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DEPRESSION - A VERY TREATABLE ILLNESS

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Dr. Marshall Lewis

Dr. Marshall Lewis earned his BA in English Literature at Yale University before attending Vanderbilt Medical School for his medical degree. He then trained in psychiatry at Harvard Medical School, where he remained on faculty for a number of years. After private practice and clinical leadership positions at McLean and other private sector hospitals, first at Harvard and then in Southern California, he moved to the public sector for the latter part of his career. In 2013 he retired as the Clinical Director for Behavioral Health Services for San Diego County and remained on voluntary faculty at University of California San Diego Department of Psychiatry as Clinical Professor until his retirement from teaching in 2022. He continues to do some consulting regarding medical quality of care issues as well as the integration of behavioral and medical care. He was diagnosed with Waldenstrom's in 2021.

Depression is quite common, and it is especially common in the age group most inclined to have Waldenstrom's macroglobulinemia (WM)—people in their 70s and 80s, owing to accumulated medical conditions and to the losses faced with aging. This article is intended as a brief guide to diagnosis, treatment, and when to seek referral to a psychiatrist.

Unfortunately, a great deal of stigma and misinformation have surrounded psychiatric illness, and for many physicians, depression is as mysterious as WM. When I was in medical school in the mid-70s, I was cautioned by some senior faculty not to specialize in psychiatry, because they believed that psychiatric illnesses didn't exist. However, after more than four decades in the field, it is clear to me that not only do psychiatric illnesses exist, but our treatments work with as much regularity as is true in the rest of medicine. The mechanisms of brain and emotional dysfunction are complex, and we do not entirely understand how the various psychiatric treatments work—but the same can be said for much of medicine, including some of the efforts to cure WM.

Depression is particularly common among people with cancers of all sorts, but, independent of that, the National Council on Aging cites a prevalence of 1-5% of older adults living in the community who have what is called "major depression," the most serious form, which I will define later. An article in the *Journal of Affective Disorders,* December 2022, examined past-year major depressive episodes in non-institutionalized people over the age of 65 in the US. Using National Drug Surveys on Drug Use and Health from 2010-2019, the authors discovered a trending increase in prevalence over that time—from 2.0% in 2010/11, to 3.2% in 2018/19.

Around the world, depression has an even more significant impact than in the US. The January 2022 *Neuroscience & Biobehavioral Review* published a "meta-analysis" (i.e. an analysis of 20 other published studies involving 18,953 participants around the world) and found the prevalence of major depression to be 13.3% among "the elderly," who were variously defined in the underlying studies as above age 65 or 70. Such "meta" reviews, especially those involving worldwide data, often show higher prevalence because their diagnostic criteria and/or definitions of illness aren't as consistent and tight as single country-focused studies.

In any case, globally, the World Health Organization (WHO) website depression fact sheet states that 5% of the world adult population and 5.7% of adults over 60 years of age suffer from depression at any time. In 2017, the WHO cited depression as the greatest cause of medical

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disability worldwide. It estimated more than 700,000 deaths from suicide worldwide yearly, and the Centers for Disease Control and Prevention reported almost 48,000 such deaths in the US alone in 2021.

As cancer patients, we have psychological work to do in confronting our WM diagnosis. It's depressing. We need to resign ourselves to it and then learn to become optimistic about all the great new research that offers the promise of healthy years of living.

Medical illnesses are like losses from the deaths of loved ones and friends. They are all losses, and losses in general are depressing. Something is taken from us. We relied on something, and it is no longer there. Our lives have changed.

Most such losses may not require psychiatric treatment, although often counseling or even just good talks with friends can be comforting and restorative. Numerous articles, including a study published in the *British Journal of Sports Medicine* (November 12, 2022), have suggested that in less severe depression, exercise can help as much as medication. Time also heals.

So, when one develops cancer or suffers another loss—whether from a medical condition or the loss of a loved one—how can someone know if talking, counseling, time, perhaps exercise, can help without needing something else to treat a more serious depression? Given the high prevalence of major depression in the general population, someone could obviously have a coincidental major depression illness as well as a reaction to cancer or another loss.

When depression becomes more serious, it affects energy, thinking, and the ability to experience pleasure in a profound way. In fact, a person may be so compromised that he or she virtually cannot think or act, and attempts to talk or exercise can be experienced as complete failure, adding to distress—and potential suicidality.

The field of psychiatry has a unique method for defining diagnoses. We periodically update our diagnostic nomenclature based on the latest research driven by international expert consensus, which gets formulated in the *Diagnostic and Statistical Manual of Mental Disorders* or *DSM*, now in its 5th iteration. The DSM-5 diagnostic criteria for major depression have been very useful over the years in defining the syndrome of severe, often very profound, depression, which seems to have a biological basis and which generally responds to medication or other physical-based treatment. It is this profile that would ordinarily suggest the presence of a more significant depression and the usefulness of psychiatric referral.

Interestingly, major depression does NOT require depressed mood, per se. Some people with this illness can have what is known as "anhedonia," a loss of capacity to experience pleasure or a loss of interest in usual pleasures, rather than the subjective feeling of depression—because some people, especially men, may not allow themselves to experience depression. To qualify for the diagnosis, one must have, over at least a two-week period, at least five of the following (including one of the first two): depression, loss of interests or pleasure, weight change, sleep change, physical and/or mental slowing or agitation, fatigue or loss of energy, inappropriate feelings of guilt, problems with concentration or indecisiveness, and thoughts of death or suicidal ideas. Also, these symptoms must not be attributable to another medical condition, substance, or medication.

Unfortunately, many medications list depression as a side effect. In fact, one of our original biological models for depression was based on the action of a blood pressure medicine, reserpine, which was observed to cause depression and was thought to do so by depleting chemicals that transmit nerve impulses in the brain. In the case of reserpine, depression was common, because that pharmacological mechanism is central to its action on blood pressure. However, depression is probably a much rarer side effect of most other medications, like those given for WM, where the primary action is far from the central nervous system. Still, if a drug does cause depression as a side effect, it could mimic major depression and potentially cause a very serious condition.

Whether related to a medication side effect, coping with a WM diagnosis, or simply coincidental with WM, the development of the major depression syndrome would ordinarily be a good reason for a psychiatric referral, unless one has a primary care physician who is well versed in the treatment of depression. Depression from medication side effects may still respond well to treatment for depression, so, if there is a good response to WM, it may be worth trying to treat the depression rather than coming off the WM treatment prematurely. Of course, the development of suicidal thinking or just wanting to "give up" would suggest more rapid psychiatric referral. Getting someone additional medical help for another medical problem like serious depression is not abandoning them. We all need to recognize our limits, and when people are profoundly depressed, no one can cheer them up, no matter how hard they try.

Treatment for major depression, until the last decade or so, was largely confined to medications, and in the case of very severe, usually psychotic and/or suicidal depression, to the somewhat controversial electro-convulsive therapy, which is rarely provided but is extremely effective and well tolerated. Dozens of new approaches have been developed, including new medications and physical treatments that modulate brain function, like vagus nerve stimulation (VNS) and repetitive transcranial magnetic stimulation (rTMS). We have gone from thinking that depression is caused by a deficit in one or two of the "neurotransmitter" chemicals that allow cells to communicate in the brain, to developing complex new models of brain chemistry that suggest the use of entirely new medications, with very promising clinical results. More drugs are coming on the market all the time. Antidepressants are not addictive like opiates (though patients might stay on them to stay in remission), and the side effects are generally benign.

We know WM isn't curable, though many are doing well in spite of the diagnosis, and there are exciting treatments on the horizon. Anyone with the additional burden of serious depression should be comforted by the fact the people with depression do get better, and there is plenty of help available.

DEPRESSION – SOME PERSONAL PERSPECTIVES

By Julianne Flora-Tostado, PhD, Moderator for IWMF Connect
Leader, Orange and San Diego Counties Support Group

Editor's note: Dr. Julianne Flora-Tostado, PhD, is a psychologist and psychotherapist. Her husband John was diagnosed with WM; in addition to being his care partner, she has had her own personal experiences with a cancer diagnosis. In a companion piece to Dr. Marshall Lewis's article on depression, she speaks from all these perspectives, as well as how she has dealt with the mental stress of the COVID pandemic in her personal life and work.

Observations from my experiences as a psychotherapist

To illustrate some of the issues that come up in cancer treatment, I am sharing an anonymous case summary of my work with a client who had WM. She has given me permission to share her story in the hope that it will help others.

About a decade ago, this client came in asking for help with extreme social anxiety and feelings of hopelessness. Right from the start she explained that she had had too much medication with chemo and did not want to see a psychiatrist for an evaluation. I could see that she was probably a hands-on learner; her rapid fire hyperverbal style meant that an insight-oriented approach would not be the best fit for her. Even though she reported being happy with her close family relationships, she missed her church and work friendships. She had been a professional designer, but anxiety about intense work hours with large contracts had become too much for her, and she had stopped working 14 years earlier, when she was first diagnosed with a cancer. She missed painting. She felt burdened with caregiving duties for her father and her grandkids. She worried, what if something happened to her, and she'd have to take all of them with her to the doctor?

Given time and practice, ***therapy*** *can make a* ***huge difference****.*

I wondered why didn't she leave the house, other than to see me. This is when I learned that she still had cancer, an incurable cancer, WM, and that she had had an allogeneic bone marrow transplant which cured a different lymphoma, but not the WM. After the transplant, she basically stopped leaving the house. She knew she was more afraid than she needed to be—in fact, she had developed a fear of leaving the house, called agoraphobia.

As a therapist I have learned that helping people requires trying many different strategies and customizing care to a client's needs. I recommended that we start with tools she could learn in our sessions and practice at home to wind down her anxiety.

It took progressive relaxation practice before she was able to use mindfulness or breathing techniques, because at first, just thinking about her breathing made her more nervous. The next focus was to choose substitute words, encouraging words, to say to herself during breathing practice. Gradually she reported that practicing with audiotapes from our sessions helped her to not panic during the week.

To help her with nightmares about the time a Rituxan flare had briefly stopped her heart, we used bilateral desensitization, which uses the distraction of stimulation on alternating sides of the body to help it calm down while upset about an event. Once she was proficient in my office at staying calm while imagining herself getting out of the house, she started planning "baby steps" for progress.

When she gradually went from being in the parking lot, to being in the back of her church for a little while, to attending fully, she was encouraged. After speaking up to explain her needs to her siblings and to her daughter, she was able to get out and enjoy an art class with one of her friends. When we celebrated that she met the goals she had set, her mood was stable and her focus was on appreciating the moments in life that were meaningful to her. This did not happen in six weeks, in spite of what the treatment manuals may say; with this client, it took two years and many different approaches to therapy to resolve her issues.

It can take time for a client to build new skills until they become habits that counteract fears. Given time and practice, therapy can make a huge difference. I find that when clients build confidence from overcoming anxiety, they can begin to work their way out from mild depression.

My client taught me many things, including about WM, and her successes have stayed with me.

Observations from my experiences as a care partner

For some people, one coping method is a good match, but a different method might be best for others. For instance, when he focused on WM as incurable, my husband John had trouble sleeping, but after our older son showed him breathing exercises designed to help people reduce and avoid stress. John's focus on the moment and on mindful breathing helped him.

Often one person's strengths in a caregiving partnership can be a good complement to the other's. When John and I found

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the IWMF, learning about WM made me feel better, whereas for him, it was NOT thinking about cancer that helped. He prefers to wait to think about it until the next MD visit or the next Ed Forum or support group meeting. While John appreciates that I keep up (and I think of my volunteer efforts with IWMF Connect as my gift to him), it's also good for me, as it helps me feel oriented.

> *...**talk therapy** gave me the courage to say the scary thought, to be stronger, to learn **how to talk** with others about how I feel, **and to listen** more carefully to how others feel.*

Before COVID, we both enjoyed support group meetings in San Diego and hosting Chili Day in our home. With COVID restrictions, John went back to walking outdoors and exercising at home, instead of at a gym, and added masking when out and about. Now we both look forward to our support group talks on Zoom. While we thought we might like the idea of meeting again in person, our group spans three counties, not all our members can drive, and we wouldn't want anyone to feel left out. But we have lost our local book group, as most members want to meet indoors without masks and are sick and tired of Zoom, having never learned how to use it reliably.

Being on the other side of caregiving for John's brother, who suffers with schizophrenia, has given both of us a deeper understanding of caregiving. It took a while to realize what a help it is to have a companion caregiver for his brother, now that he cannot drive. We both are humbled by this experience and are more seriously researching the option of buying into a senior life care community for ourselves. If we were to stay in our home to the end, all our new acquaintances would be plumbers and gardeners! For now, life has been more relaxed and less worry-worn, and John has been able to plan events with his own friends and with couples we enjoy.

Observations from experiences in my own life

When I was diagnosed with a Stage 1 cancer at age 19, I had my first experience of anxiety, but I didn't know what it was. What I wish I'd known at the time is that I could have taken steps to learn skills to be aware of, and to prevent the buildup of, anxiety. I started having hives "out of the blue for no good reason at all." Even though early intervention and a follow-up test proved I was fine, it took a full year afterward for my body to stop misinterpreting activation of the nervous system as dangerous, so I broke out in hives every time I ran to class or was excited or was slightly worried about an exam.

The second time I was asked to go through cancer testing, it was for a lump on my thyroid. This time I was aware that I was frightened. That lump in the mirror scared the heck out of me.

I was already seeing my own therapist at that time, and it helped a lot to be able to talk about my thoughts and fears. I started to get to know myself better as I told her about my life. That helped me to be better able to tell others in my everyday life how I was feeling. I came away from that cancer scare filled with purpose—nothing was going to stop me from finishing my degree, cancer or not. It showed me that my life matters to me and that I have determination in the face of probably surmountable, but maybe painful, days ahead.

Thinking back to the self-awareness I gained while working with that therapist, talk therapy gave me the courage to say the scary thought, to be stronger, to learn how to talk with others about how I feel, and to listen more carefully to how others feel.

I had always been irritable during the winter months with no sunlight when I lived in Illinois, so "down days" were familiar to me and not worrisome. But later in life, I had different symptoms of depression. My mother had died after ten years with Alzheimer's, and I was over-exhausted from juggling

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caregiving for her and for my mentors from college days, the college application process with our teens, practicing with private patients on top of my day job, and working for a non-profit children's clinic.

Thank goodness I was already seeing a psychiatrist from Kaiser I admired, who had been prescribing 5 mg Adderall for me. She recommended that I take Prozac, too, at least for a year. I was a little surprised, but indeed I had been crying every time I was alone in the car, not just during sessions. After a year or so on Prozac, I weaned off very slowly, grateful for having had that help.

When we were all instructed to stay indoors because of COVID, I was quick to learn how to use Zoom and Signal to keep private practice therapy sessions on track because I understood from helping the client discussed above, how devastating isolation can be.

John went back to the patterns he used while in the middle of chemotherapy, using non-gym walks and workouts. In some ways, John and I felt closer as we were spending more time with each other. I helped myself stay engaged with the outside world by taking *plein air* (outdoor) and Zoom art classes and an excellent, year-long zoom/website training on a developmental model for helping couples. I also dealt with COVID by researching resources outside of Kaiser. As such a large organization, they were slow to offer vaccines, for example. I've kept up with my friends, with whom I enjoy walking and talking. Now when I see clients in person, we wear masks. As we are getting out more, I've tried to not overpopulate my calendar with too many friend outings. Accepting what we are facing and choosing the best safety measures that we can live with, I am using that information to go ahead and get out—which has made a difference for me. I follow the website "Your Local Epidemiologist," focus on art classes and being in the moment, and being kind to myself and my loved ones. These seem to be the hallmarks of what is helping me. I read a helpful study by researchers in Australia, who analyzed responses from over a hundred WM patients about their quality of life. One of the study authors, Colin Perrott, is a member of IWMF Connect. Those study participants with high mindful-acceptance, who avoided seclusion and held an optimistic attitude toward the present, felt the best. [The study article can be found at *https://www.scirp.org/pdf/JCT_2014102814382747.pdf.*] So, I'm also meditating more often and wishing everyone the best quality of life possible.

I hope that my stories have given you some things to think over. My main point is that sometimes we don't realize we are starting to have depression or anxiety issues, but if we seek help, therapy can make a difference. Talking through our feelings with another can help us get to know ourselves and to be more effective with self-care and with being loving to others. Even with neurotic depression, medication can also help, depending on our individual needs.

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THE TORCHBEARER REPORT

By Newton Guerin, IWMF President and CEO

Newton Guerin

In early October, I had the opportunity to participate in the Lymphoma Coalition Global Summit, in Porto, Portugal. The Lymphoma Coalition is an organization comprised of over 80 patient advocacy groups across more than 50 countries that support those affected by lymphoma. Each year, the Lymphoma Coalition brings together representatives of these organizations to build relationships and share best practices in order advance their vision of global equity in lymphoma outcomes across borders.

The Global Summit has not been held in-person in over two years because of COVID. This was my first opportunity to join this group in-person. As IWMF President and CEO, I was invited to moderate a panel discussion to address health literacy and why it matters. The panel was composed of a group of experts who shared differing perspectives and insights around issues including:

- How big is the low health literacy problem worldwide? What is the implication for health and social care if we don´t improve health literacy?
- What problems does health literacy pose for an ever-increasing digital world?
- How can we identify and make use of opportunities to improve patient-clinician communication across the cancer care continuum?

From that discussion, we identified several challenges that each of our organizations must address:

- Low health literacy can affect a person's ability to locate health care providers and services, fill out health forms, share personal health information with providers, manage chronic diseases, and engage in self-care. Literacy skills affect how people find, understand, and use information on the web.
- Many web users struggle with even the most basic tasks—for example, using a search function, navigating from a drop-down menu, and scanning a webpage for relevant information. The stakes are high when a person is trying to sign up for health insurance, learn about a new medical diagnosis, or find doctors who specialize in a particular disease. And today, these activities are more likely to occur online than off.
- Culture and literacy skills are two important factors, among others, to consider when designing health communication materials that will capture the intended audience's attention.

Another highlight of this year's Summit was a review of the 2022 Global Patient Survey (GPS). Every other year, the Coalition conducts this survey in order to better understand the patient and caregiver experience in lymphomas and the impact of treatment and care. The data serve as the foundation for scientific abstracts, joint research initiatives, policy papers, and other international collaborations and presentations. The IWMF was invited to add five additional questions that addressed some of our specific issues and concerns. Following the Summit, the Lymphoma Coalition completed a WM-specific analysis from the GPS that summarized data from all worldwide respondents affected by WM (885 patients and 69 caregivers). Several key findings are important for us to consider:

- Only 23% of patients felt well informed about processes and stages of their healthcare.
- Outside of their doctor, 43% of patients say organizations (like the IWMF) are the most useful in providing supportive care.
- 57% of patients ranked websites as their top method of receiving information.
- Only 36% of patients were given more than one treatment option.
- 55% of patients received information about clinical trials from their doctor, and only 13% have participated in a clinical trial.
- Only 40% of patients received contact details of a patient organization, support group, or information produced by a patient organization from their healthcare team, and only 12% received that during their first visit.
- When asked what organizations were sought out for information, 85% indicated the IWMF, 43% the Leukemia & Lymphoma Society, and 22% the American Cancer Society.
- Over half (55%) of the respondents live within the US and 45% outside the US. Because this gives such a large and balanced sample of the US compared to the rest of the world, Paul Kitchen, IWMF International Committee Chair, has requested that the Lymphoma Coalition provide a similar report comparing US respondents to non-US. There may be some very valuable lessons that we can learn from this data.

During its November meeting, the IWMF Board of Trustees revisited the organization's Strategic Plan and Compelling Intentions that were put in place three years ago. Our purpose was to determine if the current plan accurately reflects

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today's organizational priorities. We wanted to ensure that our plan tells our story to all IWMF stakeholders: patients, caregivers, donors, volunteers, board members, corporate partners, and the research and medical communities. We also wanted to offer a plan that outlines big ideas, is simple to understand, is optimistic, and focuses on the future. With that in mind, we determined that our current vision statement and organizational values continue to be relevant for today's IWMF.

...it is critical that we ***tell our story to all IWMF stakeholders*** *on a regular basis.*

Our mission statement was modified as follows: Support and educate everyone affected by Waldenstrom's macroglobulinemia (WM) to improve patient outcomes while advancing the search for a cure.

In reviewing our current "Compelling Intentions," the Board considered a number of things in our assessment of where we are today, including: overall financial position and outlook for the future; evaluation of current information, education and support programs; and findings from the WM Global Patient Survey outlined above. The result was a modification of the IWMF's Strategic Plan. Instead of "Compelling Intentions," these were renamed "Global Imperatives" and were stated as follows:

- **Research:** Expand our leadership role to significantly increase the number, scope, and coordination of global WM research projects.
- **Patient Support:**
  - Awareness: Ensure that everyone affected by WM knows about the resources we offer.
  - Education and Support: Be the authoritative source for patient and caregiver education and support.
- **Healthcare Professionals Awareness:** Reach more patients sooner by ensuring that every healthcare professional working in blood cancer is aware of the IWMF and its resources.
- **Partnership:** Actively pursue and develop relationships with like-minded organizations to accomplish our mission.
- **Fundraising:** Significantly increase and diversify our sources of funding.

Good leaders have a vision for their organization and can articulate it effectively. This plan provides that. Going forward, it is critical that we tell our story to all IWMF stakeholders on a regular basis. Our donors expect to hear from us about the progress we are making, the challenges we are facing, and any new opportunities as they arise.

As I begin my fourth year as IWMF President and CEO, I welcome your advice and guidance along the way. Please reach out to me whenever you want. I can be reached by email at *nguerin@iwmf.com* or by telephone at 703-986-3549.

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*

INTERNATIONAL WORKSHOP ON WALDENSTROM'S MACROGLOBULINEMIA (IWWM11)

By Dr. Glenn Cantor, IWMF Trustee and *Torch* Science Editor, and Dr. Tom Hoffmann, IWMF Trustee and Vice Chair, Research

Every two years since 2000, WM researchers and physicians from around the world meet in a workshop to discuss current research, plan new studies, and develop guidelines for better WM treatment.

This year, the International Workshop on Waldenstrom's Macroglobulinemia (IWWM), was held in Madrid, Spain. The workshop was impeccably organized and hosted by Dr. Jesús San-Miguel of the University of Navarra in Spain and Dr. Ramón García Sanz of the University Hospital of Salamanca in Spain, together with Dr. Steven Treon and Christopher Patterson of the Dana-Farber Cancer Institute in Boston, MA. Perhaps because the regularly planned 2020 meeting was cancelled as a result of COVID, attendance this year was at an all-time high—370 attendees in person and 250 remote attendees. The IWMF was represented by Dr. Tom Hoffmann (IWMF Vice Chair, Research), Dr. Glenn Cantor (IWMF Trustee and *Torch* Science Editor), Newton Guerin (IWMF President and Chief Executive Officer), and Sara McKinnie (IWMF Manager, Meetings and Partner Engagement). The WMUK, the IWMF-affiliated organization in the United Kingdom, was represented by Bob Perry (WMUK Patient Support Manager), and the WM Foundation of Italy was represented by Claudia Bedogni.

For us, the workshop was a remarkable assemblage of smart scientists and doctors, all committed to working on WM. The depth and talent of scientific research was impressive, but equally impressive was the overall feeling of community and camaraderie—a highly collaborative and friendly group of investigators. After each session, there were insightful questions, suggestions, and discussions that were intended to take the research one step further. The benefit of this collaborative culture to WM patients is clear. Investigators from many different countries work together in a climate of mutual trust and respect to plan and implement larger, more impactful trials than could be done by any one institution or one country.

Many young investigators attended and presented their work. The high caliber of science from these new investigators, including some who are rising stars of the future, made us optimistic that the future of WM research is bright indeed.

Importantly, the meeting brought together WM researchers and physicians who worked from a variety of different perspectives and approaches. Many researchers presented their work with basic molecular mechanisms or potential new therapeutic targets; one session discussed scientific work with mouse models of WM, and many physicians discussed their latest clinical findings. This combination of scientific approaches was beneficial to everyone.

Some highlights of the scientific presentations

It is increasingly obvious that **mutations of the MYD88 gene are not enough to cause WM**. The search is on, therefore, for additional "hits" which cause cells that already have abnormal MYD88 to tip over the edge and become WM cells. It is unlikely that any single event will emerge as the culprit. Many candidate genes or other abnormalities were proposed. Dr. Jian Hou, Renji Hospital, Shanghai Jiao Tong University, China, gave a fascinating talk about a set of twins who were patients of his. One of the twins had symptomatic WM, the other had asymptomatic WM, and there were a number of siblings without WM. By comparing their DNA,

IWMF representatives with Christopher Patterson at IWWM11: Dr. Stephen Ansell, Newton Guerin, Sara McKinnie, Christopher Patterson (Administrative Director of the Bing Center, Dana-Farber Cancer Institute), Dr. Tom Hoffmann, and Dr. Glenn Cantor

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Dr. Mary McMaster (National Institutes of Health, Washington DC) speaking about genetic findings in familial WM

he found a gene called FHL2 that encodes a signaling protein which may be involved in the development of WM, at least in some people. Dr. Jonas Paludo from the Mayo Clinic, Rochester, MN, presented a completely different approach. Many people study mRNA (messenger RNA) that encodes proteins. Instead, Dr. Paludo focused on long pieces of RNA inside cells that do not encode proteins but, instead, act as regulators of cell function. There are thousands of these long non-coding RNAs (abbreviated lncRNA), making their study highly complex. They also have rather formidable names, such as "RP11-1193F23.1" that don't roll off the tongue easily. Dr. Paludo reported a number of these lncRNAs that may be involved in WM.

Meanwhile, tumor suppressor genes can also go awry. These are genes encoding proteins that normally control cancer. When the genes are mutated or fail to operate, the normal control is released and malignant cells grow more easily. A gene called TP53 received prominent attention. Research from Dr. Maria Luisa Guerrera at Dana-Farber continues on another tumor suppressor gene, WNK2 (see the *IWMF Torch*, April 2022).

An increasingly recognized area of WM research is the **role of the immune system within the bone marrow in controlling WM growth.** Specific cell types in the bone marrow suppress the body's normal immune response. This allows the WM cells to grow in the bone marrow. Dr. Aldo Roccaro from Breschia, Italy, spoke about a type of lymphocyte called a T regulatory cell (Treg, for short) that suppresses other T cells so that they are less able to control the WM cells. These Tregs interact with the WM cells through a pair of signaling molecules called CD40 and CD40L. Meanwhile, Dr. Vaishali Bhardwaj, a member of Dr. Stephen Ansell's group at the Mayo Clinic, Rochester, discussed another type of bone marrow cell that also suppresses the body's immune reaction to WM cells. These cells are called myeloid-derived suppressor cells. In the bone marrow of WM patients, these suppressor cells are more numerous, more activated, and are capable of interfering with how normal T cells kill WM tumor cells. A number of companies are working on drugs to break the interaction between CD40 and CD40L, while others are working on drugs to inhibit myeloid-derived suppressor cells. These drugs may be useful in WM in the future.

Many new therapies are on the horizon and are currently in clinical trials. Dr. Stephen Ansell of the Mayo Clinic, Rochester, and Dr. Ken Anderson of Dana-Farber discussed **bispecific antibodies** that grab on to a tumor cell (in this case, a WM cell) with one arm and a T cell with the other arm. This brings the two cells—the WM cell and the T cell—closely together and allows the T cell to kill the tumor cell. Dr. Shayna Sarosiek from Dana-Farber discussed **antibody-drug conjugates**. These consist of an antibody targeted specifically to a protein on the surface of B cells (including WM cells), linked to a highly potent drug. After attaching, the antibody-drug conjugate is taken into the cell, where the drug is released and kills the cell. This helps to kill the "right" cells while minimizing side effects to the rest of the body. Dr. Mazyar Shadman from the Fred Hutchinson Cancer Research Center in Seattle, WA, discussed **CAR T cells**. They have treated two patients with WM so far. One has been nearly free of disease for 15 months now. The other person also responded favorably but unfortunately died of COVID six months later.

A special session was held on **COVID and the impaired immune response of WM patients**, particularly those who had been treated in the past 6-12 months with rituximab. Speakers pointed out the difficulty of keeping up with the new variants that continue to emerge. In general, though, symptomatic WM patients have a poor antibody response (called a titer) to their first and second vaccination but, fortunately, mount a much better response to a third or fourth vaccination. Asymptomatic, or smoldering, WM patients generally have a good, protective response to vaccination. It is encouraging that in many patients, the T cell response to vaccination is still robust, even when the antibody response is deficient.

Panel discussion, WM Genomics: Dr. Zachary Hunter (Dana-Farber Cancer Institute, Boston, MA); Dr. Cristina Jimenez (University of Salamanca, Spain); Dr. Damien Roos-Weil (Hôpital Pitié-Salpêtrière, Paris, France); and Dr. Tina Bagratuni (University of Athens, Greece)

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The Great Debates sessions on key treatment issues

Another highlight of the meeting was the Great Debates about key treatment issues in WM. These somewhat light-hearted, jovial presentations were meant to compare medical approaches that are not completely resolvable, issues for which there is truly more than one way to look at them. One doctor was selected to argue one side, and a different doctor to argue for the other side. Each debater had a period for rebuttal, and then the audience held an informal vote.

One energetic and spirited Great Debate was **whether smoldering WM should be managed by watch-and-wait or should be treated.** The underlying context is that the newer drugs are safer than those used in the past. Dr. Prashant Kapoor from the Mayo Clinic, Rochester, argued vigorously that many patients with smoldering WM live normal lives for decades without disease, that all of the currently available drugs carry side effects, and that progression of disease can be monitored before electing to treat. He even quoted Dr. Jan Waldenström, the discoverer of WM, who famously said "Let well do," when counseling young physicians not to over-treat their patients.

Lining up for questions after a lecture. Dr. Meletios Dimopoulos (University of Athens, Greece); Dr. Alessandra Tedeschi (Niguarda Cancer Center Hospital, Milano, Italy); Dr. Prashant Kapoor (Mayo Clinic, Rochester, MN); and Dr. Judith Trotman (University of Sydney, Australia)

Taking the other side, Dr. Irene Ghobrial from Dana-Farber argued that not treating smoldering WM patients puts them at risk of serious medical injury, including stroke and retinal damage. She proposed that smoldering WM patients at high risk of progression could be identified and treated to avoid serious organ damage. She also discussed the possibility of a better response to therapy if therapy could be initiated before substantial clonal evolution or immune dysregulation occurred. She proposed a randomized, controlled trial to scientifically evaluate whether smoldering WM patients would benefit more from treatment or from watch-and-wait. In a highly unofficial vote, it looked like only about 10-20 doctors agreed with Dr. Ghobrial that smoldering WM patients should be treated, while perhaps 75 thought that patients with smoldering WM should be managed with watch-and-wait and not be treated. But then, Dr. Ghobrial posed a different question: "How many think we should do research on this?" A sea of hands went up. "See," she said, holding up her fists, "I won."

Discussion with Dr. Shuhua Yi (Institute of Hematology and Blood Diseases Hospital, Chinese Academy of Medical Sciences, China) and Dr. Karima Amaador (University Medical Center Utrecht, the Netherlands)

Another Great Debate was **which BTK inhibitor to use**. Dr. Ranjana Advani of Stanford University, CA, was selected to argue for ibrutinib; Dr. Roger Owen of St. James's University Hospital, Leeds, United Kingdom, spoke for acalabrutinib; and Dr. Judith Trotman of the University of Sydney in Australia argued for what she called "za new drug," zanubrutinib. Dr. Advani said that ibrutinib, the first BTK inhibitor used for WM, is the best studied, with the longest real-world data. Dr. Trotman, on the other hand, argued that the large randomized, controlled trial called ASPEN recently compared zanubrutinib with ibrutinib and found that zanubrutinib demonstrated fewer side effects, increased quality of life, and similar efficacy. This made zanubrutinib the best choice. She also pointed out that zanubrutinib is better than ibrutinib in patients with CXCR4 mutations. She did note that the "elephant in the room" was cost, and that if there was a significant cost difference among the three BTK inhibitors, she would just choose the cheapest one. In the end, a sea of hands endorsed Dr. Trotman's position that zanubrutinib was the best choice.

Dr. Christian Buske from the University of Ulm, Germany, and Dr. Meletios Dimopoulos from the University of Athens, Greece, debated **whether BTK inhibitors (such as ibrutinib, acalabrutinib, or zanubrutinib) or bendamustine-rituximab should be used as the standard frontline induction regimen**. Dr. Dimopoulos argued for BTK inhibitors. He said that the response rates of these two treatment regimens are similar, but BTK inhibitors are less toxic. This is a particular advantage of BTK inhibitors in older or more frail patients. In older patients, he said, bendamustine-rituximab can cause serious and prolonged cytopenia (decrease in blood cells such as neutrophils, platelets, and red blood cells). On the other hand, though, he admitted the problem that BTK inhibitors must be given as continuous treatment, while bendamustine-rituximab is a fixed duration treatment. Dr. Buske, arguing for

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Great Debate: Which BTK inhibitor to use? Left to right: Dr. Judith Trotman (University of Sydney, Australia); Dr. Ranjana Advani (Stanford University, Palo Alto, CA); Dr. Eva Kimby (Karolinska Institute, Stockholm, Sweden); Dr. Christian Buske (University of Ulm, Germany); and Dr. Roger Owen (St. James's University Hospital, Leeds, UK)

bendamustine-rituximab, emphasized the lower cost and the convenience to patients of fixed-duration treatment (often six months). He pointed to a recent study of patient preference in the Netherlands that found that patients prefer fixed-duration treatment over continuous, lifetime treatment (See *http://onlinelibrary.wiley.com/doi/10.1002/cam4.5080*). In general, he said, bendamustine-rituximab is well tolerated. He also pointed out that nearly one in four patients treated with ibrutinib discontinue within two years, suggesting that for many people, ibrutinib is not so tolerable. For the newer BTK inhibitors, acalabrutinib and zanubrutinib, he pointed out that we do not have long-term experience yet. The majority of the audience voted with Dr. Buske for bendamustine-rituximab, but this is definitely a subject of controversy.

Dr. Lia Palomba, Memorial Sloan Kettering Cancer Center, NY, and Dr. Alexandra Tedeschi, Niguarda Hospital, Italy, debated **whether patients with ibrutinib intolerance should be managed by reducing their dose of ibrutinib or switched to another BTK inhibitor**, such as zanubrutinib or acalabrutinib. Dr. Palomba argued that many patients continue to experience deep responses with less toxicity if the dose of ibrutinib is reduced. She pointed to a presentation on the previous day, in which Dr. Shayna Sarosiek analyzed data from patients who required a reduced dose of ibrutinib and found that nearly all of them continued to have the same or better response, even though the dose of ibrutinib was lower. Taking the other position, Dr. Tedeschi argued that switching to another BTK inhibitor could result in fewer side effects: "If you go to a restaurant and they give you just average wine, why would you go to that restaurant a second time?" She said there were some data suggesting that 68% of the side effects of ibrutinib did not recur when patients were switched to zanubrutinib. Both speakers acknowledged, though, that there are insufficient data to settle this issue, and the audience vote was split about 50-50.

The final debate was what should be the **endpoint or goal of WM therapy, disease control or a complete response.** There have been very few complete responses (CR) with any treatment, so the debate was more about future goals or philosophies rather than a direct comparison of currently available treatments. Presently, therapy helps many WM patients achieve VGPR (very good partial response) but seldom eradicates or cures WM. Dr. Efstathios Kastritis from the University of Athens argued that disease control should be physicians' goal. He said that with VGPR, patients feel better and live longer and that it is a realistic goal, while CRs are rare and elusive. Dr. Jorge Castillo of Dana-Farber was chosen to present the other view, that the goal should be CR, even though there have been very few CRs so far. He acknowledged that with this position, he was "swimming against the current" and that CRs are "a dream." However, with other diseases, CRs predict much better overall survival. He acknowledged that treatment intended to result in CRs in WM patients may be excessively toxic. However, he said this should be our future goal. He advocated well-designed clinical trials to investigate if CR is possible.

Great Debate: Should we treat smoldering WM? Dr. Irene Ghobrial (Dana-Farber Cancer Institute, Boston, MA)

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Consensus Panels on WM management

On last day of the meeting, seven WM Consensus Panels convened to address key questions in WM management. In a session moderated by Dr. Steven Treon and Dr. Meletios Dimopoulos, the organizers of each panel presented a list of key questions, to which the audience contributed additional questions. During the next few months, the Consensus Panels will use the questions as a guide to prepare papers summarizing the WM medical community's current recommendations. After cross-review by each panel, the consensus papers will be published in 2023 in an open-source journal so that they will be widely available.

The Consensus Panels are:

- IWWM11 Recommendations for Treatment Approach in WM – Frontline (Organizers: Drs. Christian Buske, Jorge Castillo, and Judith Trotman)
- IWWM11 Recommendations for Treatment Approach in WM – Relapsed/Refractory (Organizers: Drs. Efstathios Kastritis, Shirley D'Sa, and Jeffrey Matous)
- IWWM11 Recommendations for Molecular Diagnostic Workup in WM (Organizers: Drs. Ramón Garcia-Sanz, Marzia Varettoni, and Zachary Hunter)
- Response Criteria for WM (Organizers: Drs. Steven Treon, Roger Owen, and Alessandra Tedeschi)
- COVID Prophylaxis and Management in WM (Organizers: Drs. Meletios Dimopoulos, Véronique Leblond, and Andrew Branagan)
- Management of WM-Related Amyloidosis (Organizers: Drs. Monique Minnema, Shayna Sarosiek, and Giampaolo Merlini)
- Priorities for Novel Clinical Trials (Organizers: Drs. MJ Kersten, Prashant Kapoor, Constantine Tam, and Glenn Cantor)

Coming back from the meeting, we felt a renewed sense of optimism and commitment. Clearly, WM is a complicated disease without any easy answers. As our understanding of the details of the disease improve and drug treatments evolve, there will not be a "one size fits all" treatment. Different treatment regimens will have to be developed for different types of WM. That is a big undertaking. It was inspiring to see so many dedicated physicians and researchers from around the world working together to help WM patients.

All photos courtesy of IWWM11.

IWWM11 participants, closing ceremony at the Prado Museum, Madrid, Spain

IWWM11 AWARDEES

IWWM11 honored a number of investigators and physicians for their achievements in the field of WM research. This list is a literal "Who's Who" of the great WM scientists, and it was quite inspirational. Moreover, the awards to ten highly talented young investigators were an optimistic preview for the future of WM research. Honorees were:

The Jan Gosta Waldenström Award to honor a lifetime of contributions and achievements for improving the lives of patients with WM:

Jesús San-Miguel, MD, PhD, University of Navarra, Spain

Irene Ghobrial, MD, Dana-Farber Cancer Institute, Harvard Medical School, Boston, MA

Christian Buske, MD, PhD, University of Ulm, Germany

The Robert A. Kyle Award in honor of outstanding contributions to scientific and medical advancements in WM:

Jorge J. Castillo, MD, Dana-Farber Cancer Institute, Harvard Medical School, Boston, MA

Ramón García Sanz, MD, PhD, University Hospital of Salamanca, Spain

Stephen M. Ansell, MD, PhD, Mayo Clinic, Rochester, MN

The Robert A. Kyle Award – Dr. Jorge Castillo; his wife Dr. Joanna Mitri and family

The Peter S. Bing Humanitarian Award for extraordinary humanitarian service and activism on behalf of patients with WM:

Shirley D'Sa, MD, FRCP, FRCPath, University College London Hospitals, NHS Trust, London, United Kingdom

Judith Trotman, MBchB, FRACP, FRCPA, Concord Repatriation General Hospital, University of Sydney, Australia

Mary L. McMaster, MD, National Cancer Institute, NIH, Bethesda, MD

Three Peter S. Bing Humanitarian Awardees – Christopher Patterson and Karen Lee Sobol, presenters; Dr. Shirley D'Sa, Dr. Mary L. McMaster; Dr. Ranjana Advani, presenter; Dr. Judith Trotman

Young Investigator Award

Patrizia Mondello, MD, PhD, MSc, Mayo Clinic, Rochester, MN

Karan Lal Chohan, MD, Mayo Clinic, Rochester, MN

Mélanie Khamyath, Institut de Recherche Saint-Louis, Université Paris Cité, France

Alexandros Gkiokas, MD, MSc, Laiko General Hospital of Athens, National and Kapodistrian University, Athens, Greece

David F. Moreno, MD, Hospital Clinic of Barcelona, University of Barcelona, Spain

Vaishali Bhardwaj, PhD, Mayo Clinic, Rochester, MN

Joshua Gustine, MPH, Boston University, Boston Medical Center, Boston, MA

Jahanzaib Khwaja, University College London Hospitals, London, United Kingdom

Martina Ferrante, University of Torino, Torino, Italy

Quentin Lemasson, University of Limoges, Limoges, France

Several Young Investigator Awardees – Dr. Karan Lal Chohan; Dr. Patrizia Mondello; and Dr. Vaishali Bhardwaj
Photograph courtesy of Glenn Cantor

I JUST LEARNED I HAVE WM. NOW WHAT?

By Art Brewer

It can be overwhelming—indeed terrifying—to learn you have a rare and incurable disease like Waldenstrom macroglobulinemia (WM). No one wants to hear their doctor utter the dreaded "c" word as a diagnosis. I had always been in good health and used to brag about not taking any medication, so this was truly a bombshell development in my life. Feelings of fear, disbelief, anxiety, anger, and sadness were common, yet I never succumbed to despair.

Since my diagnosis three years ago, I have learned that WM is not a death sentence. The disease, while currently incurable, is manageable with the proper treatment, and most people die with it and not from it. After recovering from the initial shock of learning I had WM, I turned my fear into action.

One of the most important decisions I made was to select a WM specialist to treat the disease. Because WM is so rare, you need to seek treatment from a medical professional who is familiar with the disease and who has cared for many WM patients before. The International Waldenstrom's Macroglobulinemia Foundation (IWMF) maintains a directory of WM specialists from around the world that can help in the selection process (*https://iwmf.com/directory-of-wm-physicians/*). If it is not feasible to procure a WM specialist because of geographical, financial, or other factors, you should ask your doctor about the possibility of consulting with such a specialist.

It is also very important to educate yourself about WM and seek out information on the disease. Every WM diagnosis and patient is different, and the treatment can differ as well. Researching the disease can help you understand your condition, treatments, medications, and the medical terms associated with the disease. The IWMF website (*www.iwmf.com*) presents a wealth of information and resources including publications, videos, presentations, webcasts, newsletters, and much more.

Educating myself about the disease has enabled me to be a more effective advocate for myself and helped me decide with my hematologist on a course of treatment. Unless you have a certain baseline knowledge, you will not know what questions to ask your doctor to decide if a particular course of treatment is right for you. I make a list of my questions and concerns before each appointment with my hematologist. You may even want to seek a second opinion if you are uncomfortable with the doctor's diagnosis or recommended treatment.

While becoming educated about the disease is important, you should also be discerning about what you read online, because not all of the information there is accurate or current. For example, when I started researching WM shortly after my diagnosis, I was alarmed to find published reports online that provided a median survival of approximately five years from the time of diagnosis. I have since learned that this information is outdated and that treatment options are

increasingly becoming more varied and effective, resulting in much longer survival times. In fact, I have met several WM patients through my WM networks who have lived with the disease for decades. You should speak to your doctor to verify the information you obtain online and rely on credible, trustworthy sources like the IWMF website for accurate, up-to-date information.

WM patients are few and far between, so you may feel isolated and alone, but there are many support groups and social media platforms to share your experience and learn from others in similar situations. They can be helpful as you go through diagnosis, treatment, and beyond. I have joined the WM Facebook page, a local WM support group, and a dedicated WM support group for people of color to address the unique concerns faced by ethnic minorities. I have found them to be effective and much-needed outlets to connect with other WM patients and learn from each other.

Finally, if you are a spiritual or religious person, turning to religion or spirituality for solace can be an effective method of coping with the disease. Facing my own mortality at a relatively young age was disturbing and unsettling to say the least. However, having a religious perspective helped me as I grappled with the mental and emotional turmoil that came with having WM.

Receiving a WM diagnosis is truly life-changing and challenging, and everyone's journey with the disease is different. My diagnosis has changed my perspective on life and given me a newfound appreciation of things I used to take for granted, from the simple to the sublime. I am grateful that my treatment has been effective and my health is good, and I am determined to enjoy life's simple pleasures for as long as possible.

Three years after beginning my journey with WM, I have come to terms with the disease and don't often think about it anymore. I encourage you to find the support—whether your family, friends, faith, fellow patients, healthcare professionals, or online resources—to help you on your journey as well.

MEDICAL NEWS ROUNDUP

By Sue Herms, IWMF Research Committee Member

Zanubrutinib Accepted for WM Treatment in England, Wales, and Scotland – The National Institute for Health and Care Excellence (NICE) in England and Wales has issued a final appraisal document that recommends zanubrutinib (Brukinsa) for the treatment of WM in patients who have had at least one previous treatment, but with certain conditions. The cost effectiveness estimates for zanubrutinib are only within what NICE considers an acceptable use of financial resources when bendamustine plus rituximab (BR) therapy is also a suitable option for these patients; however, if BR is unsuitable, as may be the case with medically fragile or elderly patients, the cost effectiveness estimates for zanubrutinib become unacceptable when compared to alternative therapies, such as rituximab alone. This guidance does not affect treatment with zanubrutinib that was started before the final guidance was published, and those receiving treatment outside the guidance may continue without change to their funding arrangements already in place. Meanwhile, after resubmission for WM treatment within Scotland, the Scottish Medicines Consortium has accepted zanubrutinib as single agent therapy for those who have received at least one prior therapy or as first-line treatment for patients unsuitable for chemoimmunotherapy.

Mustang Bio Treats First Patient in New Phase 1/2 Trial of MB-106 and Reports Interim Results from Initial Trial – Mustang Bio announced that the first patient has been treated in its multicenter Phase 1/2 clinical trial evaluating the safety and efficacy of MB-106, the first CD20-targeted CAR T cell therapy for the treatment of relapsed or refractory B cell non-Hodgkin's lymphomas and chronic lymphocytic leukemia. MB-106 is being developed in a collaboration between Mustang Bio and Fred Hutchinson Cancer Center in Seattle. The new multicenter trial under Mustang's Investigational New Drug Application, designated as NCT05360238 on *www.clinicaltrials.gov*, builds upon the initial, ongoing Phase 1/2 clinical trial taking place in a single-center outpatient study at Fred Hutchinson. In the Fred Hutchinson study, an interim overall response rate of 96% and a complete response rate of 75% were achieved in a wide range of blood cancers, including WM. Twelve patients experienced a complete response for more than one year, four patients for more than two years, and the longest patient for 33 months. Six patients with initial partial responses improved to complete responses and remain in complete responses. No serious instances of cytokine release syndrome (the excessive release of inflammatory molecules) or neurological side effects have occurred in this trial.

Chinese Study Publishes Results of Orelabrutinib Treatment in Phase 2 Study of Relapsed or Refractory WM – A Chinese study published in the journal *The Lancet* discussed results from a Phase 2 study of the BTK inhibitor orelabrutinib in 47 relapsed or refractory WM patients. The drug was administered at 150 mg daily. With a median follow-up of 16.4 months, the overall response rate was 89.4%, and the major response rate was 80.9%. The progression-free survival rate at 12 months was 89.4%. The major response rates broken down by genetic profile were: 84.6% for mutated MYD88 and unmutated CXCR4; 100% for mutated MYD88 and S338X-mutated CXCR4; and 25% for unmutated MYD88 and unmutated CXCR4. The most common serious adverse events were neutropenia (low neutrophil count), thrombocytopenia (low platelet count), and pneumonia. One treatment-related death (because of hepatitis B reactivation) was reported.

...(Velcade)-containing treatments in WM patients at frontline and at relapse are effective, even for those who have developed resistance to BTK inhibitors.

United Kingdom Study Analyzes Real-World Data for Bortezomib Regimens in the Frontline and Relapsed Settings, Including Those with Prior BTK Inhibitor Therapy – Researchers in the United Kingdom reported that bortezomib (Velcade)-containing treatments in WM patients at frontline and at relapse are effective, even for those who have developed resistance to BTK inhibitors. This was a retrospective study of WM patients between 2010 and 2022, with real-world data obtained from the Rory Morrison Registry in the UK. Of 44 bortezomib regimens identified, 12 were in the frontline setting and 32 were in the relapsed setting; of relapsed patients, ten were refractory or intolerant to prior BTK inhibitor therapy. Median follow-up after bortezomib-containing treatments was 34 months. The overall response rate to bortezomib regimens was 88%, while two-year overall survival and progression-free survival were 90% and 76%, respectively. Median time-to-next-treatment was 66 months. In the subset of patients with prior BTK inhibitor treatment, one achieved a complete response, one a very good partial response, four a partial response, one a minimal response, and one stable disease—two were too early to assess. The major response rate was comparable in those with prior BTK inhibitor therapy (75%) vs. those without (84%). Overall, neuropathy occurred in 24% but did not result in stopping treatment; gastrointestinal disturbance occurred in 7%. All patients received subcutaneous bortezomib. Bortezomib, dexamethasone, and rituximab was the most frequently delivered regimen, followed by bortezomib and dexamethasone. A median of six cycles was delivered, with

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56% receiving once-weekly doses of bortezomib at 1.3 mg/m^2 and 44% receiving once-weekly doses at 1.6 mg/m^2. The study was published in the online journal *eJHaem*.

Phase 2 Trial Reports Safety and Effectiveness of Zanubrutinib Therapy in B Cell Cancer Patients Intolerant to Other BTK Inhibitors – An ongoing Phase 2 multicenter US trial published in the journal *The Lancet Haematology* has reported the safety and effectiveness of zanubrutinib (Brukinsa) therapy in patients with B cell cancers who were previously treated with other BTK inhibitors and unable to tolerate them because of adverse side effects. From October 2019 to September 2021, 67 B cell cancer patients who were intolerant to ibrutinib (Imbruvica), acalabrutinib (Calquence), or both were enrolled and received oral zanubrutinib at 160 mg twice daily or 320 mg once daily. Most of the previous intolerance events were associated with ibrutinib. In this trial, 70% of the intolerance events associated with ibrutinib and 83% of the intolerance events associated with acalabrutinib did not recur with zanubrutinib. Some intolerance events recurred with the same or lesser severity in patients on zanubrutinib, but no events recurred at a higher severity. The most common adverse events with zanubrutinib were bruising, fatigue, muscle aches, joint aches, and diarrhea; atrial fibrillation occurred in 4% of patients on zanubrutinib. With a median follow-up of one year, the disease control rate with zanubrutinib was 93.8%, and the overall response rate was 64.1%. The median duration of response and the median progression-free survival were not reached. The trial is still recruiting, and its identifier on *www.clinicaltrials.gov* is NCT04116437.

...a ***higher incidence of transformation*** *has been reported in those* ***with MYD88 wild-type*** *(unmutated) disease.*

International Research Article Discusses Transformation in WM Patients – A multicenter international group of researchers has published an article in the journal *Hemato* discussing the rare occurrence of transformation to aggressive lymphoma that has been observed in patients with WM. It is estimated that transformation occurs in about 1-4% of WM patients, and a higher incidence of transformation has been reported in those with MYD88 wild-type (unmutated) disease. Transformation in WM is the result of additional mutations that alter the appearance and characteristics of a WM cell, resulting in more aggressive disease, and it can occur at any time during the course of WM. The reported median time range to transformation is 4.3-4.6 years. Diffuse large B cell lymphoma of activated B cell subtype, commonly called ABC subtype, is the predominant form of transformation. Clinical symptoms include physical deterioration and the rapid enlargement of lymph nodes; most transformed patients present with elevated serum lactate dehydrogenase (LDH) and often also have disease sites outside the lymph nodes. Another frequently encountered observation is a reduction in the serum IgM level. Biopsy is required to confirm the diagnosis, and the choice of biopsy site may be dictated by findings from PET (positron emission tomography) scans. The prognosis of transformation in WM tends to be unfavorable. The most common initial treatment is chemoimmunotherapy, such as R-CHOP (rituximab, cyclophosphamide, doxorubicin, vincristine, prednisone), but response duration is short and relapses are frequent. Data on treatment with autologous stem cell transplant, BTK inhibitors, BCL2 inhibitors, or CAR T cell therapy are sparse, and more study is needed to determine how best to treat transformation in WM.

CDC Updates COVID-19 Vaccination Guidance for Immunocompromised Adults – 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 addresses the use of Novavax booster shots in limited situations.** 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 Schedules," and click on the heading "Guidance for people who are immunocompromised." To briefly summarize the guidelines:

- For those who receive the two primary Pfizer or Moderna vaccines, a third primary shot of original Pfizer or Moderna vaccine should be received at least four weeks afterward. An updated bivalent booster shot of Pfizer or Moderna should be received at least two months after the third primary shot or after a previous booster.
- Novavax was recently authorized as a primary vaccine for those 12 years and older in a two-shot regimen. In the immunocompromised, the second shot should be received three weeks after the first. For those who receive the primary two-shot Novavax vaccine, an updated bivalent booster shot of Pfizer or Moderna is preferred and should be received at least two months after the second primary Novavax shot.
- In limited situations, a Novavax booster shot may be received by those who have had primary COVID vaccination of any kind as long as they have not already received a booster shot, are unable or unwilling to receive a Pfizer or Moderna booster, and would otherwise decline a booster. A Novavax booster shot should be received at least six months after completion of primary vaccination.

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- For those who receive the primary J&J vaccine, a second primary shot of original Pfizer or Moderna vaccine should be received at least four weeks afterward. An updated bivalent booster shot of Pfizer or Moderna should be received at least two months after the second primary shot or after a previous booster. The US Food and Drug Administration has strictly limited the use of the J&J vaccine because of a rare but serious risk of blood clots. The J&J vaccine is 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 Authorization for Bebtelovimab Treatment for COVID-19 Infections – The US Food and Drug Administration (FDA) announced that the monoclonal antibody bebtelovimab, used as treatment for mild-to-moderate COVID-19 infections in those at high risk of developing serious disease, has been removed from authorization in the US. The newest data indicate that the combined proportion of COVID cases caused by the omicron BQ.1 and BQ.1.1 subvariants is above 57% nationally and above 50% in all individual regions, except one, and that bebtelovimab is not expected to be able to neutralize these variants.

CDC COVID-19 Treatment Guidelines Panel Raises Concerns About Resistance of New Omicron Variants to Prevention and Treatment Therapies – The Centers for Disease Control and Prevention (CDC) is recognizing the rapid increase in COVID-19 omicron subvariants in the US that are likely to be resistant to Evusheld. The CDC's COVID-19 Treatment Guidelines Panel has provided interim recommendations for the continued use of Evusheld, as well as appropriate treatments for COVID infection, and will closely monitor the prevalence of circulating variants for updates to these recommendations that, at the time of the *Torch* deadline, included the following:

- In the absence of an alternative option for pre-exposure prevention, the Panel continues to recommend the use of Evusheld for eligible individuals. The decision to use Evusheld should also be based on the regional prevalence of the resistant omicron subvariants, the individual patient's risks, and available resources. Individuals who receive Evusheld should continue to take precautions to avoid exposure to COVID-19 and should receive bivalent COVID-19 boosters unless their use is contraindicated.
- The Panel prefers Paxlovid and remdesivir (Veklury), in that order, for the treatment of mild-to-moderate COVID-19 disease in those individuals who are at high risk of developing severe disease. Molnupiravir (Lagevrio) should only be used for the treatment of mild-to-moderate COVID-19 disease in high-risk patients when Paxlovid and remdesivir are not available, not feasible to use, or clinically inappropriate.

Evusheld Approved by Health Canada to Treat COVID-19 Infection – Meanwhile, Evusheld has been approved by Health Canada as a treatment for mild-to-moderate COVID-19 infection in adults and adolescents. It was previously approved as a preventative for COVID in Canada and is authorized only as a preventative in the US. The Canadian approval was based on results from the Phase 3 TACKLE clinical trial, in which Evusheld reduced the relative risk of progressing from mild or moderate to severe COVID infection or death, especially if given within five days of symptom appearance.

The CDC is recognizing the ***rapid increase*** *in COVID-19* ***omicron subvariants*** *in the US that are likely to be* ***resistant to Evusheld****.*

LLS Publishes New Study Analyzing T Cell Responses in COVID-Vaccinated Blood Cancer Patients – The Leukemia & Lymphoma Society (LLS) has published a new study in the journal *Blood Cancer Discovery*, which reports that 45% of blood cancer patients who do not produce detectable antibodies after COVID-19 vaccination may have protection from T cells that target the virus. Antibodies neutralize the virus as soon as it enters the respiratory system, but T cells work later in the process, attacking the virus once it is inside cells and limiting its ability to cause damage. The article also reports on the effect of the third primary Pfizer or Moderna vaccine dose on antibody levels in blood cancer patients. About one in four such patients will not develop antibodies after the first two vaccine doses, but the third dose is helpful, spurring significant antibody levels in 20% of those who lag behind after two doses. These results were not the same across all forms of blood cancer, as those with B cell-derived cancers (including WM) have a reduced ability to make antibodies compared to patients with other blood cancers; however, even in B cell cancer patients, the T cell part of the immune system may still respond to vaccination. For this and previous LLS COVID-19 vaccination studies, information was obtained from the LLS National Patient Registry, a volunteer database of more than 12,000 blood cancer patients.

Preliminary Phase 1 Trial Results Reported for Novel BCL2 Inhibitor Used to Treat Relapsed or Refractory B Cell Cancers – Preliminary results have been reported from a Phase 1 trial of the novel BCL2 inhibitor BGB-11417 as single agent therapy or in combination with zanubrutinib

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(Brukinsa) for the treatment of patients with relapsed or refractory B cell cancers. BGB-11417 was evaluated at different dosing strengths in 58 patients, 32 of whom received it as single agent therapy and 26 of whom received it in combination therapy, with zanubrutinib beginning 8-12 weeks prior to BGB-11417 administration in the second set of patients. Median follow-up was 3.9 months. Two moderate-to-severe adverse events, one of neutropenia (low neutrophil count) and one of autoimmune hemolytic anemia (immune system destruction of red blood cells), occurred in participants on the combination treatment. Twenty patients discontinued treatment, the majority because of disease progression. Two patients with non-Hodgkin's lymphoma had responses to single agent BGB-11417; two patients with chronic lymphocytic leukemia or small lymphocytic lymphoma had responses to single agent BGB-11417, and 12 had responses to the combination. Enrollment is ongoing, and data for WM will be forthcoming. The trial identifier on *www.clinicaltrials.gov* is NCT04277637.

US FDA Committee Advises That Risks Outweigh Benefits with Duvelisib Treatment for CLL and SLL – In concerning news for the entire drug class of PI3K inhibitors, the Oncologic Drugs Advisory Committee of the US Food and Drug Administration (FDA) has advised that the risks associated with taking duvelisib (Copiktra) by patients with chronic lymphocytic leukemia (CLL) or small lymphocytic lymphoma (SLL) appear to outweigh the benefits and noted an increased risk of death after five years of follow-up data from the DUO clinical trial that led to the drug's initial approval for these two cancers. That follow-up data indicated that the median overall survival among patients who received duvelisib was 11 months shorter than for patients who received ofatumumab (Arzerra) in the trial. Toxicities associated with duvelisib included risk of serious or fatal infections, diarrhea, colitis, rash, pneumonitis, liver toxicity, and neutropenia (low neutrophil count). WM patients have been included in clinical trials of several PI3K inhibitors.

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.*

INTERNATIONAL SCENE

EDITED BY ANNETTE ABURDENE

CANADA

History of the Quebec Support Group
By Danielle Gagnon, Montreal Support Group Co-Leader and Caregiver

We first heard of Waldenstrom's when my husband, Robert Perrault, was diagnosed in August 2019. It is always a shock when you hear the word cancer. We started looking on the web for information about the disease and found that the Waldenstrom's Macroglobulinemia Foundation of Canada (WMFC) had support groups in every province, except in Quebec. We did not waste any time and in September 2019 went to the closest support group meeting in Ottawa. We were a bit nervous about what we would find out, but it was very encouraging. The group gave us a warm welcome, and patients were surprisingly healthy looking. We realized that life continues even with cancer. Some support group members were not attending because they were away. One patient was on a trip going scuba diving, one was golfing, and another was kayaking. We said to ourselves that the disease was not so bad after all. We now know that some patients have more difficulties than others.

After a few months, we attended a conference at the Jewish General Hospital in Montreal with Dr. Steven Treon presenting, and we met Betty McPhee of the WMFC. I mentioned to Betty that it was sad that we did not have a support group in Quebec. It was then that the idea of starting one came. Betty introduced me to Paul Cadrin, and with their help we finally had our first meeting in March 2020. We were supposed to meet in person, but because of COVID, our meeting had to be held via Zoom. We are still meeting on Zoom, because it is easier with people living all over the province.

We have meetings every three months in French with a few English-speaking members. During the first two years, we had five to six attendees. It started to grow this year with more and more members, and in our last meeting, we had 14! We realize that it is very helpful to meet and share our difficulties and successes. It is also very helpful to get information about WM and learn about upcoming events.

On a personal note, my husband's first chemo treatment ended in November 2021. He is doing all the things he was doing before his treatment. We have made a few bike and skiing trips as we had always done in the past—pre-pandemic, of course!

UNITED KINGDOM

WMUK at IWWM11 in Madrid
Bob Perry, Patient Support Manager

On 27 October, I was lucky enough to find myself in Madrid, Spain, for the 11th IWWM. As a representative of the UK and Ireland affiliate to the IWMF, I had been offered a place to attend with incredible generosity from Chris Patterson at the Bing Center for WM at the Dana-Farber Cancer Institute in Boston, MA. I was able to go along and take part.

Quite simply, I was blown away by the whole four days. What I witnessed there was the attendance of some of our very top clinicians, scientists, and researchers coming together, either in person or remotely, to talk, discuss, and even debate the future of WM, its treatments, and development of new treatment strategies. The commitment by all of those present to do their absolute best to improve our prognosis and quality of life was simply outstanding.

As a patient, and I have to say, as a "layman" when it comes to the science and medical technology involved in treating WM, I was made to feel so very welcome by everyone I met (and believe me, I "worked" the room!). No question was too dumb, and everyone I spoke to gave me their time willingly.

From the left: Dr. Roger Owen, St. James's University Hospital; Dr. Jahanzaib Khwaja, UCLH; Dr. Shirley D'Sa, UCLH; Amy Christian, Researcher at Bournemouth Hospital; Dr. Suzanne Arulogun, UCLH; Dr. Jindriska Lindsay, Canterbury Hospital; Dr. Helen McCarthy, Bournemouth Hospital; Dr. Jason Mainwaring, Bournemouth Hospital; Dr. Charalampia Kyriakou, UCLH; Bob Perry, WMUK Patient Support Manager

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International Scene, cont. from page 20

Members of the University College London Hospitals (UCLH) team completing their Walk for Waldenstrom's (W4W), helping to raise vital funds for the WMUK Support Line. From the left: Dr. Ali Rismani; Dr. Shirley D'Sa; Nurse Specialist Emma Rowles; Dr. Encarl Uppal; Dr. Jahanzaib Khwaja; Sheena Logan, patient; Janet Boyle, patient; Bob Perry, WMUK Patient Support Manager

Believe me, I made sure I met all the big names from around the world. I was also delighted to meet up with Claudia Bedogni, the IWMF affiliate representative for Italy.

Two big take-home messages for me:

- Clinical trials and their importance in developing future treatments – As patients we need to get on trials wherever possible, if eligible.
- Data collection – It is crucial for us all around the world to push for our data to be submitted and collected; it is this that will make regulatory bodies sit up and listen when we submit new therapies and drugs for approval. We need to support WhiMSICAL (*https://wmozzies.com.au/index.php/whimsical/*) and get our data in, and here in the UK make sure our centres are signed up to the Rory Morrison Registry. (I managed to get myself a ripple of applause for standing up and saying so!)

So, my WM global family, be assured that we have the most incredible clinicians and researchers on our team, and the future of WM treatment is indeed BRIGHT!!

WMUK Report
By Alison McKinney, WMUK Support Line Manager
Luisa Robertson, WMUK Acting Communications Manager

WMUK Support Line

Here at WMUK, we have spent the past year or so working hard to change how we provide support and advice to WM patients, their families, their friends, and to healthcare professionals. We understand that WM is often an under-represented disease within the world of cancer, and what comes with that is the need to push harder for research, education, treatment choices, and overall specialised support. We understand how complex WM can be, not only from the clinical implications, but also from the physical and emotional costs that come alongside too.

Individuals who accessed WMUK let us know that they would like to see a dedicated WMUK support line—a line which they can call to speak with someone who has knowledge of WM and the challenges it brings and to access WM-specific and -relevant advice.

Thanks to the amazing fundraising success of our Walk for Waldenstrom's event and its WMUK team, patients, and supporters, we have been able to recruit a support line nurse; a dedicated support line launched on 21 November. The support line is a confidential service which provides a listening ear, support, and advice for people who are newly diagnosed, have been living with WM, or for those supporting a loved one affected by the disease. It is a service where people can discuss the different options or services which are available to them and consider questions that they may want to ask their consultants. It will be able to point them to other specialist services and provide information for people to make more informed choices about their care.

Before the launch date, the support line nurse took time to reach out and meet with other blood cancer support lines, not only to see how the service can be best utilised, but also to raise awareness, so that if WM patients contact them in the future, they can be directed to the WMUK. We have become a member of the Helplines Partnership, a service that helps to regulate and support UK helplines, to ensure that we are operating to the highest standard and therefore providing a quality and beneficial service. We hope to raise another £25,000 in this year's Walk for Waldenstrom's campaign to continue to fund the support line for another year. We also hope that it will grow and evolve along with us as a charity and that we can expand the offering in the future.

Nurses Study Day

In September we hosted our first Nurses Study Day in London, where we had some of the leading WM consultants

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International Scene, cont. from page 21

WMUK Nurses Study Day

and WM-specific nurse specialists come to talk to nurses from around the country, both in person and virtually. They covered topics from the diagnosis of WM and associated complications, to treatment options, research, and data, but most of all, to patient support. The study day was a huge success, and we are hoping to take it around the country. It has now been turned into an online learning resource, which can be watched by other healthcare professionals and counted toward their mandatory Clinical Professional Development hours. We are hoping that this will help to raise awareness and knowledge of WM within the healthcare setting, so that when patients are diagnosed, they are able to speak to someone who has knowledge of the disease and who can inform them of available support.

Zanubrutinib in the UK

So, what else has changed in WM in the UK? Zanubrutinib is still a hot topic here right now. The National Institute for Health and Care Excellence (NICE) has approved the use of zanubrutinib for second line treatment for some patients, but it depends on what treatment you had first (although there are ways around this, depending on the wording). We published a handy guide to help you ask your consultant about how to access it (please note that this is only applicable in England and Wales). In Scotland, zanubrutinib initially got refused by the Scottish Medicines Consortium (SMC), but this was overturned on appeal earlier this month, which means Scottish WM patients now have two home treatment options.

All these decisions rely not only on medical trials and huge amounts of evidence and data, but they also rely on patient stories and experiences. We're thankful to everyone who participates in these consultations to ensure the patient voice is heard. The main message we heard is how much we need to improve on data and research, and we're working hard to ensure that we play a part in that through Patient Related Outcome Measures (PROMS), the Rory Morrison Registry, and other quality-of-life data.

Patient-Doctor Summit

Now on to the Summit! And wow—what an event it was! This was the first hybrid event we've held at WMUK, and we're really pleased with how it went. We heard from all the greats: Dr. Shirley D'Sa, Dr. Dima El-Sharkawi, the inimitable Bob Perry, and lots, lots more. We heard all about the future of WM and treatment, the COVID landscape, and the current Evusheld debate here in the UK. We heard from Jane Nicholson, CEO, and Charles Lilley on the importance of data and how WM patients can help us to build upon data collection to help future research.

In November, on the grimmest of days in Wales, 34 of us met in a wet and dull car park in the Brecon Beacons. There was a weather warning in existence, so we decided just to try to make the summit and back before the heavy rain set in. Very quickly we were engulfed in clouds with high winds. We pressed on and made the summit—and met 45 mph winds. A quick photoshoot followed, and then we retreated down to the car park. The party consisted of four consultant haematologists, a nurse practitioner, 12 WM patients ranging from 41 to 68 years of age, and 12 friends and family. We raised £12,000, an amazing day's work in very tough conditions!!

Finally, we held our first ever online auction here in the UK. We had some very generous donations, including a day in a pottery studio from a kind WMer, and with the donors' help we raised £1636. A huge thank you to everyone who participated and donated great prizes.

WMUK Patient-Doctor Summit

INDIA

By Saurabh Seroo, India Affiliate Leader

WM India spent the past few months revamping its patient outreach programs and all member-facing touchpoints. This included the WM India logo, WhatsApp, brand guidelines, and technical architecture for our website. This was a large and important project that will help us improve how we reach

International Scene, cont. on page 23

International Scene, cont. from page 22

Hikers braving the elements at Brecon Beacons in Wales to raise money for WMUK

new patients and better support existing ones. When we first started WM India, our immediate goal was to give hope and inspiration to patients who had registered with the IWMF, as well as to communicate to doctors that they could henceforth rely on us to also support their patients, as an affiliate of the IWMF. As we slowly gained trust within the community, we developed our website and created a dedicated messaging account through WhatsApp for patients to reach out to us. This helped us support more patients and caregivers and broaden our presence.

Over time, we reached a local maximum, and saw a ceiling to how many patients we could support. Recruiting members through physical networks at hospitals was cumbersome and often fruitless, as doctors were hesitant to connect us with their patients. They feared that we would refer their patients to other, possibly better, doctors. After plenty of visits (and plenty of time in waiting rooms) to hospitals across India, we realized that it would be much more efficient to reach out to new members directly, through the internet. It was also important to revamp our member-facing touchpoints, including our logo, brand tone, and design guidelines, to communicate a more confident and authoritative message to new members interacting with us for the first time. We also redeveloped the technical architecture on which our website was built to better track website analytics and get more patients to sign up for support.

We hope that this redesigned online presence will set us up for the next five years and help us attract and support even more patients and caregivers across India.

WALDENSTRÖM FINLAND

By Anne Taal

The patient association group of Waldenström Finland meets on Zoom every month to talk about a certain pre-chosen topic, such as our favorite hobbies, movies, or books, and to just chat and update each other on how everyone is doing. Our meetings are very informal and relaxed; normally we have about 10 to 15 people attending. Sometimes someone just drops in quickly only to say "hi" if they are busy elsewhere and cannot stay longer. Occasionally we have also invited a special guest to talk about an interesting topic; for example, we have had a nutritionist give us tips and recommendations for a suitable diet for cancer patients. In addition to our monthly Zoom sessions, we keep in touch via our Facebook page, our internet site, *https://www.wmfin.fi/*, and emails.

Finland's population is just under 5.6 million but our country is large, so Zoom technology has really been a real blessing for us from the start (we were established in 2019). It has allowed us to keep in touch with each other and conduct our monthly get-togethers despite the COVID pandemic. We never have to worry about infecting each other with the flu or any other ailment. In fact, some of us have joined the meetings from our sick beds while being struck down with COVID.

The Cancer Society of Finland has estimated that there are approximately 200 Waldenström patients in Finland. Every year between 10 to 20 new patients get diagnosed. This year alone we have been able to connect with and grow our

International Scene, cont. on page 24

membership by ten new people. Our membership consists of both Waldenström patients and their supporters or carers (usually family-members), and currently we have 40 patients and eight carers in our membership database.

This year we have had the extraordinary luck to have been able to organize not one, but two, actual face-to-face meetings. The first one took place in May in a hotel in Tuusula, where 22 of us were able to put faces to names for the first time and spend half a day together getting to know each other and enjoying lunch. In addition, three of our members, each in a different stage of Waldenström, shared their experiences of diagnosis, treatment, and what being a "Waldie" means in their everyday lives. This was something that especially our newly diagnosed members found valuable and interesting.

Our second in-person meeting was held at the end of November when we had 25 people coming together in a hotel in Helsinki to listen to Dr. Juha Lievonen (from Helsinki University Hospital Hematology Department) give a presentation on what he had just learned at the IWWM11 October conference in Madrid and to answer various questions we had. In addition to this, three of our Waldenström spouses led a discussion on what their experiences have been of sharing a life with someone with Waldenström.

Our Board has been busy too. As a legally registered association, we have plenty of administrative matters that need to be taken care of. The Board has been meeting on Zoom at least once a month to follow up on those topics, to exchange ideas on how to reach newly diagnosed patients, and to determine what more we could do to support our members. Each of our Board members has a specific area of responsibility, ranging from book-keeping to membership management, and so on.

We have had an eventful year, and our membership seems to grow steadily as we connect with more Waldenström patients and their family-members. One way we manage this is through our leaflets that we have distributed with the nursing staff at hematology clinics of the biggest hospitals in Finland. Our motto "Together Ahead" gives us the purpose to try to reach as many as possible—if not every—Waldenström patient in Finland to provide them with peer-support and information on new treatments, as well act as a link to the international network of the IWMF.

Finland WMF brochure

FROM THE FACEBOOK WM SUPPORT GROUP: WINTER 2023

By Betty Ann Morton

As I'm writing this column, we're entering the holiday season. The festival of Diwali is past, and Canadians have already had Thanksgiving. In the US, Thanksgiving is followed by celebrations of Rohatsu, Simbang Gabi, Winter Solstice, Hanukkah, Christmas, and then the New Year. And yet, many WMers do not feel celebratory. Instead, depression is a common reaction to not feeling well or to receiving a cancer diagnosis. Members of the Facebook WM Support Group often discuss mental health concerns.

LD recently posted on the Facebook WM Support Group page, "I am wondering if anyone has experienced deep depression after finishing six rounds of Rituxan and bendamustine. I just finished mine in the middle of July. I am on a three-month waiting period before I go back to my cancer doctor. So I didn't know if chemo can all of a sudden hit me with depression. Or if something else was the culprit? (I'm) trying to ride this out until my appointment."

Many WMers wrote about their own experiences, making suggestions about how to cope. **CR** posted, "There was a period of time where I felt overwhelmed with a couple of health issues. It soon became apparent that I was spending my days crying and fretting about everything. I needed HELP. Without further delay, I communicated with my oncologist AND PCP. Also, I reached out to my church counselor. It was a TEAM! I had great confidence in the care and support with my mental health needs. Please reach out to your TEAM. You DESERVE it! Keeping you in my thoughts and prayers."

SS added, "I wouldn't be surprised if it could impact a person in that way. Like **BM** wrote, 'don't wait to seek help.' Drugs might not be necessary. Are you in a local cancer support group? They can be very helpful. This disease is tough to endure and takes real effort to deal with. Like they say, the only easy day was yesterday." **PS** agreed, "Yes. I got a psychiatrist that specializes in cancer patients!"

CC elaborated, "Being diagnosed with cancer, even if it is an indolent one, is a real blow. Dealing with a 'chronic condition' alters our lives and perception of ourselves. Depression and anxiety are often the results. I think they are a normal reaction to such a blow. At first we concentrate so hard on dealing with the physical issues, treatment, and outcomes that we push all those emotions down, but they resurface. At least, that is what happened with me. I asked for counseling, and it did help a lot. I still work with a fabulous social worker who has given me the tools to deal with those feelings. Most oncology clinics have social workers available. I hope you find the right help. My best!"

KGB summed up that discussion. "Regardless of what is causing it, I'm glad you spoke up. It's hard. Sometimes talking about the fact that that's how you're feeling helps someone else to open up too. You are never alone…there are always people within this group who will listen if you need an ear, offer guidance if you want advice, and offer camaraderie always. Take it one day at a time…breathe. This, too, shall pass."

> ...***depression*** *is a* ***common reaction*** *to not feeling well or to receiving a* ***cancer diagnosis****.*

VH started another conversation about the emotional aspect of WM and treatments. "Hi all. Has anyone been through chemo and been weepy for no apparent reason afterwards? Was there anything you did that alleviated this?" **SS** posted, "This illness and all of the accompanying challenges aren't easy. Are you exercising regularly? I discovered pickleball. It's easy to learn, not physically demanding, and very social." **JW** noted, "Dexamethasone can cause mood changes." **BDB** agreed, "Yes, the steroids can make you moody. I know I'm moody when I cry at those cheesy Hallmark card commercials." **MEL** also shared from personal experience, "I was weepy SO OFTEN before I made real headway in treatment. For me, the anemia and fatigue seem to drain my battery so badly that there isn't enough left to reliably regulate my mood. So relieved to say this has passed!! I hope the same for you."

Yet another conversation about depression began when **BDS** wrote, "Young doctor taking new patients. I'm his first WM patient. Rituxan didn't work. I'm now taking (an oral) medication. Iron infusions brought iron levels in range, (but) fatigue still an issue. My oncologist said I'm probably depressed! He has said silly things before, however, to put that thought in my mind! I do feel better; symptoms (are) tolerable. How did you select (your) first oncologist? Depression? Don't need this on my records if it's not an issue. Confused."

CC responded, "I was lucky. The hematologist I was referred to said, 'No, she should be seen by the expert'—fortunately my hospital has several WM experts. I have to confess that I did feel depressed. The cancer diagnosis

From the Facebook WM Support Group, cont. on page 26

was incredibly traumatic to me. I asked for help in dealing with it, and I was assigned to an excellent social worker."

DS had a different experience. "We can live with this; it is indolent, treatable, and manageable. No depression here. Sure I was bummed out at the beginning, 'why me' and all that but it passed as I learned more about it."

However, **DT** also has felt depressed. "I've been experiencing depression the past several weeks. The combination of my diagnosis six months ago and chronic back pain has combined to make day-to-day life difficult. I have a good support system and am going to talk with a professional this week but wondered if anyone else has gone through this and what has helped them."

*...our **WM friends** have so many **helpful suggestions** for coping while **we heal**.*

CEC observed, "I'm a senior so I rather expect my body to begin breaking down at my age, but it's still very difficult at times keeping upbeat and in a positive mood. It helps if I focus on the little things and feel grateful for what I do have. My pets sure help with that...they bring me immense joy every day. I hope you can find some comfort, too,"

CBM had several suggestions. "I took a meditation class that helps me relax and practice centering prayer. Gentle exercises help increase serotonin. My back hurts too. But I keep walking short amounts daily. You will get better one day at a time!"

SV commented, "The whole experience from the symptoms, being diagnosed, and now on watch-and-wait is traumatic for me, and having chronic pain on top of it, is a 'natural recipe' for depression. My coping tools are yin yoga (helped/helping me so much with (my) pains and quieting my scared mind). You could also look into yoga therapy." [Note: the IWMF offers chair yoga weekly on Zoom.]

MWW contributed additional ideas, "Well, this may sound crazy. I started drawing daily in sketch-type books. I left all the terrible ugly pages. I didn't tell anyone. It's like a vacation…I listen to pod casts or music and just draw."

GW added some new perspectives. "I have had PTSD for years since Vietnam and then this cancer hit me hard with 14 minor and one major operations, but I'm blessed to have a loving wife and two wonderful dogs, a Great Pyrenees and a Swiss Shepherd, oh, and a cat. I find praying for others and reaching out to people in need really helps me to worry less about my own problems. God bless. May we all find the peace and healing we desire."

CC empathized, "I understand what you are going through. I believe that it is a totally normal reaction to this kind of a diagnosis. You are very smart to talk with a professional. I did go for counseling, and it helped me tremendously. I still get depressed at times, as I never expected my old age to be like this."

Reading these comments helps me to be gentler with myself during times when I feel down or even depressed because I know that my feelings are shared and understood by other WMers. They wisely encourage asking for help with mental health, just as with physical health. Moreover, our WM friends have so many helpful suggestions for coping while we heal. May 2023 bring joy to each of you.

Note: WMers and their family members and support people are welcome to join this group. We all need friends. To join the Facebook WM Support Group, go to *https://facebook.com/groups/wmsupportgroup*. In order to join, people must answer two membership questions. 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*.

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/***

2022 STATISTICS FOR SUPPORT GROUPS

Reported attendance this year at support groups: 1,167

Total US support groups this year: 96

6 new support group leaders and 2 new regional contacts added in 2022

2 new wellness programs in 2022: Cardio Flow and Sound Meditation

2 new specialty topic sessions in 2022: Vietnam Vets and LPL Tumor Group

ALASKA RESIDENT BETTY WALTERS DOESN'T LET WM SLOW HER DOWN

By Art Brewer

When Betty Walters was diagnosed with Waldenstrom macroglobulinemia (WM) in 2019, she was determined not to let the disease hinder her. This 79-year-old native New Yorker and current resident of Kodiak, Alaska, maintains a very active lifestyle and is dedicated to making a difference in her close-knit community.

Betty has worn many hats over the course of her career and has been active in education since 1964. After spending seven years teaching in Kodiak High School and three years as a gifted education teacher and assistant principal for Kodiak Middle School, she went on to become the principal at Kodiak Middle School for four years, assistant superintendent in the Kodiak Island Borough School District for five years, and superintendent there for 11 years. Outside of Alaska, Betty taught several subjects and grades in North Carolina, Florida, New York, Pennsylvania and Naples, Italy.

"My paternal aunt was a Catholic nun and a teacher, so I guess I followed in her footsteps by becoming an educator too," Betty said. "I had a great career, and the stars aligned just right for me to make significant advancements."

Betty didn't slow down after retiring in 2007. She has served as a mentor to new teachers in the Alaska Statewide Mentor Project, served on the Alaska State Standards Steering Committee and then stepped into the position of Interim Deputy Commissioner of the Alaska Department of Education and Early Development. Most recently she served as the Interim Director of Kodiak College. She also volunteers at her church, on the local senior center board, and for the Rotary Club.

With such a full schedule, Betty, who had always been healthy and energetic, was surprised when her blood work

Betty Walters, Kodiak

from a routine physical examination in September 2019 came back abnormal. Melissa Witteveen, the physician assistant who examined her (and whose father served as the assistant principal at Kodiak High School when Betty was teaching there), wanted her to undergo additional tests. Dr. Curtis Mortenson, the Medical Director at the Kodiak Community Health Center (whose high school diploma was signed by Betty when she was superintendent), suspected Betty had WM after consulting with his colleague in Anchorage. Based on this consultation, he made an appointment for Betty to have a bone marrow biopsy with Dr. Steven Liu, a hematologist at Alaska Oncology and Hematology in Anchorage. The bone marrow biopsy indicated she had WM, but Betty was relieved she didn't need immediate treatment.

Spotlight on Support Groups, cont. on page 28

A year later, Dr. Liu decided to begin treating Betty with a 420 mg daily oral dose of ibrutinib, a BTK inhibitor that she tolerated very well at first. Unfortunately, after two and a half months, the ibrutinib began to have an adverse effect on her liver, and she had to discontinue taking the drug. Instead, she began chemotherapy treatment with a combination of cyclophosphamide, bortezomib, dexamethasone, and rituximab, as well as drugs like acyclovir and Bactrim DS to counteract the potential side effects of the chemotherapy.

"Here I was taking all sorts of medication when all I had ever taken before was vitamins," Betty said.

Although Anchorage, the nearest city, is 250 air miles away, Betty is fortunate to have a local outpatient infusion department at Providence Kodiak Island Medical Center where many local cancer patients are treated. In years past, cancer patients had to travel to Anchorage or the lower 48 states for extended periods of time. Thankfully, Betty didn't have to do that, although she could have moved to her native New York for treatment and lived with her mother if her mother were still alive.

"Had my mom still been alive and living in Manhattan—she was 100 years old when she passed—I could have easily transitioned to city life without blinking an eye since I visited her every summer, often during the holidays and more often throughout the years as she aged," Betty said.

During the course of her six-month chemotherapy treatment, Betty's primary care physician in Kodiak met with her every week and had a standing conference call every Friday with Dr. Liu to discuss her treatment and progress. Now she is in remission and has resumed her hectic schedule and volunteer work.

Though it all, Betty has maintained a sanguine attitude about her disease. "I was brought up to believe you accept what you get, and I didn't have any of the anger or resentment that you sometimes hear about," she said. "I've enjoyed good health all my life, and I know that can come to a screeching halt, but for now, I'm doing exceptionally well and am very hopeful."

On day one of her diagnosis, Betty learned about the IWMF from Dr. Liu, and she immediately began educating herself about WM through the resources offered by the organization. She also learned about the benefits of WM support groups, but unfortunately the Alaska support group no longer existed at the time she was diagnosed. The former Alaska WM support group leader directed her to the Seattle WM support group, the closest one to her, and she has been a regular participant ever since.

*"A lot of my **positive attitude** and optimism comes from living in **a small community** like Kodiak **where everybody cares**, and I'm grateful for that,"*

Betty also regularly joins the monthly Leukemia & Lymphoma Society support group online meetings that are based in Kenai, Alaska, south of Anchorage. "It's a smaller group than the Seattle WM support group, and the members don't all suffer from the same blood cancers," Betty said. "However, many of them have ties to Dr. Liu."

Betty has lived on Kodiak Island since 1977 when her former husband was transferred there while in the Coast Guard. Kodiak Island, where the city of Kodiak is situated, is the size of the state of Connecticut. Located on the southern coast of Alaska, it is called the "Emerald Isle" because of the lush vegetation that thrives in the abundant rainfall and temperate climate. It is considered a sportsperson's paradise, and people travel there from all over the world to fish, hunt, hike, kayak, mountain climb, and watch Kodiak bears and other wildlife. The area does receive snow and wind, but the climate is mild compared to most places in Alaska.

The small and supportive community of Kodiak has been a great benefit to Betty as she copes with her disease, and she also appreciates the support of her four children and three grandchildren who live away from the city. "A lot of my positive attitude and optimism comes from living in a small community like Kodiak where everybody cares, and I'm grateful for that," she said. "It's a great and wholesome environment that has helped me live a fulfilling life despite the disease."

Spotlight on Support Groups, cont. on page 29

A TRIBUTE TO NEIL MASSOTH, IWMF BOARD MEMBER AND SUPPORT GROUP LEADER

It is with heavy hearts that we announce the passing of Neil Massoth (River Edge, NJ) on October 13, 2022. Neil joined the IWMF Board in 2002 and remained on it until 2004, when he stepped back from that because of work-related commitments. During that time, and for the ensuing 18 years, Neil continued to be active within the IWMF. He and his wife, Joyce, only missed two Ed Forums in 23 years. Joyce also led support group breakout sessions and sometimes helped at the Ed Forum information desk with Sara McKinnie, Laurie Rude, and a few other volunteers.

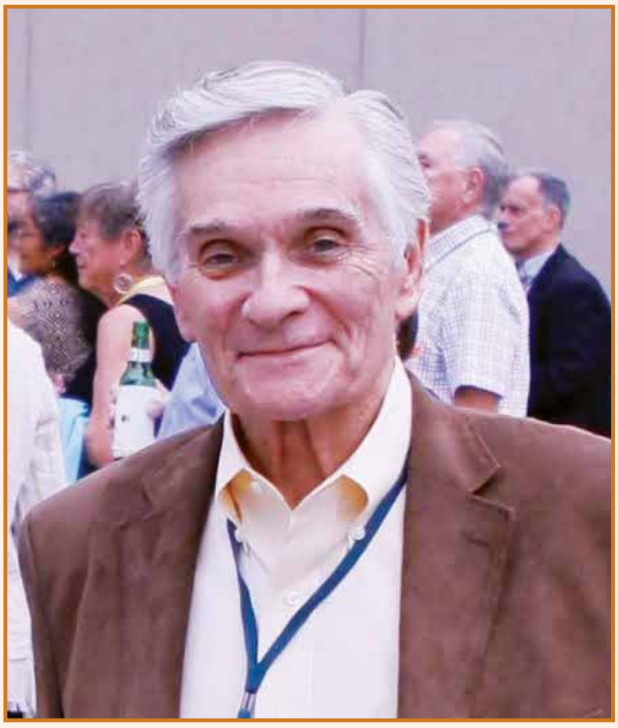
Neil presented breakout sessions on peripheral neuropathy during Ed Forums, and at several, he also moderated a session for long-time WM patients. He recommended establishing the Jack Gelber Memorial Research Fund, which was done in May 2003; renamed the Million Dollar Club to the IWMF Research Fund; and asked that all physicians on the mailing list receive a printed *Torch* and IWMF brochure. He also asked the Board to allocate $5,000 for printing and mailing IWMF materials to oncologists in Florida. With all these activities, it's no wonder Joyce said "We considered the IWMF as part of our extended family."

Neil's involvement in the IWMF helped him with decisions about treatment throughout the years.

That is how he connected with Dr. Steven Treon and later, Dr. Jorge Castillo, at Dana-Farber Cancer Institute. While he was in treatment with his local hematologist, the people at Dana-Farber were able to assist in treatment decisions.

Neil became leader of the NY Support Group after Jack Gelber's leadership and ran it until Mitch Orfuss took on the job. Lloyd Hoffman, a member of Neil's support group, offered his memories of Neil:

With the IWMF providing the phone number, "…a call to Neil in 2006, when I received my WM diagnosis, proved to be my 911 call, my lifeline phone call. Neil received the call with all the warmth and understanding I needed at that moment. He had a wealth of information on Waldenstrom's and gave it a positive twist. Neil would always tell you that it was the best cancer to have, if you had to have cancer. He conducted the support group meetings the same way, always prepared with notes on the latest studies, trials, and drugs. He would teach and listen, always respecting every individual who spoke. With his smile, mellow voice, and positive outlook, he put every newbie at ease. I was in no way unique with that initial call. Neil offered his time and expertise for anyone who desired it. Neil, the gentle warrior, will forever be in my memory and in the memories of all those whose lives he touched."



Neil Massoth

Neil is survived by his wife, Joyce Massoth, his children, Penny Massoth Bechman and Craig Massoth, and his sister, Joan Ann Massoth.

Spotlight on Support Groups, cont. on page 30

Spotlight on Support Groups, cont. from page 29

IWMF VIETNAM VETERANS SUPPORT GROUP ZOOM MEETING

By Don Callahan

The first Zoom meeting of the IWMF Vietnam Veterans Support Group was held on November 30, led by Ray Vance, a fellow Vietnam vet, Tampa Bay Area Support Group leader, and LIFELINE volunteer for military veterans.

Fifteen of us were in attendance, and all of us had varying connections to Vietnam. We had a few sailors, a couple of the gentlemen were connected by commercial involvement in Vietnam, and the majority of us were boots on the ground in Vietnam as soldiers. In fact, at least three of the 15 were stationed at the same small area of Phouc Vinh, Vietnam. We were all three assigned to the First Cavalry Division and performed different duties.

Most all of us were in discussion on this Zoom about the Veterans Administration (VA) and how it has helped us, or, more often, about the problems involved to get the VA to recognize that WM is a non-Hodgkin's lymphoma. It has taken years for a couple of these guys, and only a few months for others, to have their WM recognized by the VA.

The group had various IgM levels up to 7,000 mg/dL, and almost all seem to suffer from peripheral neuropathy and fatigue. What I personally found interesting is that those three mentioned above were stationed in the same place at the same time. Altogether over 19 million gallons of Agent Orange (AO) were sprayed in Vietnam. Our Division made up less than 10% of the total personnel in Vietnam, and, from my research, 6% of the AO was sprayed over our base camp of Phouc Vinh (9,000 gal/sq mile). It seems to me that so much exposure could have a connection to our WM.

The three ribbons at the bottom of the hat are the National Defense Service Medal, Vietnam Service Medal, and the Vietnam Campaign Medal.

It was a great group of vets, and we had some great discussion; we probably could have talked for quite a while longer. We are all looking forward to the next IWMF Vietnam Veterans Support Group Zoom meeting. Thank you, IWMF!

THE BIRTH OF THE WM WELLNESS COMMUNITY

By Ann Grace MacMullan, E-RYT 500,
WM Community Yoga Instructor and Yoga Therapist Candidate

I initially found the IWMF website while researching my father's 2019 diagnosis of Waldenstrom's. "What an incredible resource," I thought, and immediately signed up to receive the newsletter so that I could continue to learn and show my support. Deeply grateful, I also wanted to contribute to the IWMF somehow; in November 2020, I offered to donate my time as a certified yoga teacher, in training to become a yoga therapist.

During my previous six years as a yoga teacher and as a yoga therapist-in-training, I'd been tailoring the tools of yoga for special populations with varying health challenges—making yoga accessible to anyone with the ability to breathe. My Dad's illness became a nut to crack. "How could yoga help him and those affected by Waldenstrom's?", I wondered. Although still in the infancy stage, studies of yoga as a complementary, or integrative, practice are promising, as noted here from Memorial Sloan Kettering Cancer Center:

"Studies show that yoga can help patients with many types of chronic conditions. Cancer survivors report reduced fatigue, better sleep, less stress, and improved strength, mood, and quality of life. Among less active cancer survivors, restorative yoga may be easier and also have benefits. Regular practice also increases benefits. Both the American Society of Clinical Oncology and Society of Integrative Oncology (ASCO and SIO) recommend yoga for anxiety, stress reduction, depression, mood disturbance, and improved quality of life in cancer patients." (See *https://www.mskcc.org/cancer-care/integrative-medicine/therapies/yoga*.)

Spotlight on Support Groups, cont. on page 31

Ann with her Dad, Hugh MacMullan, who receives excellent care from hematologist Dr. Sunita Nasta at Penn Medicine, Philadelphia

What happened over the next two years is beyond anything I could have imagined. Working collaboratively with Michelle Postek, the IWMF's incredible manager of Information and Support, we created "Get Moving in May," four Zoom Chair Yoga classes tailored to those affected by Waldenstrom's. This donated pilot program was well attended by folks from all over the country and the world, and we received a lot of wonderful feedback right away from our survey results, as well as financial contributions to keep the program running.

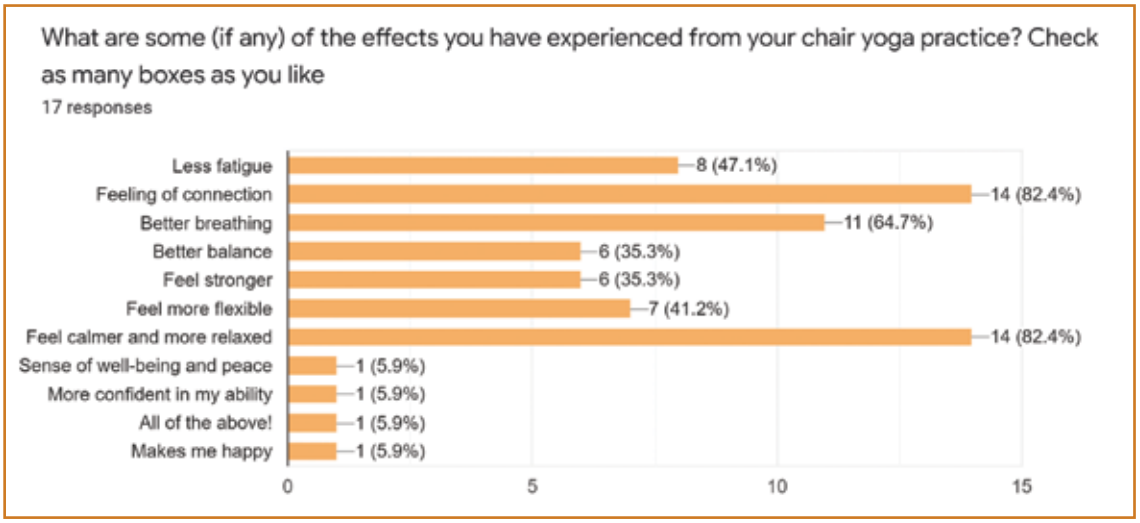
In designing the classes, I wanted to provide a safe space to move, breathe, and connect with each other, while addressing some common side effects, such as fatigue, compromised immune system health, decreased bone mineral density, peripheral neuropathy, balance issues, and stress. In any given class, you'll receive options for varying fatigue and mobility levels as well as personalized cues. You can expect:

- 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
- Meditations like body scans to facilitate mindfulness, acceptance, and relaxation.
- Optional non-recorded community chat afterwards

The word "yoga" translates as "to yoke or join," and this can mean connecting mind, body, and spirit, but it can also mean connecting with each other. One of the most therapeutic aspects of our classes has been the community support chat after we've done our movement practice. Even within the confines of our Zoom gallery view, we are able to hear, see, and feel each other's unique experiences and offer support and advice to one another. I have learned so much from this rich experience, both for my Dad's benefit and for advancing my knowledge as a yoga therapist. I am now in my third and final clinical practicum, sharing the WM special population curriculum and two Waldenstrom's patients as case studies to complete my yoga therapy certification.

Thanks to the requests of such enthusiastic participants, the community offerings are growing! The Cardio Flow class is a medium-paced class designed to get your blood and lymph fluid moving, and the Sound Meditation and Yoga Nidra sessions are more restorative and restful practices that can be done fully reclining, for those times when you might need guided relaxation and a little extra nourishment. For more information on our class schedule and how to join, visit Ann Grace Yoga at *https://anngraceyoga.com/cancer-care/*.

You are welcome, in whatever state of being you are in. If you can breathe, you can do yoga.



Part of the survey results from May 2021's IWMF yoga class pilot offering

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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PENNI WISNER
JAMES P. YEAGER*
RALPH ZUCKERMAN*

* Deceased
◊ Founding Member

RESEARCH PARTNERS

For a commitment of $50,000 per year for a minimum of two years, or a lump sum of $100,000 or more, you can become a research partner supporting a specific IWMF research project approved by the IWMF's Scientific Advisory and Research Committees. Research Partners will have an opportunity to be kept informed of the progress of the research project and will be formally acknowledged by the investigators in their report of the project as well as in any resulting publications. Generally 10 to 12 research projects are underway with new projects under consideration each year. The following funds support current IWMF research:

The David and Janet Bingham Research Fund of the IWMF has supported the following research projects:

- Brad H Nelson PhD & Julie S Nielsen PhD, Deeley Research Centre - *Mutant MYD88: A target for adoptive T cell therapy of WM*
- Aldo M Roccaro MD, PhD, Dana-Farber Cancer Institute - *Further genomic characterization of Waldenstrom's macroglobulinemia: unveiling the role of the CXCR4 somatic mutation, a crucial regulator of pathogenesis and important target for therapy*

The Elting Family Research Fund of the IWMF has supported the following research projects:

- Shahrzad Jalali, PhD, Mayo Clinic - *Modulation of T-cell function by metabolomic signature of the bone marrow microenvironment in Waldenstrom's Macroglobulinemia*
- Larry W Kwak, MD, PhD, Beckman Research Institute of the City of Hope - *Anti-tumor and immune microenvironment responses following a first-in-human DNA fusion vaccine for asymptomatic WM*
- Sherie L. Morrison, PhD, The Regents of the University of California - *Novel antibody-targeted interferons in combinatorial therapies for Waldenstrom's macroglobulinemia*
- Dr. Bruno Paiva & Dr. Jose Angel Martinez Climent, Clinica University of Navarra - *Single-cell next-generation flow and sequencing to unravel the pathogenesis of Waldenström's Macroglobulinemia and to design genetically driven human-like experimental models*
- Dr. Marzia Varettoni, Fondazione Italiana Linfomi Onlus - *Non-invasive diagnostics and monitoring of MRD and clonal evolution in Waldenström's Macroglobulinemia*
- Dr. Gareth Morgan, New York University Grossman School of Medicine - *Using mutographs to define the molecular landscape and cell of origin of Waldenstrom's Macroglobulinemia*

The Lynn M. Fischer Research Fund of the IWMF

The Robert Douglas Hawkins Research Fund of the IWMF

The K. Edward Jacobi Research Fund of the IWMF has supported the following research project:

- Dr. Morie Gertz, Mayo Clinic - *Biology to Treatment: Prognostic factors, Bone Marrow Microenvironment, Genomic and Proteomic Profile of Light Chain Amyloidosis in Waldenström's Macroglobulinemia*

The Michael and Rosealie Larsen Research Fund of the IWMF

The Leukaemia Foundation of Australia has supported the following research projects:

- Zachary Hunter, PhD, Dana-Farber Cancer Institute - *Multiomic analysis of DNA, RNA and epigenomic networks for prognostication and novel target identification in Waldenstrom's Macroglobulinemia*
- Gareth J. Morgan, PhD, New York University Grossman School of Medicine - *Using mutographs to define the molecular landscape and cell of origin of Waldenstrom's Macroglobulinemia*

The Ed and Toni Saboe Research Fund of the IWMF has supported the following research project:

- Larry W Kwak, MD, PhD, Beckman Research Institute of the City of Hope - *Anti-tumor and immune microenvironment responses following a first-in-human DNA fusion vaccine for asymptomatic WM*

The Paul and Ronnie Siegel Family Research Fund of the IWMF

The Carolyn Morris Research Fund of the IWMF

The Poh Family Research Fund of the IWMF has supported the following research project:

- Dr. Signy Chow, Sunnybrook Research Institute - *Characterization of Genomic Alterations in Treatment Naive Patients with Waldenstrom's Macroglobulinemia Through a Course of Targeted Treatment and Disease Progression*

The Ed and Toni Saboe Research Fund of the IWMF has supported the following research project:

- Larry W Kwak, MD, PhD, Beckman Research Institute of the City of Hope - *Anti-tumor and immune microenvironment responses following a first in-human DNA fusion vaccine for asymptomatic WM*

The Robert and Nadeline White Family has supported the following research project:

- Steven Treon, MD, PhD, Dana-Farber Cancer Institute - *Targeting MYD88 in Waldenstrom's Macroglobulinemia*

The Marcia Wierda Research Fund of the IWMF

The WMFC has supported the following research projects:

- Zachary Hunter, PhD, Dana-Farber Cancer Institute - *Multiomic analysis of DNA, RNA and epigenomic networks for prognostication and novel target identification in Waldenstrom's Macroglobulinemia*
- Dr. Signy Chow, Sunnybrook Research Institute - *Characterization of Genomic Alterations in Treatment Naive Patients with Waldenstrom's Macroglobulinemia Through a Course of Targeted Treatment and Disease Progression*

The Yang Family Research Fund of the IWMF has supported the following research projects:

- Steven Treon, MD, PhD, Dana-Farber Cancer Institute - *Targeting MYD88 in Waldenstrom's Macroglobulinemia*
- Zachary Hunter, PhD, Dana-Farber Cancer Institute - *Multiomic analysis of DNA, RNA and epigenomic networks for prognostication and novel target identification in Waldenstrom's Macroglobulinemia*

NAMED GIFT FUNDS

For a commitment of $10,000 per year for five years, or a lump sum of $50,000 or more, you can establish a named fund at the IWMF in your own name or in the name of someone you wish to honor. The following funds support information, education, mission programs, research, or a combination of each:

Baker Family
Research Fund of the IWMF

Yoshiko Button
Mission Support Fund of the IWMF

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Helene Ettelson
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Dr. Robert A. Kyle and
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Rosen Family Foundation

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Research Fund of the IWMF

Donald and Alison Weiss and Family
Research Fund of the IWMF

Donald and Kathryn Wolgemuth
Research Fund of the IWMF

Joseph and Maureen L. Janda
Research Fund of the IWMF

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*.

BETWEEN SEPTEMBER 1, 2022, AND NOVEMBER 30, 2022, THE FOLLOWING CONTRIBUTIONS TO THE INTERNATIONAL WALDENSTROM'S MACROGLOBULINEMIA FOUNDATION WERE MADE IN MEMORY OF:

Monique Baumann
Maya and Hans Meyer

Dr Blythe Kevin Victor Brown
Marina Skulsky

Bruce M. Buyer
Anita Buyer

Milton A. Casey
Danny Casey
Colleen Funk

Jane Dobies
Karen Dobies

Charles Vincent Doherty
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Barbara Swain

Barbara Sykes-Austin
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Timothy and Sidney Hoesch

Ronald Yee
Suzanne L. Herms

International Waldenstrom's Macroglobulinemia Foundation

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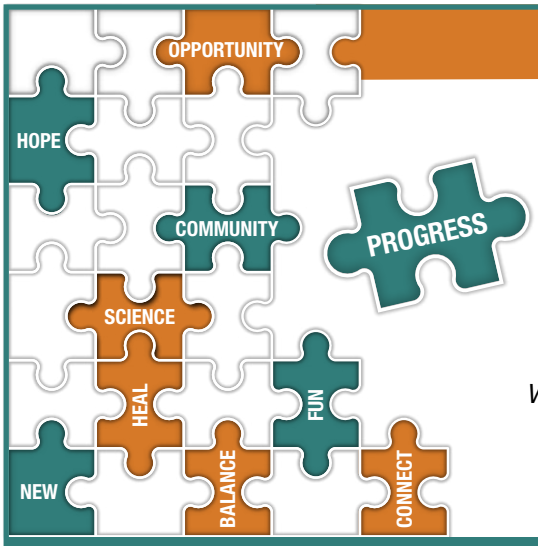

LEARN, GROW, EMPOWER

The 2023 IWMF Educational Forum will be a hybrid event.

APRIL 21-23, 2023

St. Louis Hilton at the Ballpark
St. Louis, Missouri

Whether you join in person or virtually, the Educational Forum is a unique opportunity to learn from medical experts and WM community members from around the world.

REGISTRATION OPENS SOON!

St. Louis, once known for rails and rivers, has a fast-growing downtown, an expanded network of greenways that connect rivers and parks, the National Blues Museum, Cardinals baseball, The King of Beers, and a multitude of vibrant and eclectic shops and restaurants. Points of interest you might consider visiting during your stay are:

- The Arch, known as the symbol of the city, is America's tallest monument. Inside, trams will transport you to the top of the monument for breathtaking vistas of the Midwest. Beneath the Arch, explore the museum with six galleries tracing St. Louis's role in US history. Museum admission is free to all. **Gateway Arch National Park**
- The **Budweiser Brewery Experience** offers tours, a biergarten, and Clydesdales events.
- **Laclede's Landing** is a neighborhood featuring former 18th and 19th century factories and warehouses converted to nightclubs, restaurants and bars set along cobblestone streets on the Mississippi River. **Forest Park,** named best urban park by *USA Today,* is rich in grand architecture, home to nature reserves, history, art museums, one of the best zoos in the country, and outdoor musical theatre.
- **The Hill** is a friendly and walkable district with family-style Italian markets, bakeries, and restaurants.
- The St. Louis Aquarium at Union Station is known for its six galleries that include life in our rivers worldwide and a visit to Shark Canyon. **Come See The Sea!**