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THE STORM IS COMING: T CELL REDIRECTION IN WALDENSTROM MACROGLOBULINEMIA

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Prashant Kapoor, MD, FACP, is a consultant and Associate Professor of Medicine at Mayo Clinic, Rochester, MN. He is also the Chair of the Mayo Clinic Waldenström Macroglobulinemia Working Group. He is a recipient of the American Society of Clinical Oncology (ASCO) Merit Award, Department of Medicine (DOM) Career Development Award, Research Innovation Award, Transplant Center Scholar Award, and the Department of Medicine Faculty Scholar Award. His research is focused on evaluating novel agents in plasma cell disorders.

T cell redirecting therapies have proven to be an asset against many blood cancers. These groundbreaking therapies work by harnessing the power of the patient's own immune system to kill cancer cells. T cells or T lymphocytes are a type of white blood cells, or immune effector cells, that play an essential role in helping the immune system fight bacterial, viral, fungal, and parasitic infections, as well as harmful cells like cancer cells that are constantly looking for ways to outsmart and overpower the host's immune system. One way through which the cancer cells attempt to stay under the radar is by dominating the T cells and compromising their function. As

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such, the cancer cells go unnoticed by the patient's immune system. The weakened T cells are unable to adequately perform immune surveillance and fail to detect or recognize cancer cells as foreigners, leading to their uncontrollable growth. At that point, T cells in fact need assistance to get back into shape to outmaneuver the cancer cells. This is where the T cell redirection therapies come in handy.

Available T cell redirection therapies currently include bispecific antibodies and chimeric antigen receptor T cell therapy (CAR-T) which are approved for use in patients with multiple myeloma and a variety of non-Hodgkin lymphomas (NHL) by regulatory bodies (such as the US Food and Drug Administration). Studies are ongoing to determine their safety and effectiveness in Waldenstrom macroglobulinemia (WM), a type of indolent NHL that still remains incurable in the year 2025.

Unlike monospecific monoclonal antibodies such as rituximab, directed against the CD20 antigen (protein) on WM cells, bispecific antibodies offer unique appeal by binding two different antigens. They have two antigen-binding sites which simultaneously recognize different targets on the desired cells to bring them closer together and create a bridge between the different cell types. (see **Figure 1**). Most available bispecific antibodies target the CD3 antigen on our T cells and a marker more specific to the cancer cells, such as CD19 or CD20 on lymphoma cells or B cell maturation antigen (BCMA) on myeloma cells. As a result of this contact between the cancer (intruder) cell and the T (soldier) cell, the latter wake up, and a battle ensues within the patient's body, leading to cancer cell destruction by the activated T cells. Many chemicals (cytokines) are released during this fight, with some untoward consequences (discussed later) within the battlefield, i.e., the patient's body.

Bispecific antibodies are a more readily available, "off-the-shelf" treatment option than CAR-T therapy. They can be started right away, without any manufacturing-associated delay in their administration, but are often continued until the cancer relapses or an unacceptable side effect occurs, prompting the oncologist to discontinue treatment. Studies are underway to evaluate the value of a finite duration of bispecific antibody-based immunotherapy, thereby limiting any side effects associated with continuous or indefinite therapy. Bispecific antibodies can be given in the veins or under the skin as a shot. Many bispecific antibodies, such as epcoritamab, glofitamab, mosunetuzumab, teclistamab, elranatamab, and talquetamab, are approved for various NHLs or multiple myeloma.

Figure 1. *Bispecific Antibody Mechanism of Action*

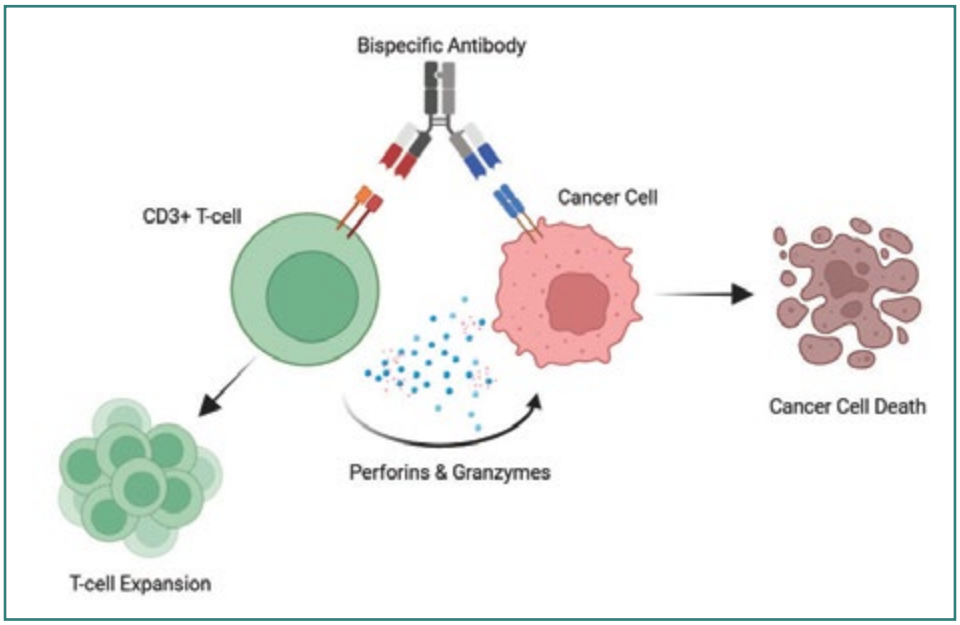

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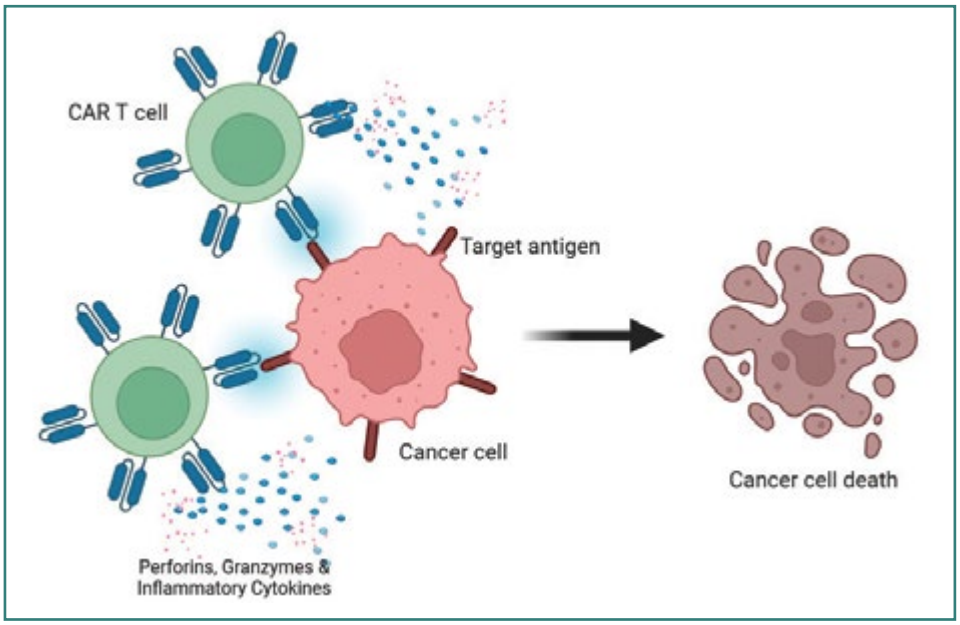
Figure 2. *CAR-T Cell Mechanism of Action*



The CAR-T cell therapy approach typically uses a patient's own T cells, which are then manufactured to recognize specific target(s) on the cancer cells, latch on to them, and eventually kill them. With this approach, T cells are first collected from the patient's blood through a process called apheresis. They are sent to the manufacturer to be genetically engineered to express a special receptor called chimeric antigen receptor (CAR) that enhances the T cells' function and empowers them to find the specific cancer cells that express the desired marker, such as CD19, CD20, BCMA, or another marker on cancer cells (see **Figure 2**). A large number of genetically modified T cells are then returned to the collection site and infused back into the patient where they can further expand and attack the cancer cells. However, in the interim, the patients may require some other form of treatment, termed "bridging therapy" to keep their cancer at bay. Additionally, patients require lymphodepletion chemotherapy before the administration of CAR-T cells to reduce and subdue existing lymphocytes in the patient's body and condition the microenvironment around the cancer cells, thereby enabling it to become more receptive and welcoming of the newly-armed T cells. This approach leads to improved CAR-T cell expansion and persistence, as well as a reduction of the overall cancer load. The longer the CAR-T cells persist in the body, the greater the likelihood of a durable remission.

Toxicities may be more severe up front with CAR-T than those seen with bispecific antibodies; however, it is considered a "one-and-done" approach that can allow for longer treatment-free intervals.

Harnessing the power of the immune system can cause some unique side effects for patients receiving bispecific antibodies or CAR-T, including cytokine release syndrome (CRS) and neurotoxicity. These treatments can also increase the risk of infections by lowering blood cell counts and/or immunoglobulins (antibodies) that help fight infections. Sometimes the blood cell count can remain low for months on end, and patients may require transfusion of blood products such as red blood cells and platelets as supportive care until their blood counts recover to an acceptable level. Moreover, CAR-T cell products also carry a higher risk of treatment-related deaths and are known to increase the risk of second cancers.

Cytokine release syndrome (CRS)

CRS occurs because of rapid immune stimulation. T cells release inflammatory substances called cytokines that are typically in response to a foreign invader, like viruses or bacteria. Because the immune response to cancer cells can be similar to that seen with infection, the side effects can overlap as well and include fever, chills, fatigue, body aches, nausea,

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increased heart rate, and headache (see **Figure 3**). More severe forms of CRS can lead to low blood pressure (hypotension), shortness of breath, organ (for example, liver or kidney) dysfunction, and even death if not managed promptly. CRS is often treated with steroids and interleukin-blocking medications like tocilizumab to reduce the inflammatory response rapidly and calm down the resultant collateral damage on the battlefield. CRS usually occurs early, and to reduce its associated ill effects, bispecific antibody therapy typically uses a step-up dosing strategy during the initial phase of administration. The doses are "stepped-up" or escalated every few days, with close monitoring to ensure that the patients are able to tolerate the side effects and are promptly treated if CRS-related symptoms develop. Once the patients are able to tolerate the full dose without complications, close monitoring (discussed later) is no longer required, and the subsequent doses can then typically be given one to four weeks apart depending on the specific dosing schedule and bispecific antibody used.

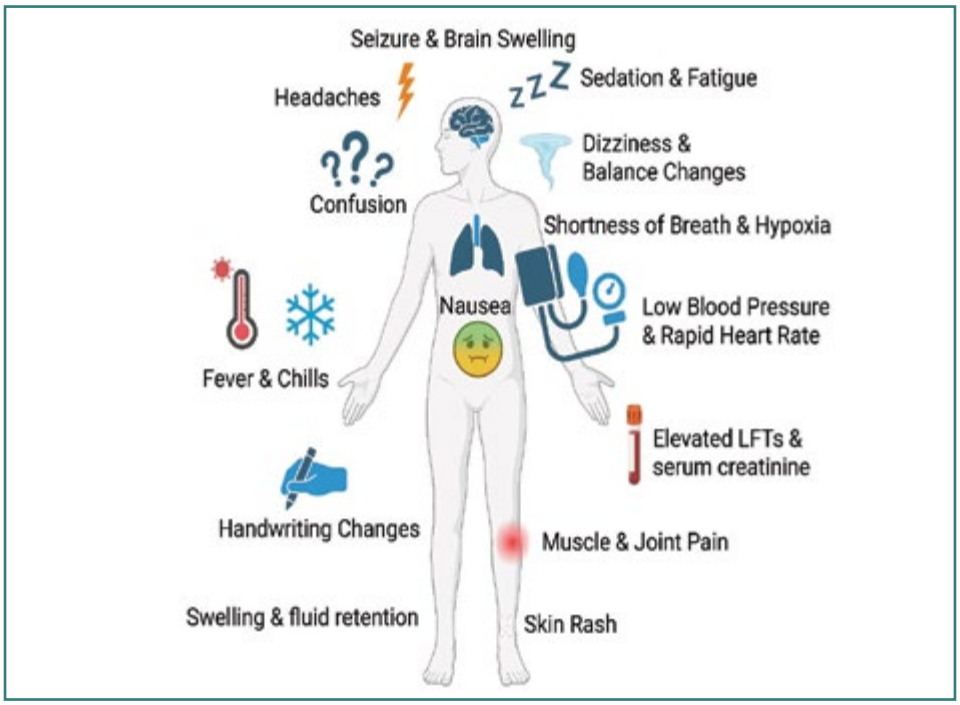
Neurotoxicity

Immune effector cell associated neurotoxicity (ICANS) from bispecific antibodies and CAR-T cell therapy is also a result of the robust immune stimulation that can occur. Although neurotoxicity (damage to the nervous system) occurs in only a subset of patients, symptoms can range from mild to severe. Signs of neurotoxicity can include frequent or severe headaches, excessive confusion, word finding difficulties, altered sense of balance, difficulty in writing or texting, and in more severe cases, even seizures or coma (see **Figure 3**). This type of neurotoxicity is typically reversible and managed with steroids but can be quite distressing, especially to caregivers. Close monitoring is required when ICANS occurs.

Infections

Both bispecific antibodies and CAR-T cell products can lead to cytopenias, or reduced blood cell counts. CAR-T often causes more profound drops in blood cell counts initially because of the impact of lymphodepleting chemotherapy, but the CAR-T cell product itself may also contribute to delayed count recovery. White blood cells play a vital role in protecting the patient's body from infections, and delayed white blood cell count recovery can be quite common following CAR-T therapy and with continuous administration of bispecific antibodies.

Figure 3. *CRS and ICANS Symptoms*



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Antimicrobial prophylaxis is essential to prevent infections in patients receiving both bispecific antibodies and CAR-T cell therapy. Shingles reactivation is reduced with the use of antiviral medications such as acyclovir or valacyclovir. *Pneumocystis* pneumonia, which typically only affects immunocompromised individuals, can be prevented with sulfamethoxazole/trimethoprim, pentamidine, dapsone, or atovaquone. When neutrophil counts are at their lowest, healthcare providers may choose to include additional antimicrobials to prevent bacterial and fungal infections as well.

These drugs can also lead to reduced production of immunoglobulins that help the body identify and fight off infectious organisms. Monthly monitoring of immunoglobulin levels and supplementation with intravenous immunoglobulin G can help prevent recurrent infections or reduce the severity of infections in patients receiving bispecific antibodies and CAR-T cell therapy.

Toxicity monitoring

Because these agents have the potential to cause life threatening toxicities, monitoring protocols and access to rapid escalation of care are essential. Depending on the institution, monitoring may be done in either an inpatient or outpatient setting. CAR-T cell therapy is administered as a one-time infusion of cells and often carries a higher risk of CRS and neurotoxicity, including more severe forms, than bispecific antibodies, which are initiated in a step-up dosing fashion as discussed previously.

Outpatient monitoring during CAR-T or bispecific antibody step-up dosing typically requires the presence of a 24-hour caregiver, vital sign monitoring, and regular check-in with either a nurse or advanced practice provider. Vital sign monitoring often includes blood pressure, oxygen saturation, and temperature monitoring at regular intervals and at additional time points if symptoms are present. Laboratory monitoring often includes blood counts, electrolytes, kidney function, liver function, and inflammatory markers. Providers and caregivers should also remain vigilant for any signs of neurotoxicity during step-up dosing. Patients may be asked to stay within a pre-determined distance, commonly 30-60 minutes, from the treating facility for the duration of step-up dosing, depending on the product-specific dosing schedule and monitoring parameters. Patients are often required to stay in town for the first 30 days following CAR-T cell infusion for monitoring and toxicity management.

Clinical experience with CAR-T cell therapy in patients with WM is rather limited. A case series reported three multiply relapsed WM patients who had received CD19-directed CAR-T therapy via two clinical trials (trial identifiers NCT00466531 and NCT03085173) conducted at Memorial Sloan Kettering Cancer Center. All three patients required bridging therapy to keep their disease under control during the CAR-T cell manufacturing period. Two patients achieved a major response, with one patient attaining a complete response and the other a partial response. The third patient demonstrated stable disease post-therapy. Unfortunately, all three patients eventually relapsed at varying intervals of 3, 7 and 26 months from the time of CAR-T cell infusion. Overall, therapy was deemed safe and no new unexpected side effects unique to WM patients were observed. CRS, although low-grade, was noted in all patients, and one patient experienced treatment-related neurotoxicity.

Although a substudy (NCT05537766) utilizing brexucabtagene autoleucel (a CD19-directed CAR-T) in patients with WM has been terminated early, another one (NCT04892277) targeting this antigen in patients with WM and other lymphomas is ongoing at Mayo Clinic, Rochester. Another trial from Stanford University is recruiting patients with WM to target the CD22 antigen (NCT06340737).

The role of MB-106, a third-generation CD20-targeting CAR-T cell, is currently being examined (NCT03277729) for patients with NHL, including WM. The preliminary data presented at the 12th International Workshop on Waldenstrom's Macroglobulinemia (IWWM-12) were very promising. Among 20 evaluable patients with WM, 95% attained a response, with 80% of patients achieving a complete response. Low-grade CRS was noted in 30% of patients, and no patient exhibited

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ICANS-related symptoms, suggesting a favorable side effect profile. At the time of the data cut-off, WM remained under control in ten (50%) patients. Fatal events (one COVID-19-related and one second cancer-related death) occurred in two patients, who had ongoing complete remission at the time of their deaths.

Data regarding efficacy of bispecific antibodies in WM are still in their infancy. At present, no published results are available regarding their use for WM, except for a case report from Mayo Clinic demonstrating activity of plamotamab, a CD20- and CD3-directed bispecific antibody in a patient with high-risk extramedullary (outside the bone marrow) WM present in the soft tissues of both thighs. The patient's cancer had previously recurred on ibrutinib therapy. With plamotamab given in a clinical trial (NCT02924402), the patient showed evidence of response as suggested by near complete resolution of the extramedullary disease initially. However, cancer progression was evident on the seventh cycle.

A few clinical trials with bispecific antibodies targeting different antigens present on WM cells are either currently underway with anti-CD-20 and anti-CD3 bispecific antibodies, such as odronextamab (NCT02290951) and epcoritamab (NCT06510491), or in development, for example the anti-BCMA bispecific antibody called etentamig, which was previously found to be effective in patients with multiple myeloma and is administered once every four weeks.

Conclusion

It is yet to be determined if bispecific antibodies and CAR-T will eventually become standards of care for all patients with relapsed and/or refractory WM. However, we remain optimistic that encouraging data generated with these new immunotherapies will likely allow them to find their way slowly, but surely, into the treatment algorithm in the near future. While T cell redirection therapies can be incredibly effective, they do not come without risks. Continued focus is necessary on strategies to overcome resistance, optimally sequence these treatments, improve patient safety, and reduce treatment-related costs and the burden of these treatments on quality of life, given the ever-growing role of bispecific antibodies and CAR-T in the care of cancer patients.

ECWM MEETING: ROADMAP TO A CURE

By Carl Harrington, IWMF Trustee and Vice Chair, Fundraising, and Lisa Kaiser

On May 19-21, the European Consortium on Waldenstrom's Macroglobulinemia (ECWM) met for its 10th annual meeting in Chantilly, France, about an hour north of Paris. This meeting included 80 doctors across Europe with a shared goal: to move one step closer to a cure for Waldenström macroglobulinemia (WM).

The overarching "leitmotif" of the meeting, "A Roadmap to Cure," united WM doctors and patients from Europe and the US for the first time in a joint session to advance Waldenstrom's research and to learn from each other. The meeting was organized and run by Professor Christian Buske and Lisa Kaiser from the University of Ulm in Germany and Dr. Pierre Morel and his French team. The event was held in collaboration with the International Waldenstrom's Macroglobulinemia Foundation (IWMF), with Carl Harrington serving as its representative.

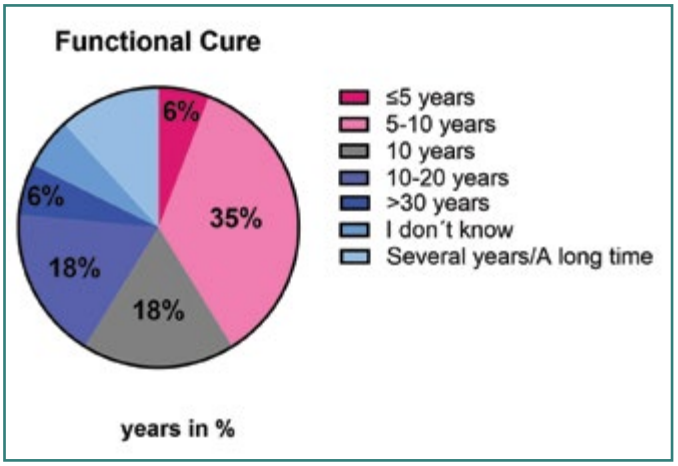
Before the meeting, Lisa Kaiser conducted a survey that asked doctors from ECWM and WM-NET in the US to identify when they thought a cure for WM might be achieved. She asked about two kinds of cure: a functional cure and complete eradication. Here are the definitions:

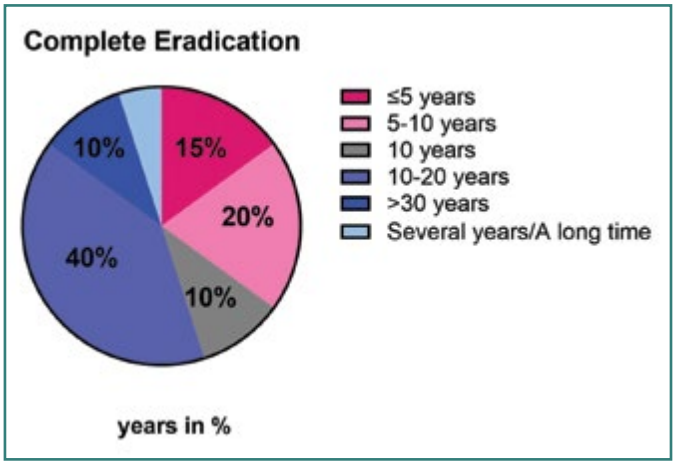
- Functional cure: The patient is in a prolonged remission, but residual disease is detected. The patient dies of reasons unrelated to the disease. The survival must be similar or equal to the survival of a matched individual where age, gender, and co-morbidities (i.e., other diseases or illnesses) are considered.
- Complete eradication: A cure means that the cancer has gone away with treatment, no more treatment is needed, and the cancer is not expected to come back. The survival must be similar or equal to the survival of a matched individual where age, gender, and co-morbidities are considered.

For perspective, Dr. Jan Waldenström first identified WM as a separate disease in 1944, but it wasn't until nearly 60 years later in 2002 at the Second International Workship on Waldenstrom's Macroglobulinemia that the disease was first defined and initial treatment protocols established. Some of you will remember the early days when we had three treatments (bad, worse, and worst, according to Carl Harrington), difficult side effects, and a generally poor quality of life. Now, just 23 years later, over 80 different combinations of treatments are available, life expectancy is 15 to 20 years or more, and deeper, longer remissions with fewer side effects are possible.

Here are the results of the ECWM/WM-NET survey:

- 59% of doctors believed we would achieve a functional cure within ten years, and 77% said we would within 20 years;





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- 45% of doctors believed we would achieve complete eradication within ten years, while 85% said we would within 20 years.

Since WM was defined only 23 years ago, these expectations are astounding.

Prof. Christian Buske welcoming meeting participants

The meeting began on an inspiring note with a visionary talk by Professor Dieter Borchmeyer, who set the tone for the days ahead. In his thoughtful opening, he drew an unexpected yet powerful parallel—inviting us to revisit the world of Thomas Mann's novel *The Magic Mountain*, a literary work offering a glimpse into the era when tuberculosis (TB), then a chronic and often deadly disease, shaped entire lives. A hundred years ago, TB was considered incurable, much like WM is now. Yet today, TB is largely treatable and manageable, thanks to scientific breakthroughs and decades of collaboration.

This reflection served not only as a historical reminder but also as a profound message of hope. Just as tuberculosis moved from despair to cure, so too can the story of WM evolve—with continued research, open dialogue, and a shared vision. It was a powerful way to open a meeting dedicated to charting our "Roadmap to Cure."

In the first keynote, Professor Meletios Dimopoulos from Greece delivered an insightful presentation titled "How to Approach Cure: Lessons from Multiple Myeloma." He shared encouraging data showing that 8% of multiple myeloma patients achieve ultra-long-term progression-free survival, remaining progression-free even 15 years after treatment.

Professor Dimopoulos emphasized key elements that contribute to the possibility of a cure in multiple myeloma:

- Clear definitions of "cure,"
- The central role of minimal residual disease (MRD) negativity, and
- The effectiveness of intensified combination regimens, including triple and quadruple therapies.

These concepts have meaningful implications for WM. For example, the ECWM-2 clinical trial used a triple combination treatment regimen in WM patients, and Professor Buske noted in his presentation of results that it showed excellent disease control—with only one case of progression after a median follow-up of more than 40 months.

A major focus of the discussion was the importance of achieving MRD negativity in WM as a potential pathway to a cure. The panel stressed the need to develop new biomarkers to measure true disease eradication and recommended that biosampling (samples of material such as tissue, blood, saliva, plasma, and purified DNA) become a standard component in prospective clinical trials. Further discussions explored the critical role of achieving complete response (CR) in the pursuit of a cure, as well as the challenges posed by tumor heterogeneity (the differences among cancer cells within the same tumor). Of particular interest was the idea

Prof. Christian Buske, Lisa Marie Kaiser

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Ask the Doctors session - From left: Dr. Eva Kimby (Sweden), Dr. M. J. Kersten (Netherlands), Prof. Christian Buske (Germany), Dr. Troels Hammer (Denmark), Prof. Shirley D'Sa (UK), and Dr. Pierre Morel (France)

of identifying and targeting a WM stem cell or propagating cell, which could open the door to deeper, more durable responses.

ECWM general session

Looking ahead, future treatment strategies in WM are expected to shift toward fixed-duration, chemotherapy-free regimens. A notable example is the ongoing VIWA-1 trial, which compares traditional DRC (dexamethasone, rituximab, cyclophosphamide) to a one-year treatment with venetoclax plus rituximab and which is coordinated by the ECWM and Professor Buske. Exciting developments also include clinical trials exploring bispecific antibodies and BTK degraders—innovative therapies that are being actively pursued within the ECWM consortium.

What stood out most was the atmosphere of deep collaboration during this meeting. Researchers and clinicians exchanged ideas in open, passionate discussions, sharing not only their latest findings but also their hopes, questions, and challenges.

Equally inspiring was the involvement of patients and carers, who were not only present but actively engaged, such as Anna, the daughter of a patient, working together with Lisa Kaiser on the survey presented at the beginning of this article and at the joint session of the ECWM and the 2024 European WM Patient Forum on the last day. This set-up offered patients the opportunity to connect, learn, and ask questions directly. Their voices brought a powerful and personal dimension to the event, reminding everyone why this work matters so deeply.

In a field where every insight counts, the ECWM meeting proved once again that progress is not only about data—it's about people coming together. With continued research, open collaboration, and patient involvement, the path toward a cure for

IWMF Trustee Carl Harrington and Roger Brown

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Waldenstrom's is growing clearer and, with examples of other diseases in mind like TB, also brighter.

So now our job is to support the leading minds in WM as they work toward a cure. In 2024, the IWMF introduced the "Accelerate the Cure" campaign. What can you do to help?

Donate as generously as possible to IWMF and ask those who love you to help too. We will be spending your gifts on what will get us better treatments faster. It's up to each of us: 95% of IWMF funding comes from WM patients and their friends and family. IWMF receives no funding from any government anywhere. We need everyone to pitch in!

Participate in a clinical trial if that it is appropriate for you. All the treatments available today are the result of trials of WM patients who have gone before us. Now it's our turn to pay it forward and help ourselves and future patients accelerate and achieve a cure.

Prof. Meletios Dimopoulos asking a question

ECWM attendees

A SHARED DIAGNOSIS: FORMER SPOUSES FACE WALDENSTROM'S WITH INDIVIDUAL STRENGTHS AND PERSPECTIVES

By Art Brewer

Waldenstrom's macroglobulinemia (WM) is a rare and often unexpected diagnosis. But for Susan Cook and her former husband Aven Crisman, it's a diagnosis they now share despite having divorced over two decades ago.

Susan, 71, lives in Redmond, Oregon, while Aven, 74, lives in Bull Mountain, Oregon. Their only child, Johanna Crisman, is a 33-year-old professional caregiver in Bend, Oregon. When both of her parents were diagnosed with WM, Johanna sought genetic testing to better understand any potential risks. Although the results have been unremarkable so far, she continues to stay informed and vigilant, aware of the unique position she holds as the daughter of two individuals facing the same rare blood cancer.

Two patients, two paths

Aven was diagnosed first, about five years ago following a routine physical, and after undergoing a bone marrow biopsy and PET scan. Though the tests confirmed WM, Aven remains asymptomatic and is not currently receiving treatment. A bone marrow biopsy four years ago showed no issues, and his condition remains stable with no treatment needed. "The doctor said it could be ten years before we need to consider treatment," he said. "Of course, that's just a guess — things can always change." His case is being monitored, and like many patients on the "watch-and-wait" track, he continues regular checkups with his hematologist.

Aven, who is single, lives a remarkably active life. "At 74, I'm still in pretty good shape and able to do just about anything I want to do," he said. A painter by trade, he's currently preparing to paint the exterior of his three-story house by himself. He walks eight to nine miles a day, and aside from a statin he started a couple of years ago at his doctor's insistence, he doesn't take any medication. He considers himself semi-retired and spends about three months a year traveling throughout Asia. He has a home in Taiwan, which serves as a base for visiting nearby countries like China, the Philippines, Vietnam, Thailand, and Malaysia. Aven has only shared his diagnosis with a few close friends and his sister. "I don't want anyone to feel sorry for me," he explained. In fact, he rarely thinks about having WM at all.

While Aven continues his monitoring quietly and without symptoms, Susan has taken a more holistic approach to managing the disease.

Susan's diagnosis came later, in 2023, following an MRI of her left hip. She had already undergone a right hip replacement, and discomfort in her other hip led her to seek imaging. The MRI revealed a lymph abnormality, which prompted further testing. A lymph node biopsy, elevated IgM levels, and abnormal blood counts were all signs pointing to WM.

Unlike Aven, Susan chose not to pursue additional procedures such as bone marrow biopsies or PET scans. Having previously dealt with a breast tumor and growing increasingly cautious of radiation exposure, she decided to forgo additional testing—a decision supported by her hematologist since further imaging would not have changed her treatment plan. She, too, is following a watchful monitoring approach, with lab tests every six months. Her IgM levels have slowly increased from 1,647 mg/dL in September 2023 to 1,830 mg/dL in January 2025.

Medical choices and personal beliefs

While Aven continues his monitoring quietly and without symptoms, Susan has taken a more holistic approach to managing the disease. Living alone, she

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sometimes experiences fatigue, lightheadedness, inflammation, and shortness of breath, but she feels her symptoms are generally under control. She uses acupuncture, laser therapy, diagnostic and therapeutic frequency treatments, and a carefully structured supplement and dietary regimen. She also limits environmental exposures, aware that her immune system may be more vulnerable.

For Susan, the diagnosis adds another layer to a life shaped by caregiving and health challenges. She spent two stressful years caring for her subsequent husband, who suffered from Parkinson's disease and dementia until his passing three years ago. Though she followed expert advice and leaned on private caregivers, Susan believes the intense stress may have contributed to her current diagnosis.

Her health concerns go back even further. While married to Aven, she developed severe sensitivities to chemical smells inside their home that Aven had built. She couldn't tolerate common household products like laundry detergent, deodorant, or dish soap. Eventually, she was diagnosed with chronic fatigue syndrome and environmental syndrome. "I couldn't stand going to the gas station and filling up my car because of the smell of gasoline," she said. Looking back, Susan wonders whether these sensitivities were an early sign of immune system dysfunction and the beginning of her WM.

Though Susan and Aven's doctors have not explored possible environmental triggers behind their dual diagnoses, they can't help but consider the potential connection. Aven has worked with paint his whole life, but he doesn't believe it played a role in developing the disease.

Despite their different approaches, both Susan and Aven remain committed to understanding their condition and staying engaged in their own care. Susan's personal philosophy is one of independence and inquiry. "Don't take what others say at face value," she advises. "Do your own research—whether it's about medicine, politics, lifestyle, or relationships. That applies to almost every area of life. Make sure you know why you believe what you believe. Don't blindly follow the herd."

Aven's advice to others newly diagnosed with WM is simple. "Get a good doctor that you trust and follow the doctor's instructions." For now, he continues to live life fully, embracing each day with energy and gratitude. "I've been blessed for sure," he said.

Looking ahead

Living with WM is a deeply personal experience, shaped by symptoms, values and each patient's approach to care. It is especially striking that two people who once shared a life as husband and wife now also share in a diagnosis of such a rare disease. WM affects only about 1,500 people in the United States each year, making it an extraordinary coincidence that both Susan and Aven, once partners in marriage, would each face the same uncommon health journey—a shared diagnosis navigated in their own ways.

HAVE YOUR SAY

The *Torch* welcomes letters, articles, or suggestions for articles. Please contact *IWMF Torch* editor Shirley Ganse at *shirleyganse@hotmail.com*

Retrospective US Study Looks at Venetoclax Therapy for Relapsed/Refractory WM – A retrospective study from nine US centers reported on the outcomes of venetoclax (Venclexta) therapy in 76 relapsed/refractory WM patients who had been treated with the drug between January 2010 and December 2022. This was a heavily pretreated group of patients, with a median number of three prior lines of therapy. Venetoclax resulted in an overall response rate of 70%, a major response rate (complete + very good partial + partial responses) of 63%, and a median progression-free survival of 28.5 months. Responses to treatment were rapid, with a median time-to-best-response of 3.8 months. A trend was noted toward improved progression-free survival in those receiving 800 mg daily of venetoclax vs. 400 mg daily, but this did not reach statistical significance. There was no difference in overall response or progression-free survival based on CXCR4 mutation status, but patients with TP53 mutations did show an inferior progression-free survival. Prior therapy with a BTK inhibitor had a negative impact on overall response and progression-free survival. Venetoclax dose interruptions and reductions were common (in 40%), with neutropenia (low neutrophil count) likely a significant factor. Tumor lysis syndrome occurred in 7% of patients, despite the use of standard strategies to prevent it. This syndrome, which can be associated with the start of venetoclax therapy, is a group of metabolic abnormalities that occur as large amounts of tumor cells are killed off, releasing their contents into the bloodstream. The study was published in *Blood Cancer Journal*.

Chinese Researchers Publish Interim Results for Phase 2 Trial of ZID as First-Line WM Therapy – An article in the journal *Clinical Cancer Research* discussed interim results from a Phase 2 clinical trial with time-limited oral therapy called ZID, consisting of zanubrutinib (Brukinsa) plus the proteasome inhibitor ixazomib (Ninlaro) and dexamethasone. In this Chinese trial of 27 newly diagnosed and symptomatic WM patients, the dosing protocol was zanubrutinib at 160 mg/twice daily; ixazomib at 4 mg on days 1, 8, and 15; and dexamethasone at 20 mg on days 1, 8, and 15 of each 28-day cycle, for a total of up to 24 cycles. The primary outcome was to assess the depth of response after six cycles, which were completed by 24 of the 27 enrolled patients. The response rates of overall, major, and deep (complete + very good partial responses) were 100%, 95.8%, and 45.8% respectively. Those with a CXCR4 mutation showed a similar rate of deep responses as those without. With a median follow-up of 30.9 months, the estimated progression-free survival was 40 months, and the overall survival was not reached, with no significant differences in survival noted between those with and without CXCR4 mutations. The most common side effects were hematological (low blood cell counts).

...oral BTK degrader NX-5948 (now known as bexobrutideg) has been granted Orphan Drug Designation for the treatment of WM.

BTK Degrader NX-5948 Receives Orphan Drug Designation for WM – Nurix Therapeutics announced that its oral BTK degrader NX-5948 (now known as bexobrutideg) has been granted Orphan Drug Designation for the treatment of WM. In contrast to BTK inhibitors like ibrutinib or zanubrutinib that suppress the BTK protein, BTK degraders like bexobrutideg target the protein for destruction by the cellular "garbage system" called the proteasome. Orphan Drug Designation applies to treatment for rare diseases or conditions and provides financial incentives for further development. Bexobrutideg is in a Phase 1 trial still actively recruiting patients with relapsed or refractory B cell malignancies, including WM, at locations in the US and internationally. Preliminary results on its safety and effectiveness led to the designation. The trial identifier on *www.clinicaltrials.gov* is NCT05131022.

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Poster Analyzes Long-Term Data from LTE1 Study of WM Patients Enrolled from ASPEN Trial – A poster presented during the British Society of Hematology Annual Scientific Meeting provided an analysis of WM patients enrolled in a long-term extension study (LTE1) conducted as a follow-up to the pivotal Phase 3 ASPEN trial of zanubrutinib (Brukinsa). Upon enrollment in the LTE1 study, patients received safety assessments every three months and disease response assessments at least every six months. Between November 2021 and June 2022, 75 of the 129 patients treated with zanubrutinib in the ASPEN trial were enrolled in LTE1. At the time of enrollment in LTEI, their median time on zanubrutinib treatment was 50.6 months. As of April 2024, 69.3% remained on treatment, and their median total time on treatment was 73.5 months. Grade 3 (moderate) or greater adverse events occurred in 29% of patients during LTE1. Except for the number of second malignancies, the prevalence of typical side effects associated with the use of BTK inhibitors decreased over time. Responses remained durable and deepened over time and were observed regardless of CXCR4 and TP53 mutation status. Patients with the MYD88 mutation improved their very good partial response rate from 36.3% in the ASPEN trial to 40.2% during their time in the LTE1 study; patients without the MYD88 mutation (wild-type MYD88) maintained the same very good partial response rate of 30.8% in the LTE1 study as in the ASPEN trial.

...they designated the two subtypes as memory B cell-like (MBC-like) and plasma cell-like (PC-like), based on the cells' expression of several genes.

Real-World Study Assesses BDR in Both Treatment Naïve and Previously Treated WM – A retrospective real-world assessment of bortezomib (Velcade), rituximab, and dexamethasone (BDR) therapy for both treatment naïve and previously treated WM was conducted by French researchers between January 2008 and June 2021 and published in the online journal *eJHaem*. All 87 patients received BDR with an initial intravenous bortezomib dose of 1.3 mg/m^2 twice a week for the first 21-day cycle; 27 patients continued with this bortezomib dose for eight cycles, while 60 switched to an intravenous bortezomib dose of 1.6 mg/m^2 once weekly for four 35-day cycles. Among 84 evaluated patients, the overall response rate was 88%, with 6% achieving a complete response, 24% a very good partial response, 45% a partial response, and 13% a minor response. The median follow-up in this study was seven years, with a median overall survival of 90.7 months; however, those who received BDR therapy as a first- or second-line therapy had a significantly higher overall survival than those who received it as third-line or further therapy. Among patients for whom mutational status was available, neither MYD88 nor CXCR4 mutations affected overall survival. Side effects, particularly neuropathy, remained a major concern, with 23% of patients exhibiting some degree of peripheral neuropathy, including 7% with severe neuropathy who had to discontinue treatment.

IWMF-Sponsored Research Study Describes Two Subtypes of WM – A research study from Perlmutter Cancer Center in New York, partially sponsored by the IWMF and published in the journal *Blood*, described and further defined two distinct disease subtypes found in a series of bone marrow samples from treatment naïve WM patients with the MYD88 mutation. Using multiple single cell analyses and whole genome sequencing, they designated the two subtypes as memory B cell-like (MBC-like) and plasma cell-like (PC-like), based on the cells' expression of several genes. The MBC-like subtype was unable to differentiate beyond the memory B cell stage, upregulated key memory B cell genes, had an increased frequency of CXCR4 mutations, and was characterized by upregulated B cell receptor (BCR) and AKT/mTOR signaling pathways. The PC-like subtype partially differentiated toward a plasma cell, upregulated key plasma cell genes, and had enhanced NF-kappa B signaling. The significance of the subtypes was further revealed from whole genome sequencing, where it was demonstrated that CXCR4, NIK, and ARID1A mutations occurred

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predominantly in the MBC-like subtype, and deletions of chromosome 6q occurred predominantly in the PC-like subtype. Clinically, the MBC-like patients had greater circulating IgM levels, greater splenic enlargement, less lymph node enlargement, and an elevated LDH (lactate dehydrogenase), while the PC-like patients were associated with higher levels of platelets and lymph node enlargement. The researchers concluded that the similarities and differences of these two subtypes provide a model for understanding in more detail the molecular patterns that underlie treatment responses and disease progression in WM.

Few treatment options have been studied for WM patients who are relapsed or refractory to these covalent BTKi's,...

International Study Looks at Depth of Response and Its Impact on Survival Outcomes After First-Line, Fixed Duration WM Treatment – A multicenter international study evaluated the depth of response to first-line, fixed duration treatment and its impact on progression-free survival and overall survival in WM. In this study published in the *American Journal of Hematology*, a total of 440 WM patients from several centers who received one of the following as first-line therapy were included: bendamustine and rituximab (BR); dexamethasone, rituximab, and cyclophosphamide (DRC); or bortezomib, dexamethasone, and rituximab (BDR). Attaining a major response to therapy at six months resulted in an estimated five-year progression-free survival rate of 50% vs. 32% for those who had not achieved a major response at six months. Similarly, the estimated overall survival rate for those who achieved a major response at six months was 89% vs. 70% for those who had not.

Salvage Therapies Assessed for WM Patients Who Discontinue Covalent BTK Inhibitor Therapy – Despite the effectiveness of covalent BTK inhibitors (BTKi's) such as ibrutinib (Imbruvica) and zanubrutinib (Brukinsa), continuous treatment with these drugs is associated with the development of treatment resistance and disease progression, as well as intolerance because of side effects. Few treatment options have been studied for WM patients who are relapsed or refractory to these covalent BTKi's, making this a significant unmet need. A retrospective study by researchers at 22 Italian medical centers assessed outcomes from relapsed or refractory—also called salvage—therapy in these patients. From December 2015 to November 2023, 233 consecutive WM patients treated with covalent BTKi's were analyzed. Of these, 78 (33.5%) discontinued covalent BTKi therapy and received subsequent salvage therapies. The reasons for discontinuation included disease progression (69.2%), side effect intolerance (29.5%), and second cancers (1.3%). Their median time on covalent BTKi treatment was 16.0 months. The overall response rates for various types of salvage therapies in these patients were as follows: 90.0% for alternative covalent BTKi therapy, 75.0% for clinical trial treatment, 66.7% for venetoclax (Venclexta) therapy, 38.7% for chemoimmunotherapy, 37.5% for proteasome inhibitors with rituximab, and 37.5% for non-covalent BTKi therapies such as pirtobrutinib (Jaypirca). Median progression-free survival and overall survival for the entire group of salvage therapy patients were 8.1 months and 21.0 months, respectively. Patients with the MYD88 L265P mutation had significantly better progression-free and overall survival after salvage therapy compared to wild-type (unmutated) MYD88 patients. Patients who received salvage therapy because of side effects from covalent BTKi's demonstrated improved progression-free survival compared to those who received it because of disease progression, but no significant difference was observed in overall survival between these two groups. This study was published in the journal *HemaSphere*.

International Study Discusses Zanubrutinib Therapy for Bing-Neel Syndrome – A letter to the editor in the journal *Lymphoma* reported a retrospective study involving ten international centers that assessed the use of the second-generation BTK inhibitor zanubrutinib (Brukinsa) for treating

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Bing-Neel syndrome, a rare central nervous system complication of WM. BNS is defined as infiltration of the brain and spinal cord by WM cells. Traditionally, the treatment for BNS has been chemotherapy, but recently the first-generation BTK inhibitor ibrutinib (Imbruvica) has become the standard therapy. In this study, 30 BNS patients received zanubrutinib, 12 of whom had been previously treated for the condition. The median follow-up from the start of zanubrutinib was 13 months. Of the 25 patients who had neurological symptoms at the start of therapy, 23 (92%) experienced clinical improvement, with complete resolution of symptoms in 11 (44%). During treatment, 14 patients (47%) experienced a side effect of any severity. The authors concluded that zanubrutinib may be regarded as an effective and safe treatment option for BNS.

The authors concluded that zanubrutinib may be regarded as an effective and safe treatment option for BNS.

Dana-Farber Study Analyzes Zanubrutinib Treatment for Bing-Neel Syndrome - A short report in the journal *Hematological Malignancy* by researchers at Dana-Farber Cancer Institute also discussed the treatment of Bing-Neel syndrome (BNS) with zanubrutinib (Brukinsa). In this study, zanubrutinib was used to treat nine patients with BNS. All patients had the MYD88 L265P mutation, no tested patients had CXCR4 mutations, and three tested patients had a TP53 mutation. The diagnosis of BNS followed their WM diagnosis by a median of 4.3 years. At the time of zanubrutinib treatment, four patients had never been treated for BNS, and five had received prior BNS therapy, including ibrutinib. All nine patients achieved or maintained a partial response from zanubrutinib therapy and had improved neurological symptoms. At the time of this report, no one had progression of their BNS. Zanubrutinib dosing varied in this small group of patients; therefore, the researchers were unable to comment on any difference in effectiveness based on dosing, although they favored maintaining a full dose of 320 mg daily, when possible, to help maximize the concentration of the drug across the blood-brain barrier.

Researchers Discuss Characteristics and Outcomes of WM Patients in India – A retrospective analysis from India, published in the *Indian Journal of Hematology and Blood Transfusion*, discussed the clinical characteristics and treatment outcomes of WM patients from a single medical center in that country. From 2009-2023, 55 patient records at the Postgraduate Institute of Medical Education and Research were available for analysis. The median age at diagnosis of WM was 62 years, with males outnumbering females. The median hemoglobin was 7.4 g/dL, and the median serum IgM level was 4.87 g/L. MYD88 mutation testing was done for 30 patients and was positive in 53.3%, which was notably less than in western countries. The most common first-line therapy was chemoimmunotherapy, typically bendamustine-rituximab or rituximab-cyclophosphamide-dexamethasone. The overall response rate to first-line therapy was 78.2%, time-to-next-treatment was 51 months, and overall survival was 150 months.

WM Patient Characteristics and Outcomes Reported for Taiwan – A group of Taiwanese researchers evaluated the clinical characteristics, treatment types, and survival outcomes of WM patients in their country, with a specific focus on the significance of comorbidities (coexisting medical conditions such as diabetes, high blood pressure, etc.) in these patients. The analysis included data derived from 135 patients from September 2002 to September 2023. At diagnosis, the median age was 66.8 years, and the majority were male. Anemia was the most common indication for treatment, followed by hyperviscosity syndrome. The most prevalent first-line treatment was an oral alkylating agent, such as chlorambucil or cyclophosphamide, combined with steroids and received by 56.7% of patients, while 29.6% received a rituximab-containing regimen such as bendamustine plus rituximab. Bendamustine plus rituximab was the most commonly used second- and third-line therapy. The combined

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overall response rate to any line of treatment was 79.5%, but bendamustine plus rituximab resulted in an overall response rate of 87.5%. In this group, 68.1% of patients had at least one comorbidity, with high blood pressure the most common, followed by chronic kidney disease and peptic ulcer disease. Also, 10.4% had a history of solid cancers. Notably, 12.6% were carriers of hepatitis B, and those who did not receive anti-hepatitis B prophylaxis during their WM therapy experienced reactivation of the virus. The median progression-free survival of the whole group was 5.5 years, and overall survival was 9.2 years. A higher burden of comorbidities was associated with worse survival outcomes. This article was published in the journal *Hematologic Malignancies*.

The author gratefully acknowledges the efforts of Grete Cooper, Peter DeNardis, Dr. Tom Hoffmann, Richard Savoy, and others in communicating news of interest to the WM community. The author can be contacted at suenchas@bellsouth.net *for questions or additional information.*

DID YOU KNOW?

YOU CAN CREATE A FACEBOOK FUNDRAISER FOR IWMF

Celebrate your birthday, anniversary, or other special event while accelerating the search for a WM cure! IWMF has put together a step-by-step guide for setting up a Facebook fundraiser to share with your family, friends, and co-workers. All the donations go to IWMF. You can see the guide on our website at *https://iwmf.com/facebook-fundraiser/*. Or for more information, contact Kellye Jacob, IWMF Development Associate, at 941-927-4963

REFLECTIONS ON THE 2025 IWMF EDUCATIONAL FORUM

By Peter Denardis, IWMF Board Chair Emeritus,
and Sue Herms, IWMF Research Committee Member

Signs announcing the Ed Forum were prominently displayed at the entrance and throughout the lobby area of the Sawgrass Marriott Golf Resort & Spa in Ponte Vedra Beach, FL, to welcome participants to this year's Ed Forum, whose theme was "Turn the Tide on WM."

Thursday is usually dedicated to register attendees and to provide an opportunity for hands-on training and sharing of best practices among support group and global partner leaders, and this year was no different. Following the training session, a reception was held for those support leaders and volunteers in attendance who have been instrumental throughout the past year in helping people with WM around the world.

This year's venue included a popular lobby cocktail bar, staffed by one of the top five mixologists in the state of Florida—and attendees took advantage of the opportunity to sample some drinks and to chat a bit more into the night. Much comfort, support, and laughter were shared each evening.

Day 1 – Friday, May 30, 2025

Each day began at 7:30 with a half hour session on mindful movement with IWMF Wellness Program Coordinator Ann MacMullan and a breakfast buffet with several food options. Paul Kitchen, Chair of the IWMF Board of Trustees, kicked off the event with a heartfelt welcome to attendees. He recognized first-time attendees and those dealing with their new WM diagnosis and provided inspiration by pointing out those who have had WM for over 15, 20, and 25 years (and who are still going strong!).

IWMF Volunteer Appreciation Dinner – Left to right: Chuck Ross, Alyce Pine, Steve Pine, Maria Palmisano, Paula Eastmond

Paul also noted that the global WM community should be on the lookout for news and updates regarding WM-NET (a consortium of US medical centers working together to improve access to clinical trials for WM patients), as well as a new and improved IWMF website.

Dr. Jorge Castillo, Dana-Farber Cancer Institute

The agenda for the day included several general sessions:

- A patient panel sharing their experiences, journeys, and advice for fellow WM patients and caregivers
- A primer on WM by Dr. Morie Gertz of Mayo Clinic in Rochester, MN—his ever-popular and relevant "Garden Talk"
- An explanation of WM complications from Dr. Shayna Sarosiek of Dana-Farber Cancer Institute, Boston, MA

There were also smaller breakout sessions and events, several of them focusing on wellness and social connections:

- A speed networking session for attendees, moderated by WM patients Bob Perry and Sharon Rivet

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Ed Forum general session

- The management of peripheral neuropathy in WM by Dr. Shirley D'Sa of University College London Hospitals NHS Foundation Trust, United Kingdom
- The genetics of WM from Dr. Zachary Hunter of Dana-Farber Cancer Institute
- Integrative oncology by Jacqui Bauers of Joint Joint LLC
- Mindfulness for mental health by Leigh Ann Caulkins of Innova Peterson Life with Cancer Team
- Eating well for WM cooking demonstration from Laura Pole, chef and Director of Smith Center Nourishment Education Programs
- An art therapy workshop by Jacqueline Carmody of Twist Out Cancer
- A leisure walk led by Peter DeNardis, IWMF Board Chair Emeritus
- A sound bath rest session led by Ann MacMullan

The day concluded with the Welcome Reception and Dinner. Patients, care partners, presenters, clinicians, and researchers all sat together for some good food, good company, and support. Paul Kitchen presented the 2025 Judith May Volunteer Award to Sharon Piotrowski (see accompanying article), and the night ended with attendees dancing together to some popular tunes. (Did anyone know that Dr. Shirley D'Sa has some amazing dance moves…not to mention several IWMF staff members, including Donna Cutillo?)

Day 2 – Saturday, May 31, 2025

The sessions began with a formal welcome and recap of the prior day's activities by Paul Kitchen and Peter DeNardis. Pete presented Paul with a ceremonial gavel used for Board meetings—a gavel that has been passed down from Judith May to Carl Harrington to Pete. Pete also provided an update on the WhiMSICAL patient database/registry and encouraged all in attendance to continue to participate and look forward to a new format (and app) that will be available near the end of the year. For more details, go to *https://iwmf.com/participate-in-patient-registries/*.

The day's general sessions included the following:

- Information of how to be a well-informed patient and an advocate for your own care from Dr. Jeffrey Matous of Colorado Blood Cancer Institute, a frequent and popular Ed Forum speaker

Patient panel - Left to right: Gene Batiste, Eileen Sullivan, Jason Euzukonis, Lynn Milliman, Bob Perry, and David Kahn, panel moderator

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- A presentation by Dr. Steven Treon, world-renowned WM expert from Dana-Farber Cancer Institute, who highlighted the exciting research activities being conducted around the world—developments that point toward a cure actually being possible in the near future
- Case studies in WM, moderated by IWMF Board Trustee Meg Mangin and including Dr. D'Sa, Dr. Matous, Dr. Sarosiek, Dr. Rachid Baz of Moffitt Cancer Center in Tampa, FL, and Dr. Jorge Castillo of Dana-Farber Cancer Institute
- Exploring WM-NET and clinical trials by Dr. Castillo and Leah Szumita from The Leukemia & Lymphoma Society

Several breakout sessions were repeats for those unable to attend one on Friday and included networking, integrative oncology, mindfulness for mental health, eating well for WM, and the art therapy workshop. New breakout sessions focused on the following topics:

- Understanding WM test results from Dr. Baz
- Managing the side effects of treatment by Dr. Lia Palomba, Memorial Sloan Kettering Cancer Center, New York, NY
- Wearable devices in WM care by Andrea Preston of Sanius Health and Dr. Shirley D'Sa

After the sessions were over, attendees were free to go out on their own to have dinner. And, of course, several could still be found later in the evening huddled together in the cocktail bar. Old friendships were cemented, and new friendships were forged.

Day 3 – Sunday, June 1, 2025

It should be noted that this day also happened to be National Cancer Survivors Day—and appropriately so! The day began with Paul Kitchen and Dr. Treon introducing recipients of last year's Robert Kyle Career Development Awards for young investigators: Dr. David Cordas dos Santos, Dr. Filip Garbicz, Dr. Tina Bagratuni, and Dr. David F. Moreno. Each awardee presented either an in-person or virtual summary of the research they are conducting, along with some insights into why they chose to focus on WM.

The last session of the Ed Forum was the Ask the Doctors panel, moderated by Dr. Treon and

Twist Out Cancer Art Therapy Workshop

Left to right: Dr. Steven Treon, Dr. Filip Garbicz, Dr. David Cordas dos Santos, all of Dana-Farber Cancer Institute, and IWMF Board Chair Paul Kitchen

Sharon Rivet, IWMF Board Chair Emeritus Peter DeNardis, IWMF Trustee Meg Mangin, and Laurie Rude-Betts

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including Dr. D'Sa, Dr. Castillo, and Dr. Yazeed Sawalha of The Ohio State University. Topics included a wide variety of items from treatments (bendamustine, BTK inhibitors, IVIG, etc.), to how to manage WM symptoms.

Laurie Rude-Betts, a long-time Ed Forum attendee and spouse of former IWMF President Ben Rude, spoke along with IWMF Trustee Carol Gray about the importance of continued financial support for the IWMF and its research platform. They noted that the pursuit of a cure for WM depends almost exclusively upon donations from WM patients and the people who love them. Paul Kitchen provided closing remarks to end the Forum, and attendees gave a standing ovation to the researchers and clinicians who took time out of their busy schedules to talk to and meet with the attendees and to the WM staff members who made the entire weekend an unforgettable experience.

Attending an Ed Forum in person provides the opportunity to learn first-hand the critical aspects of WM diagnosis, treatment, and management, and to meet one-on-one with amazing researchers and clinicians from around the world. But, perhaps more importantly, it provides the opportunity to get a true sense of the humanity and dedication of the medical professionals who devote their lives to helping those affected by WM. Also, on a very personal level, attendees can engage with others on the same WM journey and share experiences and lessons learned.

With the conclusion of a successful 2025 Ed Forum, Paul announced that next year's Ed Forum will be May 1-3, 2026, in Columbus, Ohio! We look forward to seeing you there!

SHARON PIOTROWSKI, 2025 JUDITH MAY VOLUNTEER AWARD WINNER!

The Judith May Volunteer Award was created to recognize the spirit of volunteerism, which IWMF President Emerita Judith May aptly demonstrated throughout her involvement with the Foundation. Our 2025 award recipient has made significant contributions to furthering IWMF's mission and positively impacting the well-being of the IWMF community.

Sharon Piotrowski was diagnosed with WM in July 2019. Sharon was highly symptomatic with a massively enlarged spleen, enlarged abdominal lymph nodes, digestive issues, anemia, fatigue, and loss of weight. Sharon had treatment right away, which helped her recover. She also went to Dana-Farber Cancer Institute (Boston, MA) to get a second opinion. Sharon has relapsed twice (in five years) and finished bendamustine and rituximab in April of 2024.

Sharon is so grateful for IWMF and wants to help in any way she can. She is a LIFELINE volunteer, Co-Leader for the Sarasota Support Group in Florida, and on the Support Group Leader's Committee. Sharon has participated in many pharmaceutical research projects on behalf of IWMF. She has been an ACE-certified personal trainer for almost 17 years and has conducted live workouts as part of the IWMF's Wellness Program. She is 64 years old, has been married for almost 39 years, and has two adult daughters. Sharon is an exercise enthusiast who likes to bike and attends group fitness classes for strength training and cardio.

Thank you, Sharon!

FROM THE FACEBOOK WM SUPPORT GROUP: JULY 2025

By Betty Ann Morton, Editor

Receiving a cancer diagnosis can be frightening and lonely. You may feel isolated in the midst of people who have no idea what Waldenstrom macroglobulinemia (WM) is. As it has for years, the Facebook WM Support Group provides support for WM patients and caregivers around the clock. With over 7,600 group members around the world, there's always someone online to answer questions, encourage, or just listen.

A recent discussion was initiated by **JS** who wrote, "Once a BTK (Bruton's tyrosine kinase) inhibitor (such as Imbruvica or Brukinsa) stops working, what has been the next treatment and was it successful?"

SAP responded, "I went from BTKi to bendamustine and rituximab (Benda-R). Now one year out. I'm not sure how one can answer success, as each person's journey is different."

"Current treatment options for WM patients refractory to covalent BTKi include alkylating agents, nucleoside analogs, anti-CD20 monoclonal antibodies, proteasome inhibitors, BCL-2 inhibitors, and noncovalent Bruton tyrosine kinase (BTK) inhibitors," explained **MCM**. She added, "Nurix is conducting three Phase 1 clinical trials across its protein modulation portfolio: two drug candidates from its protein degradation portfolio are under investigation for the treatment of relapsed/refractory B-cell malignancies, and one drug candidate from its protein elevation portfolio is under investigation for immuno-oncology indications including a range of solid tumor types and lymphoma."

CC endorsed participating in a clinical trial. "Look into a clinical trial for a BTK degrader instead. I was on Brukinsa but could not tolerate side effects. I'm now on the clinical trial with the BTK degrader, and I have had very minimal side effects so far!"

GV shared personal experience, "I was on Brukinsa for three years when it quit working. I switched to Jaypirca. I've been taking it for a little over a year and it's been working great."

CH added another perspective, "It also depends where you live. There are not as many options in the UK as in the US."

Longtime WM patient **ES** wrote, "Given the pace of research these days, I think it's an impossible question to answer if you are talking about the future. Treatments and trials change constantly, and the new trials that are combining targeted therapies to achieve limited duration treatments rather than lifetime treatments are very promising."

Peripheral neuropathy is a perennial concern among the WM Facebook members. Recently **MB** posted, "I was diagnosed in July 2023. I've been on the watch-and-wait protocol ever since with the only symptom I'm aware of being peripheral neuropathy. However, it's getting worse. I've had doctors tell me that's not enough to get treated. There's no super high IgM, (mine has been between 900 and 1,000 mg/dL consistently); there's no viscosity, or high anti-MAG. I have different opinions from several doctors, most telling me to not get treated because it'll be worse with the side effects of chemo. What do you think? Has anybody else experienced the same? Just neuropathy?"

SC responded by describing his own experiences. "I was diagnosed in Feb '23. One symptom I developed was a mild buzzing in my feet. I still have that. I was tested for neuropathy, but that was inconclusive. I started to get more symptomatic in the fall of 2024. I know now that my immune system was failing. Later in the fall a blood test found my neutrophils had disappeared. I have my 5th Benda-R next week. Going into treatment, my IgM was 6,200 mg/dL. A blood test this week showed my IgM has dropped to 1,200. I can't say chemo has been easy, especially the first two. After the first I ended up in hospital with a high fever. They were never able to find the cause of the infection/high temperature. I'm feeling really good these days."

PA wrote, "I was diagnosed in 2024 with the same symptoms—worsening peripheral neuropathy. I have high normal IgM (174 mg/dL last time but it fluctuates a bit), and M-spike of 0.3 g/dL and sky-high MAG antibody (>60,000 consistently). Dr. Castillo recommended treating the WM (not the neuropathy alone) when I hit a Rankin score of 2 or

From the Facebook WM Support Group, cont. on page 24

if the neuropathy started to change very quickly. My neurologist has me at a solid 1 on the Rankin scale right now. I have numbness and tingling, which is slowly progressing through my feet to the heels at the moment, and some balance issues, but they aren't seriously affecting my lifestyle yet. I do need trekking poles when hiking on very rough or steep ground, and I can no longer balance in the dark or with very poor visibility. Both doctors have told me they will treat me when I feel the neuropathy is affecting my lifestyle significantly, not just based on some (somewhat subjective) score or blood work. I hope that helps. It is the toughest ongoing decision I have ever had to make. Right now, the good days outnumber the bad. Best of luck."

HW noted, "Neuropathy can have other causes than WM. A negative anti-MAG test would indicate that. You may need to treat the neuropathy with a neurologist rather than an oncologist."

JL contributed to the discussion, "I presented with anti-MAG neuropathy and was treated with solo 4x Rituxan in 2017 with a good partial response. Five years later I was treated with 8x Rituxan, again with a good response. PN has improved each time, but keeps progressing."

SPD added, "My PN worsened with Benda-R. It went from feeling I had a short sock on to 3" above my knee! And, my IgM is climbing again after just 1.5 years post 6x BR."

FB asked **SPD**, "Have you been told by an oncologist that the worsening symptoms are attributed to treatment or just a natural progression of PN? I'm asking because mine keeps progressing and treatment hasn't helped." **SPD** responded that she needed to discuss that question with her doctor.

SS wrote, "I had low IgM, but increasing neuropathy in my feet and eventually my hands. I was concerned with the trend and had a bone marrow biopsy showing 40% infiltration. I'm getting bendamustine and rituximab. The treatment hasn't made the neuropathy worse and after four sessions it seems to be stabilizing. I'm glad I started because nerve damage is either irreversible or very slow healing, so I didn't want it to go far. I saw a neurologist and ruled out some common causes of PN, but they couldn't say definitively WM was 'the cause.'"

"I'm sorry that you are also dealing with neuropathy," wrote **FB**. "I was diagnosed with WM in December 2022. My IgM at the highest was 2,300 mg/dL. I first heard of neuropathy at the IWMF conference in April 2023. And then I connected the dots after three foot surgeries that had nothing to do with the root cause of the pain. It is critical to work with a neurologist and an expert WM hematologist-oncologist. I live in Canada but go to Dana-Farber Cancer Institute in Boston annually for a second opinion. I am also scheduled to see the neurologist who works with them in a clinical trial for WM patients with neuropathy affecting the myelin. They are doing a clinical trial for such patients—I didn't qualify since mine is axonal but you should look into it.

"My neuropathy has progressed to my knees, and my hands are very much impacted—three fingers in each hand are numb and tingly. It has affected my dexterity and the pain is sometimes unbearable. I am now trying bi-weekly IVIG transfusions as recommended by my WM expert. It's early days with four treatments only, but I believe that it may be working to regenerate damaged nerves. My advice is not to wait to seek expert opinion as your best chances are to stop PN progression or reverse damage in the first two years. All the best to you. You should consider attending the IWMF conference either in person or online. You get a lot of answers by hearing what experts have to say."

By the time this issue of the *Torch* comes out July 1, the 2025 Ed Forum will be over, but recordings of sessions are available at *iwmf.com*. It's not too early to make plans to attend the 2026 Ed Forum: excellent presentations about WM topics from our expert doctors and researchers, conversations with old and new friends, good food, and plenty of relaxation.

If you would like to become more connected with the WM community and join the Facebook WM Support Group, go to *https://www.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 at 941-927-4963 or email to *office@iwmf.com*.

WM INDIA REPORT

By Saurabh Seroo, IWMF Board Member

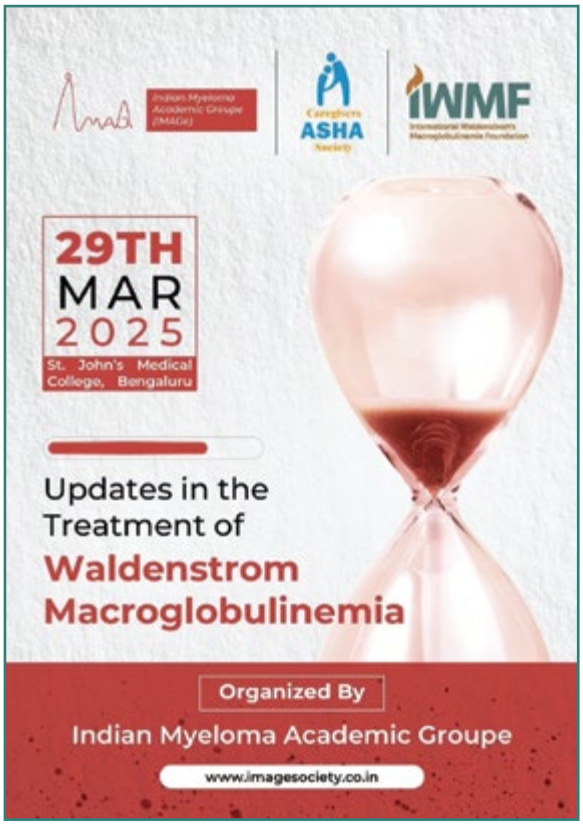
WM India recently achieved a significant milestone by holding its first doctor-patient meeting dedicated specifically to Waldenstrom's macroglobulinemia. The meeting was held in Bangalore, India, on March 29 and saw many top physicians from across the country in attendance.

The agenda of the conference bore similarity to that at the IWMF Ed Forum, with topics ranging from navigating the unique manifestations of WM in each patient to considering various treatment options available today.

Our inaugural event marked an important step forward in enhancing awareness, support, and coordination among WM stakeholders in India. It also laid the groundwork for a clear five-year vision to establish WM India as a central hub around which WM meetings, patient support groups, and advocacy activities can consistently revolve in the country.

A month earlier on February 15, WM India also held its second support group meeting of the year, in Bangalore, India.

IWMF Trustee Saurabh Seroo, Rajini, and Prashanth



WM patients at the doctor-patient meeting

BEING WALDENSTRONG IN ULM, GERMANY

By Juergen R. Goetz

The self-help group Waldenstrong SHG, founded in April 2021 by Uwe Kerscher from Regensburg and three other Waldenström macroglobulinemia (WM) patients, has grown to over 140 members as of this April. There are patients from seven nations, but also relatives, in a communication network supported exclusively by WhatsApp, which enables exchanges of information about the WM with great openness.

The membership of Dr. Michaela Sternke is extremely helpful, as her expertise and experience as a patient enable her to reassuringly clarify many questions that arise during discussions which cannot be answered based on members' experiences.

That alone would be an efficient set-up for many. But by chance, the group came into contact with Prof. Christian Buske from the University of Ulm, an internationally recognized expert in the field of WM. He is a highly respected mentor to our group and is also available for individual consultations.

Ulm, a medieval university town on the Danube in the southern part of Germany, has become an obvious choice for annual meetings. A growing number of members of the Waldenstrong group have been meeting there in person for the past four years, where, in addition to discussions among the members, there are also fascinating presentations. Of course, the presentations always deal with areas related to our disease that were addressed in the WhatsApp group.

This year's meeting took place March 20-22, 2025, and on Friday, the patient day, after a member discussion, lectures were offered on polyneuropathy by Dr. Georgia Schilling, and another on cancer survivorship (living with and after cancer) by Dr. Anke Pregler. In a final lecture and discussion, our mentor Prof. Buske informed us in his usual excellent manner about the latest developments and research results in the field of WM. As in the past, all presentations were made available via video conference to those who were unable to attend.

On two evenings, the participants of the meeting in Ulm had dinner together. On the first evening, Thursday, we welcomed Prof. Buske and his assistant Ms. Lisa Kaiser. This turned out to be very successful, because after dinner there was a discussion in which numerous questions were asked by the participants without a fixed agenda. These were patiently answered by Prof. Buske and Ms. Kaiser in a way that was very easy to understand for lay people.

Saturday morning was dedicated to a visit to the museum, "The Einsteins," which brought us closer to the life of a famous Jewish family from Ulm and, of course, to the great physicist Albert Einstein.

The large number of members in our Waldenstrong group led Uwe to structure the WhatsApp communication thematically by forming subgroups, which proved helpful during the familiarization period and has been generally accepted.

The group is very active and the face-to-face meetings are important and popular. Now that all presentations have been made accessible via video conference, they also remain available to members on the website maintained by Uwe. The motto is: Keep up the good work! It seems certain that further ideas will be developed to keep Waldenstrong appealing and helpful for those affected and their relatives.

ISLAND OF IRELAND WM SUPPORT GROUP MEETING

By IWMF Trustee Bob Perry

The first face-to-face meeting of the Island of Ireland WM Support Group was held March 22 in the Kilmainham Hilton Hotel in Dublin. The meeting consisted of an amazing 45 people comprised of 23 WM patients, 11 family/carers, nine health care professionals (HCP) and two IWMF representatives.

The day consisted of a series of educational presentations from the HCPs about WM, including what it is, how it manifests, its treatment options, side effects, and active surveillance. In addition, we were joined by Professor Shirley D'Sa from London to talk about the future of WM and the innovative treatments that are coming along as we try to "Accelerate the Cure."

The good amount of time during the day over lunch/coffee was just as important for our patients and carers/family members to meet each other and engage with the HCPs. It was so heartwarming to see people meeting another WMer for the FIRST TIME!! There were many friendships and contacts made, and everyone went home full of knowledge and enthusiasm for the ongoing progress of the group. In fact, we now have a WhatsApp group of 22 members.

It should be noted that we had patients, as well as a consultant haematologist and clinical nurse specialists (CNSs) from Belfast, Northern Ireland. We also had a clinical professor and CNSs from Dublin—

Meeting of the Island of Ireland group

testament to the overall feeling on the Island of Ireland that WM has no border.

Many thanks go to Professor Elisabeth Vandenburghe from Dublin for being our Guest of Honour, Dr. Carmel Waldron and her CNS colleagues, Grace Faulkner and Melissa Martin, from Dublin, and Dr. Oonagh Sheehy and her CNS colleague Christine Coyle from Belfast. Also, a massive thanks to Beth Mitchell and Hannah Syed, Consultants, IWMF Global Partner Engagement, for their invaluable help in setting up and running the meeting. I would also personally like to thank Mr. Charles Kyriacou from the UK for his generous donation to assist with the cost of the meeting.

In conclusion, this meeting really emphasized the importance of sharing experiences and knowledge and of forming friendships as we all move forward on our individual WM journeys. I have no doubt this group will grow as word gets out. We hope to meet again in 2027 or sooner, if possible.

From left: Beth Mitchell, IWMF Global Partner Engagement Consultant; Dr. Carmel Waldron, Consultant; CNS Grace Faulkner, St James's Hospital, Dublin; IWMF Trustee Bob Perry; CNS Melissa Martin and Professor Elisabeth Vandenburghe, both of St James's Hospital, Dublin; and Prof. Shirley D'Sa (UCLH, UK)

FITNESS IS KEY TO MANAGING MY WM

By Deborah Kelly

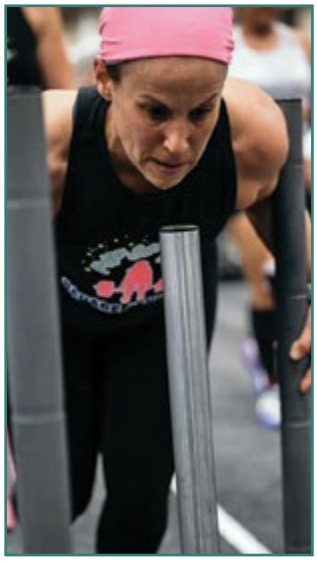
I was diagnosed with WM in September of 2019 at 36 years old, six months after my youngest daughter was born. Upon diagnosis, I was on watch-and-wait status; however, several months later, after contracting RSV from my baby, it became clear I needed treatment. This was right before COVID began, and life was uncertain. My local doctor communicated with the experts at Dana-Farber Cancer Institute and concluded that I needed to start on a BTK inhibitor. I have been taking it since 2020, and I feel fantastic.

I got involved with the IWMF shortly after my diagnosis when seeking support. Initially, I was anxious and struggling to live with my diagnosis. I found the IWMF LIFELINE resource, and I also contacted Ryan Scofield, a member of the Young WM Affinity Group. He was so helpful to me and gave me a lot of comfort. He told me about his life and how he had navigated the anxiety and physical symptoms of WM. In addition to his support, I worked with a life coach to manage my feelings. My father passed away from another B cell lymphoma in 2005, so the anxiety of a cancer diagnosis was terrible. The life coach was exceptionally helpful, and the experience inspired me to become a life coach. I got certified and then returned to the IWMF to volunteer for other young people with WM. I now facilitate the Young WM Affinity Group along with Ryan and Jason Euzukonis.

I am a busy mom, life coach, personal trainer, and group fitness instructor. I have four kids, two of my own and two amazing stepchildren. My family and I live in the Washington DC area, but are originally from Texas. I am very thankful to be able to live my life just the way I want it. My WM does not hold me back at this point, and I am very grateful. I have always been a strong believer in health and wellness and taking care of myself; this diagnosis further solidified my passion for that. I am managing so well as a result of my efforts to be healthy. I exercise five days a week and just finished training for and completing an endurance fitness race called HYROX, the Washington DC race, about 45 minutes from where I live.

A HYROX race is a competitive fitness event that combines running with functional workout stations, designed to test strength, endurance, and overall athleticism in a standardized format. Every race follows the same format, performed eight times: one kilometer (0.62 miles, totaling 4.97 miles) run, followed by one of eight different workout stations: 1. SkiErg – Similar to cross-country skiing using a resistance machine for 1,000 meters, 2. Sled Push – pushing a heavy sled across turf for 50 meters, 3. Sled Pull – using a rope to pull the sled back for 50 meters, 4. Burpee Broad Jumps – jumping forward after each burpee for 80 meters, 5. Rowing on a machine for 1,000 meters, 6. Farmers Carry – walking with heavy weights in each hand for 200 meters, 7. Sandbag Lunges – lunges while carrying a sandbag on your back for 100 meters, and 8. 75 or 100 Wall Balls – squatting and throwing a medicine ball to a target (repetitions vary by division).

Rowing competition



Sled push competition

The race was an intense challenge that I prepared for over a three-month period in a group with a trainer. I loved the challenge and felt very well prepared. I exercise for health, for stress management, for fun, and to challenge myself. I plan to do another HYROX race later this year with one of my sisters and my husband and am already making plans to do another race in Toronto this fall.

I love to travel and recently went on an incredible trip to Costa Rica with my husband for our 10th anniversary. We are adventurous people and take all the chances we get to try new things! In future years, I plan to continue challenging myself with fitness goals, traveling the world, and being an active parent in my kids' lives.

OUR SUPPORT COMMUNITIES ARE A GIFT

By Sharon Rivet, Support Group News Editor

"Sangha" is an ancient Sanskrit word that, according to the Merriam-Webster Dictionary, means "Buddhist religious community or monastic order." Today, it is often described as an association or assembly and is used in yoga to describe a group of students and teachers who practice together.

I have a yoga sangha every week with students I teach, many of whom have practiced with me for over ten years. As I reflect on how many things have changed since I was diagnosed in 2018 with Waldenstrom's, I think about all the new sanghas, or communities, that have come into my life. As an IWMF support group leader for the Eastern Massachusetts Support Group, another sangha, I have community with other group leaders and the IWMF staff who support us. As members, we share our stories, hopes, fears, and overall care for each other. I am also honored to be in the IWMF Yoga Wellness group sangha, practicing yoga together every month.

Recently I found a new sangha, as the Ambassador to the Lymphoma Research Foundation (LRF) representing Waldenstrom's. In February, I was invited to attend an Ambassadors meeting at the new World Trade Center (yes, the view was spectacular!). The participants included LRF staff and Ambassadors representing the many different types of lymphomas. There were presentations discussing a variety of topics, from the Foundation's rebranding to the Early Career Researcher program, research projects in progress, and how Ambassadors can offer support. We learned that, as Ambassadors, we can give support by sharing our personal stories (written articles or videos as a Story of Hope), providing staffing at different events (walk-a-thons, charity events, etc.), and dispensing materials to local hospitals, cancer centers, and doctors. Some long-time Ambassadors speak at legislative hearings in Washington DC, and several of us already participate on a patient advisory council for BeiGene Pharmaceuticals.

The LRF offers a helpline (which sends new callers diagnosed with WM to the IWMF), education programs (Ask the Doctor, Lymphoma Talks), clinical trial and financial information, and different charity events, just to name a few. What resonated with me was their message that the Lymphoma Research Foundation focuses on all types of lymphomas, and, just like IWMF, everything they do begins with scientific research and insights from the world's leading experts.

Yes, we are absolutely blessed with our own IWMF, which supports us in every possible way, and we also have LRF, another sangha, which offers us their support as well. All of these sangha communities share awareness, wisdom, support, understanding, and acceptance. What a gift!

The LRF Ambassadors Meeting, NYC

IWMF'S 2025 SPRING GIVING CHALLENGE

Tra-la-la! IWMF Chair Paul Kitchen and his sidekick, our IWMF Correspondent, are back from their highly successful virtual tour of five WM research labs on three continents. Our "Accelerate the Cure" campaign raised $416,000—a spring record! We are deeply grateful to those 432 international donors who invested in our future dreams to knock this disease flat.

Post tour, on Facebook young patients conversed about being breadwinners and parents of young children. They shared fears about being diagnosed at an early age. One man reached out to his doctor, Dr. Shayna Sarosiek of Dana-Farber Cancer Institute, about a publication's lifespan statistic for WM that scared him.

Here is Dr. Sarosiek's response:

"To study the survival of patients with WM you need to have decades of data. In manuscripts discussing overall survival of patients with WM, you will often notice that they are analyzing data from patients that were treated prior to 2015 (which is when ibrutinib first became FDA approved for WM). If that is the case, then many of the novel therapies that we have available now would not have been used in those patients. Since 2015 and beyond, we have started routinely using more novel therapies, including ibrutinib or zanubrutinib, venetoclax, and pirtobrutinib.

"We have also learned to try to avoid many therapies that have high risk of causing other future health issues (i.e., fludarabine, which can cause secondary cancers). In addition to the new medications that are available, we have many exciting regimens in trials now (combination of pirtobrutinib/venetoclax, combination of chemotherapy/BTK inhibitor, loncastuximab, multiple BTK degraders, sonrotoclax, epcoritamab, etc.) that would not have been utilized in any publication examining survival of patients with WM over the last 20-40 years but will likely be routinely used in the future.

"So, these novel therapies all need to be considered when thinking about the future survival of a young patient with WM now—and hence why our group believes the outlook for young patients with WM is very optimistic."

A big thank you to Dr. Sarosiek. "Accelerate the Cure" campaign funds WM-NET—a clinical trials network of 22 US academic institutions. Dr. Sarosiek leads a WM-NET clinical trial, and she happens to be the medical reviewer of our latest Frequently Asked Questions (FAQ) booklet. Downloadable copies are at *https://iwmf.com/frequently-asked-questions-waldenstrom-macroglobulinemia/.*

A colleague on the "Giving Challenge" global tour, Dr. Judith Trotman of Sydney, Australia, reflected on the medical meaning of the word "cure" for those with WM. It's not too late to hear how her thinking correlates with the words of Dr. Sarosiek. See the video at *https://www.youtube.com/watch?v=1C_zkT_wydY.*

When you invest in the "Accelerate the Cure" campaign, you support IWMF's engagement of these exceptional scientist physician partners. We are grateful to have their wise counsel as we work together toward our common goal.

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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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:

David and Janet Bingham Research Fund of the IWMF

- 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 targets for therapy* 03/01/14 - 02/28/16
- Brad H Nelson PhD & Julie S Nielsen PhD, Deeley Research Centre, *Mutant MYD88: A target for adoptive T cell therapy of WM* 10/01/14 - 09/30/16

Elting Family Research Fund of the IWMF

- Dr. Marzia Varettoni, Fondazione Italiana Linfomi Onlus, *Non-invasive diagnostics and monitoring of MRD and clonal evolution in Waldenstrom's Macroglobulinemia* 10/15/17 - 10/15/19
- 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* 10/15/17 - 10/15/21
- Sherie L Morrison, PhD, The Regents of the University of California, *Novel antibody-targeted interferons in combinational therapies for Waldenstrom's Macroglobulinemia* 10/15/17 - 10/15/20
- Shahrzad Jalali, PhD, Mayo Clinic, *Modulation of T-cell function by metabolomic signature of the bone marrow microenvironment in Waldenstrom's Macroglobulinemia* 09/15/17 - 09/15/19
- Dr. Bruno Paiva & Dr. Jose Angel Martinez, Climent Clinica University of Navarra, *Single-cell next-generation flow and sequencing to unravel the pathogenesis of Waldenstrom's Macroglobulinemia and to design genetically driven human-like experimental models* 09/15/17 - 09/15/19
- 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* 01/01/23 - 12/31/25

Hamberg Family Research Fund of the IWMF

- Jorge Castillo, MD Dana-Farber Cancer Institute, *WM-Net* 09/01/23 – 08/31/2028

Robert Douglas Hawkins Research Fund of the IWMF

The Lynn M. Fischer Research Fund of the IWMF

Michael and Rosalie Larsen Research Fund of the IWMF

Leukaemia Foundation of Australia

- 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* 09/01/20 - 09/01/22
- Gareth J Morgan, PhD, New York University Grossman School of Medicine, *Using mutographs to define the molecular landscape and cell of the origin of Waldenstrom's Macroglobulinemia* 09/30/22 - 09/26/24

K. Edward Jacobi Research Fund of the IWMF

- Dr. Morie Gertz, Mayo Clinic, *Biology to Treatment: Prognostic factors, Bone Marrow Microenvironment, Genomic and Proteomic Profile of Light Chain Amyloidosis in Waldenstrom's Macroglobulinemia* 10/01/17 - 10/01/19

Carolyn K. Morris Research Fund of the IWMF

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- 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* 09/01/22 – 08/31/24

Ed and Toni Saboe Research Fund of the IWMF

- 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* 10/15/17 - 10/15/21

The Paul and Ronnie Siegel Family Research Fund of the IWMF

Waldenstrom's Macroglobulinemia Foundation of Canada

- 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* 09/01/20 - 09/01/22
- 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* 09/30/22 - 09/29/24
- Zachary Hunter, PhD, Dana-Farber Cancer Institute, *Characterization of Isoform Usage, Novel Isoforms, and Tumor Evolution in WM* 07/01/23 - 06/30/25
- Patrizia Mondello, M.D. PhD, Mayo Clinic, *Identifying the oncogenic cooperation between IRF4 and MYD88 L265P and their impact on the Tumor Microenvironment of Waldenstrom Macroglobulinemia* 08/21/23 - 08/20/25

Robert and Nadeline White Family Research Fund of the IWMF

- Steven Treon, MD, PhD, Dana-Farber Cancer Institute, *Targeting MYD88 in Waldenstrom's Macroglobulinemia* 09/01/18 - 08/31/20

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- Steven Treon, MD, PhD, Dana-Farber Cancer Institute, *Targeting MYD88 in Waldenstrom's Macroglobulinemia* 09/1/18 - 08/31/20
- 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* 09/01/20 - 09/01/22

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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:

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