IWMF TORCH

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INSIDE THIS ISSUE

A VISITOR'S ASH EXPERIENCE

BY PAUL KITCHEN, CHAIR OF THE IWMF BOARD OF TRUSTEES

Paul Kitchen

Editor's note: Paul Kitchen, former Chair of WMFC (Canada) and now Chair of the IWMF Board of Trustees, was one of three IWMF officials representing the organization at the 66th American Society of Hematology (ASH) Annual Meeting in San Diego in December. Here is his account of his experience at that meeting; selected abstracts concerning WM presented at the meeting are then summarized.

Make no mistake, although the full name of the ASH Annual Meeting starts with the word "American," this is a global meeting. It is the largest meeting of hematologists in the world, with over 30,000 attendees from more than 100 countries.

The only way IWMF, as a small organization, can have influence in the global hematological world is by forming partnerships. IWMF partners with LLS (Leukemia & Lymphoma Society), American Cancer Society, WM European Doctors' Consortium, NCCN (National Comprehensive Cancer Network), Lymphoma Coalition, Cancer Support Community, Cancer*Care,* NORD (National Organization for Rare Disorders), and many more. We also have partnerships in the pharmaceutical world helping to inform WM patients of clinical trials, the availability of new drugs, and the direction of the latest research.

The ASH Annual Meeting is the perfect setting for IWMF to meet other patient advocacy organizations, partners, and leading-edge cancer researchers, including those we are currently sponsoring. With the numbers in attendance and the huge, multiple football field-size space in the San Diego Convention Center, there are lots of opportunities to meet these organizations and share information.

I attended with our former IWMF CEO Newton Guerin, who helped show me the ropes, and Dr. Tom Hoffmann, IWMF Vice-Chair, Research. One real opportunity for us was to visit the various pharma organizations and discuss areas of mutual interest: drug development, clinical trials, and priorities that pharma has and that IWMF is contemplating. In that vein, we met with AstraZeneca, Nurix, BeiGene, and Lilly. Each meeting was prearranged, and Newton and I were able to visit and understand how we could work together with pharma to help accelerate the cure for WM. Every partnership must be a two-way street.

We also had meetings with LLS representatives, who have been such a help to us in setting up our Strategic Research Roadmap Initiative, and with the Mayo Clinic.

A Visitor's ASH Experience, cont. on page 3

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From these meetings, I learned about their directions and priorities as we enter a new year. LLS had lots of news of exactly where they are going and how they are going to rebrand.

With ASH attracting so many attendees, we were able to gather with several of the widely-scattered members of the IWMF Scientific Advisory Committee (SAC). Co-chaired by Dr. Stephen Ansell from the Mayo Clinic and Dr. Steven Treon from the Dana-Farber Cancer Institute, the IWMF SAC includes leading WM researchers and clinicians from around the world. We had an hour-long discussion about the priorities and direction of the SAC, and on the last evening, we had a lovely meeting with the WM-NET research center participants. WM-NET has been established to enable clinical trials involving WM therapies to take place at multiple centers. Presently we have 22 WM-NET sites across the US, making it much easier for clinical trial enrollment. If 30 patients are needed for a clinical trial, to gather all 30 at one site is a huge challenge. But if you have six different sites and each site averages five patients, the clinical trial can enroll and become active more quickly.

At ASH, we saw abstracts about research that reported both interim and completed results. Sometimes the abstracts dealt with clinical trials, sometimes with basic scientific research trying to answer a question. Every evening the abstracts from that day were taken down and a new set put up. There were thousands and thousand of abstracts, with some focused on WM, each day. Many of these abstracts were from the young researchers we are sponsoring across the world. One of the really satisfying realizations for me was that every abstract about WM thanked the IWMF as a sponsor.

I appreciate the opportunity of attending ASH and seeing just how crucial it is that we are seen as an active partner in the fight against blood cancers. We represent a small percentage of those with blood cancers, but our disease is unique because of its effect on the bone marrow and potentially other organ systems. Because of WM's indolent nature, it is an ideal disease to study and thereby help understand not only WM but also other non-Hodgkin's lymphomas.

As we talked to leaders of huge organizations like LLS or AstraZeneca, we learned that they know of WM and the great work that IWMF is doing, and we realized that IWMF is respected and well-known among other blood cancer advocacy organizations, pharma companies, and hematologists around the world. Because of our partnerships, our investment in research, our clear strategic vision, and the strong support of WM patients like you, IWMF "punches" well above our weight. Thank you for your support that has helped make this possible. I was proud to represent you at ASH. With your continued support, we will work with our partners to support the goals of our "Accelerate the Cure Campaign" for WM.

DID YOU KNOW?

IWMF HAS UPDATED ITS POPULAR FAQ BOOKLET

IWMF's popular *Frequently Asked Questions* booklet is in a very readable format designed for those who are new to WM or who may not have a strong background in biology. The updated booklet has even more of the important questions that we all ask and want answers to when we are diagnosed! Be sure to go to the IWMF and Affiliate Publications page of the IWMF website at the following link where you can download it in English. While you're there, check out our other publications, including a new Fact Sheet on the BTK inhibitor pirtobrutinib!

https://iwmf.com/publications/

SUMMARIES OF SELECTED ABSTRACTS FROM THE 66TH ASH ANNUAL MEETING

By Sue Herms, IWMF Research Committee Member

The following are summaries of selected online abstracts of clinical trial results and prognosis and survival trends for WM that were selected for presentation during the 66th ASH (American Society of Hematology) Annual Meeting in San Diego, CA, on December 7-10, 2024. These and other abstracts can be found at https://ash.confex.com/ash/2024/webprogram/start.html.

Bortezomib in Combination with Ibrutinib/Rituximab Is a Highly Effective and Well Tolerated First Line Treatment for Waldenström's Macroglobulinemia: Results of the Multicenter Phase II Trial (ECWM-2) of the European Consortium for Waldenström's Macroglobulinemia (Abstract 859) – In this trial, 53 treatment naïve WM patients requiring therapy received six 28-day cycles of the combination of bortezomib, rituximab, and ibrutinib, followed by maintenance therapy with rituximab and ibrutinib for 24 months and then ibrutinib alone until disease progression or unacceptable side effects. For this so-called B-IR therapy, rituximab was administered intravenously for the first cycle, with subsequent cycles administered subcutaneously; bortezomib was dosed subcutaneously. Responses were rapid, and at best response, the overall response and major response rates were 100% and 98%, respectively. The proportion of patients with a combined very good partial response/complete response increased over time from 19% after six cycles to 38% at best response. Responses were mostly not influenced by the presence of CXCR4 mutations. The one-year progression-free survival rate was 93%. Grade 3 (severe) adverse events related to treatment occurred in 45% of participants, the most common events being COVID-19 pneumonia, lower respiratory tract infections, and anemia. All deaths (15% of participants) during the course of the trial were caused by respiratory infections, with COVID-19 as the primary cause, and it was noted that trial recruiting occurred during the height of the COVID-19 pandemic. Peripheral neuropathy was mild-to-moderate and occurred in 15% of patients.

Preliminary Efficacy and Safety of the Bruton Tyrosine Kinase Degrader BGB-16673 in Patients with Relapsed or Refractory Waldenström Macroglobulinemia: Results from the Phase 1 CaDAnCe-101 Study (Abstract 860) – This multicenter international study recruited patients with a range of B cell cancers to evaluate the use of the oral BTK degrader BGB-16673, dosed once daily. This abstract focused on the 22 patients in the study with relapsed or refractory WM, all of whom had received prior BTK inhibitor therapy. In contrast to BTK inhibitors like ibrutinib or zanubrutinib that suppress the BTK protein, BTK degraders target the protein for destruction by the cellular "garbage system" called the proteasome. In 21 patients eligible for evaluation, the overall response rate was 90%, the major response rate was 81%, and the very good partial response or better rate was 14%. Responses were seen in those with or without mutations in MYD88, CXCR4, and BTK. Treatment-related adverse events occurred in 95% of patients, the most common of which were low neutrophil counts, bruising, and diarrhea. No atrial fibrillation, high blood pressure, low neutrophil counts with fever, or major hemorrhage occurred. Three participants (14%) did experience severe infections, one of whom died. Another patient died because of disease progression. At the time of this report, 17 patients remained on treatment.

Iopofosine I 131 in Previously Treated Patients with Waldenstrom Macroglobulinemia (WM): Efficacy and Safety Results from the International, Multicenter, Open-Label Phase 2 Study (CLOVER-WaM) (Abstract 861) – Iopofosine I 131 delivers a radioisotope of iodine that is toxic to the cancer cells it targets. Eligible WM patients in this study had received a median of four prior therapies, including BTK inhibitors. Treatment consisted of two cycles of iopofosine I 131 administered intravenously on days 1 and 15 of each 57-day cycle. Dose reduction was allowed in the second cycle if blood counts had

Summaries of Selected Abstracts, cont. on page 5

not recovered from the first cycle. Of 65 patients enrolled, 55 were eligible for evaluation in this updated report. The overall response rate was 80% in all patients; those with wild-type (unmutated) MYD88 had an overall response rate of 81%, and those with previous BTK inhibitor treatment had an overall response rate of 72%. The estimated progression-free survival rate at 18 months was 72%. Grade 3 (severe) or greater adverse events occurring in at least 10% of patients included low platelet counts, low neutrophil counts, anemia, low lymphocyte counts, infections, and low neutrophil counts with fever. There was one death because of bacterial sepsis (commonly called blood poisoning). *(Editor's note: Cellectar Biosciences recently announced that it is discontinuing further development and commercialization of iopofosine I 131, stating that the drug may best be brought to market by a larger organization with greater resources.)*

Bing-Neel syndrome (BNS) occurs in about 1% of WM patients when the WM cells invade the central nervous system...

Zanubrutinib Is Effective in the Treatment of Patients with Waldenström's Macroglobulinemia and Bing-Neel Syndrome: A Retrospective Multicenter Study (Abstract 1642) – Bing-Neel syndrome (BNS) occurs in about 1% of WM patients when the WM cells invade the central nervous system (brain and spinal cord). This Spanish study consisted of 11 WM patients with BNS treated with zanubrutinib between 2022-2024. Their most common symptoms were sensory deficits and visual abnormalities, followed by language disorders, motor deficits, and altered mental status. BNS was the first presenting feature of WM in six patients, while in five it was diagnosed during the course of WM, with a mean time from WM diagnosis to BNS of 8.2 years. Nine received zanubrutinib as their first-line treatment for BNS; the dosage was 160 mg twice daily in seven patients and 320 mg once daily in four. A clinical response to zanubrutinib was observed in eight patients, two with complete responses and six with partial responses. Two patients developed low neutrophil counts. With a median follow-up of seven months, the overall survival was 82%.

Two-Year Follow-up After Ibrutinib and Venetoclax in Symptomatic, Treatment-Naïve Patients with Waldenström Macroglobulinemia (Abstract 1647) – Dana-Farber Cancer Institute presented data after additional follow-up from the Phase 2 trial combining ibrutinib and venetoclax as first-line treatment of WM. Between July 2020 and January 2022, 45 participants were enrolled for what was intended to be a fixed-duration treatment of 24 months. The trial was halted because of four ventricular heart arrhythmia events. No patient completed the 24 months of treatment; instead, the median time on treatment was 10.2 months. At 36 months of follow-up, the progression-free survival rate was 51%, and the overall survival rate was 93%. There were two treatment-related deaths during the therapy and one death of unknown cause two years after therapy was stopped. CXCR4 mutations did not impact survival rates. No treatment-related adverse events, especially arrhythmia, were observed after treatment was stopped.

Zanubrutinib Plus Ixazomib and Dexamethasone in Newly Diagnosed Symptomatic Waldenström Macroglobulinemia: A Phase II Study Short Title: ZID for Waldenström Macroglobulinemia (Abtract 1648) – This trial from China evaluated zanubrutinib combined with the oral proteasome inhibitor ixazomib and dexamethasone (called ZID therapy) in 27 newly diagnosed symptomatic WM patients, who received the combination for up to six 28-day cycles, followed by zanubrutinib alone for up to 24 total cycles. Of 24 patients who completed the six combination cycles, the overall, major, and deep response rates were 100%, 95.8%, and 45.8% respectively. The median time to response was two months. Five of 22 patients had CXCR4 mutations, with no difference in the deep response rate between those with and without these mutations. With a median follow-up of 30.9 months, five patients had progressed. The median progression-free survival and overall survival were both estimated at 40 months. The most common adverse advent was hematological (low blood counts).

Summaries of Selected Abstracts, cont. on page 6

Real World Treatment Outcomes in the First Line Management of Waldenström Macroglobulinemia from the Global Patient Derived Data Registry, WhiMSICAL (Abstract 1654) – The WhiMSICAL (Waldenstrom Macroglobulinemia Study Involving CArt-wheeL) global data registry uses patient-reported data to address important research questions in the treatment of WM and is linked with data on quality of life. This study assessed outcomes and quality of life for patients treated with bendamustine and rituximab or with BTK inhibitors in the first-line setting. A total of 704 patients from 23 countries entered data into the registry, with the majority from the US and Australia; 501 underwent first-line treatment, the most common being the combination of bendamustine and rituximab. With a median follow-up of 45 months after first-line treatment, the time-to-next treatment was not significantly different between first-line bendamustine and rituximab vs. BTK inhibitors; however, patients on BTK inhibitors reported significantly improved quality of life. Additional assessments over time are planned.

Long Term Outcomes of Hematopoietic Stem Cell Transplantation in Patients with Waldenström's Macroglobulinemia. Report from the Lymphoma Working Party of the European Society for Blood and Marrow Transplantation (LWP EBMT) (Abstract 3010) – In the European Society for Blood and Marrow Transplantation registry, 772 WM patients underwent autologous bone marrow stem cell transplantation (using their own stem cells) from 2000-2021. The median follow-up was 4.6 years. At two, five, and ten years, the estimated overall survival rates were 89.4%, 70.4%, and 55.3%, respectively. From the same registry, 330 WM patients received allogeneic bone marrow stem cell transplantation (using donor stem cells) during the same period. With a median follow-up of 8.3 years, the two, five, and ten year estimated overall survival rates were 62.9%, 54.0%, and 47.3%., respectively. Graft vs. host disease, a serious complication of allogeneic transplantation, occurs when the transplanted immune cells from the donor recognize the patient's cells as foreign and attack them. The incidence of acute (occurs early) graft vs. host disease was 26.7%, while the cumulative incidence of chronic (occurs later) graft vs. host disease at five years was 45.5%. The researchers concluded that stem cell transplantation is still a viable alternative for some patients, even in the era of targeted pathway inhibitors, bispecific antibodies, and CAR T cell therapies for lymphoma.

...responses and outcomes of second-line therapy with ibrutinib were compared with chemoimmunotherapy...

A Phase II Study of Pirtobrutinib and Venetoclax in Previously Treated Patients with Waldenström Macroglobulinemia: An Interim Analysis (Abstract 3011) – A multicenter trial in the US consisted of a fixed-duration treatment combination of the non-covalent BTK inhibitor pirtobrutinib and the BCL2 inhibitor venetoclax. Therapy was given in four-week cycles. Cycle 1 consisted of pirtobrutinib only at 200 mg/day, with venetoclax added stepwise in increasing dosages during cycle 2; cycles 3-24 used the same pirtobrutinib dose along with 400 mg/day of venetoclax. Between May 2023-June 2024, 16 patients were enrolled. With a median follow-up of six months, a very good partial response was reached in 56%, a partial response in 31%, and a minor response in 13%, for an overall response rate of 100%. No complete responses occurred. Two patients experienced disease progression, both with wild-type (unmutated) MYD88 disease. The six-month progression-free survival rate was 84%, and the six-month overall survival rate was 98%. At the time of this report, there were no heart arrhythmia events. The trial expects to enroll 26 more participants.

Ibrutinib or Chemo-Immunotherapy as Second Line Treatment in Waldenstrom Macroglobulinaemia? A Real-Life Multicentre Study (Abstract 3013) – In this Italian study, responses and outcomes of second-line therapy with ibrutinib were compared with chemoimmunotherapy regimens in 169 WM patients who required treatment

Summaries of Selected Abstracts, cont. on page 7

at some point during the period 2008-2022. Of this number, 85 were treated with ibrutinib and 84 with chemoimmunotherapy (with bendamustine and rituximab therapy the most common, followed by dexamethasone, rituximab, and cyclophosphamide therapy and bortezomib-based regimens). The overall response rates were 84.7% for the ibrutinib group and 69% for the chemoimmunotherapy group; the ibrutinib group showed a better four-year progression-free survival (67%) than the chemoimmunotherapy group (48%), but there were no statistical differences in terms of time-to-next-treatment and overall survival between the two groups. Of patients within the chemoimmunotherapy group, bendamustine and rituximab therapy demonstrated the best progression-free survival.

Focal Symptomatic Bone Involvement with Waldenström's Macroglobulinaemia and Non-IgM Lymphoplasmacytic Lymphoma (Abstract 3023) – Unlike multiple myeloma, bone involvement is not typically described in WM/LPL (lymphoplasmacytic lymphoma). Researchers from the University College London Hospitals NHS Foundation Trust discussed a group of patients treated at their center for skeletal involvement or bone complications from WM/LPL. All patients had experienced skeletal pain, prompting further investigation. Of 570 patients diagnosed with WM/LPL, 17 (3%) had symptomatic bone involvement not otherwise linked to another condition. Median time from WM/LPL diagnosis to confirmed bone involvement was 53 months. Imaging with CT or MRI was used to diagnose bone involvement, with MRI determined to be the most sensitive imaging method. Limb involvement was present in 59%, axial involvement (spine and rib cage) in 47%, and skull involvement in 12%. Fracture was seen in only one of the 17 patients. Treatment was given to 14 patients, primarily with a variety of chemoimmunotherapy regimens. Radiation therapy was incorporated in three cases. Symptomatic improvement was seen in all, with complete resolution of symptoms in ten patients. Median follow-up from diagnosis of bone disease was 102.5 months, and 16 of the 17 patients were still alive at the time of data collection for this report.

Prognostic Significance of TP53 Mutations in Lymphoplasmacytic Lymphoma (Abstract 3024) – While the presence of TP53 mutations leads to a negative prognosis in multiple myeloma and chronic lymphocytic leukemia, its impact in WM is not well understood. The MD Anderson Cancer Center in Texas evaluated TP53 mutations in 255 patients at its institution with either WM, non-IgM LPL (lymphoplasmacytic lymphoma), or IgM MGUS (monoclonal gammopathy of undetermined significance), who had undergone gene testing on their bone marrow samples. Genes with the highest percentage of mutations were MYD88 (73%), CXCR4 (31%), IGLL5 (26%), ARID1A (11.5%), and TP53 (11%). TP53 mutations were most common in patients with symptomatic WM, followed by those with symptomatic non-IgM LPL and smoldering WM; no patients with smoldering non-IgM LPL or IgM MGUS showed these mutations. TP53 mutations were associated with a shorter median overall survival (50.4 months vs. not reached) and a significantly higher risk of death. No statistically significant differences were noted in the incidences of neuropathy, hyperviscosity, Bing-Neel syndrome, bone lesions, acquired von Willebrand disease, and cold agglutinin hemolytic anemia between those with and without TP53 mutations. The researchers concluded that TP53 mutation testing should be a part of routine clinical testing for LPL/WM patients and that new treatment strategies are needed to improve outcomes in LPL/WM patients with TP53 mutations.

The researchers concluded that TP53 mutation testing should be a part of routine clinical testing for LPL/WM patients...

Bing-Neel Syndrome – a Case Series of 46 Patients from the United Kingdom (Abstract 3039) – Central nervous system involvement with WM or

Summaries of Selected Abstracts, cont. on page 8

LPL (lymphoplasmacytic lymphoma) is termed Bing-Neel syndrome (BNS), a rare complication. Using the University College London Hospitals registry of WM patients, researchers there studied 46 patients with BNS between 2012-2024. A preceding diagnosis of WM/LPL was present in 34 cases, and the median time from WM diagnosis to BNS was 55 months. Symptoms included sensory and/or motor deficits in 21 cases, cognitive changes in eight, impairment of one or more of the cranial nerves in five, headaches in four, seizures in three, hearing loss in three, and eye or eye orbit involvement in two. In addition to magnetic resonance imaging (MRI), cerebrospinal fluid (CSF) testing was performed to diagnose the majority of cases, with the detection of the MYD88 L265P mutation in the CSF an important diagnostic factor. Patients whose CSF was negative for MYD88 L265P after treatment did not relapse in this study. High-dose methotrexate-based therapy had excellent response rates, but subsequent disease progression occurred in a majority of these patients at three years. Therapies using BTK inhibitors appeared to result in much-improved progression-free survival rates at three years.

Impact of Baseline Osseous Involvement on Outcomes in Patients with Lymphoplasmacytic Lymphoma (LPL)/Waldenstrom's Macroglobulinemia (WM) (Abstract 3737) – The Ohio State University assessed the presence of osseous (bone) involvement on outcomes in patients with LPL/WM seen at its institution. They defined bone involvement as the presence of lytic bone lesions (areas of bone destruction that appear as holes), bone lesions noted on PET scans, pathological fractures, or osteopenia/osteoporosis not explained by other reasons. A total of 77 LPL/WM patients were identified, 20 of whom (26%) had bone involvement at diagnosis. Patients with bone involvement tended to be older at diagnosis and at treatment initiation and were exclusively of the White race. Treatment types varied; among treated patients, the overall response rate, major response rate, progression-free survival, and overall survival were similar in patients with and without bone involvement.

A Phase II Trial of Loncastuximab Tesirine in Patients with Previously Treated Waldenström Macroglobulinemia (Abstract 4404) – This multicenter trial, part of the recently established WM-NET clinical trial network, is continuing to enroll previously treated WM patients with at least two lines of therapy, including rituximab and a BTK inhibitor. Loncastuximab tesirine is a CD19 antibody drug conjugate that targets the CD19 surface antigen on B cells (including malignant B cells) and delivers a toxic payload to kill those cells. This intravenous therapy was administered once every four weeks for a total of six doses. To date, the first seven patients have enrolled out of an anticipated total of 36. Early data demonstrated an overall response rate of 86% in these patients, with three achieving a very good partial response, three a partial response, and one with progressing disease. One patient with a very good partial response later developed the central nervous system complication called Bing-Neel syndrome. Toxicities included skin rash, fluid retention, low blood counts, and asymptomatic elevation of the liver enzyme GGT (gamma-glutamyl transferase).

Patients with bone involvement tended to be older at diagnosis ... and were exclusively of the White race

Clinical Outcomes of Lymphoplasmacytic Lymphoma/Waldenstrom Macroglobulinemia (LPL/WM) in the Targeted Therapy Era: A US Multicenter Retrospective Analysis (Abstract 4392) – Researchers assessed 709 patients diagnosed with LPL/WM between January 2003 and March 2024 at seven US academic centers. An IgM monoclonal protein was present in 98% of all patients, followed by IgG in 1% and IgA in 0.4%. The MYD88 mutation was present in 85% who were tested; mutations in CXCR4 and TP53 were present in 5% and 14%, respectively, at diagnosis. During this period, 20% of patients did not require treatment. Of those who did, the most common first-line treatment was chemoimmunotherapy (primarily bendamustine and rituximab, followed by cyclophosphamide and

Summaries of Selected Abstracts, cont. on page 9

rituximab combinations), single agent rituximab, BTK inhibitors, proteasome inhibitors, and chemotherapy alone. The highest overall response rate was for chemoimmunotherapy at 68%, followed by BTK inhibitors at 54%, proteasome inhibitors at 53%, and single agent rituximab at 34%. The median time-to-next-treatment between first- and second-line therapy was longest with chemoimmunotherapy at 79 months, followed by BTK inhibitor therapy at 60 months, chemotherapy alone at 40 months, and single agent rituximab at 31 months. For all patients, the seven-year and ten-year overall survival estimates were 81% and 74%, respectively.

Prognostication in IgM and Lymphoplasmacytic Lymphoma Associated Systemic AL Amyloidosis (Abstract 4684) – This study from University College London Hospitals NHS Foundation Trust discussed IgM-associated systemic light-chain (IgM-AL) amyloidosis, which accounts for 7% of all systemic AL amyloidosis. This type of amyloidosis is a condition that results in misfolding of the monoclonal IgM antibody light chains, which subsequently deposit in tissues and organs and interfere with their normal function. Included in the study were 221 patients treated from 2012-2024. A median of two organs were affected, the most common being kidneys, heart, soft tissue, liver, and peripheral nerves. Lambda light chains were involved in 67% of patients and kappa light chains in 33%. Study participants were treated with a variety of first-line therapies, primarily either bendamustine-based or bortezomib/cyclophosphamide/dexamethasone-based; none in this study received an autologous stem cell transplant (using their own stem cells). At a median follow-up of 46 months, the median overall survival was 58 months, and longer for bendamustine-based than other therapies. The researchers noted that survival for IgM-AL appears to have improved from their previous report (58 months in this report vs. 42 months in a previous report). Survival is still largely dependent on the IgM level and the presence of heart involvement.

"Birches" by Diane Mazza

THE 2025 IWMF GIVING CHALLENGE – YOUR PASSPORT TO ACHIEVE A WORLD WITHOUT WM

This year, you and your family are invited to take a vicarious worldwide tour to visit researchers funded by our "Accelerate the Cure" campaign. For TEN days—from April 8 to April 17—the 2025 Giving Challenge will be your passport to find out how we can achieve a world without WM. From the comfort of your computer or smartphone, you'll go to Minnesota, Italy, Australia, New York City, and Boston. Along the way, you'll meet with dedicated researchers working to cure our rare cancer. This is an all-out opportunity to support their work.

How? Your gifts up to $1,500 will be DOUBLED during this Giving Challenge. That's right—generous individuals have pledged over $250,000 to make your donation go a lot further. You give $100, and the IWMF will receive $200; you donate $1,500, and the IWMF will receive $3,000—all to fund research to find a cure for WM.

So, grab your digital passport and come along on video visits to five "rock star" scientist-physicians. Here's our tour itinerary:

1. **Rochester, Minnesota: The Mayo Clinic** – Paul Kitchen, Chair of the IWMF Board of Trustees, kicks off the tour on *Tuesday, April 8*, with an e-blast from New Brunswick, Canada, to our WM community. He and his news correspondent will then land at the Mayo Clinic lab of Dr. Stephen Ansell, who will share research about genetic changes in WM cancer cells that seem to create surface proteins which make them invisible to the immune system.

Dr. Stephen Ansell

Dr. Simone Ferrero

2. **Turin, Italy: Universita Di Torino** – On *Thursday, April 10*, we arrive in Italy for a visit with Dr. Simone Ferrero, an IWMF-funded researcher. Dr. Ferrero will tell us what he's discovered about WM blood biomarkers—research that might mean fewer bone marrow biopsies in your future.

The 2025 IWMF Giving Challenge, cont. on page 11

3. **Sydney, Australia: Concord Repatriation General Hospital** – The tour continues in the "Land Down Under" on *Monday, April 14*. We'll visit with Prof. Judith Trotman, Director of the Clinical Research Unit in the Hematology Department. Prof. Trotman will explain her advice to patients about "playing the long game" and will reflect on clinical trials and their critical role in accelerating the cure.

Prof. Judith Trotman

Dylan Gagler

4. **New York City, New York: New York University, Langone Medical Center** – Jet back to the States on *Wednesday, April 16,* as we join Dylan Gagler, a young investigator working on an IWMF-funded project in the lab of Dr. Gareth Morgan in New York City. We'll learn about the field of bioinformatics and emerging research on WM subtypes, with the day coming when disease subtypes call for specific treatment protocols.

5. **Boston, Massachusetts: Dana-Farber Cancer Institute** – The last 24 hours of the Giving Challenge on *Thursday, April 17,* land on the birthday of Dr. Jan Waldenström, the man who first described WM in 1943. While we honor Dr. Waldenström, Dr. Steven Treon will reflect on today's global collaboration to find a cure.

Dr. Steven Treon

Join the tour and absorb the infectious enthusiasm of researchers working on our behalf. Donate as generously as you can. Every dollar, euro, pound, yen, and renminbi counts, so remember that double match!

Invite your friends and family to donate. After all, finding a cure is up to each one of us. The IWMF gets no support from government. Our funding comes entirely from the WM community. Don't be bashful. Your personal network of family and friends will enjoy giving a gift that doubles, as an expression of love for you.

The more funds we raise, the more we invest in research. The more research we fund, the closer we move to a world without Waldenstrom's macroglobulinemia. So join us April 8-17 on our world tour and have your donation doubled! Go to *https://iwmf.com/wm-giving-challenge/***.**

WATCH-AND-WAIT? WATCH AND LIVE

By Paul Bryan, Southern New Jersey/Eastern PA Support Group

I was diagnosed with Waldenstrom's macroglobulinemia (WM) in October 2022, and, while it may sound strange to say, the news and its timing fit right in with other changes occurring in my life at that time. Frankly, it all made sense.

Everyone with WM has their own, unique diagnosis story. My path, oddly enough, started because I was feeling great. I had recently changed jobs—stepping down from the most all-encompassing, challenging, rewarding, and stressful position of my lengthy career as a college administrator. I had lost weight and was in excellent physical condition, so I applied for an upgraded life insurance policy. It was the life insurance physical that raised a red flag and, after much follow-up testing, led to my diagnosis. Unsurprisingly, I did not qualify for the new policy.

Two and a half years later, I am still on watch-and-wait, which, as I've learned, has its own challenges. With the knowledge that WM will continue its slow growth, I have a seemingly built-in, plausible explanation for any health concerns that come up.

This past fall, I was experiencing significant pain and the loss of sensation in my right hand and fingers. Of course, my initial instinct was that it must be some form of peripheral neuropathy. I was able to see my primary care physician quickly, and, while he knew about my WM and its potential symptoms, he felt certain that what I was experiencing was carpal tunnel syndrome. After follow-up testing, this was confirmed, and I was scheduled for a carpal tunnel release procedure. I was thrilled to be diagnosed with something so…normal! My peace of mind was short-lived, however. When I relayed the news to my hematologist, I was told that a tissue sample should be collected during the procedure to test for amyloid protein. I had the procedure in December, and in early January was informed that the Congo red test performed for it was, thankfully, negative.

My WM is a permanent and present companion. I feel powerless at times, as the term watch-and-wait perhaps suggests. The disease will run its course regardless of how proactive I try to be.

For better or worse, though, I am a pragmatic, get-it-done, creative, glass-half-full, quick-thinking, master problem-solver. While watch-and-wait might describe my current course of treatment, I decided in October 2022 that it would not be the means with which I approached living my life. I will reiterate that my positive attitude—due to my improved physical conditioning, different job, and new opportunities around the time of my diagnosis—made, and continues to make, an enormous difference on my outlook and in my life.

Paul conducting a performance in Philadelphia's Marian Anderson Hall (photo credit: Peter Blaikie)

New job, new opportunities, new mindset

I'm a musician—from the age of thirteen, I knew music was what I wanted to do—and I've been lucky that all my professional endeavors have, in some way, been musically-related. For college, I attended the Curtis Institute of Music in Philadelphia, a small, selective, tuition-free classical music conservatory. Upon graduation, I joined the school's staff and have spent the last 32 years as an administrator there, including nearly ten years, from 2013-2022, as dean. Away from Curtis, I've concurrently maintained my musical pursuits as a conductor and educator. My decision to step down from the dean position and accept a job with fewer responsibilities was rejuvenating, and it also allowed me the time and

Watch-and-Wait, cont. on page 13

mental bandwidth to take on additional teaching and performing opportunities that I greatly enjoy. My improved mindset had a great deal to do with my ability to put my diagnosis into perspective and live with WM.

I'm not going to wait

My wife and I have always loved to travel and be outside. Walking, hiking, snowshoeing—we enjoy being active. That's a good thing because our other hobby is food! We've always said there are more beautiful places and interesting restaurants than we have time to visit. Knowing what I knew in October 2022, it was time to get going and experience as many of those destinations as we could. There was no time to waste. I didn't know when I might start feeling too winded to enjoy, or even go on, our trips. Quite simply, I had no intention to just watch-and-wait. With my shifted priorities, making the time to explore the places on our collective bucket list was no longer as difficult as it once had been.

Since my diagnosis, we've traveled to San Francisco and twice to London, hiked the Dingle Way in Ireland and Scotland's West Highland Way, and explored some of our country's most beautiful places like Lake Huron, the Grand Canyon, and Zion National Park. Even my check-ups at Dana-Farber Cancer Institute in Boston give us an excuse to schedule an extended weekend in Vermont. Our upcoming travels include a return to England to explore Windsor Castle and enjoy chef Heston Blumenthal's nearby Michelin-starred restaurants and a trip to hike the Salt Trail in the Bavarian Alps.

Paul and his wife, Gerry, hiking Scotland's West Highland Way

Everything happens for a reason

I have always felt that everything happens for a reason, and WM certainly falls into that category. My diagnosis has given me a different sense of purpose. Obviously, there's no way to accurately predict what will happen and when with my health, but I'm grateful to enjoy each day more than I did before.

HAVE YOUR SAY

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

Chinese Study Reports Phase 2 Trial Results for Zanubrutinib, Bendamustine, and Rituximab Combination Therapy in WM – Chinese scientists reported interim results from a Phase 2 clinical trial of zanubrutinib (Brukinsa) combined with bendamustine and rituximab for a one-year, time-limited treatment of newly diagnosed, symptomatic WM patients. This so-designated ZBR trial enrolled 25 patients. Bendamustine was given intravenously at 70 mg/m^2 on days 1 and 2 of each monthly cycle for six cycles. Rituximab was given on day 1 of each cycle for six cycles, while zanubrutinib was given orally at 160 mg twice per day, up to 12 cycles. At the time of this report in the journal *Blood*, all 25 patients had completed the first six months of treatment with ZBR, and seven had completed all therapy; the overall, major, and deep response rates were 100%, 85.7%, and 71.4%, respectively. The median time to at least a partial response was one month, and the median time to best response was three months. The ZBR combination was effective in reducing enlarged lymph nodes and extramedullary masses. The most common adverse events were low neutrophil counts, infection, low platelet counts, rash, fatigue, and cerebral hemorrhage. At the time of this report, one patient had died from cerebral hemorrhage.

Final Analysis Published for Phase 2 Trial of Combined Bendamustine, Rituximab, and Bortezomib Therapy – Italian researchers associated with the Fondazione Italiana Linfomi (FIL) conducted a Phase 2 clinical trial of bendamustine, rituximab, and bortezomib (BRB) therapy in 38 relapsed or refractory WM patients, who were enrolled from 2014-2017. Bendamustine was given at 90 mg/m^2 on days 1-2 of each monthly cycle for six cycles, rituximab was given intravenously on day 1 of each cycle, and bortezomib (Velcade) was given at 1.3 mg/m^2 subcutaneously on days 1, 8, 15, and 22 of each cycle. Median follow-up was 39 months. The overall response rate at the end of therapy was 84.6%, including 11% complete responses and 39% very good partial responses. Moreover, BRB induced high rates of undetectable minimal residual disease, meaning that any remaining cancer cells were so few that they could not be detected. Progression-free survival was 78.8% at 30 months, while overall survival was 92.1% at 18 months. The primary toxicities were low blood counts, such as low neutrophil and low platelet counts, which occurred in 50% of patients. Neuropathy developed in 10%, but while some patients had to reduce their bortezomib dosage, the neuropathy was not severe enough to result in treatment discontinuation. These results appeared in the *British Journal of Hematology*.

The ZBR combination was effective in reducing enlarged lymph nodes and extramedullary masses.

Italian Researchers Discuss Effectiveness and Safety of Different First-Line Chemoimmunotherapy Treatments for WM – A correspondence article in the *American Journal of Hematology* discussed the effectiveness and safety of different first-line chemoimmunotherapy treatments for WM patients seen between January 2008 and December 2022 at 14 Italian centers that are part of the Fondazione Italiana Linfomi (FIL). The retrospective study compared four different groups of treatments: bendamustine and rituximab (BR); dexamethasone, rituximab, and cyclophosphamide (DRC); other rituximab (R)-chemo regimens; and chemo alone. Participating were 547 WM patients, with 245 receiving BR, 116 receiving DRC, 86 receiving other R-chemo regimens, and 52 receiving chemo alone. The overall response rate was 93.3% for BR, 79.2% for DRC, 75% for other R-chemo regimens, and 44% for chemo alone. The four-year progression-free survival rate was 80% for BR, 68% for other R-chemo regimens, 60% for DRC, and 25% for chemo alone. Overall survival at four years was 58% for chemo alone, compared to the other three treatment groups, whose overall survival rate varied slightly from 86-93%. Regarding safety, a significantly higher rate of hematological toxicities (low blood counts) was seen with BR when

Medical News Roundup, cont. on page 15

compared to the DRC and other R-chemo groups, resulting in more frequent dose reductions in BR patients. Among several other analyses performed, BR dosing regimens of either 90 mg/m^2 or 70 mg/m^2 for six monthly cycles were compared. Generally, patients receiving the lower dose were older, but there were no other notable differences in patient characteristics associated with these two dosing groups. Neither group had dose reductions during treatment. No significant difference was observed with respect to four-year progression-free survival, which was 84% for the 90 mg/m^2 group and 85% for the 70 mg/m^2 group.

BTK Degrader NX-5948 Receives FDA Fast Track Designation for WM – Nurix Therapeutics has received Fast Track designation from the US Food and Drug Administration (FDA) for its BTK degrader NX-5948 as treatment of relapsed or refractory WM patients who have had at least two prior lines of therapy, including a BTK inhibitor. This designation is designed to fast track the development and expedite the review of drugs to treat serious conditions and fill an unmet medical need, in this case as therapy for WM patients whose disease has progressed following other BTK inhibitor treatment. In contrast to BTK inhibitors like ibrutinib or zanubrutinib that suppress the BTK protein, BTK degraders like NX-5948 target the protein for destruction by the cellular "garbage system" called the proteasome. The Fast Track designation was based on Phase 1 trial data presented at the recent 12th International Workshop on WM; the company is continuing to enroll WM patients in the ongoing Phase 1b expansion part of the trial. The clinical trial identifier on *www.clinicaltrials.gov* is NCT05131022.

Nurix Therapeutics has received Fast Track designation from the US Food and Drug Administration (FDA) for its BTK degrader NX-5948...

Phase 3 ASPEN Trial Analysis Determines Effect of BTK Inhibitor Treatment on Peripheral Neuropathy in WM – Investigators involved in the pivotal Phase 3 ASPEN clinical trial, which compared treatment of zanubrutinib (Brukinsa) to ibrutinib (Imbruvica) in WM patients, also performed an analysis to determine the effect of these BTK inhibitor treatments on peripheral neuropathy (PN) symptoms. Of 49 patients with PN symptoms, 27 received zanubrutinib and 22 received ibrutinib. Quality of life, including PN, was assessed with a standardized questionnaire. Overall, 71.4% experienced resolution of their PN symptoms, with a median time to resolution of 10.1 months. In patients with mutated MYD88, the median time to PN symptom resolution was 4.6 months with zanubrutinib and 14.1 months with ibrutinib. There was a significant association between resolution of PN symptoms and a major response to BTK inhibitor treatment. This analysis was reported in the journal *Blood Advances*.

Retrospective Study Looks at Outcomes of WM Patients Receiving Plasma Exchange at First-Line Therapy – A study from Case Western Reserve University and Taussig Cancer Center at Cleveland Clinic analyzed survival outcomes in WM patients who received plasma exchange (also called plasmapheresis) for symptomatic hyperviscosity just prior to or along with their first systemic drug therapy. This retrospective study, published in the journal *Blood*, included 138 patients diagnosed from 2008-2023, 17 of whom received plasma exchange at the time of first therapy. Median IgM level and median serum viscosity were 6.1 g/dL and 4.9 cp, respectively, at the time of plasma exchange. The median time-to-next-treatment for patients receiving plasma exchange was 2.61 months vs. 54 months for patients who did not require plasma exchange; median progression-free survival was 3.4 months for patients receiving plasma exchange vs. 55.0 months for those did not require it. After 66.3 months of follow-up, the median overall survival was not reached for either group. The researchers concluded that patients needing plasma exchange for hyperviscosity at first treatment have a more aggressive disease, with increased risk of

Medical News Roundup, cont. on page 16

progression and shorter time-to-next treatment, and suggested that improved early treatment strategies are need for these high-risk patients.

Study Discusses Transformation of Indolent Lymphomas to Diffuse Large B-Cell Lymphoma – Transformation of indolent (slow growing) non-Hodgkin's lymphoma to diffuse large B-cell lymphoma (DLBCL) is not common but usually has a poor prognosis; it occurs when the indolent lymphoma cells acquire additional mutations that result in the development of the more aggressive DLBCL. The rates of transformation and outcomes vary among the different types of indolent lymphomas, but data is limited for comparing transformed indolent lymphoma to de novo DLBCL, or DLBCL that arises on its own, without a previous indolent lymphoma diagnosis. A multicenter study, reported in the *Blood Cancer Journal*, used data acquired from the US Surveillance, Epidemiology, and End Results (SEER)-17 database to look at survival outcomes for patients who transformed from follicular lymphoma, marginal zone lymphoma, and lymphoplasmacytic lymphoma (LPL)/WM, and compared them to a control group of de novo DLBCL patients. This study included 19,921 patients diagnosed with indolent lymphoma between 2010-2015 and followed through 2020. Compared to patients with de novo DLBCL, patients with transformed lymphoma of all subtypes were generally younger at diagnosis, more likely to be White, more likely to have advanced disease, and less likely to have documented B symptoms (fevers, night sweats, weight loss). Of the study's total number of indolent lymphoma patients, 1,622 were diagnosed with LPL/WM. The rate of transformation of LPL/WM to DLBCL was 2.2% over a median period of 7.67 years. The five-year overall survival rate was highest for de novo DLBCL patients at 59%, compared to the transformed indolent lymphoma patients. Notably, the transformed LPL/WM group had the lowest five-year overall survival rate among the transformed lymphoma subtypes, at 33%.

International Researchers Study Outcomes of Stem Cell Transplant in Transformed WM – A multicenter international study investigated the outcomes of patients with transformed WM who underwent autologous stem cell transplant (auto-HSCT) or allogeneic stem cell transplant (allo-HSCT), reporting the results in a correspondence article from the *American Journal of Hematology*. Transformation in WM is uncommon and occurs when the WM cells acquire additional mutations that result in the development of a more aggressive cancer, usually diffuse large B cell lymphoma. Typically, transformed WM patients are treated with chemoimmunotherapy, but survival outcomes are poor. This retrospective study of patients with transformed WM, treated at 29 centers between 1995-2021, was divided into three groups: 46 who received an auto-HSCT (using their own stem cells), 10 who received an allo-HSCT (using donor stem cells), and 227 who were not transplanted. The median age of those receiving an auto-HSCT was 63 years, while the median age of those receiving an allo-HSCT was 51 years. Among other analyses, median overall survival rates were 11 years for the auto-HSCT patients, 3.2 years for the allo-HSCT patients, and 1.3 years for the non-transplanted patients. Patients who had received a single line of therapy before auto-HSCT transplant and achieved a complete response to it had especially favorable survival outcomes after transplant. The researchers noted some limitations to their study, including lack of information about patient co-morbidities (co-existing diseases) and differing transplantation practices among the centers involved in the study.

The author gratefully acknowledges the efforts of Grete Cooper, Peter DeNardis, Julianne Flora-Tostado, 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.*

ADDING MORE LIFE TO YOUR YEARS: QUALITY OF LIFE WITH WM

By Ann Grace MacMullan

Never has the term, quality of life, meant so much to me as it does now, while I'm helping to care for my father on home hospice. He was diagnosed with Waldenstrom's macroglobulinemia (WM) in 2019 and successfully treated for it, although chronic fatigue, low hemoglobin levels, and recurring infections linger. Like so many other folks with WM, it's sometimes difficult to distinguish which symptoms can be attributed to this rare lymphoma.

In 2023, however, Dad's PSA levels began to climb, and his decades-long battle with prostate cancer required more aggressive treatment. After enduring chemotherapy, targeted radioactive therapy, and finally an immunotherapy drug being tested in a Phase 2 clinical trial, he'd had enough. Dad had lost 30 pounds and was barely able to care for himself; his symptom burden was high, and his functionality low. In December 2024, the difficult decision to stop treatment for advanced metastatic prostate cancer had finally come. Home hospice was the logical next step.

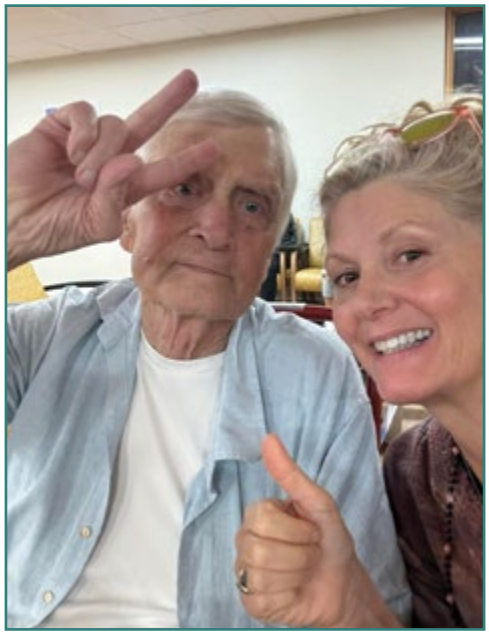
Ever a striver, Dad asked his palliative care doctor what he should do next. The answer was, "Do whatever you want. Eat whatever you want." And his long-time oncologist echoed the sentiment, advising us to "focus on quality of life." This was the first time that quality of life had entered the medical conversation, although we as a family had been reflecting on it. The book *Being Mortal*, written by a surgeon named Dr. Atul Gawande, had given us a helpful lens through which to see Dad's medical situation:

> "We've been wrong about what our job is in medicine. We think our job is to ensure health and survival. But really it is larger than that. It is to enable well-being. And well-being is about the reasons one wishes to be alive."

I began to reconsider the concept of quality of life. What contributes to life's richness or fullness? Could simply becoming aware of one's own "aliveness" be a step toward improving it? Through my work with IWMF's Wellness Program, I've encountered the quality of life variable. Though they are not specific to WM, many studies show that mind-body practices such as yoga and t'ai chi are feasible interventions used to reduce symptom burden and improve quality of life in cancer patients. See "Yoga into Cancer Care: A Review of the Evidence-based Research," at *https://pmc.ncbi.nlm.nih.gov/articles/PMC5769195/*.

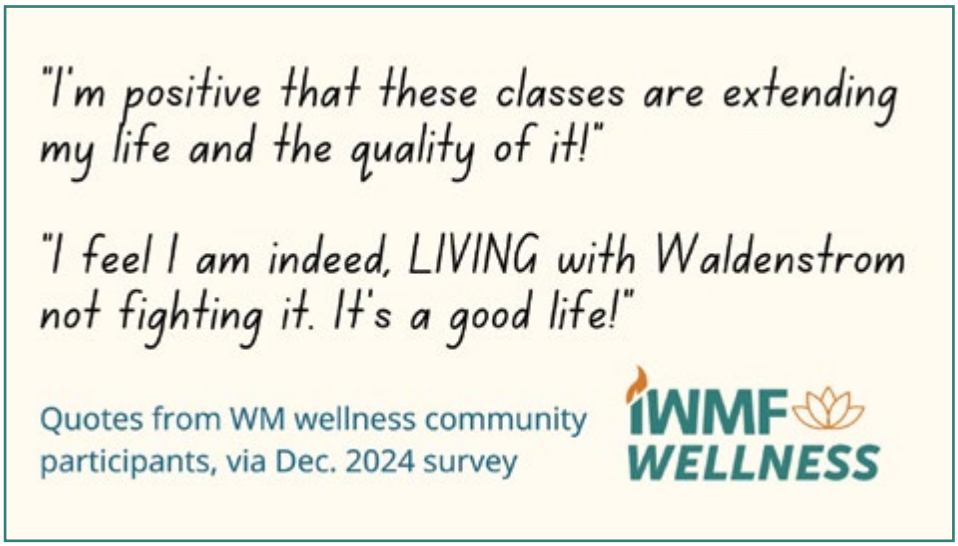
Abbreviated as "QoL," quality of life is difficult to define, as it can mean something different to each person and is constantly shifting and evolving. For my father, age 85, physical health is still a high priority. He gives himself a "30 out of 100" in this area. As the North American Orienteering Champion at age 77, it's been hard for him to say goodbye to competitive trail-running and long-distance runs. However, being able to stay in his home of 45 years and having a large family who surrounds him with loving support scores a "90 out of 100," according to him. What aspects of your life are most important to you?

To those with Waldenstrom's, QoL is a very valuable consideration, as you can expect to live for many years



Ann Grace and her Dad

Quality of Life with WM, cont. on page 18



with the proper care: "It's a marathon, not a sprint."

> "For many patients, a diagnosis will manifest as a lifelong multisystem relapsing-remitting chronic inflammatory condition, and an appreciation of this, as well as the subsequent psychological and social impact on patients and their families, is important." See "Indolent lymphoma: addressing the needs of survivors" at *https://www.tandfonline.com/doi/full/10.1080/10428194.2025.2456970*.

Having a sense of what contributes to your own well-being can be helpful when making treatment decisions while also providing a foundation for the marathon ahead. Frustratingly, QoL cancer questionnaires are not specific to this unique disease, and the concept of quality of life is often left out of the conversation altogether. Fortunately, there are some WM specialists who are contributing meaningfully to this QoL discussion.

In January 2024's *IWMF Torch*, Dr. Jonas Paludo wrote in his article "Beyond Remission: Understanding the Goal of Therapy in WM":

> "Since we are not yet capable of eradicating this disease…the overarching goal of WM-directed therapy is to **improve quality of life**. This is the why, the reason to start, continue, and stop/change treatments. The primary mechanism by which WM affects quality of life is through symptoms. For example, fatigue interferes with your daily life, or peripheral neuropathy causes discomfort or affects your balance. Once the interference of WM with your quality of life is enough to counterbalance the potential side effects of therapy, it is time to consider initiation of treatment." See *https://iwmf.com/wp-content/uploads/2024/01/N52606-Torch-January-2024_web.pdf*.

In a study (see *https://ascopubs.org/doi/10.1200/JCO.2024.42.23_suppl.168*) published in August 2024, Dr. Shirley D'Sa recognized the need for a "tailored QoL tool for WM to reflect the unique disease and treatment impacts. This would help optimize treatment decisions and improve patient care."

D'Sa and her colleagues set out to enrich understanding of the patient experience by giving WM participants a smartwatch that continuously captured their activity levels, sleep, and heart rate. Using a mobile app, patients were asked to input treatments taken, if any. They filled out a standard QoL questionnaire which measures mobility, self-care, usual activities, anxiety/depression, and pain/discomfort. Participants also rated their disease symptom severity.

The data collected were extremely helpful in creating baseline physiological and QoL metrics for patients with WM and in demonstrating the feasibility of a digital ecosystem of wearable-

Quality of Life with WM, cont. on page 19

captured and patient-reported outcome metrics. Many of us hope we'll be able to take part in the continuation of such research soon. One interesting takeaway from the study: increasing activity levels significantly correlated with decreasing symptom severity and increasing QoL scores.

During a recent IWMF Wellness Seminar, Dr. D'Sa shared how hopeful she is about the future of this technology in helping doctors monitor their patients in real-time (see *https://www.youtube.com/watch?v=93ywrE3Rj2Q&feature=youtu.be*). She believes "you can live well with WM, and our work demonstrates that digital technologies can enhance the capture of the experience." She sees wellness as a proactive choice, shifting focus away from the disease to living fully. Thanks to Drs. Paludo and D'Sa, we are beginning to understand the importance of considering quality of life in those living with WM, a unique and rare disease that can have a lifelong impact on many levels.

In the same article cited above, "Indolent lymphoma: addressing the needs of survivors," its authors believe that well-being should play a more significant role in cancer survivorship and advise the need for broader, more holistic care for populations like those affected by Waldenstrom's:

> "Traditionally survivorship care has been limited to 'survivors' of curable malignancies who have completed treatment of finite duration. However, the importance of this holistic approach is now recognized in those with incurable malignancies, including chronic lymphocytic leukemia (CLL). Patients with CLL…suffer chronic multisystem physical and psychosocial effects, driven directly or indirectly by their disease, as well as therapy. These require specific attention by the treating clinicians and broader planning for health service delivery…A holistic approach which empowers patients to be active participants in their survivorship care is paramount."

As IWMF's Wellness Program coordinator and yoga therapist, I meet a lot of folks affected by WM. Many have become advocates for their own care, and some know more about their disease than their doctors do and are personally committed to improving their quality of life on many levels. In fact, the WM wellness community we now enjoy was born out of these empowered individuals trying to fill the gap in their own care.

Integrative interventions (see *https://cancerblog.mayoclinic.org/2022/03/15/integrative-oncology-lifestyle-medicine-for-people-with-cancer)* like yoga, fitness, and meditation can help reduce fatigue, improve physical well-being, manage stress, and increase focus and awareness—at any stage of the cancer journey. Wouldn't an increased sense of awareness also enrich one's basic experience of being alive?

In attending the variety of IWMF Wellness Program sessions, participants can address their physical, mental, social, and spiritual well-being, all of which contribute to QoL. The sheer fact that there is something they can do to contribute to their own outcome, alongside others with their same rare diagnosis, is incredibly therapeutic; it provides a crucial sense of control.

Recently, one participant reported, "I feel more alive," after a very short practice including simple breath-infused movements and a breathing exercise. That sense of vitality is integral in exploring quality of life. What makes you feel more alive? If you stop, take a breath, and let yourself be, you might hear the answer. Simply being present is a key element of defining and even experiencing the "quality" in quality of life. Again, the article "Indolent lymphoma: addressing the needs of survivors" offers an appropriate comment:

> "…It is now time for us to engage our patients, their caregivers, and other healthcare providers in care aspects beyond the lymphoma diagnosis, so they can anticipate a rich and full life, free from both direct and indirect consequences of the lymphoma diagnosis."

Quality of Life with WM, cont. on page 20

A rich and full life is something we all deserve. You can explore measuring quality of life as a thought experiment by creating lists and scoring various elements. Or you can experience the "quality" in quality of life by cultivating awareness. I suggest you try both, staying alert to the peaks and valleys that are inevitable. Share important QoL information with your doctors and stop by a wellness class sometime if you'd like some support in this vital endeavor.

As for my father, when he stopped being a patient, he opened a magic door to his own rhythms, wants, and needs. Dad is more himself, laughing as we reminisce about the fish he's caught and the races he's won. He's gained weight. And he's back out walking—one mile at a time. Focusing on quality of life has proven surprisingly therapeutic! Imagine if more oncologists empowered their patients to take part in their own well-being, encouraging them to seek quality over quantity of life—and sooner in the conversation. We might just add more life to our years!

Eat what you want

Ann Grace MacMullan, E-RYT 500, C-IAYT, is IWMF's Wellness Program Coordinator. A certified yoga therapist, Ann specializes in tailoring the practice of yoga to a wide range of practitioners, especially to help navigate chronic illness and support aging gracefully. Since 2021, Ann has collaborated with IWMF to create a holistic, integrative wellness curriculum to address common side effects of WM and WM treatments. Her Dad was diagnosed with WM in 2019.

FROM THE FACEBOOK WM SUPPORT GROUP: SPRING 2025

By Betty Ann Morton, Editor

The Facebook WM Support Group continues to be very active; most days bring about eight new posts, along with comments on each. On a typical day, 600-900 people post, comment, or react to what others have written. Most posts are written in English, but IWMF is an international organization and some prefer to write in other languages, including French, Italian, Spanish, and German. If you are more comfortable writing in a language other than English, please feel free to use the language that is best for you. Facebook will provide translations, although it is still learning to speak WM.

New member **KH** started a lengthy discussion of WM symptoms that led to treatment. "First time posting. I was diagnosed in November 2024. My symptoms are fatigue (sleeping 11+ hours a day including naps), shortness of breath and light-headedness when doing everyday chores, and weakness. My questions are: What symptoms led you to begin treatment? Have your symptoms improved with treatment? Or did you just have changes in numbers?"

DDW responded quickly, "Progressive anemia with slowly declining hemoglobin over about five years (down to 8.7 g/dL in February 2024). Shortness of breath in 2023 when hiking led to my diagnosis in November 2023. I lost about 20 lbs. at the beginning of COVID, but I was happy to lose it. I had five rounds of bendamustine and rituximab over six months in 2024. Numbers all look really good now, and I feel great; no shortness of breath and Hg is 12.1 g/dL. IgM has dropped from around 5,500 mg/dL to 634 so far (it has continued to drop since treatment ended in June.) I have gained about eight pounds but was diagnosed with Stage 0-1 breast cancer in October 2024. After surgery in November, I began taking hormone blockers—one side effect is weight gain. So that may be unrelated to WM."

RH's experience was, "Shortness of breath coupled with discomfort underneath my left side rib cage. I had been experiencing fatigue also. My primary care doctor was convinced sleep apnea was causing my fatigue, but I don't have it. CT scans revealed major clues towards my diagnosis."

MD wrote, "My major symptoms were continual fatigue, extremely low internal energy, shortness of breath, and sudden unexplained weight loss. On a few occasions, I experienced night sweats. My blood tests showed my paraprotein was increasing. I was scheduled for bendamustine-rituximab chemotherapy, but it was not effective on me. I plateaued well below expected/desired levels. I was then placed on zanubrutinib (BTK inhibitor) which I have taken for the past 15+ months. My cancer fatigue still remains, while my internal energy and shortness of breath have both ameliorated somewhat. Since being on zanubrutinib, my paraprotein continues to be relatively high but not increasing. As a result, I am considered stable."

TR's experience with symptoms leading to treatment were, "I had neuropathy from toes to calves and fingertips to forearms, severe fatigue, severe headaches, hemoglobin below 10 g/dL. Treatment with bendamustine and rituximab resolved the symptoms. Neuropathy is returning a bit after nine months post-treatment, but I'm otherwise symptom free. I am still slightly anemic and red blood count is just below normal, but fatigue is greatly reduced."

KL described her husband's experience, "My husband's initial symptom was anemia…in the second year the GP sent him to a hematologist. We feel lucky he was diagnosed without major issues. He started treatment after about a year of watch-and-wait when he lost a bunch of weight, including muscle mass, and was extremely fatigued. We should've figured it out faster and gotten him in before his three-month bloodwork was due."

Based on this discussion, anemia, fatigue, and shortness of breath are common symptoms at diagnosis. Weight loss and peripheral neuropathy were also frequently mentioned. The majority of those who responded said they felt better after treatment,

From the Facebook WM Support Group, cont. on page 22

noting that weight loss stopped and shortness of breath and anemia improved. Neuropathy and fatigue seem less responsive to treatment.

Sometimes a WMer writes seeking advice. When the question is medical, others may share their knowledge, citing their personal experience, as well as scientific/medical articles, and advise checking with their own doctor. A recent example started with **RS**'s post, "Hello all. I have a zanubrutinib question. When I started taking zanubrutinib, I took two in the morning and two in the evening. It seems like I felt better then than when I switched to four in the morning. I'd appreciate your feedback. I'm thinking about switching back to the two and two."

JBS replied, "My husband was told to make sure you only take two in the morning, then again at night, 12 hours apart. Never take all four together. I have no idea why or if it makes a difference but it must. I would say if you did better separating the dose and that's the way it is recommended, then I would go back to it. Good luck."

SAP wrote, "I believe I read here that in the clinical trial the dosage was two in the morning and two in the evening. Was there a reason for the switch? The research company for the drug has a great patient website: *https://www.mybeigene.com/*. They have on-staff oncology nurses who should be able to answer your questions about dosing. Of course, check with your doctor. When I was on it, I took two in the morning and two in the evening. Wishing you well too!"

Group expert **MCM** added, "Hi **RS**. The prescribing info that comes with zanubrutinib (Brukinsa) states you may take the tablets all at the same time or split the dose by taking two tablets in the AM and two in the PM. During a clinical trial, subjects took two tablets in the AM and two tablets in the PM. Comparison of the overall response between daily and twice-daily dosing did not indicate advantage of either regimen. See *https://www.ncbi.nlm.nih.gov/pmc/articles/PMC10430288/*.

MD shared personal experience, "When I started zanubrutinib 15+ months ago, my oncologist said the choice was mine: either take two in the morning and two in the afternoon OR take all four at once in the morning. I've taken all four in the morning each day and haven't had any issues."

CBM added, "My Mayo doctor said taking the entire dose at once was fine. I think they make me feel strange so I take them in the evening."

There's always room for more in our Facebook WM Support Group. If you're considering whether to join, here's **DE**'s opinion. "This is a note of appreciation for this support group. I was diagnosed with Waldenstrom's in 2017 and have been on watch-and-wait since then. My time has finally come to start treatment based on my symptoms and an enlarged spleen, and I will start on zanubrutinib in January.

"As I've been updating my family and close friends with this news, everyone is so surprised at how calm and rational my attitude is in dealing with this situation. Well, I have this group to thank for that! I've been reading all your questions and thoughts and notes of encouragement as well as learning a great deal about this disease (again through this group!) for the past seven years. For me, this education combined with all your personal stories have taken away much of the fear and the unknown. I'm confident and comfortable that everything will turn out for the best.

"Earlier this year, during an appointment with my oncologist at Northwestern, she commented, 'Wow, you really know a lot about Waldenstrom's—are you in that Facebook group?' Of course, I replied in the affirmative, and she said, 'Yes, I can always tell when one of my patients is active in that group—you're all so well informed.' I loved hearing this. Thanks to all of you for helping me on this journey!"

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

NAVIGATING THE CLINICAL TRIAL PROCESS: THE LLS CLINICAL TRIAL SUPPORT CENTER

While there is no cure for WM, it is typically a slow-growing lymphoma that can be managed with treatment. Standard treatments for WM include chemotherapy, targeted therapies, immunotherapy, stem cell transplant, and clinical trials. Without clinical trials, the current treatment choices for WM would not exist; clinical trials are an important option for WM patients seeking new therapies. Unfortunately, the clinical trial process can be complex and overwhelming for patients and healthcare providers (HCP), requiring personalized navigation and support. IWMF has partnered with The Leukemia & Lymphoma Society's Clinical Trial Support Center (LLS CTSC) to help WM patients navigate the clinical trial process. The CTSC is a comprehensive navigation program that supports WM patients, their loved ones, and healthcare providers throughout the clinical trial process.

Understanding clinical trials for WM

Clinical trials are carefully controlled research studies that seek to improve the care and treatment of patients by identifying more effective and less harmful therapies. They may involve a new drug or a combination of drugs and are also the key step in advancing cancer treatment and providing patients access to innovative and potentially lifesaving therapies.

Identifying better treatments and cures for all patients through clinical trials is critical, yet participation is low; only 5-8% of adult cancer patients in the United States ever participate in a trial. Low participation rates are the result of a clinical trial process that is highly complex and overwhelming with many obstacles. Common barriers to participation include lack of awareness and understanding about clinical trials; ineffective patient identification and provider communication; difficulty identifying appropriate trials (particularly if no trials are available at the physician's institution); reluctance to refer patients to trials at another institution; restrictive inclusion/exclusion criteria; travel and financial constraints; time commitment; and fear, mistrust, and attitudes and preferences toward treatment decisions among providers and patients. Barriers to clinical trials exist for all cancer patients, including those with WM.

As mentioned before, without clinical trials, current treatment options for WM would not exist. To continue moving the science forward, clinical trials should be discussed as a potential treatment option at the time of diagnosis and at every change in treatment. Current clinical trials for WM include patients who are not yet treated, patients whose disease has relapsed (returned after a period of improvement), and patients whose disease is refractory (has not responded) to treatment. It is important to discuss all your treatment options, including clinical trials, with your WM specialist. If your specialist does not mention clinical trials as a potential option, it is okay to ask! Understanding each treatment option, the goals of treatment, potential risks and benefits, and factoring in your personal beliefs, goals of care, and unique situation are critical considerations when making such an important decision. Deciding to explore clinical trials may seem overwhelming, and identifying and enrolling into a trial can be equally daunting.

How The LLS Clinical Trial Support Center can help

In 2016, The Leukemia & Lymphoma Society created the Clinical Trial Support Center. This free service provides comprehensive, individualized support to blood cancer patients, their loved ones, and healthcare providers to navigate the clinical trial process. The CTSC is a team of 12 nurse navigators, with expertise in both pediatric and adult blood cancer, who work one-on-one with patients to identify potential clinical trials, overcome the barriers to enrollment, and empower patients to be active participants in their care. This patient-centered approach to clinical trial navigation is unique. This relationship starts with a comprehensive assessment of past medical history, diagnosis, and treatment and with an educational assessment to identify the patient's understanding of the diagnosis and treatment options, including clinical trials.

Providing education is critical in improving awareness of clinical trials, and it is an opportunity to better understand what the patient's goals and

Navigating the Clinical Trial Process, cont. on page 24

preferences for treatment are. It is also important to understand what support and resources a patient has that may impact participation in a clinical trial, as it could take someone away from home frequently or for an extended period. This also includes identifying other potential barriers to participation.

Taking all these unique characteristics into account, the CTSC nurse navigator searches for potential clinical trials utilizing a proprietary database. That database includes WM-NET trials and all others available on *clinicaltrials.gov*. It also includes up-to-date information gathered from interactions with principal investigators, study sponsors and site contacts. Providing patients and their healthcare team, with curated, up-to-date, and easy-to-understand clinical trial information allows them to have a shared decision-making conversation to decide what is the next best treatment option. The nurse navigator continues to help with enrollment by reaching out to trial sponsors, investigators, and site contacts to learn more about a patient's eligibility and by identifying resources to overcome any barriers to enrollment. The LLS CTSC nurse navigators provide comprehensive and personalized support throughout the entire clinical trials process.

It is important to emphasize that the goal of the CTSC is not to enroll every patient into a trial but to increase opportunities for trial participation; this is done by facilitating informed, shared decision-making and minimizing logistical barriers if the patient decides that a clinical trial is right for them. Ultimately, the goal of the CTSC is to educate, support, and empower patients to be active participants in—and have control over—their treatment decisions. CTSC nurse navigators support patients in accessing the care they need, whether it is standard of care or a clinical trial.

Conclusion

Helping WM patients participate in clinical trials is important to offer hope, access to new treatment options, and the possibility for better outcomes. Navigating the clinical trial process can be overwhelming, but The Leukemia & Lymphoma Society's Clinical Trial Support Center is available to provide free education, support, and resources to empower patients to be active participants in their care and access the treatment they need. Improving participation in WM clinical trials will help provide improved quality of life and identify more effective therapies that can bring us closer to a cure.

To speak with an LLS Clinical Trial Support Center Nurse Navigator:
Email: *ctsc@lls.org*
Phone: 800-955-4572
To learn more, go to: *www.lls.org/ctsc*

CTSC Process for Supporting Patients

AUSTRALIA REPORT: WMOZZIES

By David Young

The WMozzies Facebook Support Group (which we co-moderate with the Australian Leukaemia Foundation) continues to grow and provides WM patients and their carers with the latest information about WM. It also posts online information and helpful webinars and, of course, the community chat page, which is always busy with personal stories, questions, and support from other WM patients. Our current membership is 344.

WM-VOICE survey gets huge Australian participation

Of the total membership of WMozzies, 75% submitted responses to the WM-VOICE survey. As of February 17, the goal of 188 people for the VOICE project was reached in an outstanding level of participation, reflecting the great appreciation of this IWMF-sponsored research project. There was strong Australian recognition of the valuable opportunity to have a say about WM patient treatment preferences. It is of special value that a separate analysis of Australian responses will be provided. It will be particularly interesting to see if treatment preferences are influenced significantly by differing country factors. For example, in Australia the government funds the total treatment costs for common treatments such as bendamustine, zanubrutinib, and rituximab. Professor Judith Trotman, one of the leading Australian WM research investigators, has stated that having a well-researched analysis of Australian patient treatment preferences is valuable in the design of local WM clinical trials and the support of future treatment funding applications to the Australian government.

Last year an international survey on patient perception of the relevance of quality of life questionnaires in Waldenström macroglobulinaemia was completed by University College London Hospitals NHS Trust, with input from WMozzies and WMUK. The survey was recently submitted to a research publisher for review, and we await the outcome with anticipation.

WM INDIA UPDATE

By Saurabh Seroo, IWMF Trustee

WM India representatives travelled to Kolkata to conduct our first support group meeting of the year on February 26. We had a wonderful meeting with WM patients Anil Somani and Rajat Saha, along with caregivers Joyita Sinha and her mother, Jaba.

Rajat and Anil, both of whom have battled WM for a decade, shared their experiences and deep knowledge of the disease and its manifestations. They also spoke in-depth of their experiences of undergoing treatment, how the landscape has evolved, and how their lives had changed over time.

Joyita and Jaba, caregivers of Jaba's brother, spoke of their experiences and personal journeys of supporting a loved one who lives in another city, and the isolation that someone living with WM could have from such an experience.

The impact of living with WM without immediate support highlighted how important support group meetings and community are for a disease like ours. This is especially evident in an environment such as India's, where awareness of WM amongst the doctors is not as advanced as that in more developed countries.

This was our second meeting in Kolkata, the first since the pandemic. We had a special and fascinating discussion and did not realise how quickly time flew by.

WMUK: WM BUDDY SERVICE AND WM CLINICAL TRIALS HUB

By Kat Tucker, WMUK Deputy CEO

The year has started at full pace, with a series of new and exciting programmes being launched, all thanks to the amazing fundraising efforts by the WM community.

In December 2024 we asked people to contribute to expand our Support Line services. We were truly amazed and humbled by your support and response. In one week, your donations—all doubled by our generous pledgers and the Big Give—helped us raise over £50,000. A huge thank you to everyone who supported the campaign.

This phenomenal amount of money has meant we have already been able to launch our much-asked-for Buddy Service. The Service will match a trained volunteer "Buddy" with any individual seeking one-to-one peer support, providing an opportunity to talk to someone who has gone through something similar and to feel less isolated. We were inundated with enthusiastic applications from people wanting to become a Buddy and support their fellow WMers—a wonderful reflection on the positive and supportive WM community.

We were also thrilled to publish a summary of the findings for our Big WM Survey, the largest WM-specific patient survey in the world. The results made for compelling reading, and have focussed our work for the next year into three broad categories:

- Providing mental health support
- Filling the gaps in providing information
- Improving the route to diagnosis

You can read the results and more about how to plan to tackle the issues raised here: *https://www.wmuk.org.uk/2025/01/the-big-wm-survey-results/*.

Amongst the findings on information, over 60% of you told us you didn't know about resources on how to find clinical trials. Trials play a huge role in helping to get more treatment options and improve existing therapies and care, but it's clear from the survey that some people with WM can find it a hard path to navigate. That's why on 5 March we launched the UK's only WM Clinical Trials Hub. With a searchable database of clinical trials and an ever-expanding library of resources, this hub is your one stop shop for all things clinical trials: *https://www.wmuk.org.uk/wm-clinical-trials-hub/*.

As always, we're open to feedback and insight from the WM community to help improve and expand our services, so that everyone with WM can live well. Please don't hesitate to reach out: *info@wmuk.org.uk*.

WM INCLUDED IN RARE CANCER RESEARCH PROJECT

By Sharon Piotrowski

I have Waldenstrom's macroglobulinemia (WM), and I'm excited to share my involvement in a groundbreaking project designed to bring more attention to rare cancers like WM.

This initiative stems from the US Food and Drug Administration's (FDA) Oncology Center of Excellence Rare Cancer and Real-World Evidence Programs and involves a collaboration with Ontada, a McKesson business. Ontada was awarded a contract by the FDA to leverage its iKnowMed EHR data for studies on the natural history of rare cancers treated in US community oncology settings.

The Ontada Rare Cancer Research (ORCA) project has three overarching objectives:

1. Enhance understanding of the clinical experience of rare cancer patients in community oncology.
2. Contextualize these findings with other data sources, such as national registries.
3. Generate insights to inform clinical care, research, and regulatory evaluation.

This project aims to generate real-world evidence to understand how patients with rare cancers present and are treated, describe patient outcomes under the standard of care, and inform drug development, including improved clinical trial design.

The Rare Cancer Scientific Council

To address the unique challenges associated with studying rare cancers, Ontada established the Rare Cancer Scientific Council (the Council). This multi-disciplinary team provides insights and recommendations to the Ontada Research Team, helping to interpret findings and maximize the learning derived from these studies. The Council comprises representatives from various sectors, including patients, patient advocacy organizations, oncology practitioners, payers, government/policy organizations, and rare cancer experts from academia.

The Council's responsibilities include:

- Assessing and interpreting pilot data and trends.
- Providing input on key variables and narratives.
- Reviewing analyses and identifying areas for further exploration.
- Offering recommendations for future cancer types to be studied, subject to data availability.
- Assisting in publication and presentation opportunities.

My role

I am privileged to represent WM on this Council, joining as one of up to eight volunteer members. My two-year term includes biannual meetings to provide a patient's perspective on WM and contribute to the Council's broader objectives.

First meeting October 2024

During our inaugural meeting, all Council members, along with FDA and Ontada personnel (observing only), discussed critical topics such as:

- Challenges in clinical trials for rare cancers due to limited sample sizes.
- The importance of collecting comprehensive health data to improve early diagnosis.

I was struck by how much the Council's non-patient members valued the perspectives of patients. Their openness reinforced the importance of involving individuals with lived experience in shaping research.

The FDA's collaboration with Ontada highlights a growing commitment to addressing the unique needs of rare cancer patients. By focusing on real-world evidence and leveraging Ontada's expertise, this project has the potential to create meaningful advancements in care and research for rare cancers, starting with WM and gallbladder cancer.

I look forward to continuing my work on this project and sharing updates as we progress.

WHAT'S THE BEST PART OF A SUPPORT GROUP? DISCOVERING YOU ARE NOT ALONE.

By Kathy Chapman, Southern New Jersey/Eastern PA Support Group

On January 12, Lisa Wise graciously hosted our Southern New Jersey/Eastern PA Support Group at her home for her annual IWMF Chili in Philly. Our group has enjoyed Lisa's chili for a number of years, but COVID concerns put her chili fest on hold for a while. Now we were looking forward to Lisa's party and to seeing our many WM friends and their caregivers.

My husband, Jim, and I arrived at Lisa's home at the same time as five other guests. Introductions ensued, and it turned out that three guests were newly diagnosed, with this the first Waldenstrom's support meeting for all of them. Of course, they wondered what to expect. I reassured them that we would shortly be sharing a delicious meal with a houseful of WM patients, and they would discover that Waldenstrom's is not so rare as many of us think.

In all, 25 people arrived to enjoy Lisa's delicious chili buffet. We gathered together and began our meeting. Lisa welcomed our newest guests and invited each of them to share how they were doing. Our support group has an exceptional range of survivor years, from single digits to 25 years. This is always very reassuring for newly diagnosed patients.

Lisa touched base with everyone, and we launched into a multitude of topics. Several of us are on watch-and-wait, while others have completed various treatments. What about side effects and why do certain treatments help some but not others? We currently have two members participating in clinical trials, and several in our group did so in the past. We spoke about the personal commitment a trial requires, but also how participating helps many others in the future. As always, IWMF Trustee Carl Harrington shared the latest news about new drugs and treatments that are in the pipeline and how the IWMF is funding this critical research. Another important topic was where to find Waldenstrom's specialists. Carl explained there is a list of volunteers that patients can call. He also extended an invitation to everyone to attend the upcoming IWMF Ed Forum in Florida.

As our meeting came to a close, our new WM friends felt reassured and positive, and they left with plenty of helpful information. On their way out the door, people very happily took home some of Jim's banana bread (and other leftovers) as a warm souvenir of a cozy fireside gathering full of meaningful connections on a chilly wintry Sunday afternoon. I am pretty sure they discovered they are not alone!

The annual Chili in Philly support group meeting and buffet

BEST BANANA BREAD RECIPE

By Jim Chapman, Southern New Jersey/Eastern PA Support Group

Ingredients

14 ounces of raw organic durum wheat, which you then take to a licensed miller and have ground coarsely into semolina flour. Who am I kidding, just buy a Pillsbury Banana Bread mix.

1 banana purchased from an FDA, EPA, and FBI approved organic farmer, size medium (but does size really matter?). Or just buy a banana from any supermarket. You will need to acquire the banana roughly 7-10 days prior to baking, as it needs to be overripe.

2 large purple eggs laid by free range Black Copper Maron hens which have been raised listening to classical music (but NOT opera). Or just buy any color eggs you can find at any supermarket, given the shortage due to the bird flu epidemic. However, do not substitute ostrich eggs (too large) or quail eggs (too small).

⅓ cup of vegetable oil, preferably canola oil, but definitely not peanut oil (possible allergic reaction for some) and avoid using any oils with numbers like 5-W30 or 10-W40, as these are only for use in vehicle engines.

Although the package indicates one cup of water, I substitute ¾ cup of pulp-free orange juice and ¼ cup of vanilla extract (seriously!). Pure Mexican vanilla is preferable, but after tariffs are imposed, use whatever is cheapest.

½ cup (118.3 milliliters for you metric fans) of semi-sweet chocolate chips sourced from ethically grown cacao plants. Or you can use whatever chips you can find at the supermarket, if your conscience doesn't bother you.

Preparation

If you followed my suggestion and bought the Pillsbury mix, you can follow the directions on the box for the temperature (375 degrees Fahrenheit) and time (depends on loaf pan size). However, you should first mash the overripe banana dramatically, so that it will mix well with the other ingredients. You can either mix manually with a spatula (the box suggests 50 strokes, but if you think that would cause **you** to have a stroke, use an electric mixer to be safe).

Note that the chocolate chips do not get mixed in; they are added later, in layers, as the mixture is slowly poured into the loaf pans. I suggest you sprinkle in a generous amount of chips after about ¾ of an inch of mixture has been poured, another sprinkling after another layer, and one more sprinkling after a third layer of mixture. If you choose, you can save some for the top (unless you are like my wife, who thinks that makes it messy). Bake per directions.

Serving

After cooling, slice into ½ inch thick slices (or thicker if you are not watching your weight), microwave for 15 seconds, and top with whipped cream. I hope you enjoy it!

DID YOU KNOW?

MEDICARE PART D HAS IMPORTANT UPDATES FOR 2025

1) The Medicare Part D annual out-of-pocket annual cap, which limits the amount you must pay each year for prescription medicines, has changed to $2,000. This means that the donut hole has been closed. After you hit the $2,000 out-of-pocket limit, you enter the catastrophic coverage phase when you owe nothing for covered medications for the rest of the year. Note, however, that these drugs must be covered under your Part D plan to be eligible for the cap.

2) There is now a voluntary option to pay for your Part D medications in monthly installments. This free program doesn't alter the cost of your medications, but it can make it easier to manage high drug costs that occur earlier in the calendar year by smoothing out payments throughout the year. To sign up, visit your drug plan's website or contact your plan's administrator.

3) As part of the Inflation Reduction Act, Medicare began negotiating directly with drug manufacturers last year to lower drug prices for a range of prescription medications. The first negotiated round included ten drugs, one of which was Imbruvica (ibrutinib); those negotiated prices will become effective on January 1, 2026. The 2025 negotiations will include the following drugs: Ozempic/Rybelsus/Wegovy, Trelegy Ellipta, Xtandi, Pomalyst, Ibrance, Ofev, Linzess, Calquence, Austedo/Austedo XR, Breo Ellipta, Tradjenta, Xifaxan, Vraylar, Janumet/Janumet XR, and Otezla. Negotiated prices for this second round will become effective in 2027. The negotiation program is slated to continue over the next several years.

4) Expanded vaccine coverage allows you to receive the following vaccines without paying out-of-pocket costs: COVID-19, hepatitis B, influenza, pneumococcal pneumonia, and shingles.

5) Insulin prices have been capped at $35 per month, with no deductible requirement for Part D-covered insulin. For insulin received every three months, the cost cannot exceed $105.

BEN RUDE HERITAGE SOCIETY

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

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*Deceased ✧Founding Member

RESEARCH PARTNERS

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

David and Janet Bingham Research Fund of the IWMF

- Aldo M Roccaro MD, PhD, Dana-Farber Cancer Institute, *Further genomic characterization of Waldenstrom's Macroglobulinemia: unveiling the role of the CXCR4 somatic mutation, a crucial regulator of pathogenesis and important targets for therapy* 03/01/14 - 02/28/16
- Brad H Nelson PhD & Julie S Nielsen PhD, Deeley Research Centre, *Mutant MYD88: A target for adoptive T cell therapy of WM* 10/01/14 - 09/30/16

Elting Family Research Fund of the IWMF

- Dr. Marzia Varettoni, Fondazione Italiana Linfomi Onlus, *Non-invasive diagnostics and monitoring of MRD and clonal evolution in Waldenstrom's Macroglobulinemia* 10/15/17 - 10/15/19
- Larry W Kwak, MD, PhD, Beckman Research Institute of the City of Hope, *Anti-tumor and immune microenvironment responses following a first in-human DNA fusion vaccine for asymptomatic WM* 10/15/17 - 10/15/21
- Sherie L Morrison, PhD, The Regents of the University of California, *Novel antibody-targeted interferons in combinational therapies for Waldenstrom's Macroglobulinemia* 10/15/17 - 10/15/20
- Shahrzad Jalali, PhD, Mayo Clinic, *Modulation of T-cell function by metabolomic signature of the bone marrow microenvironment in Waldenstrom's Macroglobulinemia* 09/15/17 - 09/15/19
- Dr. Bruno Paiva & Dr. Jose Angel Martinez, Climent Clinica University of Navarra, *Single-cell next-generation flow and sequencing to unravel the pathogenesis of Waldenstrom's Macroglobulinemia and to design genetically driven human-like experimental models* 09/15/17 - 09/15/19
- Dr. Gareth Morgan, New York University Grossman School of Medicine, *Using mutographs to define the molecular landscape and cell of origin of Waldenstrom's Macroglobulinemia* 01/01/23 - 12/31/25

Hamberg Family Research Fund of the IWMF

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

Robert Douglas Hawkins Research Fund of the IWMF

The Lynn M. Fischer Research Fund of the IWMF

Michael and Rosalie Larsen Research Fund of the IWMF

Leukaemia Foundation of Australia

- Zachary Hunter, PhD, Dana-Farber Cancer Institute, *Multiomic analysis of DNA, RNA and epigenomic networks for prognostication and novel target identification in Waldenstrom's Macroglobulinemia* 09/01/20 - 09/01/22
- Gareth J Morgan, PhD, New York University Grossman School of Medicine, *Using mutographs to define the molecular landscape and cell of the origin of Waldenstrom's Macroglobulinemia* 09/30/22 - 09/26/24

K. Edward Jacobi Research Fund of the IWMF

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

Carolyn K. Morris Research Fund of the IWMF

Pharmacyclics LLC

The Poh Family Research Fund of the IWMF

- Dr. Signy Chow, Sunnybrook Research Institute, *Characterization of Genomic Alterations in Treatment Naive Patients with Waldenstrom's Macroglobulinemia Through a Course of Targeted Treatment and Disease Progression* 09/01/22 – 08/31/24

Ed and Toni Saboe Research Fund of the IWMF

- Larry W Kwak, MD, PhD, Beckman Research Institute of the City of Hope, *Anti-tumor and immune microenvironment responses following a first in-human DNA fusion vaccine for asymptomatic WM* 10/15/17 - 10/15/21

The Paul and Ronnie Siegel Family Research Fund of the IWMF

Waldenstrom's Macroglobulinemia Foundation of Canada

- Zachary Hunter, PhD, Dana-Farber Cancer Institute, *Multiomic analysis of DNA, RNA and epigenomic networks for prognostication and novel target identification in Waldenstrom's Macroglobulinemia* 09/01/20 - 09/01/22
- Dr. Signy Chow, Sunnybrook Research Institute, *Characterization of Genomic Alterations in Treatment Naive Patients with Waldenstrom's Macroglobulinemia Through a Course of Targeted Treatment and Disease Progression* 09/30/22 - 09/29/24
- Zachary Hunter, PhD, Dana-Farber Cancer Institute, *Characterization of Isoform Usage, Novel Isoforms, and Tumor Evolution in WM* 07/01/23 - 06/30/25
- Patrizia Mondello, M.D. PhD, Mayo Clinic, *Identifying the oncogenic cooperation between IRF4 and MYD88 L265P and their impact on the Tumor Microenvironment of Waldenstrom Macroglobulinemia* 08/21/23 - 08/20/25

Robert and Nadeline White Family Research Fund of the IWMF

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

Marcia Wierda Memorial Research Fund of the IWMF

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- Steven Treon, MD, PhD, Dana-Farber Cancer Institute, *Targeting MYD88 in Waldenstrom's Macroglobulinemia* 09/1/18 - 08/31/20
- Zachary Hunter, PhD, Dana-Farber Cancer Institute, *Multiomic analysis of DNA, RNA and epigenomic networks for prognostication and novel target identification in Waldenstrom's Macroglobulinemia* 09/01/20 - 09/01/22

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

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Thank you for the work and support IWMF does and Ann's yoga class

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With gratitude for the work of the IWMF in fighting for my grandmother, Julie Couyoumjian, and the many others like her who beat WM.

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