wanted to know if a conventional treatment or a clinical trial might extend his life—his top goal. However, for Susan, the questions are focused on side effects and how treatment might impact her current quality of life.

Knowing each patient's goals has been critical. Twelve years ago, we were told that Susan must start treatment

A Caregiver's Tips, cont. on page 20

A Caregiver's Tips, cont. from page 19

immediately. However, when we focused her care team on her goal of quality of life we all came to the decision to wait. Recently, when her quality of life deteriorated due to her disease burden, we were able to weigh the pros and cons of treatment options against her current condition, and we all agreed that it was time to start treatment, as well as a particular treatment plan that was synergistic to her treatment goals.

TIP 5: Caregiving is hard. It is emotional. To watch someone you care about suffer and perhaps, at some point, die is extremely difficult. You must have your own support group: family, friends, other caregivers. You need people to share the tears with.

Years ago, I worked as a practitioner in a medical treatment program where every patient was terminal. Our patients would spend hours each week in intensive therapy, and so we became very close to them. Unfortunately, all were on a terminal "glide path." When we "lost" a patient from our shift, it was incredibly painful and difficult. Before the next shift, we would all gather in a conference room and have a good cry. Doctors, nurses, and technicians, all would have a good fifteen minutes of tears and hugs. Then, it was back to work.

Just recently, we enjoyed a Zoom meeting to offer support for WM caregivers. The presenter delivered a relevant presentation about caregiving, after which the caregivers had the opportunity to socialize virtually with each other. When the IWMF has another session for caregivers like this, I highly recommend it for anyone involved with caring for a WM patient. You can find further information for caregivers on the IWMF website at *https://iwmf.com/support-for-caregivers/*.

Spotlight ON SUPPORT GROUPS

EDITOR'S NOTE:

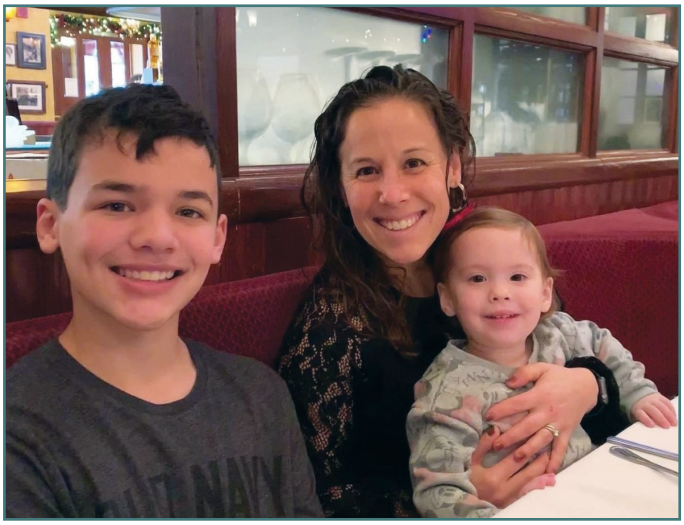
As the support group section continues to evolve away from individual reports, we begin to spotlight certain groups, activities, or people. As always, for particular information about when and where meetings are being held, go to the Events Calendar for listings: ***https://iwmf.com/events-calendar/***

YOUNG WM SUPPORT GROUP GOES WORLDWIDE

The most recent meeting of the Young WM group was in March, and the ten attendees had a really supportive and informal discussion of what's happening in the group members' worlds. The members, newly diagnosed or experiencing new treatment, shared their experiences and asked questions, and shared resources about updated survival data and new research about WM in young patients.

A presentation by Dr. Shayna Sarosiek with be featured at the next meeting; she will share information about current and upcoming clinical trials at Dana-Farber Cancer Institute.

The Zoom meetings provide opportunities to connect young WMers around the world. Although time zones present scheduling problems, anyone who can get online can participate. As a result, we have had people join from India, Chile, Canada, and New Zealand. Young WMers



Deborah Kelly with Cooper and Isabelle

Spotlight on Support Groups, cont. on page 21

who have felt left out now have a place to come for support from others who are navigating this disease in similar situations. Our group shares the unique concern of managing this illness while working and potentially also caring for our young children.

If you are under 50 years old and living with WM, please consider joining the group, and feel free to reach out to the co-leaders with any questions or concerns:

Deborah Kelly - *Deborah982@gmail.com* and
Ryan Scofield - *Ryanscofield@gmail.com*

Ryan Scofield, after finishing a half marathon in 2021

A YEAR OF HEALTHY EXERCISE

One year ago, the IWMF launched a "Get Moving in May" program, which introduced weekly chair yoga classes to our community. What was planned as a month-long pilot program has now celebrated one year! Our mailing list now has 192 participants, and interest continues to grow. Many thanks to Ann MacMullan, the WM yoga instructor, for providing classes to our WM community members in honor of her father, Mac (pictured to the right, caught taking a rare moment of rest).

WM chair yoga classes are tailored just for those managing WM. No experience needed! We move the breath and body to help battle fatigue, compromised immune system health, and balance issues. While we remain seated for most of the class, we stand and use a chair for support for some poses, with modifications so all levels can practice.

The 45-minute classes incorporate some of the following:

- Breath exercises for reducing stress and boosting the immune system
- Gentle stretches designed to energize the whole body
- Yoga poses that move the lymph fluid and improve balance and steadiness
- Meditation-like body scans to facilitate mindfulness, acceptance, and relaxation

To join the WM chair yoga mailing list, Michelle Postek at *mpostek@iwmf.com*. Classes are on Mondays at 2pm US EDT and are recorded for those who cannot attend live.

Spotlight on Support Groups, cont. on page 22

MANAGING THE SOUTHERN CALIFORNIA SUPPORT GROUPS

By Julianne Flora-Tostado

To expound a bit to help other SG Leaders understand how we manage our group(s), I will explain my thoughts when planning ahead for a meeting, as well as while it is happening. For context, in our Southern California area, we now have two support groups, one headed by Marla Chao, who chairs a large group focused twice a year on a presentation from a speaker, usually a local MD, with time set aside for Q&A. I offer a "chat style" support group where we keep up-to-date with one another and share information and questions. We met monthly during the more intense phases of the pandemic, then we met every other month for a while, and now we aim for every six weeks, which Goldilocks might agree is "just right."

Before we met in April, Michelle Postek from the IWMF office sent out a member list with new IWMF members and their contact information highlighted. Since a few of the folks in our area like to attend the support group chats just once in a while, and a few new people join every time, catching up with how everyone is doing can take a variable amount of time. The timing usually seems to work out naturally, but I wanted to make sure that any new members who joined the Zoom chat would have a chance to share their story—so, for the April meeting I decided to invite just the first half of the new member list this month, and I will invite the other new members next month.

Having a chance to invite new members makes me smile and reminds me of the relief my husband, John, and I felt the first time we attended Marla's support group meeting in LA. It's always a good thing to see and talk with others who are thriving with WM.

Getting an email out before the next meeting is a bit of a quandary. If sent too early, the Zoom link gets buried by the everyday emails we get. If sent too late, there's no time to plan ahead to attend. I now send out reminders on my day off, the Wednesday ahead of our Saturday meeting. I send reminders of group meetings to all who have ever asked to attend, which has grown to about 80 members. However, I do not send reminders to those who have not responded for six months in a row. I can't guess if newly invited members might attend in a higher proportion than our usual attendance ratio, but a pattern of around one in six holds up. I have decided to mention here the ratios of invitees to actual attendance to check if it's the same for others around the country. I'm also curious if these ratios are different for different types of meetings. Please, if you are a support group leader, send me a note on IWMF Connect to let me know!

Attendance is usually about 12 for each meeting. One of the new members joined us this time, and it happened to be especially delightful to welcome her, as we remembered each other from an American Association of University Women book group 30 years before. Her story is unusual in that she worked as a nurse for years for an MD who is now her doctor. I'm sure whenever she's able to join in our Zoom chats, her years of experience will be an added help to others!

For the April meeting, I expected that there would be follow-up on several issues that had been discussed recently during previous meetings and on Connect. Indeed, discussion was lively, and topics included efforts to get Evusheld for COVID protection before travel; Consumer Lab, a commercial website with information on the purity of supplements; each individual's dilemmas, symptoms, and questions for the group; treatments that look hopeful, including pirtobrutinib, zanubrutinib, CLR 131 (a radioisotope); and just what does CAR T cell therapy do, really?

Zoom has made support groups accessible to everyone. As a leader, I now can attend IWMF trainings to talk with and learn from other leaders, so it's a great time to sign up for anyone who wants to start a support group!

INTERNATIONAL SCENE

EDITED BY ANNETTE ABURDENE

INDIA

By Saurabh Seroo, WM India

WM India conducted its first in-person support group meeting in Bangalore since 2020. We were fortunate to have a diverse group of members join us, from newly diagnosed patients to members undergoing treatment and those in remission. We had a wonderful meeting in which patients and caregivers shared their experiences and deep knowledge of the disease and its manifestations.

As we shared our stories of overcoming Waldenstrom's, it was fascinating to note the variety of treatments offered to our members and their different paths to recovery. Our members also spoke in-depth of their experiences of undergoing treatment, how the landscape has evolved, and how their lives have changed over time. We had a special and fascinating discussion, and it was great to meet in person after two years!

What struck us most was the special role that doctors and caregivers play in the lives of our patients. We remain in awe of their selflessness to serve our members during their times of need. We are also deeply inspired by our patients, and especially awestruck by their will and determination to live better lives, despite their diagnosis and subsequent illness. We hope that this year brings them good health and joy.

GERMANY

By Uwe Josef (UJ) Kerscher, founder of Waldenstrong Germany

My WM journey: One day in the spring of 2019 at the age of 47 I noticed a rapid drop in performance while jogging. To be on the safe side, I went to my family doctor in mid-May for a check on lung function, an EKG, and a small blood test. My doctor informed me in a faltering voice that my hemoglobin value was just over 5, that it was life-threateningly low, and that I should immediately drive to the next clinic. I called in sick at my workplace, informed my shocked family, and experienced the next few hours as if in a trance.

Uwe Josef (UJ) Kerscher, founder of Waldenstrong Germany

I had known hospitals only as a visitor and had experienced until then no significant medical events. In the local hospital—I live in a city of 150,000 inhabitants in Bavaria in the south of Germany—I got blood transfusions, and tissue samples were taken. On the third day I was diagnosed with Waldenström's macroglobulinemia. I had never heard the name, and before I could even deal with the disease, an hour after the diagnosis I was given my first chemotherapy infusion with bendamustine, followed two days later with the first session of rituximab. Fortunately, I tolerated the treatment well. Five days later I was discharged, and during the following six months I was given another four rounds of bendamustine, a high dose of cyclophosphamide (because of possible stem cell collection, which unfortunately did not work), and another five rounds of rituximab, all administered in an outpatient setting. Due to the cyclo session, my hair fell out, my stomach and digestion have been extremely sensitive since, my diet is limited, and I have been suffering from neuropathy. Nevertheless, I am aware that without this therapy I would no longer be here to write this report. Optimism is a must! Overall, I am well adjusted to medication and have been able to work full-time again since the end of 2019.

*With such a **serious illness** as ours, we want to get quick help and answers in the event of a problem. That's why on April 26, 2021, I founded the virtual self-help WhatsApp group **"Waldenstrong."***

In March 2020, the COVID-19 lockdowns began in Germany. I found myself with enough time in the home office and decided to understand my illness better. Since our common illness is comparatively rare, it was difficult for me to exchange ideas with fellow sufferers. Unfortunately, Waldi [WM] was only a marginal topic in the German self-help groups. But when I had found four more fellow patients via social media such as Facebook, a cancer app, and a tip from my oncologist, I thought about building a digital exchange option. I created a WordPress website with associated domain *https://waldenstroem.de*. With such a serious illness as ours, we want to get quick help and answers in the event of a problem. That's why on April 26, 2021, I founded the virtual self-help WhatsApp group "Waldenstrong." The first active Waldenstrongers were Anja, Ines, and Jörg, scattered offline across Germany. I found Jörg by chance when I was fishing on a river and overheard the word "Waldenström" as two women walked by. After I assured them that this was not a new pick-up line, one of them passed on my e-mail address to the newly diagnosed Waldenström patient Jörg.

We are now almost thirty patients from German-speaking countries, including patients in Austria and Switzerland. We

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International Scene, cont. from page 23

have grown solely by word of mouth. When a group member learns about a new Waldenström patient, he/she will be invited via WhatsApp group link. We like to be low-threshold and democratic. Our topics of conversation primarily concern the exchange of experience in therapies. Our own experience has already provided some watch-and-wait and new patients with important tips for pre- and after-care. Alternative healing methods are discussed in detail. Discussions and exchange of experiences with the COVID-19 vaccinations have been very helpful for me and have taken away fears about the new vaccinations. Blood pressure levels and blood values are shared, compared, and interpreted. We exchange doctor and clinic recommendations.

I have contacted the German support group for leukemia and lymphoma at *https://leukaemiehilfe-rhein-main.de* (LHRM), which led to fruitful exchanges and joint online meetings.

Due to the great work of the IWMF, I became aware of an online lecture on "Living with Peripheral Neuropathy" in May 2021 at *https://iwmf.com/event/iwmf-global-educational-webinar-peripheral-neuropathy-no-easy-feat*. Since I suffer from peripheral neuropathy, I followed the lecture with great interest and learned how to deal with this disease; my thanks to Dr. Guy Sherwood and Dr. Todd Levine. Since some of our older patients are not familiar with the English language, I prepared the lecture in German and shared it via an online session. The presentation is still available for download on our website.

Our Waldenstrong WhatsApp group has become an important channel for communication and compassion. Someone is always there who understands 100%. Although our self-help group only exists digitally, and I only know most of the members through their messages, I feel deeply connected by our common fate and shared experiences. We exchanged over 5,000 messages last year and, in addition to medical specialists, have collected the largest body of Waldenström know-how in the German-speaking world. For our group mantra "Shared suffering is half suffering and shared knowledge is more knowledge" to continue, we warmly welcome every new Waldenstrong member.

UNITED KINGDOM

By Kat Tucker,
Fundraising and Communications Manager WMUK

The WM community has been doing amazing things in the UK these last few months, notably raising an incredible £36,000 towards a brand new WMUK Support Line. We cannot say thank you enough to everyone who took part in Walk for Waldenstrom's to raise this amount—almost double our original target. We are currently in the process of recruiting a healthcare professional to set up, manage, and staff the line, which we aim to launch later this summer.

WMers in the UK have been invited to get a "spring booster," a second booster jab to help protect them from COVID over the summer months. This is the fifth vaccination that immunocompromised people—including people with WM—have been offered and can be received three months after the fourth dose. We know that some people are still struggling to get their jabs. We have all the facts, including useful links to take along to vaccine appointments on our website: *https://wmuk.org.uk/news/fifth-dose-of-covid-19-vaccine-available-to-wmers/*

Rebecca Milburn finishing the Tonbridge Sprint Triathlon

Earlier in the year, we reported that the BTK inhibitor ibrutinib had failed to get funding, meaning it would become unavailable to WMers in England and Wales. We're disappointed to report that the drug has failed at its second review. This is a big blow to many people in the WM community, for whom ibrutinib provides a kinder alternative to chemotherapy. People who are already taking the drug will continue to be able to do so, until they and their doctor decide it's time to stop. The drug is still available in Scotland.

Zanubrutinib, another, newer BTK inhibitor, also failed at its first review. However, there is some hope that this decision will be overturned in its second review in June, once again giving WMers the option of an oral treatment. We are working closely with healthcare professionals, pharma companies, and the National Institute for Health and Care Excellence (NICE) to do all we can for a positive decision, and we will keep the WM community updated on the decision and any next steps.

Keep an eye out on our website—we have got a new look and expanded range of information coming very soon. The team has been working hard behind the scenes to produce a website that people with WM deserve. With more information on the subjects you have asked for and better navigation, we hope it will be a valuable resource, no matter the stage of your WM journey. A big thank you to our expert clinicians, nurses, and patients, who have reviewed the information.

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Our fundraisers have been as busy as ever. Rebecca Milburn is completing not one, but three triathlons this spring and has already raised over £1,200 in support of her mum who lives with WM. We rely on donors and fundraisers like Rebecca to ensure we can continue to be there for everyone affected by WM and grow this positive and supportive community. If you want to get involved, you can find out more here: *https://wmuk.org.uk/get-involved/*

Stay up to date with everything happening in the community, including new webinars and support groups by joining our mailing list: *https://wmuk.org.uk/get-involved/sign-up/*.

NEW ZEALAND

By Lea Hullett
IWMF Affiliate Leader for New Zealand

First, a bit of history about our group. Sal Simson and Peter Phelan talked of forming a New Zealand patient's group affiliated to the IWMF after meeting by chance at Christchurch Hospital in 2009. Sal agreed to be the contact person, which set things in motion. Unfortunately, she passed away four months later; Michael Goldschmidt became coordinator of the group, and Michael and Peter came up with the name Waldos to describe the group they were planning. By November 2017, when the Waldos became my responsibility, about 23 members were on the list.

New Zealand Waldos at a Zoom meeting

Since then, a few Waldos have found us through the IWMF website and Facebook. The Leukaemia & Blood Cancer NZ (L&BCNZ) held meetings that Matthew Eby organized in my area, and I told him about our group, which was by then an affiliate of the IWMF. I offered to add him to my email list of Waldos. He accepted, and after that he encouraged anyone he met who had Waldenström's to join us. Through Matthew's interest in us, the L&BCNZ arranged for a NZ haematologist to give a webinar for us. Unfortunately, Matthew has taken up a new job in Australia this year, but the L&BCNZ has a link on its website to the IWMF now. Hopefully it will add a link to our website as well, at *https://waldos.kiwi/*

WMOZZIES
Australian patient support group for Waldenström's Macroglobulinemia

We congratulate WMozzies for being instrumental in Australia's funding of zanubrutinib for WM. Australia has 105 modern medicines publicly funded that are not available to New Zealand patients. Haematologists are among those questioning why a long overdue review of funding in New Zealand was presented to parliament months ago but is not yet available publicly. There are 70 medicines on the Options List of Pharmac, the government agency that decides which medicines are funded, and I found both ibrutinib and venetoclax while browsing its website, but not zanubrutinib. Bendamustine and rituximab are funded.

We are very short of nurses and doctors, who are heading to Australia and other countries for better pay and working conditions. Our health sector needs a lot more money poured into it. Recently it was estimated that we need 3,000 more specialists and doctors in community practices, along with 12,000 more nurses to match Australia's staffing level per capita. Our health system is free to New Zealand citizens, though people who can afford insurance have access to private care and pharmaceuticals not available to the general public.

While New Zealand has avoided the COVID death rate of other countries because of our high Pfizer vaccination rate, COVID has impacted our already stretched health system. Diagnosis, operations, and cancer treatments have been delayed, costing lives. As we go into winter our country is opening up to tourists, and people are enjoying the lowering of restrictions. We are advised to get vaccinated against the seasonal flu and also get boosted for COVID, as the District Health Boards throughout the country could easily be overwhelmed. We are encouraged to wear face masks, socially distance, and wash hands, but not everyone is adhering to these precautions.

On a brighter note: we Waldos had our first Zoom meeting for 2022 on May 12. Five of us enjoyed lively discussion on a number of topics including zanubrutinib, ibrutinib, the dosing of bendamustine, and other matters relating to our

International Scene, cont. on page 26

quirky ailment. At this time, we have 47 Waldos, 31 men and 16 women. There would have been more present at the meeting, but for other engagements. We are grateful for the IWMF providing our Zoom licence and intend to hold another meeting in a month or so.

AUSTRALIA

By Michael van Ewijk, Editor, WMozzies Committee

WMozzies leader David Young receives a Community Recognition Statement from the NSW Parliament Legislative Assembly

David was diagnosed with Waldenstrom macroglobulinemia in 2012. After years of fatigue, David managed to get on a trial for the BTK inhibitor zanubrutinib in 2017. His blood tests are virtually normal now, and he has all his energy is back. He climbed Cradle Mountain in Tasmania with his son in 2020.

When David was first diagnosed, he discovered there was little support on the NSW North Coast for rare cancers like WM. David set about to educate himself. He went on to set up three cancer support groups on the North Coast. His advocacy work earned him a Community Recognition Statement from the Parliament of NSW Legislative Assembly in 2021.

Zanubrutinib is now publicly funded

Rare blood cancers have until now had fewer opportunities for government subsidised pharmaceutical options available to patients through the Pharmaceutical Benefits Scheme (PBS) than the more common cancers and other illnesses. This has all changed thanks to the persistent lobbying on the parts of all patient cancer advocacy groups, including Lymphoma Australia. The process for having a drug admitted to the PBS for subsidy is that a pharmaceutical company makes application to the Public Benefits Advisory Committee (PBAC), who in turn reviews this application and then, if approved, recommends it to the PBS. BeiGene in March 2021 made a submission to the PBAC to have zanubrutinib admitted to the PBS. The government finally listened and asked BeiGene which cancer advocacy group it should invite to participate in this as a pilot project. BeiGene recommended that WMozzies be represented.

David Young and David Rabie represented WMozzies through this process. Commencing May 2021, we had numerous teleconference and Zoom meetings with Dr. Sally Wortley, the leader of the Consumer Evidence and Engagement Unit, and Jo Watson, Deputy Chair PBAC. They mentored us on the process that would be adopted in assessing this application. There was substantial preparation and reading required on our parts for these meetings. We were not privy to any of the classified material arising from the meetings of the sub committees such as the Economic Sub Committee (ESC). We were given the opportunity to make written submissions in support of BeiGene's application. Sadly, the initial application was declined. BeiGene, however, felt it was a close call and that through a further submission, they would hope to get it over the line. A Facilitated Resolution Pathway Workshop, another first for the PBAC, was set up for September 6, at which once again David Young and I were present. This time BeiGene was successful, and zanubrutinib is now publicly funded.

COVID-19 drug to reduce hospitalisations listed on Pharmaceutical Benefits Scheme (PBS)

Australians at risk of severe COVID-19 will soon be able to access through their general practitioner a drug that can lessen the disease's impact, after the federal government listed a second anti-viral treatment on the PBS.

Health Minister Greg Hunt has announced the PBS listing of Paxlovid, a combination of the drugs nirmatrelvir and ritonavir, as state governments prepare to scrap close contact rules once the omicron BA.2 wave of infections has subsided.

Andrew Warden holding his subsidised script for zanubrutinib

International Scene, cont. on page 27

David Young on Cradle Mountain, Tasmania, in 2018

Eligible adults who test positive to COVID-19 through a PCR or rapid antigen test will be able to get Paxlovid, which can prevent severe disease if taken within five days of onset of symptoms, from their local pharmacy with a GP prescription.

This medicine will help reduce the need for hospital admission. Paxlovid has been available on the PBS since May 1 to people aged 65 or older and Aboriginal or Torres Strait Islander patients aged 50 and over.

CANADA

By Janet Parcher Cherry, WMFC

Ottawa and Eastern Ontario WM Support Group

The Ottawa and Eastern Ontario Support Group started in the fall of 2001. Janelle Jones, who is still going strong 21 years after her diagnosis (!), and Terry Cherry, my husband and WM patient, met at the medical day care unit at the Civic Campus of the Ottawa Hospital. Terry had already been in contact with Arnie Smokler, the founder of IWMF, and Arlene Hinchcliffe, founder of WMFC. Arlene provided Terry with the contact information for Frances Mulligan, and thus the core of Ottawa's support group, Terry, Janelle, and Frances, was formed. The first few meetings were held at Fran or Terry's home. Once the word got out that a support group existed, our numbers started to increase. We quickly outgrew Fran's house before finding free space in the lounge of a local church, where we met for several years. Upon the completion of the Maplesoft Centre at the Ottawa Regional Cancer Centre, we began having our meetings there, up until the onset of the COVID pandemic.

When Terry was in treatment, I started to attend meetings as his support, and before long I became part of the group, gaining support from the other members and providing my own support to them as needed. When Terry died in 2009, I took over his role as the facilitator of the group. Sometime later, Murray Shaw became co-leader of the group and has become an inspiration for many of our members. Murray's "Story of Hope," published on the IWMF website *https://iwmf.com/stories-of-hope/* in June 2020, has motivated and uplifted people ranging far beyond our own group, and his continuing commitment to use knowledge and exercise as a part of the healing process remains an inspiration to our members.

From the beginning, we have encouraged partners, caregivers, and family members to attend our meetings. We are even fortunate enough to have our own therapy dog. We average 14 to 16 people per meeting, when meeting in person. Our membership has grown a lot. In the past, we have had members coming from as far away as Long Sault, Kingston, and Madoc. Thanks to our proximity to Quebec, we have also had members come from Shawville, Gatineau, Aylmer, and Montreal. We hold our sessions in September, November, February, and April. In between these formal meetings, we almost always hold a barbecue during the summer months and a winter holiday lunch in December. Over the years we have had question-and-answer sessions with a local hematologist and a grand round presentation by Dr. Steven Treon of Dana-Farber Cancer Institute.

The COVID-19 pandemic has, by necessity, changed how we meet. Zoom has become the new de facto way to meet each other, and—while I am thrilled that this allows us to continue meeting, as well as allowing those further afield to join in—many of us miss the personal contact of meeting each other in the same room.

BEN RUDE HERITAGE SOCIETY

The Ben Rude Heritage Society recognizes those who have made provisions for a future gift to the IWMF, such as a bequest, listing the IWMF as a beneficiary for a life insurance policy or qualified planned asset (such as 401k or IRA), or a life income agreement, such as a Charitable Remainder Trust. Legacy gifts represent an important component of the IWMF's financial future. There are many ways to support the IWMF through a planned gift, but a bequest is perhaps the easiest and most tangible way to leave a lasting impact. The following supporters are members of the Ben Rude Heritage Society:

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If you have discretionary giving power and would like to help move our research program forward in a special way, we invite you to join those listed above. For more information about Research Partners and Named Gift Fund opportunities and potential gifting options that might make that possible, please contact Director of Development and Communications Alix Redmonde at *aredmonde@iwmf.com*.

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