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INSIDE THIS ISSUE

TP53 IN WALDENSTROM MACROGLOBULINEMIA: WHAT IT MEANS FOR YOU

By Jithma Abeykoon, MD, and Thomas E. Witzig, MD

Dr. Jithma Abeykoon

Dr. Jithma Abeykoon is an Assistant Professor in the Division of Hematology, Department of Internal Medicine, Mayo Clinic College of Medicine and Science, MN. His research encompasses basic, translational, and clinical studies in non-Hodgkin lymphoma, including Waldenstrom macroglobulinemia (WM). Dr. Abeykoon is a recipient of the 2023 Robert A. Kyle Career Development Award from IWMF. He has a particular interest in investigating TP53 alterations in WM and leveraging these insights for therapeutic development.

Dr. Thomas E. Witzig

Dr. Thomas Witzig has been on the staff at Mayo Clinic since 1986. His clinical and research interests focus on blood cancers, especially non-Hodgkin and Hodgkin lymphoma. His current focus is on agents that interfere with the DNA damage repair pathways and understanding the role of maladaptive inflammation in lymphoproliferative diseases. He has been a leader in the development of radioimmunotherapy, mTOR inhibitors, and immunomodulatory drugs such as lenalidomide. Dr. Witzig has been honored with several awards during his career, including the Department of Medicine Outstanding Investigator, the Henry S. Plummer Distinguished Physician, and, most recently, the Barbara Woodward Lips Professor 1.

Case presentation

A 65-year-old male presented with a two-week history of progressive blurred vision, headaches, fatigue, mild night sweats, and unintentional weight loss over the past month. Physical examination revealed swelling of the veins in the back of the eye consistent with blood that was too thick (hyperviscosity syndrome), pale skin, and swollen lymph glands. Laboratory tests showed anemia with a hemoglobin of 8.5 g/dL and elevated serum viscosity due to an increase in immunoglobulin M (IgM) to over 5,000 mg/dL. Serum calcium and kidney function were normal. Bone marrow biopsy demonstrated 55% infiltration by small lymphoplasmacytic cells producing the IgM protein. Analysis of the genes in these cells revealed a *MYD88*^{L265P} mutation, while the *CXCR4* gene was normal

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(referred to as wild-type *CXCR4*). This confirmed the diagnosis of Waldenstrom macroglobulinemia (WM). Because of his hyperviscosity symptoms, urgent treatment was initiated to rapidly lower the IgM protein levels and improve visual and neurological symptoms. This treatment, called plasma exchange, involves removing abnormal proteins using a machine and replacing them with healthy donor plasma, quickly reducing blood viscosity.

Following stabilization, he was started on first-line therapy with bendamustine plus rituximab (BR regimen), which targets the abnormal cells (cancer cells) that are making the protein. The patient responded promptly, with symptoms resolved following plasma exchange, and subsequent disease control was achieved with BR.

After achieving a complete response initially, the patient experienced a relapse three years later. He now presents with worsening anemia (hemoglobin 7 g/dL), thrombocytopenia (low number of platelets at 65,000/μL), and significant fatigue. Bone marrow biopsy reveals extensive involvement with lymphoplasmacytic lymphoma, accounting for approximately 60% of marrow cellularity. Next-generation sequencing (NGS or genetic sequencing of the DNA of the cancer cells) confirms the persistent *MYD88*^{L265P} mutation and wild-type *CXCR4*, but also a new *TP53* alteration, indicating a more aggressive disease. To treat this relapse with a *TP53* mutation, current management involves starting zanubrutinib (Brukinsa), an oral BTK inhibitor aimed at targeting his mutated pathways.

After three months of treatment with zanubrutinib, he achieved a very good partial response, with normalization of IgM levels and only a very small detectable abnormal IgM in the blood, and is now feeling back to his normal self. However, he now asks three important questions about the significance of the new *TP53* mutation.

1. **What is the meaning of the *TP53* mutation found when my cancer came back?**
2. **Why was the *TP53* mutation not detected when my WM was initially diagnosed?**
3. **Do I have an increased chance of another relapse compared to patients without the *TP53* mutation?**

The presence of a *TP53* mutation at relapse suggests that the patient's disease has become more aggressive and may be more resistant to traditional therapy like BR. The *TP53* gene is a tumor suppressor gene, and its mutation is associated with poorer prognosis and higher relapse risk in WM. This mutation was not detected at his initial diagnosis three years ago, most likely because it was not there or was at a very low level for the techniques used at that time. This mutation is often acquired as the cancer cells that (in this case) survived BR recur in the marrow. Finally, he wondered if having this mutation increases his chance of disease relapse compared to patients without it. The answer is yes—*TP53* mutations are considered high-risk mutations and are linked to a higher likelihood of relapse and a more challenging disease course, which means that close monitoring and potentially different management strategies are important for his ongoing care. However, the BTK inhibitors, such as zanubrutinib, and other non-chemotherapy approaches, can work relatively well in WM with *TP53* mutations, and thus, there is hope for a long response.

Let's delve a little deeper…

What is a gene mutation or gene alteration in WM?

Genes are like instruction books inside your cells, telling the cells what to manufacture. Sometimes, these instructions can change or get "altered." When this happens, it's called a mutation. Mutations can make the cell underperform or overperform—either way, they can harm the body.

Certain genes, like *MYD88* or *CXCR4*, mutate in WM, making the cancer cells grow or behave differently. These mutations can be important because they help the cancer develop and influence how the disease progresses and how well treatments work.

Think of it like a typo in a recipe that changes the finished dish. In this case, a change in the

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gene "recipe" causes the production of abnormal proteins—the finished dish—leading to abnormal cell growth in the bone marrow, contributing to WM.

MYD88 mutation

The *MYD88* mutation, particularly the L265P variant, is the most common genetic alteration in WM, detected in over 90% of patients. This mutation turns on signaling pathways that promote the survival of the malignant cells and causes them to grow. Thus, the *MYD88* mutation is "activating." Identifying the *MYD88* mutation is a valuable diagnostic marker with implications for treatment selection. For example, BTK inhibitors like zanubrutinib are likely to be more effective in WM with the *MYD88* mutation compared to unmutated *MYD88*, while the efficacy of chemoimmunotherapy regimens like BR does not appear to depend upon *MYD88* mutation status.

CXCR4 mutations

CXCR4 mutations, present in about 30-40% of WM patients, often occur alongside the *MYD88* mutation. These mutations can drive the disease by enabling the cancer cells to better interact with their surrounding environment, aiding their survival and growth. *CXCR4* mutations are associated with more aggressive disease features and can affect the response to certain treatments. Targeted therapies aimed at inhibiting the *CXCR4* pathway are being explored to reduce the aggressive nature of the disease in patients harboring these mutations.

TP53: the guardian of the genome

The short arm of chromosome 17 has a gene called *TP53* that makes a protein known as p53. This protein helps prevent cancer. Healthy cells have two copies of this gene, and usually, having at least one working copy produces enough p53 protein to keep your cells working properly and healthy.

In WM, *TP53* mutations can occur, affecting the resulting protein p53. Sometimes one copy of chromosome 17 is lost (called monoallelic 17p loss or deletion 17p). Other times, both copies of the gene are damaged or turned off, leaving little to no functional p53. This loss or mutation of *TP53* can make it harder for the body to prevent normal cells from becoming cancer cells and stopping their growth. *TP53* changes can also occur together with mutations in *CXCR4*. Most evidence suggests that these *TP53* alterations are rare in patients who haven't been treated yet, but when present, they are linked to a higher cancer burden and a more aggressive form of the disease.

Because *TP53* is a tumor suppressor gene, it is often called the "guardian of the genome." It plays a crucial role in ensuring the cell has preserved integrity in all its instructions (DNA) before the cell gives birth to a daughter cell. The *TP53* protein does this by regulating DNA repair and the proteins that control cell growth and cell death (see left side of **Figure 1,** next page). For example, *TP53* watches as the cell tries to duplicate itself and divide. If a mistake is made, *TP53* will stop the process and not let it proceed, thus preventing a poor product that might develop into a tumor. However, if the *TP53* gene mutates, the resulting protein may be misfolded, leading to dysfunction, or it may be absent altogether, allowing unchecked cellular proliferation—a hallmark of cancer (see right side of Figure 1). In WM, changes (mutations or deletions) in the *TP53* gene are relatively uncommon as compared to $MYD88^{L265P}$ mutations, but when they do occur, they are important for several reasons.

TP53 alterations are not specific to WM but, when found, can help identify patients with a more aggressive form of the disease right at the start. These changes are usually detected through specialized genetic tests performed on bone marrow samples, often as part of a broader panel that looks for other mutations in the *MYD88* and *CXCR4* genes, which are more common in WM.

Understanding *TP53* alterations

The prevalence of *TP53* gene alterations in WM at diagnosis ranges from approximately 7% to 15%, depending on the patient group being studied and the definition of alteration (mutation, deletion, or other abnormalities). Specifically, studies using next-generation sequencing and chromosome analyses have reported *TP53* mutations in about 7–10% of patients at diagnosis, while broader definitions, including deletions and other abnormalities, can reach up to 15% of cases. Moreover, similar to

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our case study patient above, some studies have identified that *TP53* alterations increase in frequency in patients after the first line of treatment; thus, the frequency is about 15-25% in relapsed WM patients compared to 5-15% in newly diagnosed WM.

The presence of *TP53* mutations typically correlates with a more aggressive disease, underscoring the importance of early genetic testing in managing the disease. One study found that patients with *TP53* alterations tend to have the disease come back more frequently (42%) compared to patients without *TP53* alterations (20%).

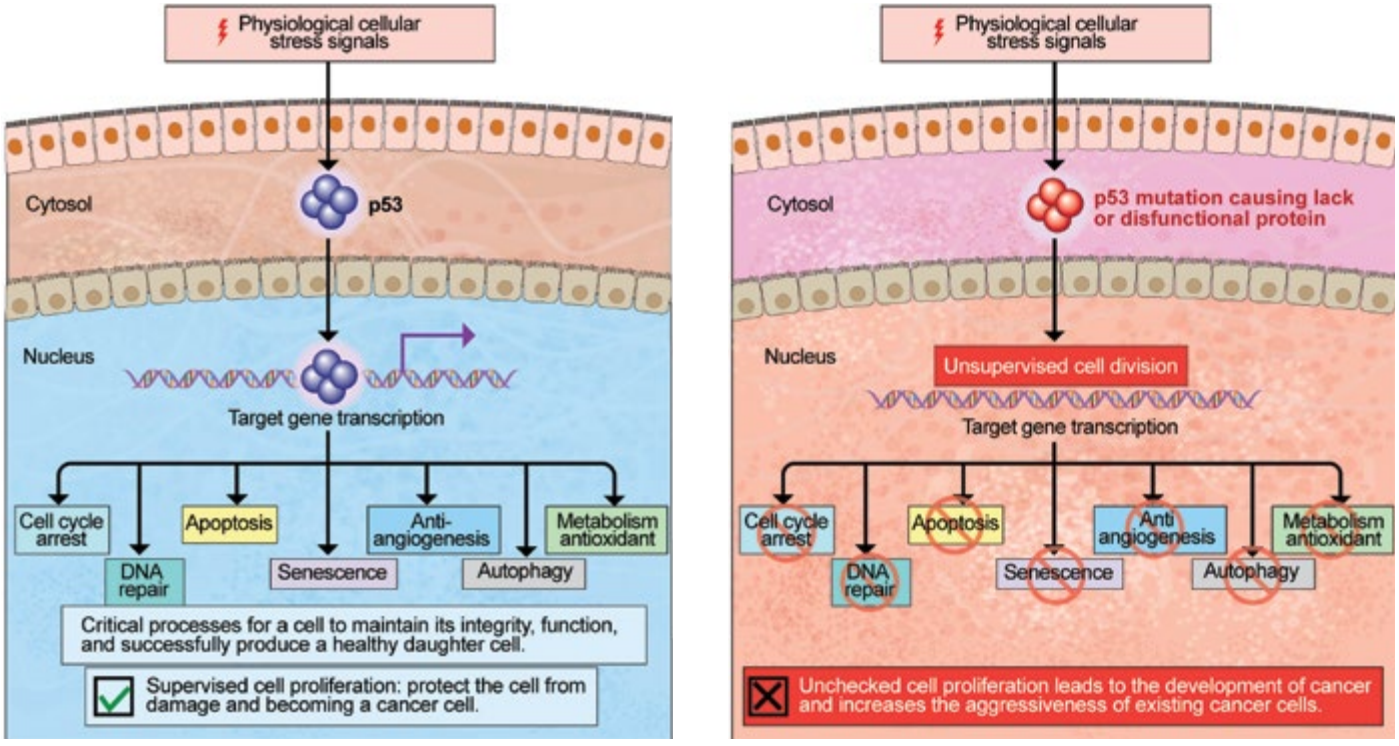
Treatment implications of *TP53* alterations

TP53 alterations may influence therapy choices. While standard treatments such as rituximab-based regimens and BTK inhibitors like ibrutinib or zanubrutinib are used in WM, patients with *TP53* mutations may respond less to chemoimmunotherapy (BR, for example). Some evidence suggests that BTK inhibitors can still be effective in these patients, but outcomes are generally poorer, and clinical trial participation is encouraged for high-risk cases. The IWWM-12 Consensus Panel recommends genetic screening for *TP53* alterations at diagnosis and before therapy to guide treatment strategies and monitoring.

Novel therapeutics: Research is underway to develop drugs specifically targeting signaling pathways that have become more active due to *TP53* mutations in WM. One exciting area of research involves approaches that either fix the mutated p53 protein so that it works normally or prevent the normal, functioning p53 from being broken down. These drugs aim to rehabilitate the tumor-suppressing abilities of *TP53*, encouraging cancer cells to either repair their damaged DNA or self-destruct.

Combination therapies: Drug combinations that target specific genetic pathways can be more effective than single-agent therapies. For instance, combining drugs that target *TP53*-associated biological pathways, such as cell death, DNA damage repair and DNA replication, with agents that inhibit other pathways, like those activated by *MYD88* and *CXCR4* mutations, might provide a comprehensive approach to disrupting cancer cell growth.

Figure 1. *Physiological Cellular Stress Signals*



TP53 *In Waldenstrom Macroglobulinemia, cont. on page 6*

Risk of disease transformation to aggressive lymphoma with *TP53* alterations

A mutation in the *TP53* gene in WM is linked to a higher chance of the disease transforming into a more aggressive type of lymphoma, such as diffuse large B-cell lymphoma (DLBCL). When *TP53* is mutated or missing, it can cause genetic instability and stop the body from naturally eliminating abnormal cells (see right side of **Figure 1,** previous page). This makes the disease more likely to progress rapidly and become more aggressive. Studies have shown that patients with *TP53*-mutated blood cancers often have worse outcomes, including shorter times without disease worsening and shorter overall survival. While scientists are still studying exactly how *TP53* mutations contribute to transformation, it's clear that having them indicates a more complex and aggressive form of WM. Patients with these mutations need close follow-up and possibly different treatment approaches.

Integrating genomic insights into clinical practice

The integration of genomic data into clinical practice is transforming the management of WM. Genetic testing allows for a more personalized approach to treatment, enabling healthcare providers to tailor therapies based on the specific mutations in a patient's cancer cells. This personalization helps in predicting disease progression, choosing the most effective therapies, and potentially improving patient outcomes.

Future research directions

The focus of future research on *TP53* alterations in WM will likely include several promising areas:

1. **Understanding why treatment sometimes stops working:** Scientists are studying how mutations in the *TP53* gene make cancer more challenging to treat. Learning this can help find new ways to overcome resistance and develop more effective treatments.
2. **Creating better drugs to reactivate *TP53*:** Researchers are working on improving drugs that can turn the *TP53* gene back on. Better medicines could more effectively stop cancer cells from growing.
3. **Ways to kill cancer cells with *TP53* mutations:** When the *TP53* gene is mutated, cancer cells get more DNA damage and must copy their DNA more often. This puts stress on them. If we make this stress even worse, we can push the cancer cells past their limit and kill them, while healthy cells are less affected because they don't have the same stress.
4. **Finding early warning signs:** Scientists are searching for markers in the blood or body that can detect *TP53* mutations early. Detecting these mutations sooner can help start treatment earlier and improve outcomes.
5. **More clinical trials and research teams:** Expanding studies to include more patients with different genetic types of cancer can help us understand *TP53* mutations better. Collaboration between research groups can speed up the development of new treatments.
6. **Gene editing with technologies like CRISPR:** New tools like CRISPR could someday directly fix *TP53* mutations in cancer cells. Although this is still new research, it could become a powerful way to treat cancers at their genetic source.

Conclusion

Our case study shows how managing WM can be complicated, especially when it changes over time. At first, our patient had symptoms caused by thickened blood, and his initial treatment worked well. However, when the disease came back, it was linked to a change in a gene called *TP53*, which can make the cancer more aggressive and more challenging to treat. This highlights the importance of monitoring the disease's genetic changes during treatment. Knowing such genetic changes can help doctors choose better, more personalized therapies. In the future, researchers are looking for new ways to attack WM by exploring different biological pathways, especially for patients whose cancer cells tend to be very resilient because of these genetic changes. Developing new treatments with different and new mechanisms of action will improve outcomes for our patients.

AN IWMF WELCOME TO DELORA SENFT!

Delora Senft

IWMF has a new President and CEO! Delora Senft, who began work August 18, is well prepared for the pivotal role she will play in supporting patients living with WM as she leads us toward our funding goals for breakthrough research.

In her previous position at Gateway for Cancer Research, Delora spent more than a decade in key roles supporting cancer research and patient advocacy. She managed the organization's day-to-day operations, set financial priorities, and shaped funding strategies. She built strong relationships with clinicians, scientists, cancer centers, healthcare institutions, and like-minded organizations all committed to changing the future of cancer care by discovering the cancer treatments for tomorrow. Delora's deep commitment to advancing cancer research and empowering informed patients is personal: after losing her brother to cancer, she made a promise to help spare other families from the same pain.

IWMF Board Chair Paul Kitchen stated, "Delora Senft has the experience, commitment, resolve, and energy to bring us to the culmination of our search for a cure for WM. She has all the qualities we have been seeking in a CEO. Delora is the right person to lead IWMF."

We look forward to working with Delora and hearing more from her in the January 2026 issue of the *Torch,* in which she will share with us her vision for IWMF.

IWMF GLOBAL PARTNERS AND GLOBAL PATIENT INITIATIVE

By Bob Perry, IWMF Trustee and *Torch* International Correspondent

Editor's note: In this issue we introduce Bob Perry, our newest writer for the Torch*, who, as a new Trustee and Chair of the Global Partners and Global Patient Initiative, will keep us informed about WM-related happenings around the world, on an organizational level as well as a personal level. We want to thank Annette Aburdene, who has been the international correspondent for the* Torch *since 2012, for all her years volunteering in this capacity. We appreciate her efforts to keep our readers informed and applaud her longstanding commitment to our international WM community.*

I am sitting in a thunderstorm in the south of France following several days of unbelievably hot weather, and I thought "what better time to send a report to the *Torch* about the international WM picture."

But firstly, for those of you that don't yet know me, I am Bob Perry, a 71-year-old Englishman living in the UK, who has been knowingly living with WM for ten years. I have been a patient advocate in the UK for six of those years and was responsible for setting up a total of 16 WM support groups across the UK. I continue to run two support groups, the Bournemouth and District Support Group (BAD WMers!) and also the Island of Ireland Support Group. More recently, I was voted onto the IWMF Board of Trustees as the first European on the Board, and my responsibility is the IWMF Global Patient Initiative. Together with two amazing IWMF Global Partner Engagement Consultants in London, Beth Mitchell and Hannah Syed, we are promoting a more international approach to reaching out to, supporting, and educating WM patients, carers, and

IWMF Global Partners, cont. on page 8

families from as many different countries as we can. This work follows the efforts of Elena Malunis and Carl Harrington in making us a truly global foundation and family.

You will, of course, know that we already have well-established support groups, charities, and global partners in countries like New Zealand, Australia, United Kingdom, Canada, Germany, France, Finland, Sweden, and India, to name a few, but we are keen as an organisation to really reach out and get as many countries into the fold as we can.

What we are finding in some countries, such as Holland, China, South Africa, and Portugal, is that support for WM patients comes under general lymphoma and cancer organisations. As good as these are, we all know that WM is a rare condition, and it forms a very small demographic within these large groups. Therefore, they might not provide the support, empathy, education, and encouragement that specific WM groups do.

To this end, I am really excited that in August we held Zoom meetings with patients from Holland and South Africa, during which we hoped to encourage and facilitate the setting up of dedicated WM support groups. In addition, we are in the early stages of doing the same in Russia and China.

I have not forgotten our good friends in Chile and Spain, where our language translation tools on the website are starting to pay dividends as support groups there start to grow.

So, we at IWMF are really excited about raising our profile globally and making us a truly international organisation for WM patients, wherever they are. If you are a WM patient, carer, or family member living in a country I may not have mentioned, please reach out to us via the website at *http://www.iwmf.com*, and we will be very happy to engage with you. Simply put, we want to support you in your WM journey, wherever you may be and in whatever language you speak. We are a family!

Let's aim for many more country support groups!

Next time I hope to update you on developments as well as share some encouraging stories from some of our global partners.

ANDREW WARDEN APPOINTED A MEMBER OF THE ORDER OF AUSTRALIA

Andrew Warden, an Australian Waldenstrom macroglobulinemia (WM) patient for 20 years and a patient advocate for WM and other blood cancers, was appointed a Member of the Order of Australia (AM) in the King's Birthday 2025 Honours List. His investiture was on September 9, with a recipients' lunch at NSW Parliament House ten days later.

The IWMF community is very familiar with Andrew, a member of WMozzies since 2007 and Team Leader from 2013 to 2020. He was a co-presenter at the 2018 IWMF Educational Forum in Rosemont, IL; a former IWMF LIFELINE Australian representative; *IWMF Torch* contributor; and recipient of IWMF's prestigious Judith May Volunteer Award, presented at the 2019 Educational Forum in Philadelphia, PA.

Andrew was a research team member and lead patient investigator for the WM COVID-19 Vaccination Studies at Sydney's Concord Repatriation General Hospital. He is co-founder of the WhiMSICAL International Patient Database, which IWMF supports and publicizes to the WM community.

Dr. Judith Trotman is a recognized worldwide WM expert and Senior Staff Specialist and Lead, Lymphoma and Community Partnerships in the Haematology Department, at Concord Hospital. Concerning WhiMSICAL, she says, "Through his initiative, Andrew, my colleague Dr. Ibrahim Tohidi-Esfahani, and I established this global PRO (Patient Reported Outcome) and QoL (Quality of Life) collaboration, providing an ethically approved, scientifically rigorous means of amplifying the patient voice and gathering real world data on this rare lymphoma. Based on its initial success and Andrew's connections, we secured the further investigator engagement of global leaders in WM clinical research and members of the Board of IWMF.

"WhiMSICAL, Andrew's initiative, is now the global database for WM, with more than 720 participants with a median eight years of follow-up. We had a publication in the *American Journal of Hematology* in 2022 and an updated abstract selected for presentation at the American Society of Hematology (ASH) Annual Meeting in 2024. This will be followed by our second major publication in 2026 thanks to the sustained support of 730 WM patients updating their own data entry.

Seated: Dr. Judith Trotman and Andrew Warden
Standing: Dr. Ibrahim Tohidi-Esfahani

"Andrew is an intellectual who pairs his curiosity with his passion for bettering the lives of people diagnosed with WM. Over more than 15 years, with warmth, optimism, and practical support, Andrew empowered WM patients across Australia and made then feel they were not alone. He advocated for patient access to clinical trials and medicines access on the Pharmaceutical Benefits Scheme [a program of the Australian government that subsidizes prescription medication], including, in 2022, the transformative oral BTK inhibitor therapy zanubrutinib (Brukinsa)—which he did with the use of WhiMSICAL QoL data and which became a drug that he himself finally could freely access."

Dr. Ibrahim Tohidi-Esfahani, Staff Specialist Haematologist at Concord Hospital, says, "I am overjoyed to see this wonderful recognition for Andrew. With his enthusiasm and passion, he has been energising all those around him to bring about real change for patients with WM. I have been fortunate enough to be in partnership with

Andrew Warden, cont. on page 10

him after he developed the idea for and became a co-investigator of the WhiMSICAL Registry. The study would not have been possible without Andrew's efforts, with the data produced leading to eight international conference presentations, as well as the data being used in the successful application for US Medicare funding of the lifesaving and life-changing new treatment—zanubrutinib—for WM. He is the patient chief investigator on an Australian Medical Research Future Fund grant to expand the WhiMSICAL registry to a mobile phone application, along with translations to improve the study's reach and accessibility, giving a voice to patients with WM regardless of postcode and geography."

The world-wide WM community owes a debt of gratitude to Andrew for his tireless advocacy on their behalf. His energy and persistence in support of research into such a rare disease is an incentive and inspiration to all. Thank you, Andrew, and congratulations!

Andrew Warden AM at NSW Government House, Sydney, after his Order of Australia Investiture Ceremony. He is with Her Excellency the Honourable Margaret Beazley AC KC, Administrator of the Government of the Commonwealth of Australia

Blood Cancer United

LEUKEMIA & LYMPHOMA SOCIETY (LLS) CHANGES ITS NAME

In advance of Blood Cancer Awareness Month in September, the Leukemia & Lymphoma Society (LLS) announced a change to its name, which is now Blood Cancer United. The new website address for the organization is *www.bloodcancerunited.org*.

The name change is anticipated to help the organization reach more people affected by blood cancer and make them feel more welcome under a new name that represents all 100+ types of blood cancer—not just leukemia and lymphoma. Several of the other blood cancers that the organization represents include myeloma, myelodysplastic syndromes, and myeloproliferative neoplasms.

While the name has changed, the new Blood Cancer United said that it "will continue to directly help patients by funding promising research, advancing innovative treatments, offering free support, and advocating for policies that help people access quality healthcare."

US FDA and EC Approve Tablet Formulation of Zanubrutinib – The US Food and Drug Administration (FDA) and the European Commission (EC) have approved a tablet formulation of zanubrutinib (Brukinsa) of 160 mg to replace the current 80 mg capsules, with the replacement to begin this October. This will enable users to take two tablets daily (rather than four capsules) at the recommended daily dose of 320 mg. The tablets will be smaller in size and with a coating to enhance ease of swallowing. The 160 mg tablets will be scored so that they can be split by those who require dosing adjustments.

Updated Version of NCCN Clinical Practice Guidelines® Released for WM/LPL – The NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Waldenström Macroglobulinemia/ Lymphoplasmacytic Lymphoma was recently updated to Version 1.2026. Notable changes from the previous version include the following: 1) for primary (first-line) therapy, single agent ibrutinib and ibrutinib + rituximab have been moved from the category of Preferred Regimens to the category of Other Recommended Regimens; 2) for primary (first-line) therapy, BTK inhibitors should not be used for patients with WM/LPL-associated amyloidosis; and 3) for previously treated therapy, pirtobrutinib has been moved from the category of Useful in Certain Circumstances to the category of Other Recommended Regimens. After establishing a login, one can view the complete guidelines at *https://www.nccn.org/professionals/physician_gls/pdf/waldenstroms.pdf*.

Zanubrutinib Is First BTK Inhibitor Approved in India for WM – The Drugs Controller General of India has approved zanubrutinib as the first BTK inhibitor treatment in India for five B cell malignancies, including WM. The drug will be distributed by Glenmark Pharmaceuticals and marketed in India under the Brukinsa brand name.

Iopofosine I 131 Receives Breakthrough Therapy Designation from US FDA – Cellectar Biosciences announced that the US Food and Drug Administration (FDA) has granted Breakthrough Therapy Designation to iopofosine I 131 for the treatment of patients with relapsed or refractory WM. This designation expedites the development and review of drugs for serious or life-threatening diseases when there is evidence that they offer substantial improvement over available therapies. Iopofosine I 131 is a novel agent that combines a phospholipid ether molecule targeted to the cancer cells and radioactive iodine to cause cancer cell death. During the Phase 2 CLOVER WaM clinical trial, WM patients received intravenous iopofosine I 131 on days 1 and 15 of cycle one; six weeks later, they received the final two doses on days 1 and 15 of cycle two. The total treatment and evaluation period was one year. The overall response rate was 81.4% in *MYD88* wild-type (unmutated) disease, 84.3% in *MYD88* mutated disease, 80.0% in *CXCR4* mutated disease, and 73.1% in *TP53* mutated disease. The major response rate (the sum of partial, very good partial, and complete response rates) was the trial's primary endpoint: this rate was 50.1% in *MYD88* wild-type disease, 59.0% in *MYD88* mutated disease, 100% in *CXCR4* mutated disease, and 40.0% in *TP53* mutated disease. The most common treatment side effects included low platelet counts, low neutrophil counts, anemia, decreased white blood cell counts, fatigue, nausea, diarrhea, shortness of breath, headache, dizziness, decreased lymphocyte counts, nosebleeds, decreased appetite, constipation, and low neutrophil counts with fever.

The NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Waldenström Macroglobulinemia/ Lymphoplasmacytic Lymphoma was recently updated...

Medical News Roundup, cont. on page 12

Phase 1 Trial Results Updated for Sonrotoclax in Relapsed or Refractory WM – An abstract presented during the European Hematology Association (EHA) 2025 Congress updated results of a Phase 1 international trial of sonrotoclax for relapsed/refractory B cell cancers, including WM. Sonrotoclax is a more selective and more potent inhibitor of BCL-2 than venetoclax (Venclexta). This dose escalation trial enrolled 23 participants with WM in a ramp-up schedule to reduce the risk of tumor lysis syndrome, which is a group of potentially serious metabolic abnormalities that occur as large amounts of tumor cells are killed off and release their contents into the bloodstream. Patients were treated until disease progression or unacceptable side effects. The overall, major, and very good partial response rates were 78.3%, 60.9%, and 13.0%, respectively. With a median follow-up of 22.1 months, median progression-free survival was not reached. Nine patients discontinued treatment, six because of disease progression and three because of side effects. Six patients died because of disease progression, COVID-19 pneumonia, or other pneumonia. The most common side effects that occurred in 20% or more of patients included anemia, COVID-19 infection, low neutrophil counts, nausea, and fever. No cases of tumor lysis syndrome occurred, and no cases of atrial or ventricular fibrillation were reported.

Results Presented for Phase 1 Trial of BTK Degrader BGB-16673 in Relapsed or Refractory WM – Another EHA 2025 Congress abstract updated international Phase 1 trial results for the oral BTK degrader BGB-16673 in relapsed or refractory WM patients, part of a larger study of the drug in several B cell cancers. The drug blocks BTK signaling by tagging BTK for degradation through the cell's proteasome pathway. In this ongoing dose escalation trial with 30 WM participants, the median number of prior therapies was three, including covalent and non-covalent BTK inhibitors and BCL-2 inhibitors. At the time of this report, median follow-up was 8.1 months. In the 29 patients evaluable for a response, the overall response rate was 89.7%, the major response rate was 75.9%, and the very good partial response rate was 31.0%. Responses were independent of mutations in the genes *BTK*, *MYD88*, *CXCR4*, and *TP53*. The most common side effects, occurring in 96.7% of patients, were decreased neutrophil counts, diarrhea, bruising, anemia, fever, and low platelet counts. No atrial fibrillation or major hemorrhage occurred, and there was one observed case of high blood pressure. On *www.clinicaltrials.gov*, the trial identifier is NCT05006716. The European Medicines Agency has granted PRIME designation to BGB-16673 for the treatment of WM patients previously treated with a BTK inhibitor. PRIME designation provides early and enhanced support to developers of promising medicines for patients with unmet medical needs.

Sonrotoclax is a more selective and more potent inhibitor of BCL-2 than venetoclax (Venclexta).

Phase 1 Clinical Trial Data Discussed for BTK Degrader Bexobrutideg in Relapsed or Refractory WM – Meanwhile, researchers presented international Phase 1a/b clinical trial data during the EHA 2025 Congress on another oral BTK degrader called bexobrutideg (also known as NX-5948). This ongoing trial of participants with relapsed or refractory B cell malignancies includes 18 with WM. Of these, 13 could be evaluated for responses. Their overall response rate was 84.6%, and the depth of their responses improved with longer time on treatment. The most common treatment side effects included diarrhea, low platelet counts, bruising, and petechiae (tiny spots of bleeding under the skin). No atrial fibrillation was observed. As reported in a previous issue of the *Torch*, bexobrutideg received Orphan Drug Designation from the US Food and Drug Administration for the treatment of WM; the drug just recently received the same designation from the European Medicines Agency. This designation provides incentives to encourage the development of drugs intended to treat rare diseases. The trial identifier on *www.clinicaltrials.gov* is NCT05131022.

Long-Term Follow-Up Results Presented for Phase 2 Trial of Venetoclax in Relapsed or Refractory WM – An EHA 2025 Congress abstract

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included long-term follow-up results from a Phase 2 trial of solo venetoclax (Venclexta) for relapsed or refractory WM patients, half of whom had been previously treated with BTK inhibitors. In this multicenter US trial, venetoclax was ramped up to a maximum oral dose of 800 once daily and administered for two years. With a median follow-up of 81 months, 23 patients (72%) experienced disease progression, 17 (53%) began a new treatment, and three (9%) had died. The median progression-free survival was 36 months. *CXCR4* mutation status and previous exposure to BTK inhibitors were not associated with any differences in progression-free survival. The five-year overall survival rate was 95%. Of the 17 participants who began a new treatment, six received solo venetoclax again (five achieved a response); three received venetoclax in combination with a BTK inhibitor (two achieved a response, and one had stable disease); four received a solo BTK inhibitor (all achieved a response); two received a combination of bendamustine with an anti-CD20 monoclonal antibody (both achieved a response); and two received a proteasome inhibitor with an anti-CD20 monoclonal antibody (none achieved a response).

Phase 2 BRAWM Clinical Trial in WM Reports Updated Results – The Phase 2 BRAWM clinical trial conducted at nine Canadian sites published updated results in the journal *Hematological Oncology*. This trial was a fixed-duration, one-year therapy for 63 treatment naïve WM patients, consisting of bendamustine and rituximab administered for six monthly cycles and acalabrutinib (Calquence) administered for 12 monthly cycles. At the time of this report, median follow-up was 18 months. The primary outcome of the trial was the combined rate of complete and very good partial responses, which was 62.7% by cycle 7, 62.2% by cycle 12, and 53.8% by 18 months. The progression-free survival rate and overall survival rate at 24 months were both calculated as 97.6%. Mutations in the gene *CXCR4* were not associated with an inferior rate of complete and very good partial responses. MRD (minimal residual disease) negativity rates in the peripheral blood were 82% by cycle 7, 91% by cycle 12, and 71% by 18 months. MRD negativity in the bone marrow was not as frequent but increased over time to 23% by 18 months. The most common side effects included low neutrophil counts and low platelet counts.

...the oral MALT1 inhibitor called SGR-1505...has received fast Track Designation from the US Food and Drug Administration for the treatment of WM...

MALT1 Inhibitor in Phase 1 Trial for Relapsed or Refractory B Cell Cancers Receives FDA Fast Track Designation for WM – A Phase 1 dose escalation clinical trial of the oral MALT1 inhibitor called SGR-1505 is being used to treat 33 patients with relapsed or refractory B cell cancers, and trial data were presented during the EHA 2025 Congress. MALT1 stands for "mucosal associated lymphoid translocation protein 1" and is located downstream of BTK in the NF-kappa-B signaling pathway. Of the four WM patients included in the trial, three were evaluable for responses, which included one partial response and two major responses. The overall incidence of side effects in all patients was 79%, with the most frequent including low neutrophil counts, rash, fatigue, and pneumonia. Schrödinger Inc., the maker of SGR-1505, announced that the drug has received Fast Track Designation from the US Food and Drug Administration (FDA) for the treatment of WM patients who have failed at least two lines of therapy, including a BTK inhibitor. Fast Track Designation is another program that facilitates the development and expedites the review of drug candidates to treat serious conditions and fill an unmet medical need. This trial is still recruiting patients, and its identifier on *www.clinicaltrials.gov* is NCT05544019.

Pirtobrutinib Used as Effective Treatment After Ibrutinib Therapy for Bing-Neel Syndrome – A letter published in the *American Journal of Hematology* by Italian researchers discussed their clinical experience in treating three WM patients with Bing-Neel

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syndrome (BNS) who had progressed on ibrutinib (Imbruvica) and then successfully received the non-covalent BTK inhibitor pirtobrutinib (Jaypirca). Ibrutinib and zanubrutinib (Brukinsa) are both covalent BTK inhibitors that have become standards of care to treat this rare neurological complication of WM/lymphoplasmacytic lymphoma, but there are no published data on treatments used if BNS patients fail these covalent BTK inhibitor therapies. In all three BNS patients discussed, pirtobrutinib administration resulted in improvement in both symptoms and brain imaging scans within two weeks, indicating that pirtobrutinib was crossing the blood-brain barrier.

BTK Inhibitor Tirabrutinib Studied as Treatment for Bing-Neel Syndrome in Japan – Japanese researchers conducted a retrospective study to investigate the second generation BTK inhibitor tirabrutinib as treatment for Bing-Neel syndrome, a rare neurological complication of WM/lymphoplasmacytic lymphoma, in patients diagnosed between August 2020 and April 2024. The median starting dose was 480 mg once daily. Among 19 of 22 Bing-Neel patients evaluable for response, the overall response rate was 100%, with 58% of these being complete responses. The median time to best response was 3.6 months. Overall survival at 30 months was 90.7%. Side effects were observed in 77.3%, with skin issues the most common. No patients discontinued tirabrutinib because of side effects, although dose reductions and interruptions were required in seven and eight patients, respectively. The trial results were reported during the EHA 2025 Congress.

Promising Early Results Announced for WM Patients in Phase 1 Trial of CAR-Modified Natural Killer Cell Immunotherapy – The pharmaceutical company ImmunityBio announced early findings from its ongoing Phase 1 QUILT-106 clinical trial for relapsed or refractory B cell non-Hodgkin lymphoma that included complete responses in its two WM participants. The participants were treated with a CD19 CAR-NK immunotherapy using natural killer (NK) cells rather than T cells. The trial, conducted in South Africa, had two arms, one using the immunotherapy alone and the other combining it with rituximab. Treatment was administered in the outpatient setting. No significant side effects were noted in either WM patient, both of whom remained in remission at the time of this report, which was six months following treatment. This is an off-the-shelf therapy, meaning that the company uses an engineered natural killer cell line rather than having to collect, modify, and process natural killer cells from each patient.

Greek Study Describes Potential Mechanisms of Resistance to Ibrutinib Therapy in Previously Untreated WM Patients – A study from Greek researchers, presented during the EHA 2025 Congress, identified and described the mechanisms of resistance to ibrutinib in previously untreated WM patients who received the drug as first-line therapy. Using multiple approaches to study the bone marrow of 27 WM patients and two healthy controls, samples were obtained at various points during ibrutinib treatment. Those who achieved at least a partial response to ibrutinib were compared to those who did not respond. In the responder group, genes such as *CHST15*, *EIF4E3*, *GSDME*, and *IL17RB* were upregulated, compared to the non-responder group. The non-responder group had a different set of upregulated genes, including *EGR1*, *S100A4*, and *S100A6*. There were also significant differences in the immune microenvironment between the responder group and the non-responder group, particularly in certain populations of monocytes and natural killer cells. In the T cell compartment, CD4 and CD8 T cells were significantly enriched in the responder group, while the non-responder group exhibited a more exhausted group of T cells. Whole genome sequencing identified certain mutated genes in the responder group that included *KMT2C*, *CAST*, and *SLC10A3*, while the non-responder group included mutations in *CXCR4*, *NOTCH1*, *KMT2D*, *ARID1A*, and *ARID1B*. Deletion of chromosome 6q was observed in about 40% of the non-responder group, compared to 25% in the responder group. The authors concluded that these differences highlight potential mechanisms of resistance to ibrutinib therapy that could serve to help predict responses to BTK inhibitor-based therapy in WM

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patients. This research has been supported with a grant from IWMF.

MD Anderson Evaluates Long-Term Outcomes After BTK Inhibitor Treatment Is Discontinued – MD Anderson Cancer Center retrospectively analyzed data from 153 WM patients treated at its center between January 2014 and March 2024 with BTK inhibitors, in either the first-line or previously treated setting, to evaluate long-term outcomes after their BTK inhibitor treatment was discontinued. At last follow-up, 71% had stopped treatment with their first BTK inhibitor, which was primarily ibrutinib. Their median time on BTK therapy was 12 months, with the following reasons for stopping: side effects in 44%, disease progression or transformation to a more aggressive lymphoma in 27%, physician or patient choice in 24%, and other in 6%. After discontinuation, 78% of these patients received another treatment; 51% chose an anti-CD20 antibody-based regimen with or without chemotherapy, 29% chose an alternate BTK inhibitor, 11% chose venetoclax; and 11% chose other therapies. After this next treatment, 49% of patients achieved at least a partial response, with major response rates being statistically comparable among all the treatment regimens. Patients who received an alternate BTK inhibitor had a significantly longer median progression-free survival (38 months) than those who received an anti-CD20 antibody-based regimen (29 months), venetoclax (14 months), or other regimens (six months). However, the researchers noted that when the analysis was limited to just those who discontinued their first BTK inhibitor because of disease progression, no statistically significant differences in progression-free survival among the next regimens were observed. This abstract was presented during the EHA 2025 Congress.

***TP53* Mutations Impact Overall Survival After First-Line Therapy in WM/LPL** – Previous studies have found that *TP53* mutations are associated with decreased overall survival in WM/lymphoplasmacytic lymphoma (LPL), and MD Anderson Cancer Center analyzed the impact of *TP53* mutation status on survival after first-line treatment of WM/LPL with either chemoimmunotherapy or BTK inhibitor therapy. In this retrospective study of 107 patients with a diagnosis of WM/LPL, 10% were determined to have *TP53* mutations prior to initiation of any treatment. The three-year overall survival rate was 77% for those without *TP53* mutations vs. 52% with these mutations. When evaluating overall survival in patients grouped by *TP53* mutation status and type of first-line treatment, patients with *TP53* mutations who received first-line chemoimmunotherapy trended toward having inferior outcomes compared to those without the mutations; however, patients who received first-line BTK inhibitor therapy had similar outcomes regardless of *TP53* mutation status. The researchers suggested that WM/LPL patients be tested for *TP53* mutations prior to first-line treatment and that BTK inhibitors should be given preference over chemoimmunotherapy in those with *TP53* mutations. This analysis was reported during the 2025 American Society of Clinical Oncology Annual Meeting.

Spanish Researchers Determine Drivers of Disease Progression to Active WM – The *MYD88 L265P* mutation can be found in IgM monoclonal gammopathy of undetermined significance (MGUS) and asymptomatic WM; however, its presence alone is not sufficient to drive disease progression to active (symptomatic) WM. Researchers in Spain attempted to better determine the genetic mutations leading to progression by studying the bone marrow of 19 IgM MGUS and 17 asymptomatic WM patients. They observed that patients at a low risk of progression were only characterized by the presence of the *MYD88 L265P* mutation, while those at intermediate or high risk harbored additional mutations on the genes *CXCR4*, *KMT2D*, *ARID1A*, and *EP300*. They also found that patients at low risk had a significant decrease in the number of monocytes compared to patients at high risk. The group at high risk of progression showed increased expression of genes involved in the activation of NF-kappa-B and B cell receptor (BCR) signaling. This work was partially supported by a grant from IWMF.

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.*

STILL STANDING STRONG: JENNIFER HOEGERMAN'S CONTINUING JOURNEY WITH WM

By Art Brewer, Features Correspondent

Since becoming involved with IWMF in 1999, California resident Jennifer Hoegerman has been a steady and inspiring presence in the WM community and a passionate advocate for patient education and empowerment.

Diagnosed in 1995, Jennifer has lived with WM for three decades. She first shared her story with the *Torch* in 2014 and revisited it in an update in 2020, offering fellow patients a window into her experience navigating treatment and personal growth. Now 73 and retired from a 36-year nursing career, Jennifer continues to find strength and connection from IWMF, an organization that has remained a cornerstone in her life with WM as she confronts new treatment challenges.

After about ten years of successful treatment with ibrutinib, Jennifer's WM started progressing again. Seeking guidance at Stanford University, she was advised to move to zanubrutinib. But the recommendation didn't sit right with her. Both drugs are BTK inhibitors that act on the same pathway, and she questioned whether a similar drug would work if resistance had already developed. Relying on years of knowledge gained from attending the IWMF Educational Forum (Ed Forum)—an annual event for WM patients, supporters, and caregivers to learn about WM —she sought a second opinion from the Mayo Clinic.

Jennifer and Robin Hoegerman

There, a different treatment was offered: venetoclax. It took nearly a year to get the new drug started, but it paid off. Within a few weeks on three daily pills, Jennifer said she felt dramatically better. "I came to life again," she said. "It's amazing what a difference the right treatment can make when you're armed with knowledge and have doctors willing to listen."

The power of patient education

Jennifer believes her ability to navigate complex treatment decisions stems directly from the Ed Forums she has attended over the years. She has participated in 23 Ed Forums since 1999 and says the experience transformed not only her understanding of WM, but also her relationship with her care team.

"If you have a receptive doctor who doesn't have an ego and is willing to listen, then this works really well," she said. "The Ed Forums gave me the knowledge to speak their language and advocate for what made sense."

From the beginning, Jennifer was drawn to the Ed Forum not just for the information, but for the sense of community. "The local oncologist can't know every detail of the latest research," she said. "At the Ed Forum, you meet people just like you, and you hear directly from the researchers who are shaping the future of treatment."

One of her favorite Ed Forum traditions is the moment when attendees are asked to stand based on how long they've lived with WM. "They go from five years up to 30 years," Jennifer said. "At the last Ed Forum, when they got to 30 years, the last ones standing

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were Eileen Sullivan and me." Eileen is a member of the IWMF Board of Trustees, a WM support group leader for Massachusetts, and a member of the Ed Forum Committee.

Jennifer finds it deeply meaningful to see newly diagnosed patients come into the Ed Forum feeling frightened "like deer in the headlights" and then watching their expressions change as they learn more. "By the end, they're smiling. They have a plan," she said. "It's incredibly positive."

Jennifer had symptoms of peripheral neuropathy, including numb toes, long before she was diagnosed with WM. At the time, she blamed her Birkenstock sandals. It wasn't until she attended an Ed Forum that she began to understand the connection between WM and neuropathy. That information changed how she viewed her initial treatment, which included rituximab but didn't address the nerve damage.

Staying active and grounded

Despite the neuropathy, Jennifer maintains a physically active lifestyle on her California farm. She cares for several animals including two horses (Rosie the Arabian and Rella the Quarter Horse), 11 tortoises, a cockatoo, and more. She also takes care of her 14-month-old grandson four days per week. Her daily chores keep her grounded and fit. "When I'm out shoveling horse poop every morning, I think, 'All those people go to the gym to get that exercise—I'm getting it right here in my backyard!'" she laughed. "The only times I've been really knocked off my activity level were during some of the therapies, and before I started ibrutinib when I felt completely drained."

Over the years, Jennifer has been an active member of her local WM support group and often donates to IWMF. She frequently refers newly diagnosed patients to the IWMF website, calling it a valuable starting point. "As bewildered as people are at the beginning, they'll get good guidance there," she said. "You don't need to master everything on the website, just go to what applies to you in the moment."

One of the most pivotal moments in Jennifer's treatment journey came when bendamustine failed, and she felt she was "circling the drain." It was then that she logged into IWMF Connect, the Foundation's online discussion forum, and saw a post about a clinical trial for ibrutinib at Dana-Farber Cancer Institute and Stanford. She called Stanford immediately and learned there were only a few spots left. Because of that timely post and her quick action, she enrolled. "I honestly believe it saved my life," she said.

Jennifer riding her horse

Her local oncologists, too, have come to value her participation in the Ed Forum. "They actually get excited when I tell them an Ed Forum is coming up," Jennifer said. "They want me to bring back the latest news. That's a huge compliment to IWMF and what it offers."

Bonds that last a lifetime

Jennifer's bond with IWMF extends beyond the professional. Over the years, she has developed close friendships with many involved in the Foundation. She grew especially close to Sara McKinnie, who was hired by IWMF founder Arnie Smokler to run

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the organization's office in its early days. Though Sara has since retired, she visits Jennifer and her husband, Robin, in California.

Jennifer also connected deeply with Laurie Rude-Betts, whose late husband, Ben Rude, was a former IWMF President. Their shared love of horses brought them together, and after the most recent Ed Forum in May, the two women vacationed at the beach in Florida along with Sara and Robin. It was a trip they had planned for a long time.

She also remembers fondly her friendship with the late Alice Swift Riginos, the editor of the *IWMF Torch* from 2008 to 2018. "She was the coolest lady," Jennifer said. "We bonded over our love of sailing. She was the one who convinced me to write my article for the *Torch* back in 2014."

More recently, Jennifer has found a kindred spirit in Ann Grace MacMullan, IWMF's Wellness Program Coordinator. "We're on the same wavelength," she said.

Reflecting on her long relationship with IWMF, Jennifer is amazed by how much the organization has grown. "It used to be one person running the whole Ed Forum and doing everything else," she said. "Now it's an international organization with a full staff and research support. IWMF has been instrumental in funding the research that's saving our lives."

For most of those years, she noted, you didn't hear the word "cure" when applied to WM. Now, the possibility of a cure is being seriously discussed. "That's a huge change," she remarked.

Gratitude and compassion

Spiritual practice has played a central role in Jennifer's ability to cope with WM. A devoted student of Tibetan Buddhism, she views her illness through the lens of those teachings. "Your life is your practice," she explained. "Whatever life throws at you, that's what you work with."

Her mother, a devout Catholic who lived to be 102, surprised Jennifer by recognizing how much her daughter's Buddhist practice helped her cope with her disease. "She told people she didn't think I could handle my illness without it," Jennifer said. "That was big for her to say."

The teachings she draws from emphasize moving beyond both hope and fear toward a state of equanimity. "It's not that you stop caring," Jennifer said. "It's that you're better able to roll with it. I know it may sound cliché, but I'm just grateful for everything."

While Jennifer looks forward to new treatments and perhaps a cure one day, she's also realistic. "That's still a way off," she said. "What's more important is how we respond right now. For some people, a diagnosis like this slows you down and helps you see what's really important. For others, it opens the door to compassion. Along with gratitude, compassion rises."

Through it all, Jennifer continues to lean on IWMF and to live with purpose and an unwavering commitment to making each day count.

2025 IWMF RESEARCH GRANTS

By Paul S. Kitchen, IWMF Board Chair

In June of this year, the 2025 IWMF Research Grants were announced. You funded these projects—you and others in our WM community who believe progress is possible. What our investigators are discovering will shape the future for everyone living with WM. Two articles immediately follow to explain Dr. Eric Durot's and Dr. Hao Sun's research.

Pieter Langerhorst will use blood-based protein profiling to better understand why some patients respond differently to treatment or progress more quickly. This project has an international collaboration that includes scientists from The Netherlands, the United States, and Iceland.

Drs. Kevin Miller and Lia Palomba at Memorial Sloan Kettering in New York will use machine learning to identify patterns of inflammation in WM that could help guide treatment decisions.

In France, a team led by **Dr. Eric Durot** is studying the tumor microenvironment in people whose WM has transformed into a more aggressive form, using detailed tissue analysis to understand how cancer cells interact with their surroundings and to search for treatment targets.

At Mayo Clinic, chief investigator **Dr. Saurabh Zanwar** is using artificial intelligence to analyze bone marrow biopsies and predict which patients are more likely to relapse early.

City of Hope's **Dr. Szymon Szymura** explores how T cells, key immune cells that normally attack cancer, may slow or stop WM by changing how cancer cells read their own genetic code.

Dana-Farber Cancer Institute's **Dr. Hao Sun** is tracking how both the cancer and the immune system change over time in patients taking ibrutinib, to understand why some responses last and others do not.

I'll close with a wonderful reflection from our lead WM physician-scientist in Australia, Dr. Judith Trotman: "Pretty nice to be on a winning team, isn't it?"

We count on you. And you can count on us.

HAVE YOUR SAY

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

RESEARCHER SPOTLIGHT: A FIRST-EVER DEEP DIVE INTO THE TRANSFORMED TUMOR MICROENVIRONMENT

Dr. Eric Durot is conducting a bold, long-overdue study that asks a crucial question: What exactly happens inside the body when WM transforms into a fast-growing, life-threatening disease?

Dr. Eric Durot

For years, we've known that some cases of Waldenstrom macroglobulinemia (WM) change into something much more dangerous—a process called *histological transformation*. But we haven't understood **why**.

Cracking the code

In this project, Dr. Durot, who is a senior consultant at Robert Debre Hospital in Reims, France, uses two breakthrough technologies to look at tumors like never before. One technology is imaging mass cytometry, which allows him to analyze individual cells and measure dozens of markers on those cells at the same time to dissect their identity, communication patterns, and roles in disease. The other tool is single-cell RNA sequencing, which acts like a microphone, allowing scientists to listen in on what each cell is doing—fighting or helping the tumor.

Together, these tools go far beyond old methods. They don't just count cells. They show who's talking, who's helping, and who's being silenced inside the tumor.

One-of-a-kind study

Dr. Durot draws from 52 rare tumor samples, the largest set ever assembled from patients whose WM became aggressive. These were gathered through years of collaboration across France. Every tumor lives in a community. It's not just cancer cells, it's also immune cells, connective tissue, blood vessels, and chemical messengers.

In WM, this bone microenvironment gets hijacked. Our immune system normally has "brakes" that prevent it from attacking healthy cells. Cancer can exploit these brakes to avoid being attacked. In some aggressive transformed lymphomas, doctors are now using immune-based drugs called inhibitors to try to block the cancer cell's ability to hide from the immune system's T cells. But for WM, we still don't fully understand what is happening in the tumor's environment when it transforms. That's what this study aims to change.

Dr. Durot is creating a cancer cell map from these French tissue samples, linking what's happened at the cellular level to how real patients responded to treatment. The focus is on these types of cells:

- **Exhausted T cells**
  These are immune cells that should be fighting the cancer but are worn out and ineffective.
- **Macrophages and suppressor cells**
  These cells normally help the body heal. But in this setting, they're helping the tumor grow, hide, and resist treatment.
- **Signaling molecules**
  These are chemical messengers that cancer uses to recruit help or block attacks. Some of these may be targetable with immune therapies, drugs already being used in related cancers.

When WM transforms, it's one of the most dangerous events a patient can face. Chemotherapy often fails. Even newer treatments may only work briefly. But with this research, Dr. Durot hopes to find earlier warning signs, so high-risk patients are watched more closely. When he identifies the types of cells and how they interact in transformed WM, he expects to uncover potential ways to reprogram the immune response and stop the tumor from gaining strength.

Backed by cutting-edge science and grounded in patient need, this IWMF-funded project fits squarely within IWMF's mission to accelerate discovery and improve lives. Funding begins this fall. We expect results in a year.

Thank you to everyone who donates to IWMF. This is your investment at work.

RESEARCHER SPOTLIGHT: HOW WM ADAPTS—AND HOW THE IMMUNE SYSTEM FIGHTS BACK

Dr. Hao Sun, Robert A. Kyle Career Development Award winner, explores the mechanics of treatment resistance.

Dr. Hao Sun

The Robert A. Kyle Career Development Awards are two-year grants designed to support exceptional post-doctoral researchers and junior faculty who are advancing the science of Waldenstrom macroglobulinemia (WM). Named in honor of Dr. Robert Kyle—whose decades of insight shaped the field—these awards do more than fund a project. They accelerate bold, high-quality research already in motion.

Each grant supports a rising WM-focused young investigator, working in close partnership with a senior mentor who is an established leader in B cell or plasma cell malignancies. Together, they form a powerful team: combining deep disease insight with fluency in the latest scientific tools and technologies. These scientists bring fresh perspective, creative momentum, and a drive to push boundaries by asking sharper questions and uncovering new opportunities.

Late this summer, Dr. Hao Sun launched his exciting project unpacking just how WM tumor cells fight ibrutinib.

What happens when WM is under pressure?

Dr. Hao Sun is determined to find out. As treatment begins, some tumor cells die, others adapt, and the immune system either rallies or falters. It's a hidden battle inside the bone marrow. Why do some patients stay in remission for years, while others relapse early? What clues are buried in the behavior of individual tumor and immune cells that could help us predict—and prevent—resistance?

As a highly promising investigator at Dana-Farber Cancer Institute, Dr. Sun has 82 co-authored publications and nearly 900 citations to his name. He earned his PhD in biochemistry from the Institute of Hematology and Blood Diseases Hospital in Tianjin, China, and joined Dana-Farber in 2023 as a postdoctoral fellow in blood cancer biology.

Powered by a world-class mentoring team

Dr. Sun is backed by an exceptional, hand-picked mentoring team, each fully committed to this project. Led by Dr. Steven Treon, who discovered the *MYD88* mutation in WM and helped launch BTK inhibitor therapies for it, the team includes Drs. Jorge Castillo, Romanos Sklavenitis-Pistofidis, Zachary Hunter, and Shirong Liu. Together, they bring unmatched expertise in clinical trials, tumor microenvironment research, genomics, and computational biology, ensuring this project is supported from every scientific and clinical angle.

Tracking tumor evolution over five years of real patient treatment

In earlier work, the team conducted the first long-term, single-cell analysis of how WM tumor cells evolve during ibrutinib treatment. Using real patient samples collected over five years, researchers analyzed thousands of individual tumor and immune cells at multiple time points. This allowed them to map how specific tumor clones changed and how some became dominant or disappeared during treatment. They discovered that patients follow one of three evolutionary paths, each closely tied to treatment outcomes.

In some cases, signs of aggressive clonal evolution were detectable up to **two years before** clinical relapse, offering a crucial opportunity for earlier intervention.

Using next-generation technologies to decode resistance

With this new phase of research, Dr. Sun is applying newly available cutting-edge tools. Technologies like high-throughput single-cell sequencing and advanced pathway analysis now allow him to track how individual tumor and immune cells behave at

Researcher Spotlight, cont. on page 22

each stage of treatment, as if replaying the disease in slow motion. This gives him a "real-time" view of how resistance unfolds, even though the samples were collected in the past.

Dr. Sun will focus on the immune system to understand how it influences these patterns. By analyzing individual immune cells, such as T cells and other defenders in the bone marrow, he aims to uncover which immune responses help keep the cancer in check and which may allow WM to return.

Dr. Sun will also zero in on what makes some WM tumor cells resistant to treatment. By identifying weak spots in those cells, he can test new drug combinations in the lab that could block resistance before it takes hold. This work may help explain why ibrutinib works so well for some people, but not for others, and point the way toward smarter, longer-lasting treatment strategies.

It's research like this—ambitious and patient-centered—that accelerates the cure.

WHAT DOES *THAT* MEAN?

If you're reading through the *Torch*, listening to a presentation on WM, or talking to your doctor about treatment, do you wonder what some of the medical terms mean?

Complete response (CR) – A way to measure the response to treatment for WM. The criteria are a normal quantitative serum IgM; the absence of monoclonal IgM; the absence of WM cells in the bone marrow; and no enlarged lymph nodes, enlarged spleen, or WM masses in other tissues.

Major response – A way to measure the response to treatment for WM. It is any response that meets the criteria for a partial response, very good partial response, or complete response.

Overall survival (OS) – The length of time during and after diagnosis or treatment that someone remains alive.

Partial response (PR) – A way to measure the response to treatment for WM. The criterion is a reduction in quantitative serum IgM between 50-90%.

Progression-free survival (PFS) – The length of time during and after treatment that someone lives with a disease but it does not get worse.

Refractory – Not responding to treatment.

Relapse – The return of disease after someone was treated and had a response.

Very good partial response (VGPR) – A way to measure the response to treatment for WM. The criterion is a reduction in quantitative serum IgM of at least 90%.

HEALING POWER OF MUSIC AND COMMUNITY

BY DECLAN COSGROVE

Just weeks before my Waldenstrom macroglobulinemia (WM) diagnosis, I was walking miles on holiday in Iceland, feeling healthy and vibrant. Soon after, walking my collie dog Blue up a small hill near home, everything changed. Severe dizziness led to blood tests which revealed dangerously low hemoglobin levels.

By November 2023, the words "Waldenstrom macroglobulinemia" entered my vocabulary for the first time. Like most people, I'd never heard of this rare blood cancer. The symptoms had been building: the dizziness, dangerously low hemoglobin, and heavy, frequent nosebleeds that I'd dismissed as minor inconveniences. With enlarged lymph nodes scattered throughout my body, my mind immediately went to worst-case scenarios. But as someone who's always focused on making the best of any situation, I accepted what was and began preparing for the journey ahead.

What I couldn't have prepared for was how a medical mishap would compound this crisis—and ultimately lead me to discover the true healing power of the piano method I'd spent years developing.

When everything went wrong

A couple of days after my WM diagnosis, my world was further rocked by a medical mishap following a biopsy, which led to weeks in hospital including intensive care. Suddenly, I had gone from thinking of myself as incredibly healthy to someone barely hanging onto life, with a very uncertain future.

The irony wasn't lost on me. For years, I'd been transforming lives through my DecPlay piano method, a patented system combining numbers and patterns that harnesses our natural musical ability without the barrier of traditional notation. Thousands of students aged 60 to 96 across 72 countries had discovered they could play songs within hours rather than weeks using this approach.

Many had shared remarkable stories of how learning piano provided mental, emotional, and even physical health benefits. I'd listened with interest, pleased that my method was helping people, but I didn't truly understand the depth of transformation they were describing.

Declan with his dog, Blue, in the studio

The DecPlay community was already thriving, we had our Piano Buddy program connecting students individually or in small groups, online private groups, and regular Zoom calls where people shared their musical progress and life stories. I knew logically that students gained great support from this community, but I hadn't felt the emotional impact myself.

That was about to change.

DRC treatment and the power of music therapy

Once I was well enough to go home from hospital, I started several months of outpatient dexamethasone, rituximab, and cyclophosphamide (DRC) treatment. Unable to access my piano studio (which required walking up stairs), I decided to cheer myself up, and I made what turned out to be one of the most important purchases of my life: a grand piano. I positioned it right beside my recuperation chair, and something magical happened.

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Healing Power of Music, cont. from page 23

My brain fog meant I couldn't play complex pieces, but to distract me from the physical discomfort, I would reach over and randomly play a few notes, which I call "doodling." The beautiful resonance of the strings seemed to instantly soothe me, lifting my spirits and taking my mind away from pain. Each note inspired the next, leading to new songs being composed virtually every day. I felt more creative than I had since my early twenties.

Even more surprising were the songs that emerged unconsciously about my hospital experience. Though I didn't think I had emotions to process, music became my therapist, bringing out feelings I didn't even know I had. One particular song about my trauma took me fifteen attempts to record before I could get through it without tears.

Finally, I understood what my students had been telling me for years. Music wasn't just entertainment or a hobby—it was healing. This led me to develop a simple technique to enable absolute beginners to "doodle" on piano, for relaxation or distraction from discomfort and pain.

The IWMF revelation

During my treatment, it was heartwarming to see the messages of support and genuine care that flowed from the DecPlay community. However, it was attending the IWMF/WMUK conference in London several months later that provided another profound "aha moment." Being around people in a similar position, sharing experiences, making genuine friendships, I suddenly understood the emotional impact of community in a way I never had before. It was exactly like our DecPlay Buddy program, but now I felt it from the inside.

The parallels were striking: just as my piano students found healing through music and connection, I discovered the same dynamic in the WM community. We weren't just sharing medical information, we were sharing hope, understanding, and mutual support.

Meeting medical professionals like Dr. Shirley D'Sa and connecting with other WM patients reminded me that healing happens not just through treatment, but through community and shared experience.

Stories that inspire

Among my students, the transformation stories continue to amaze me. Claudine, who promised herself during cancer treatment that she would learn piano once she finished, is not only playing beautifully, but she has evolved to become a community leader. She shares how the experience has massively boosted her confidence, helped her mental health, and given her a huge sense of fulfillment.

Alex, at 85, discovered that playing piano has brought him great joy and helped manage his anxiety and depression. It also helped him with a number of medical issues, including regaining movement in his arm after a stroke.

When I started creating my piano course, I wanted it to be friendly and informal, so I allowed my collie Blue to wander in and out of the video recordings as she pleased. Blue has become a favourite with our students and has made me realise that for many students, especially those who live alone, a pet can be another form of therapy.

The Health and Piano podcast

After experiencing firsthand the transformational power of music during my own recuperation, combined with the profound support and valuable insights I gained from the WM community, I was inspired to create the Health and Piano podcast. I realized I was uniquely positioned, having access to tens of thousands of DecPlay subscribers with countless inspirational stories of health transformation through music, to combine practical tips, student stories, and medical expert interviews into a resource that could help others.

Dr. Shirley D'Sa was a recent guest, discussing topics of interest to WM patients, including managing stress, holistic health approaches, optimizing medical consultations, and the importance of social connections. You can view the video podcast at *decplay.com/podcast2.*

A silver lining from fragility

My WM diagnosis and medical crisis brought life's fragility into sharp focus. This experience, rather

Healing Power of Music, cont. on page 25

DecPlay Club group. Declan on the right

than being depressing, became liberating. It gave me a huge sense of gratitude and appreciation for things I had taken for granted, like walking, eating, not being in constant pain and even just being alive. It also helped me to gain clarity on what is important in my life and has clarified my sense of purpose.

It became clear that I'd been given an extraordinary opportunity: to combine my teaching method, the experiences of my student community, and my personal understanding of illness, to help others in a deeper way. Teaching piano was no longer the end goal, it became the vehicle through which I could help people improve their health and wellbeing through fun, creativity, and connection.

Current health

Over a year since finishing DRC treatment, my blood results continue improving, and I don't have any significant WM symptoms. I feel incredibly fortunate to have access to such effective treatment and to have recovered so well. But more than that, I've discovered that helping others creates an enormous sense of wellbeing, perhaps the most powerful therapy of all.

My illness has led me to deep reflection on life's priorities. I don't take time or health for granted anymore, and I've discovered that I've been given an opportunity to use my gifts and experience to help others, which feels deeply fulfilling.

A future of hope and action

Living with WM has forced me to face life's uncertainty, but I've realized it's also given me a unique opportunity to focus on what truly matters. For me, that's been discovering how my gifts and experiences can help others find healing through music and community.

I would encourage everyone to consider engaging with communities and support services from organisations like IWMF and WMUK. My experiences with the conference, group Zoom calls, and support line have given me a deep sense of connection. There's something powerful about being with people who understand your journey. Supporting others in a community creates an incredible sense of purpose, and many people have existing life skills and experience that, when shared, can genuinely support others, creating something beautiful from challenging circumstances.

Beyond community support, you might also discover the therapeutic benefits of a creative hobby, such as piano, music, gardening, singing, art, indeed anything that connects you with others and genuinely brings you joy.

FINANCIAL ASSISTANCE AND OTHER SUPPORT FROM THE PAN FOUNDATION

By Amy Niles, Chief Mission Officer, PAN Foundation

At the PAN Foundation, our primary goal is to accelerate access to affordable, equitable healthcare for patients. As the Chief Mission Officer at PAN, I am proud to be a part of a national charitable assistance and healthcare advocacy organization that has helped more than 1.3 million people living with chronic, rare, and life-threatening conditions—including thousands living with Waldenstrom macroglobulinemia (WM).

Our financial assistance programs help people afford their health insurance premiums, copays, and other treatment costs, as well as transportation to support their care. We also address ongoing barriers to care of patients by advocating for policy changes and empowering people through education as they navigate their healthcare journey.

Immediate financial help for WM patients

Through a dedicated WM program, PAN has immediate financial assistance of up to $13,500 per year for WM patients to cover the cost of treatment-related deductibles, copays, and coinsurance. If you or a loved one is living with WM, you could receive an initial grant of $9,500 and can receive additional funding for up to $13,500 total per year.

How our financial assistance works

PAN provides patient assistance grants for more than 80 diagnoses, including WM. Through these grants, we offer a fast, reliable way for eligible patients to get help paying for their out-of-pocket prescription medication costs, health insurance premiums, and transportation expenses. Our online eligibility checker helps patients find out whether they qualify for any of these funds in minutes.

Our grants often cover 100% of out-of-pocket costs. And we cover products that are FDA-approved or listed in an official compendia or evidence-based guidelines for each disease. This includes brand and generic medications.

You can apply online through the PAN portal or by phone. If you're new to PAN, please apply by phone at 1-866-316-7263 Monday through Friday, 9am to 5:30pm ET. In most cases, approved applicants can begin using their grants immediately.

Don't miss out on this opportunity!

PAN has significant funding available for those living with WM today. We encourage you to check your eligibility and see if you qualify for a grant.

Eligibility criteria

To qualify for our WM fund, you must:

- Be in active treatment for WM.
- Reside and receive treatment in the US or a US territory (citizenship not required).
- Have health insurance that covers your prescribed WM medication.
- Be prescribed a medication on PAN's covered medication list. PAN covers all FDA-approved treatments listed in official compendia and in published evidence-based or clinical guidelines. See the list for WM at *https://www.panfoundation.org/disease-funds/waldenstrom-macroglobulinemia/*.
- Have a household income at or below 500% of the Federal Poverty Level. Examples:
  Household of 1: Up to $78,000
  Household of 2: Up to $105,000
  Household of 3: Up to $133,000
  Household of 4: Up to $188,000

Enroll today

Funds are available immediately, and the application process is fast and straightforward—it takes under

Financial Assistance and Other Support, cont. on page 27

ten minutes. Once approved, you can begin using funds right away, with a 90-day lookback period.

Our advocacy and education initiatives

In addition to our financial assistance programs, we are also committed to supporting patients in their healthcare journey through our advocacy and education initiatives. In our role as a national healthcare advocacy organization, we're committed to amplifying patient voices around key policies that improve access to care. Go to *https://www.panfoundation.org/our-advocacy-work/*.

And as expert educators, we are dedicated to breaking down complex topics in a way that empowers patients, community leaders, and healthcare professionals along their healthcare journey. See *https://www.panfoundation.org/education-initiatives/*.

Topics include:

- Recent Medicare Part D reforms
- The federal Extra Help program
- Copay accumulators and maximizers
- Alternative funding programs
- Financial assistance

PAN resources

Website: *panfoundation.org*

Phone: 1-866-316-7263

Sign up for PAN Foundation updates: *https://www.panfoundation.org/subscribe/*

We want to help you focus on what matters most—your health and well-being. We encourage you to apply today at *https://www.panfoundation.org/apply-and-manage-grants/applying-for-grants/*. Thank you for trusting us with your healthcare journey.

FROM THE FACEBOOK WM SUPPORT GROUP: FALL 2025

By Betty Ann Morton, Editor

As a now-retired teacher, I still think of fall as the beginning of my year. That means it's a time to make decisions and plans about what I'll be doing this year. One plan is to pay attention to various aspects of my health. As I've been doing for many years now, I will continue seeing my WM doctor regularly. However, I've been thinking about all of the various support groups and opportunities that IWMF provides for each of us. I have found support in my local Chicago area support group that meets several times a year, but there is also the Facebook WM Support Group page, along with weekly WM chair yoga and additional classes provided by Ann Grace MacMullan and others through the WM Wellness community. The classes generally conclude with conversation; participants share struggles, joys, and suggestions. Regular participants morph into a community, which always has room for more.

When people ask to join the Facebook WM Support Group, they frequently say they are looking for support and for information. Support might be answering questions about WM, telling how and why to connect with an expert doctor, explaining why watch-and-wait may be appropriate, encouraging someone to seek medical attention, sharing ideas about "what worked for me," or simply (and importantly) saying, "I feel that way too." Support comes in many packages.

Shelly Postek, IWMF's Director of Information and Support, has been busy helping to organize not only new geographical support groups, but also affinity groups, including Young WM (under 50), WM People of Color, Bing-Neel Syndrome, WM Military Veterans, Watch and Wait, and Peripheral Neuropathy.

Shelly recently wrote on Facebook, "Hello everyone. We are getting some new geographical support groups started in a few areas. Please let me know if you live nearby and would like to get connected to the new leaders!

- Austin/San Antonio TX
- SE Florida (Ft. Lauderdale area)
- SW Florida (Ft. Myers/Naples area)

"Get in touch with me if you want to connect with our new leaders for these areas! And if you are inspired and would like to get a group started in YOUR area, email me at *mpostek@iwmf.com*!"

The Facebook WM Support Group is always available to members. No need to wait for a meeting to get support.

Recently **DSC** wrote, "I just joined yesterday. My husband was diagnosed in August 2022, and the watch-and-wait period is coming to an end. We're waiting for tests/PET scan to come back, then an appointment with the oncologist for the next step in the journey."

JS responded, "It's the day I dread. Any advice for the spouse during watch-and-wait? I feel like I'm on high alert watching for everything that is a symptom."

LJ replied, "**JS**, my thoughts are with you. All I can say is just breathe, one day at a time. It helps with anxiety as a spouse and a caregiver. You do need to also look after yourself so you are rested, both physically and mentally, as much as you can be. It is OK to cry. Just enjoy each moment. My husband was diagnosed 26 June and has just started his first round of treatment on 3 July, so just navigating it, five more rounds to go.

KM from Denmark posted about her caregiving experiences. "As a partner you can do a lot of supporting things during treatment. But don't forget yourself and your own interests and network, because then there's a risk that you can burn out. There are lots of way to be supportive. I have been together with him for all the tests, the meetings, and all the times he went for treatments (six rounds of rituximab and bendamustine, B and R). And as you easily get confused about all the information, I've been taking notes at every meeting in a big notebook and we've been discussing beforehand what questions he should ask. Usually we share all the work at home, but of course I took the better part

From the Facebook WM Support Group, cont. on page 29

after the treatments. I cooked all his favourites in order to stimulate his appetite."

Newly diagnosed member **MFF** shared her feelings. "I just got diagnosed through a bone marrow biopsy. I'm a little freaked out. My oncologist says we will wait and watch my bloodwork; no treatment at this time. I guess that's a good thing. I don't think my husband understands that I'm scared, and he is making me feel it's no big deal."

NH quickly responded. "Hi, we've all been where you are now, listening to words that don't feel they belong to you and fearing the worst. It takes time to get comfortable and understand your own brand of WM and what it means for you. We are all so very different—some on active monitoring for years, as their WM was found by accident whilst checking something else out and having few symptoms. Others are massively anaemic or have other big symptoms affecting their quality of life and needing more immediate treatment. The good news is there are several very effective treatments when you do need them. You have time to understand your options and get comfortable; WM treatment is seldom an emergency.

"My best advice is to find a doctor you can talk to and who understands WM. Your relationship with them will be a long one. Check out the IWMF website for information; there is a whole range of webinars and other information. Maybe your husband would be open to watching a few too. He's also in a new and scary place and we all cope with it differently."

Here's a note from a new member **SK**. "Good morning to all my WM family. I joined last week and, not being an avid FB poster/member, I completely missed so many warm welcome messages from so many of you. I want to express my gratitude for all the lovely messages I received. I was reluctant to join the group, because I feared there would be a lot of depressing posts. Much to my surprise, you all are AMAZINGLY upbeat. I join you all in support of healing and maybe even finding a cure someday. Thank you all so very much."

Group members frequently share news about their progress or setbacks, either because they have questions or because they want to celebrate or worry with their community. Sometimes posts have a mixture of feelings.

FTW's recent post read, "We interrupt this program to bring you an important message…Brukinsa (zanubrutinib) works wonders! Now in the fourth month of taking this extremely high-priced drug, blood test results indicate significant improvement in WM-related markers." After giving details, FTW added, "Side effects from use of Brukinsa appear minimal. Constipation is often a companion (although this may result from significant travel); neuropathy is nonexistent and fatigue is fictional. My primary care physician ordered an electrocardiogram, and the results will be discussed with my oncologist when we next meet. That's something to be aware of, but nothing to worry about. We now return you to your regularly scheduled program."

CPM joyfully wrote, "Hi! I just wanted to share my husband's IgM results from today. He's finally in the green (normal)! He was over 8,000 (g/dL) in the summer of 2023."

HMS's response read, "This gives me hope! I was 8,000 in June and currently on B and R treatment for 4-6 cycles."

CKL wrote, "Yay!!! I was on B and R in the fall of 2023. My IgM was at 5,500. My bloodwork from last week showed my IgM at 275!!!"

CPM responded with more details, "Thanks for all the wonderful comments. My husband started with a five-day inpatient stay to do three rounds of plasmapheresis in October 2023. Then he went on Brukinsa in the fall of 2023 to the spring of 2024. It worked initially, but his numbers started to rise. In April 2024 he started four rounds of DRC (dexamethasone along with rituximab and cyclophosphamide). In August 2024 he started venetoclax (800 mg) daily with rituximab infusions every two months. We are going to Dana-Farber Cancer Institute in September to review his meds and see if there should be any changes. There is a huge difference in his energy level since the summer of 2023. He has lost weight on venetoclax because it

From the Facebook WM Support Group, cont. on page 30

seems to affect his appetite. Thanks, everyone. Hang in there!"

Members also use the Facebook WM Support Group to request information to help guide their own WM-related decisions. For example, **APM** posted, "I am looking at knee replacement and on Brukinsa. I will talk to my oncologist later this week but wondered if anyone has been through this. Any information on their experience would be helpful. Thanks."

AWL described her own experience, "I had a knee replacement three years ago, and I'm on Imbruvica. No issues; I stopped the Imbruvica five days before and five after. I am fortunate not to have any effects when I temporarily stop Imbruvica (ibrutinib). Recovery from the surgery was uneventful—a few weeks using a walker and physical therapy for a few months. I couldn't drive (it was my right knee) for about four weeks."

KL added, "It shouldn't be an issue. You will probably need to stop Brukinsa before and after for a short hold. I was off for a week. I took low dose steroids for withdrawal symptoms."

MCM contributed information from the US NIH. "About 25% of patients develop BTK inhibitor withdrawal syndrome. You should be alert for symptoms that may include fever (unresponsive to antibiotics), body aches, night sweats, joint pain, chills, headache. Discrimination between withdrawal syndrome, infection, or disease progression can be challenging, so close monitoring is advised. Prednisone (10 mg, 2 times/day) may be used to control withdrawal symptoms if needed." *https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6029546/*

If you have questions, comments, worries, suggestions, or experiences to share, please join us. Or perhaps you prefer to lurk in the background, reading the posts, but not commenting. You're welcome, too.

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*.

IWMF INTRODUCES NEW SUPPORT GROUP LEADERS

Compiled by Sharon Rivet, Support News Group Editor

Bev Johns

Bev Johns – South Florida East Coast Support Group

My husband, LJ, a businessman and an activist in our community in central Illinois, had been energetic and purpose-driven for many years. But he was losing his energy, having stomach issues, and getting thinner, when he really couldn't afford to do so. He went through tests to see what was wrong.

So began our journey to find a diagnosis. Originally, LJ was thought to have multiple myeloma, but the bone marrow and eye tests confirmed that it was WM. We were given a manual on it to study. We discovered Dr. Daniel Dammrich at Holy Cross Hospital in Fort Lauderdale, who was the perfect match for my husband. He could read him like a book and was very sensitive to his needs. LJ's journey with WM will be ten years old this Labor Day weekend.

As his spouse and partner for 52 years, I have taken this journey with LJ through a variety of treatments. Having been in the field of special education, I knew the importance of advocacy and the need to get support. When we moved to Florida, I attended a Blood Cancer Forum to learn more about WM and looked for a support group. I found a great one, the Fort Lauderdale Support Group, just before the pandemic, and I am filled with gratitude for the help they gave us. We met on Zoom during the pandemic but slowly became inactive, and a search for a new leader began. I agreed to become the leader because I wanted to give back to IWMF for helping us. I am also grateful for the Facebook WM Support Group and its administrator, Meg Mangin, for helping us through our journey.

Charles Newton

Charles Newton – South Florida West Coast Support Group

I am a cardiothoracic surgeon and hospice and palliative medicine physician who retired 13 years ago. My plans following my retirement were simply to spend more time with my wife, children, and grandchildren—people who too often were neglected because of the demands of my profession. This year, however, my new WM diagnosis (with the question of treatment response and tolerance), plus my recent shingles outbreak and subsequent neuropathy, have impacted my capacity to travel and perform even small physical tasks. Early in my WM treatment, I sought out a local support group through IWMF, but found there was none. When Shelly Postek reached out for a volunteer to initiate a Southwest Florida group, I raised my hand, knowing that my wife, Anne, with her superb social skills, would assist. Anne and I both attended the IWMF Ed Forum this past May, where we met Shelly and several support group leaders, solidifying our resolve to move forward. After nearly 50 years of visiting, consulting on, and caring for patients facing a life-altering diagnosis, I am now the patient.

Anne and I are eager to initiate and nurture a similar program to offer support to all of us challenged in some way by WM and living here in beautiful southwest Florida. We are excited for our first meeting which will be a hybrid format (in-person and virtual) scheduled in September!

IWMF Introduces New Support Group Leaders, cont. on page 32

IWMF Introduces New Support Group Leaders, cont. from page 31

Jane Cox

Jane Cox – Northern Virginia, Washington DC, and Maryland Support Group

When I was diagnosed with WM in 2017, it was shocking to me. I remember sitting in the oncologist's office being told that it was either multiple myeloma or WM. Three weeks later, my bone marrow biopsy confirmed WM. I was dealing with extreme fatigue, breathlessness, and the inability to walk from one room to the next without feeling like I would pass out. I was hospitalized on that day, and I began bendamustine and rituximab treatment after two plasmapheresis sessions to lower the IgM. It was a whirlwind experience that didn't allow me time to process what I was going through or participate in the decision-making about my treatment plan, because of my lack of knowledge and the urgent nature of my symptoms. It has now been eight years since my diagnosis.

During the first year of my diagnosis, I attended a local IWMF support group meeting. It was an extremely informative presentation by Dr. Steven Treon of Dana-Farber Cancer Institute. I was surprised at the number of participants who had only been diagnosed one to two years prior, and many did not know about IWMF Connect and the Facebook WM Support Group. These were my lifelines in learning about our disease. It was awesome to be able to share that information with these groups.

After the recent February meeting, Shelly Postek from IWMF asked me to be a support group leader, which gave me the opportunity to participate in the excellent support group leader trainings. Being a support group leader allows me to provide timely information, tools, resources, and opportunities for conversations with others with WM. It can be a lonely walk dealing with this disease. I love being a part of a group where I can build relationships with other WM patients, have a sense of community and trust, and meet others who know about our rare disease.

Left to right: Dianna and Miriam (Las Cruces, NM), Rebecca (El Paso, TX)

Rebecca Vidales – El Paso/Las Cruces Support Group

I was diagnosed with WM and multiple myeloma in November 2021 while working as a nurse. I had tumors in my bones, soft tissues, spleen, and other areas in the lymph system. I started bendamustine and rituximab in December 2021. The treatment was taxing my system, so I retired from nursing after 44 years and finished my treatment cycles.

I immersed myself in research. In 2023, I remotely attended the IWMF Ed Forum. I submitted a question, but time did not allow for all of them to be answered. Soon after the conference, I got a text from Steve Pine, who saw my question and responded. Steve was at the Ed Forum and is a support group leader in Dallas. He invited me to his support group meeting that I attended remotely.

Steve's support group ignited a fire in me. I began to live with WM as part of my life instead of building my life around it. I wanted others to benefit as I did. I wanted to make myself available and volunteered to become a support group leader for a new support group located in the area of El Paso, TX/Las Cruces, NM. I framed the support group meetings after Steve's model, in which he positively impacts WM lives and is a motivator to all who attend! I hope others will discover they too can flourish despite having WM. We are excited to meet, greet, and share. Thank you for the opportunity to be a part of an outstanding organization. Looking forward to seeing y'all!

BEN RUDE HERITAGE SOCIETY

The Ben Rude Heritage Society recognizes those who have made provisions for a future gift to IWMF, such as a bequest, listing 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 IWMF's financial future. There are many ways to support 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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BETWEEN JUNE 11, 2025, AND SEPTEMBER 9, 2025, CONTRIBUTIONS TO INTERNATIONAL WALDENSTROM'S MACROGLOBULINEMIA FOUNDATION WERE MADE IN HONOR OF

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