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INTERNATIONAL WALDENSTROM'S MACROGLOBULINEMIA FOUNDATION

INSIDE THIS ISSUE

Laboratory Diagnosis and
Monitoring of
Waldenstrom's
Macroglobulinemia.... 1

Chairman's Corner..... 6

IWMF Doc Star:
Dr. Monique Minnema ... 7

From IWMF Connect:
Fall 2019 9

Vaccination for Adult
Immunocompromised
Patients 11

Survival 12

Medical News
Roundup 14

Cooks' Happy Hour ... 16

Support
Group News 19

International Scene.... 23

LABORATORY DIAGNOSIS AND MONITORING OF WALDENSTROM'S MACROGLOBULINEMIA

BY JANIS ATKINSON, MD



Dr. Janis Atkinson

Dr. Janis Atkinson graduated from Rush Medical College in Chicago, IL, in 1986. She completed an internal medicine internship and a residency in pathology at Northwestern University, Chicago, from 1986 through 1992 and was appointed to the medical staff of Saint Francis Hospital, Evanston, IL, in 1992.

At Saint Francis Hospital (now known as AMITA Health Saint Francis Hospital), she has served as chair of the Department of Pathology and medical director of the Laboratory since 2000. She is also an assistant clinical professor at the University of Illinois and teaches medical students and residents.

She has served in several leadership roles for her hospital and health care system, including member of the Board of Directors, president of the Medical Staff, president of the Medical Executive Committee, president of a multi-hospital pathology group, and vice president of medical affairs for Alverno Laboratories, which serves the multi-hospital system.

She lives in Wilmette, IL, with her husband Jeff. They have two children, Grant and Kelsey.

My experience with Waldenstrom's macroglobulinemia (WM) is both professional and personal. As a pathologist, one of my jobs is to recognize and diagnose this disease through analysis of biopsy material and lab test results. On a personal level, my husband was diagnosed with WM in February of 2011. He has been treated with three different monoclonal antibody and chemotherapy regimens and, after a good response to bendamustine and Rituxan, is currently in a "watch and wait" mode.

This article is for those who were just diagnosed with WM and for those who are medium- or long-term survivors. It is sub-divided into three parts. The first part will introduce what the medical profession knows about the causes of WM. This will help to form the foundation for the second and third parts, which will cover diagnosis and monitoring.

The Cause

While much is still unknown as to why any individual person will get WM, it is known that there is an association with a gene mutation that occurs after birth—a "somatic mutation"—to a gene known as MYD88. The forces that cause gene mutations during our lifetimes are many and include smoking, radiation, viruses, chemicals (carcinogens), obesity, hormones, and chronic inflammatory conditions. While the mutation can be discovered by blood testing, the cause of the WM mutation cannot. WM is usually not inherited, and most people affected have no history of the disorder in their family.

Laboratory Diagnosis, cont. on page 2

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Laboratory Diagnosis, cont. from page 1

The impact of the disease on the patient can be understood by the symptoms and by lab test abnormalities that can be seen and measured. Jan Waldenström first identified the disease in the 1940s when he noticed that some of his patients were experiencing an unusual combination of symptoms, including bleeding and blurry vision. He was able to figure out that these symptoms were a side effect of the buildup of abnormal cells and the proteins that the abnormal cells secrete into the blood. These proteins—called IgM—make the blood thicker than normal and can cause the symptoms that are collectively referred to as hyperviscosity syndrome. About 30% of patients will experience this syndrome.

The cells that are associated with WM are abnormal lymphocytes and plasma cells. While lymphocytes and plasma cells are part of our normal immune system, in WM their growth is unregulated. An overgrowth of these cells can cause tumors in the lymph glands, bone marrow, or other tissues in the body.

The term “macroglobulinemia” in the disease name is a reference to the IgM protein, because it is naturally a very large molecule. The term can be divided into its three constituent parts: “macro” means large, “globulin” is a type of protein, and “emia” means in the blood.

Diagnosis

The diagnosis of WM, from a laboratory point of view, requires identification of two main things: the abnormal lymphocytes and plasma cells and the IgM proteins made by the cells.

Identifying the Cells: Pathologists study a tissue sample using a microscope to visually identify the abnormal cells that are characteristic of WM. Usually, diagnostic tissue samples are taken from bone marrow or lymph node for this purpose. Special methods beyond simple microscopy are used to establish the diagnosis, which is not always straightforward. Other

Laboratory Diagnosis, cont. on page 3



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Waldenström's macroglobulinemia is coded 273.3 in the International
Classification of Diseases (ICD) of the World Health Organization.

diseases, like multiple myeloma, can look very similar to WM, and the two cannot always be differentiated without additional testing.

Some of these chains are referred to as “light chains” because they are smaller than the others that make up the entire molecule.

Identifying the Proteins, Including IgM and Free Light Chains: Blood and urine tests must be performed to identify the presence of the abnormal proteins associated with WM. The abnormal proteins—IgM and its constituent pieces—are produced by the tumor cells and serve as unique signatures of the disease. The IgM protein is a large molecule composed of different pieces or chains. Some of these chains are referred to as “light chains” because they are smaller than the others that make up the entire molecule.

We use the light chains to help determine whether the IgM molecules are normal or abnormal. Light chains normally come in two varieties, kappa or lambda. If an excess of one or the other type is present, that is indicative of the disease, since normally we would see a mix of the two types in a predictable ratio.

We use serum and urine protein electrophoresis (SPEP and UPEP) and immuno-focusing electrophoresis (IFE) to detect these proteins. If too many proteins with one specific charge are seen, it produces a “spike” pattern on the tracing of the protein’s electrical charges, and, in combination with the tissue sample findings, a diagnosis of WM can be made. Once the diagnosis is established, that molecule can be identified as either IgM kappa or IgM lambda and will be used to monitor disease regression or activation.

Monitoring the Disease

IgM: Since the excess IgM proteins in WM come from the abnormal tumor cells, the quantity of IgM can be used to monitor disease activity. As the disease progresses, more protein is produced and the IgM goes up. Conversely, as the disease responds to treatment, the IgM proteins decline. Normal ranges may differ at various institutions; one example of normal range from a large national lab is 40-230 mg/dL.

Normal lab values (or “reference values”) provided in this article are from the Mayo Clinic, a large Midwest reference laboratory. The ranges of normal lab values vary between laboratories and will always be provided as part of your individual lab test report for comparison purposes. If a normal value provided here differs from your lab report, you should rely on your lab report.

SPEP: The SPEP may be used in disease monitoring as well, since the abnormal proteins will produce a characteristic pattern on the tracing.

Kappa and Lambda Light Chains: The light chains are pieces of the IgM molecule and these are often monitored. The ratio will be abnormal in the presence of disease. These can be measured in serum and urine.

24-hour Urine Testing: A 24-hour urine collection is a simple lab test that measures what’s in the urine. The test is used to check kidney function and to look for the abnormal light chain proteins that can be found in WM. The entire IgM protein cannot be found in the urine because it is too large to pass through the kidney. Only the smaller pieces of the IgM protein—the light chains—can be found there. A 24-hour urine collection is done by collecting your urine in a special container over a full 24-hour period. The container must be kept cool until the urine is returned to the lab.

Serum Viscosity: Probably the single most important test to check after establishing the diagnosis is serum viscosity. This test measures the “thickness” or “sludginess” of the blood. The IgM proteins can cause red blood cells to stick or clump together, which makes blood thicker (like espresso compared to coffee). If the serum is very viscous, blood flow to the organs such as brain and kidney can be affected. This is why some patients have symptoms of blurry vision, for example. If the blood is too thick, additional therapies might be used, including plasmapheresis, to remove the unwanted protein. A plasma exchange can normalize viscosity. The normal range for serum viscosity is 1.4-1.8 and given as a ratio relative to water (which is 1.0).

Beta-2 Microglobulin: This is a small protein in the blood that is shed by the tumor cells, and it increases as the tumor cells increase, so it is used to monitor disease burden. As such, it is considered an important prognostic tumor marker. It also can spike transiently during therapy as tumor cells break down. Normal ranges for beta-2 microglobulin are 1.21-2.70 mcg/mL.

Lactate Dehydrogenase (LDH): This is an enzyme in many of the cells of the body, including white blood cells. It is involved in tumor metabolism. Tumor cells produce more LDH than normal cells. Elevated LDH can serve as a prognostic marker and to monitor treatment response and recurrence. Normal levels of LDH are 122-222 U/L.

Amyloid: Rarely, the kappa and lambda light chains that build up during WM can deposit in the tissues where they are known as amyloid. Amyloid buildup in the organs such as the liver or kidney can cause damage. Lambda light chains are more likely to form these deposits than kappa. Approximately 3% of WM patients will experience complications caused by amyloid deposits in organs. The most common method

used to diagnose amyloid is to take a small needle aspiration sample of abdominal wall fat. A Congo Red stain is applied to the fat sample in the laboratory, and, if an apple-green refractive index is seen under polarized light, the presence of amyloid is confirmed.

Lab test results provide valuable information for staging WM.

IgG Levels: IgG is the most common immunoglobulin in the body, and, as such, is very important to normal immune function to fight off infection. One consequence of WM treatment can be that normal lymphocytes are damaged along with the abnormal ones that are targeted. When this happens, IgG levels can go down, and the risk of infection increases. To avoid this, intravenous immune globulin infusions (IVIG) may be necessary to maintain healthy IgG levels. Normal reference values are 487-1,327 mg/dL. Intravenous immunoglobulin is a safe product. The donors are screened, and the plasma is heat-treated (pasteurized) and filtered.

Complete Blood Count (CBC): Several components of the CBC are carefully monitored in patients with WM, including the white blood cells (WBC), hemoglobin, and platelet count. Infection, anemia, and bleeding may be complications of the disease.

WBC: Reduction of WBCs can be seen during active disease or with treatment. Increased WBCs can be seen in the case of infection. Low WBC count is a common side-effect of therapy that targets the white cells, like bendamustine and Rituxan. These therapies usually diminish the lymphocyte portion of the WBCs. The normal range for the WBC count is 3.4 to $9.6 \times 10^9/L$.

Hemoglobin: Hemoglobin is a measure of the protein that carries oxygen in red cells. Low hemoglobin can be seen in WM if the tumor cells are interfering with normal red cell production in the bone marrow, which leads to anemia. Blood transfusion may be ordered if the hemoglobin is below 7 g/dL or if symptoms are present, such as shortness of breath. The normal hemoglobin for males is 13.2-16.6 g/dL and for females is 11.6-15.0 g/dL.

Platelets: Platelets are fragments of cells that are important for proper blood clotting. Low platelets can lead to bleeding problems. Transfusion may be necessary if they drop below $50,000 \times 10^9/L$.

CD4 Counts: Some therapies (especially bendamustine) can produce a prolonged drop in subsets of immune cells

including CD4 positive lymphocytes. These important cells, which help fight infection, often are monitored to evaluate the strength of the immune system and, if low, may predict the need for supplemental therapies like antibiotics. Normal CD4 counts are between 500 and 1500 cells/microliter.

Creatinine: Creatinine in the blood is increased when kidney function is impaired. The kidneys can be at risk if there are too many of the kappa or lambda light chains in the blood that are produced by the tumor cells. Normal creatinine is 0.6-1.2 mg/dL in males and 0.5-1.1 mg/dL in females.

ALT/AST: These enzymes are increased if a patient has liver disease (like hepatitis). This is not a typical complication of WM, but an increase in ALT/AST can be caused by some of the therapies.

Uric Acid: Uric acid can be increased in the blood following breakdown of tumor cells, so it can occur during treatment. Excess uric acid can lead to gout if the crystals deposit in the joints.

Cholesterol: Serum cholesterol has been known to drop in WM. There is some speculation that this may be because the disease increases cholesterol metabolism.

A few general points to mention about interpreting lab tests may be helpful. If a lab value is flagged as abnormal, but is only a little bit higher or lower than the normal range, that may or may not be significant. The important thing is to monitor the trend over time. Many WM patients find it helpful to trend their lab tests to get a better picture of what may be going on.

Some tests may take longer to come back because they are sent to an outside laboratory, including the tests for SPEP, the IFE, and serum viscosity.

Many laboratory tests rely on immunologic methods—meaning that immunoglobulins are used as part of the lab test—and the immunoglobulin M protein in the blood of WM patients can, occasionally, cause interference. The interference can result in falsely high or low results. A wide variety of laboratory tests can be affected including blood counts, serum sodium, calcium, phosphorous, thyroid function tests, bilirubin, HDL, and more. Luckily, these types of interferences are the exception rather than the rule.

Scoring System for WM

Lab test results provide valuable information for staging WM. The International Prognostic Scoring System for WM includes the following five features:

- 1) Age greater than 65 years
- 2) Hemoglobin less than 11.5 g/dL
- 3) Platelets less than $100,000 \times 10^9/L$
- 4) Beta-2 microglobulin greater than 3 mcg/L

- 5) IgM concentration greater than 7 g/dL (or 7000 mg/dL).

This scoring system can help predict survival. Patients with lower levels of IgM and beta-2 microglobulin tend to do better than those with higher levels. Patients with WM who are older, are anemic (based on a low blood hemoglobin level), or have a low platelet count tend to have a poorer outcome.

Except for age, each of these factors is worth a single point. The points are added to make a score, which is used to divide patients into three risk groups:

Low Risk: Includes patients 65 or younger who have no more than one point.

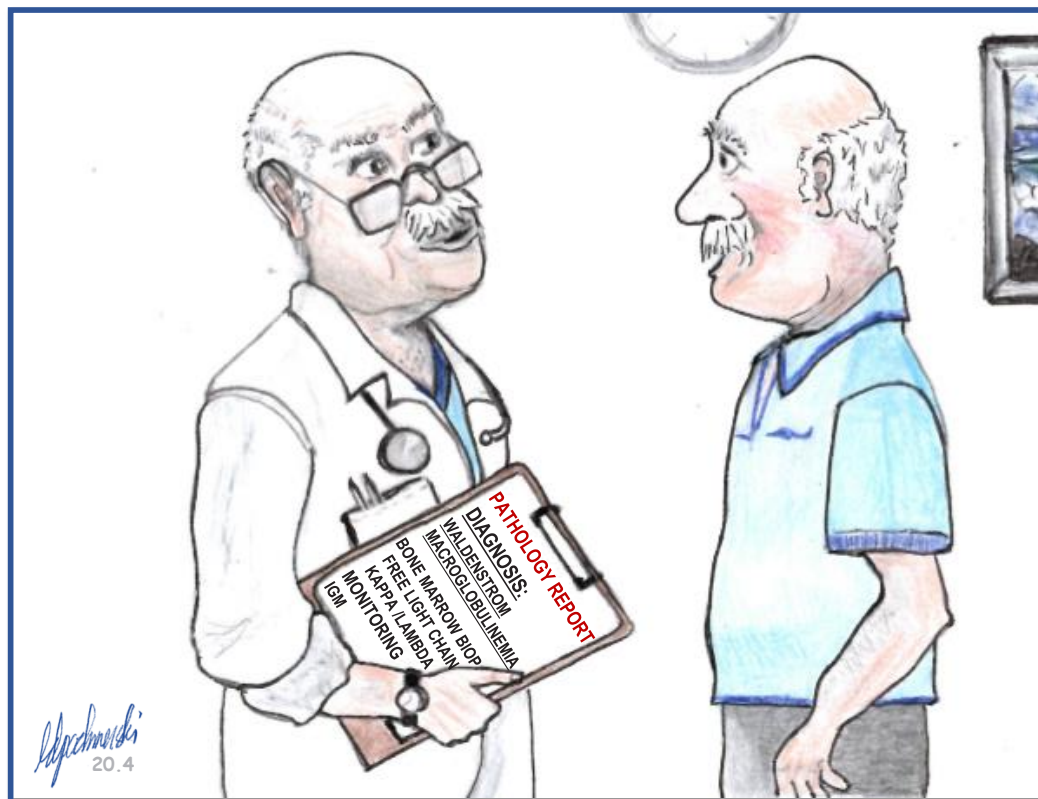
Intermediate Risk: Includes patients who are older than 65 with two or fewer points, and those younger than 65 who have two points.

High Risk: Includes those of any age who have at least three points.

Conclusion

Laboratory testing provides valuable information used for diagnosis, monitoring, and prognostic scoring for patients with WM. It is worthwhile to become familiar with the tests in order to understand their purpose and meaning. Unusual or unexpected results should be discussed with your physicians.

Torch Illustration by Linda Pochmerski



A WM diagnosis is not an end. You are braver than you believe, stronger than you seem, smarter than you think, and one day you will know how far you've come.

Have Your Say

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

CHAIRMAN'S CORNER

BY CARL HARRINGTON



Hey, look above my picture at the title of this column. It's always been called the President's Corner but now it's called the Chairman's Corner. How come? Because the IWMF has made a big change and brought in Rick Smith as our new full-time chief executive officer (CEO) and president. But don't worry. I'm still here in your corner! Instead of president, my title changes

to chairman of the Board of the IWMF.

Let me share with you the reasons for this change in our structure.

Since our inception, the IWMF Board of Trustees has been an operating board of all volunteers. That means that the Board not only directs the big picture strategy and policies of the IWMF but also is hands-on in everything we do, from writing, proofreading, and executing everything we produce, to selecting, contracting, and monitoring progress on all of our research projects. This structure means one or more IWMF Board members direct and work with our staff and other volunteers in every single aspect of our work. As the IWMF has grown, our Board has been stretched far beyond what volunteers can be expected to do. In order to accomplish our ambitious goals, in February the IWMF Board decided to move from an operating board to a governing board. This change will enable us to better serve our members and to intensify our search for a cure.

As a first step, the Board created a job description, placed an ad, and alerted all of our partners that we were looking for a full time CEO and president, in case they knew any good candidates. We received a strong response from many qualified candidates who were intrigued by the chance to make a difference in the lives of WMers. We carefully screened and reduced the resumes to eleven candidates for preliminary interviews, then to six semifinalists for more online interviews, and then to three finalists for in-person interviews. We were very careful and diligent about the process to ensure we found exactly the right person to lead us forward.

We are excited to have found an outstanding person and leader in Rick Smith, who started as the IWMF president and CEO on August 12. Rick has made non-profit work his entire career. Some highlights of his resume include:

- Area vice president with the American Diabetes Foundation

- Chapter president in several locations at the National Multiple Sclerosis Foundation
- CEO and president at the American Liver Foundation
- CEO at the International Dyslexia Foundation

If you want to know more, Rick's complete resume is here: <https://www.iwmf.com/sites/default/files/docs/documents/Smith%20RESUME.pdf>.

With such an impressive background, why did Rick choose to join the IWMF?

"I was lucky to find what I loved when I was just 20. I was a scholarship athlete at the University of New Mexico. As part of my scholarship, I was asked to do public service. I found I loved the work at the local YMCA and have made non-profit work my entire career. I've always been drawn to making a difference in people's lives. I want to go to bed each night knowing that I've done something to help someone somewhere.

*We are excited to have found an **outstanding person and leader** in Rick Smith.*

"When I saw the IWMF ad asking if I wanted to make a difference, I was intrigued. In investigating the IWMF, I found a passionate organization that was doing excellent work in three critical areas: patient education, patient support, and leading the search for a cure. I felt I could help the IWMF take the step to become an even stronger organization and touch far more people's lives at their immediate point of need. As our essential movement gets stronger and louder, we will create better future pathways for patients, caregivers, and families whose lives are impacted by Waldenstrom's macroglobulinemia."

As I mentioned, I'm not going anywhere, but with such an illustrious professional as Rick at the helm of our organization, perhaps I'll get a life...just kidding, but those 40-50+ hour weeks were getting a little tiring. Seriously, while I am honored to have steered the IWMF for the past seven years, I look forward to a less-all-consuming volunteer commitment. And as a patient, I know about watch and wait. So, I look forward to watching the IWMF grow under professional stewardship. In fact, I can't wait. As the newly titled chairman of the Board of the IWMF, I'll be helping Rick and the IWMF Board of Trustees build better tomorrows for WMers everywhere. This is a great day for WMers and bad news for WM cancer cells!

Chairman's Corner, cont. on page 7

In other good news, I want to make sure you haven't missed the following:

- The videos of all of the presentations from the 2019 IWMF Educational Forum in Philadelphia are on our website at: <https://www.iwmf.com/library/media-library/educational-forum-multimedia>.

If you haven't looked at them, do so right after you read the rest of this column. You might find the Great Debates fun and of particular interest.

- We approved another \$1.2 million in new WM research as part of the IWMF-LLS Strategic Research Roadmap. If you missed this story, see: <https://www.iwmf.com/news-and-events/news/iwmf-awards-12-million-new-research>. To date, the IWMF has funded over \$16.4 million in research that has benefited us all. We now have better treatments that give longer and deeper remissions with fewer side effects. But we won't stop until we find a cure. Please pay it forward and give as generously as you can so we can accelerate our search for a cure.
- We initiated the first Continuing Medical Education (CME) course in conjunction with Plexus Communications: <https://www.iwmf.com/news-and-events/news/iwmf-collaborates-educate-medical-community-wm>. Since WM is a rare disease, many community oncologists seldom see a WM patient. Increasing awareness and knowledge about WM among community oncologists has long

been a goal of the IWMF. As part of this course, each attendee gets information about the IWMF and a copy of our *Frequently Asked Questions* booklet.

- We created a new IWMF publication on IVIG (intravenous immunoglobulin): https://www.iwmf.com/system/files/IVIG_FactSheet-English.pdf. WM patients who have recurrent severe infections due to a compromised immune system may use IVIG. This fact sheet is available in English, Spanish, French, German, Italian, Norwegian, Traditional Chinese, and Simplified Chinese. Be sure to check out all of our publications: <https://www.iwmf.com/library/iwmf-and-affiliate-publications>.
- We announced the 25th IWMF Educational Forum, June 5-7, 2020, at the Hyatt Regency Lake Washington in Renton, WA (near Seattle). You won't want to miss this Ed Forum silver anniversary so mark your calendars now! <https://www.iwmf.com/news-and-events/news/announcing-date-and-site-2020-iwmf-educational-forum>.

We look forward to accelerating our search for a cure. And with Rick's leadership and your continued support, we will surely get there.

Stay well,

Carl



IWMF DOC STAR: DR. MONIQUE MINNEMA

AS TOLD TO RON TERNOWAY



Dr. Monique Minnema (right) and Dr. Marie-José Kersten in Paris

Dr. Monique Minnema is professor of hematology at the University Medical Center, Utrecht University, in the Netherlands. After completing her hematology training at the Academic Medical Center in Amsterdam, Minnema began her career at Utrecht in 2005.

She specialized in the diagnosis and treatment of B-cell malignancies, especially plasma cell disorders such as multiple myeloma, AL amyloidosis, and Waldenstrom macroglobulinemia

(WM). She now leads a large clinical trial team at Utrecht involved in over 20 active clinical studies, including the Phase

2 study of acalabrutinib and the Phase 3 study of zanubrutinib for WM patients. Her main focus is the development of novel therapies for plasma cell dyscrasias and lymphomas.

Minnema accepted the challenge of developing guidelines for the diagnosis and treatment of Bing-Neel syndrome (BNS), a rare complication of WM that straddles both hematology and neurology. She was a member of the organizing committee for IWWM-9 in Amsterdam in 2016 and spoke on the topic of disease presentation of WM at the 5th International Patient and Physician Summit in New York City in October 2018.

Dr. Shirley D'Sa of University College London Hospital and our January 2018 IWMF Doc Star is an enthusiastic fan of her Dutch colleague: "Monique has personally contributed to many developments in the field of WM, through her

IWMF Doc Star, cont. on page 8

enthusiasm for science and clinical trials, her robust and consistent clinical approach, and her gift for collaboration and delivering on projects. Her warmth and responsiveness have endeared her to the WM community, and she is a champion for her patients. Her recent recognition as a professor of haematology is a testament to her academic prowess. Working with Monique is a consistent highlight for me and many others in the WM community!”

Minnema grew up in a small village in the Haarlemmermeer, which is a polder, land reclaimed from a big lake (“meer”), below the normal water level and surrounded by dikes. “Typically Dutch!” she exclaimed. The youngest of three children, she admired an aunt who lived in Amsterdam. “That was what I also wanted: to move away from the small village and live in a big city! At school I loved history and was actually thinking about studying art history. But I also liked biology and chemistry and was looking for studies in that direction too.”

Her mother is a nurse and proposed to her daughter the idea of studying medicine. “I thought that I could try one year and change to something else if I did not like it. But I became enthusiastic immediately and completed my studies and medical training.”

When asked whom she considers to be her most influential personal and professional mentors, Minnema replied, “In my personal life my biggest mentor is my husband, who has always supported me and has said from the beginning that I could achieve everything I wanted. In my professional life, as an intern at the internal medicine ward of a small hospital, I do recall my supervisor. He was at the end of his career and was a very cheerful person. I remember clearly that he told me ‘Monique, I do envy you. Many new developments in the treatment of patients are approaching, the future is so exciting, and you are going to experience this!’ And he was right, I do have the feeling that we live in exciting times with so many new developments, and I’m extremely grateful that I can contribute to this.”



Dr. Monique Minnema at IWWM-10 in New York City

Minnema credits Hematon, the Dutch blood disorder patient advocacy organization, with leading her to specialization in WM. In 2010 she was concentrating on multiple myeloma when a fellow physician mentioned to her that Hematon wished to have more attention paid to WM by the Dutch medical community and wanted to send a young hematologist to Venice to the 6th International Workshop for WM, IWWM-6.

“So Hematon paid my trip to

Venice, and I really did not know anybody. I was totally surprised by the high quality and positive atmosphere of the meeting, and during this workshop I learned that a disease called Bing-Neel syndrome (BNS) existed. At the end of the meeting I knew more people and was invited to a beautiful dinner at a Venetian palace.”

She was so enthusiastic about the Venice workshop that for the next meeting in 2012 she brought three colleagues with her. At IWWM-8 in London in 2014, she spoke about BNS and started her work on the first guidelines for the disease. “Being a part of this inclusive community was and is really important to me, both in my personal life as well as my professional life, and I have to thank the Dutch patient organization for this!”

Approximately 1500 WM patients are in the Netherlands, with more than 50 being treated at UMC Utrecht. When asked what advice she gives newly diagnosed Wallies, Minnema replied, “Take time for decisions, get informed, get connected, and try to accept that the disease will be with you for the rest of your life. Heed the advice of Dr. Bob Kyle: know your M-protein! In addition, be assured that we will do everything possible to help as much we can.

“The most important challenge is to make other colleagues understand the diversity of the disease and that WM is not like other indolent lymphomas. It needs special considerations and expert care. The MGUS state, which can be associated with clinical symptoms, is sometimes misunderstood.”

Minnema’s comments on the challenges of balancing life as a physician, researcher, wife, and mother: “I do not think I have a good work-life balance. I do have a family, two beautiful daughters of 16 and 12 years old, and in the end that choice is always easy; my children come first. They are very proud of me, and I think it is important that I can show them that as a woman you can have a career as well as a family. So my leisure time is mostly in the holidays, and then I like to read history books. I also have an interest in politics, architecture, and art.”

The final word goes to Monique’s Dutch colleague and close friend Dr. Marie-José Kersten: “I have known Monique Minnema since I had the privilege to be her mentor at the Academic Medical Center in Amsterdam for her training as an internist and hematologist. It has always been such a pleasure for me to work with Monique, and together with Josephine Vos, we have developed the Dutch WM Task Force, which we began after IWWM-7 in Newport, Rhode Island, in 2012.

“Monique is extremely dedicated to her patients and to her research, and she has become an international expert on rare syndromes such as Bing-Neel syndrome and AL amyloidosis. I consider her to be a true friend and look forward to further improving care for WM patients together with her in the Netherlands!”

FROM IWMF CONNECT: FALL 2019

BY JACOB WEINTRAUB, MD

Now that we are past the summer, new challenges await us in reading and discussing posts about WM as we enjoy the changes that fall brings. IWMF Connect continues to be a part of our lives. As always, there are multiple links to human interest articles, scientific studies, and other important issues. Multiple issues are discussed and even old topics are presented with new twists or just reminders of information we may have forgotten.

IWMF Connect Manager and IWMF Trustee Peter DeNardis posted a link to an article of general interest. This was an article for caregivers titled “Caregiver Anger: Florence Nightingale Never Swore Like This.” It is a blog-type posting that shows how difficult the caregiving task truly is and may be cathartic in easing our anxiety over those issues. <https://blogs.psychcentral.com/full-heart/2019/06/caregiver-anger-florence-nightingale-never-swore-like-this/>

Sherry C thanked Peter for the link. She catches herself being mad at her husband when she has to repeat something over and over. She then realizes how futile it is for her to get mad because his short-term memory is about a minute and then it is gone.

*Immune globulin is used to **treat** a variety of **medical conditions**.*

Peter also posted a complete article about the status of immune globulin, which is experiencing a supply shortage. The article is from the *Wall Street Journal*, August 9, 2019, and is worth reading. Immune globulin is used to treat a variety of medical conditions, including primary immune disorders, immunodeficiency from diseases such as WM, and other conditions such as some peripheral neuropathies. Recently, many hospitals and infusion clinics have received less immune globulin than they need. Some have started to ration it, prioritizing it for patients who need it more urgently for life-threatening conditions. The shortage is, in part, due to increased demand and some manufacturing delays. Companies are boosting production, but it will take time to meet demand. The FDA is working with manufacturers to mitigate the shortages. <https://www.wsj.com/articles/drug-shortage-leaves-patients-without-immune-disorder-treatment-11565343023>

Wanda H posted links to articles of interest. One was to an article that reviewed a book of love poems celebrating the end of chemo. The book is by fellow Wally Sheree K. Nielsen.

<https://menafn.com/1098794794/St-Louis-Author-Celebrates-End-of-Chemotherapy-with-Book-of-Love-Poems-for-the-Beach>

Hally D posted that it is very inspiring when a person can use creativity to cope with treatments and life challenges in general. Hally will definitely take a look at the book and make it a point to visit the beach. Hally related very well to what the author is saying.

Wanda also sent a link to an article in *Lymphoma News Today* about cancer and becoming impatient. Wanda commented that cancer can make us impatient, but we never know what other people are going through. https://lymphomanewstoday.com/2019/07/12/change-cancer-patience/?utm_source=LYM+E-mail+List&utm_campaign=7c8895339d-RSS_THURSDAY_EMAIL_CAMPAIGN_US&utm_medium=email&utm_term=0_4783db36f7-7c8895339d-71472833

Robin S complimented Wanda on sharing the best articles. At age 70, Robin became extremely impatient, declaring to any family member who seemed to holding her back that “I don’t have forever you know!” This was before she was diagnosed with WM. Now, a few years later, she is reading four books at a time, has no patience with a lawn that refuses to survive the Virginia heat, and walks out of dumb movies. She says the time has arrived to live her life the way she should have when she was younger and thought she had all the time in the world.

Finally, **Wanda** posted a link to an article titled “How to Talk to Your Kids About Your Cancer Diagnosis.” This is from the magazine *Prevention*. The article includes helpful advice from experts and a mother who has been there twice. For the newly diagnosed person with young children, the tips in this article could be helpful. The article includes advice on talking to children of all ages and is more relevant since it appears that we now have more people diagnosed at a younger age than we have had in the past. <http://flip.it/Wt2mBh>

FATIGUE

Meg M posted a link to an instructive (and entertaining) animated presentation of cancer-related fatigue and tips for coping with it. This is a DocMikeEvans video called “Cancer-Related Fatigue” and is from *Lymphoma News Today*. <https://lymphomanewstoday.com/social-clip/2016/06/01/cancer-related-fatigue-need-know-2/?amp>

There was a separate discussion about fatigue, including a link to a lengthy article about the multitude of causes of fatigue. The article’s title is “Cancer-Related Fatigue: Approach to Assessment and Management,” and **Steven D** posted this

IWMF Connect, cont. on page 10

link for it: <https://www.mdedge.com/hematology-oncology/article/147594/patient-survivor-care/cancer-related-fatigue-approach-assessment>

The initial question on fatigue was from **Alan W**, asking if high IgM in the blood and bone marrow cause profound fatigue, even when the viscosity isn't high and the hemoglobin isn't "terribly low." He has had disabling fatigue for a long time, but his oncologist did not think it was WM-related. However, after a recent plasmapheresis, the fatigue vanished, though this relief only lasted ten days.

Linda G responded that she has severe fatigue with low IgM and normal hemoglobin. She sees Dr. Castillo, and he has many patients with similar symptoms and feels it is a subgroup of WM. Although she has had fatigue for seven years, Dr. Castillo has not yet suggested treatment.

Sue H reassured Alan that he is not alone. Cancer-associated fatigue is a recognized phenomenon that occurs even in patients who have had good responses to treatment. The reasons for it are not always well understood, but researchers are studying it. Cytokines (chemical messaging molecules of the immune system) have been suggested as one reason for unusual fatigue in cancer patients. Sue suggested to Alan that hypothyroidism (underactive thyroid) might be a condition causing fatigue, and it easily can be tested for and treated.

Brad S added that his fatigue was related to his low hemoglobin. He had several suggestions for dealing with it, including making a list of what you would like to do the next day. In the morning, don't look at the entire list, but just one thing, and do it. Rest if needed, and then look at the next thing on the list and do that. Celebrate any items that you complete. Also, he suggested not to be hard on yourself if you have to do fewer things, don't be shy about letting family and friends know what you need, and accept help that is offered.

ANKLE SWELLING

Jane P posted that she has had swollen ankles for a while. She didn't know if it is related to WM. She has asked both her oncologist and cardiologist for opinions. Her oncologist wasn't concerned. The cardiologist ordered a couple of tests which were OK. She has an increasing neuropathy but is watch and wait, IgM 617.

Karen R answered that she only has had swollen ankles when taking dexamethasone during treatment. Her ankles now are normal but swell some when she eats food with high sodium content. She has stayed hydrated and does not salt her food when she eats.

Joanne B posted that she had drastic swelling in her limbs and feet. She takes daily Celebrex, but her doctor says the swelling is not related to her WM.

Kathy W added that she has learned that Celebrex can cause fluid retention.

Robin S answered that she has had some swelling in her ankles since starting treatment, which includes dexamethasone. She has obtained compression socks, and they've helped a lot. However, wearing them in the summer heat has been a challenge. Most of the swelling is in her right ankle, and the right knee has been causing her pain.

Gordon G posted that his swollen ankles were linked to his amlodipine, the heart medicine he was taking to counter the ibrutinib-related hypertension and arrhythmia. When he switched to a different medicine, Ramipril, the swelling subsided.

Richard B spoke with his family physician, and he said the swelling is due to the leaking of valves in the veins, allowing blood and fluid to pool in the ankle. His doctor said compression hose would help. Venous studies a couple of years ago showed this leakage.

SUN EXPOSURE

This discussion was held during the summer. Now that it is fall, it might not be so relevant but should be remembered next summer.

Lela H asked about sun exposure. She and her husband asked his oncologist about sun exposure, and the doctor wasn't certain what they should do other than wear long sleeves and use sunscreen. She wanted to know if the danger from the sun was because of his WM or because her husband is taking Imbruvica (ibrutinib). She later added that they tried UV arm sleeves, but the brand they bought was not helpful, so they are looking for shirts, hats, and sleeves that have 50 UV rating. They also use sunscreen.

Dr. Tom Hoffmann, IWMF Trustee, commented that anyone who has cancer has a higher risk of getting another cancer than does the general population. However, here it is the drug, not WM. Ibrutinib is an EGFR (epidermal [skin] growth factor receptor) inhibitor. That leads to skin problems and higher rates of skin cancer. <https://www.uwhealth.org/healthfacts/cancer/7124.pdf>

Pat J posted that she saw a specialist for a second opinion, and he was very strong in recommending she wear high SPF sunscreen, applying at least two times a day, and wearing a large sun hat with sun protection, too. If possible, a light cover-up would be helpful. The doctor said patients with any lymphoma are especially susceptible to developing melanomas.

As always, the discussions and links here represent only a small portion of the wide range of topics discussed. Everyone is invited to join in the group. We hope you will participate, but just "lurking" and reading on the sidelines also are welcomed. If you have any questions or wish to see more from our discussions on a particular topic, please let me know and I will try to include those discussions in a future column. I wish you all continued good health.

VACCINATION FOR ADULT IMMUNOCOMPROMISED PATIENTS

BY SUE HERMS, IWMF RESEARCH COMMITTEE MEMBER

Since flu season is fast approaching, the subject of vaccination for flu and other diseases is expected to be of special interest to WMers, and it is timely to review the recommendations for the vaccination of adult immunocompromised patients.

General Considerations

In general, patients who have a hematologic cancer such as leukemia and lymphoma, have had stem cell transplantation or spleen removal, or are receiving chemotherapy, radiation, or long-term or high dose steroid therapy are considered to be immunocompromised, meaning that they have an impaired immune system. For this reason, they may not be able to develop as effective an immune response to vaccination as a “normal” person. Also, vaccines that are composed of live, attenuated (weakened) bacteria or viruses are typically not recommended for these patients, as they can cause serious, albeit rare, side effects that may include the actual infection they are intended to prevent.

Vaccines manufactured from killed bacteria or viruses, toxoids (inactivated toxins), or partial bacterial or viral components are considered safe for people with immune system deficiencies.

The vaccination of immunocompromised patients may necessitate giving an extra dose, altering the timing of doses, or selecting a different vaccine formulation (such as “killed” versus “live” vaccine). For instance, with the exception of the influenza vaccine, vaccination during chemotherapy or radiation therapy should generally be avoided because the immune response may be suboptimal. If a vaccine is given right before or during therapy, it should be repeated three months after therapy if immune competence has been restored. Patients who have B-cell deficiencies and are receiving immune globulin therapy should not be vaccinated because of concerns about vaccine effectiveness. Patients on therapy that includes anti-B-cell antibodies (such as rituximab) ideally should wait at least six months after therapy before being vaccinated.

If someone with immune deficiency has received exposure to a specific disease for which a safe vaccine is not available, it may be desirable for that person to receive immune globulin therapy instead.

Travel to areas where certain diseases are endemic may require the administration of special vaccines, such as for typhoid, dengue fever, cholera, or yellow fever. In this situation, the general principle for immunocompromised adults still applies: live vaccines are not recommended.

The recommendations below are general in nature and may not apply in certain cases. Pregnant women and stem cell transplant patients should follow special guidelines. For more

information on vaccination for adult immunocompromised patients, go to: <https://www.cdc.gov/vaccines/schedules/hcp/imz/adult-conditions.html#note-zoster>.

You should consult with your physician or an infectious disease practitioner if you have any questions about vaccination.

Vaccines Considered Safe for Adult Immunocompromised Patients

The US Advisory Committee on Immunization Practices (ACIP) considers the following vaccines to be safe for adult immunocompromised patients:

- Haemophilus influenzae* type b*
- Hepatitis A*
- Hepatitis B*
- Human papilloma virus
- Influenza shot
- Meningococcal*
- Pneumococcal (PCV13 and/or PPSV23)*
- Tetanus/diphtheria/pertussis (Tdap) or tetanus/diphtheria (Td)

*These vaccines are used for adults with additional risk factors because of age, travel, potential exposure, or specific medical conditions

Vaccines Contraindicated for Adult Immunocompromised Patients

Vaccines that are live and generally should **not** be administered to patients with hematologic cancers or on immunosuppressive therapy include the following:

- Chicken pox
- Measles/mumps/rubella
- Influenza nasal spray
- Zostavax for shingles

*...exception to the general rule that **vaccination** should be avoided during immunosuppressive therapy is the **influenza vaccine**.*

More About Influenza Vaccination

One notable exception to the general rule that vaccination should be avoided during immunosuppressive therapy is the influenza vaccine. Because flu can be so dangerous to the elderly and immunocompromised, the ACIP recommends

Vaccination for Adult, cont. on page 12

that these patients receive yearly vaccination against the influenza virus even when they are receiving such therapy. Preferably, vaccination should be done at least two weeks before chemotherapy begins or between cycles. Note that only the influenza shot is recommended, not the nasal spray vaccine.

There are several types of flu shots available. Trivalent shots protect against three strains of the virus; these include a high-dose shot called Fluzone and a shot called Fluad with an immune-boosting adjuvant, both of which are designed for people 65 years of age and older. Quadrivalent shots protect against four strains of the virus. There are shots which do not use eggs in their production and are suitable for those who have egg allergies.

New for the 2019-2020 flu season is the recommendation that clinicians should offer vaccination by the end of October and continue to offer it throughout the season.

More About Shingles Vaccination

Shingles vaccination is of great interest to many cancer patients, particularly those with hematologic cancers, as their risk of getting shingles increases if they are receiving immunosuppressive therapy for their disease. As noted above, the Zostavax vaccine is not indicated for such patients.

The Shingrix vaccine for shingles, approved by the US Food

and Drug Administration in 2017 for people 50 years of age and older, is not made from live virus and is thus presumably safe for the immunocompromised; however, it has not yet been officially recommended by the ACIP for patients with hematologic cancer or on immunosuppressive therapy because its effectiveness in this population is still unknown. Despite this, many clinicians are suggesting that their cancer patients receive the vaccine. Current recommendations also suggest that anyone who has received Zostavax should receive Shingrix as well. An adjuvant to boost the immune response has been added to Shingrix to make it more effective than the older Zostavax vaccine, and for maximum benefit, it must be administered in two doses, two-six months apart. Shingrix does appear to be more likely than Zostavax to cause soreness at the site of injection for up to three days afterward. Be aware that supply shortages currently exist because of high demand for this vaccine. When you receive the first Shingrix dose, check with your provider to see if your second dose can be reserved for you.

The other option for the prevention of shingles, especially during chemotherapy treatment, is to receive daily prophylaxis therapy with an oral antiviral medication such as acyclovir or valacyclovir.

SURVIVAL

BY DAVID SCHNELL

At the turn of the century I was diagnosed at the Mayo Clinic in Rochester, MN, with an extremely rare lymphoma: Waldenstrom's macroglobulinemia. The prospects were not very good—poor in fact. Thanks to astounding luck, some of the world's premier WM researchers were my doctors at Mayo, and new treatments had been recently approved. That was 18 years ago. The path has not been without obstacles, but so far, so good.

“...in landlessness alone resides the highest truth, shoreless, indefinite as God...”

Herman Melville, *Moby Dick*

“Awly, awly oxen free.” A phrase from my childhood had returned and I chanted it over and over in my misery.

I couldn't sleep, my feet ached, my head ached, my heart pounded, and the doctors said my kidneys were failing. It was my first night in the hospital. They didn't have a diagnosis and didn't want to confound their tests with any medications.

In the coming days I would have ultrasounds, MRIs, biopsies, and innumerable blood tests.

All I could do now was stand in the midnight shower, while my wife slept in the big chair, let the hot, slowly flowing water spill over my head, run down my shoulders, and eventually wash over my feet as I chanted over and over “Awly, awly oxen free.” Many people know the phrase, few can explain it. Weeks later, a friend told me she thought it came from Liverpool and originally sounded like, “All ye, all ye out, are in now free.”

Whether it was conscious thought, hallucination, imagination, or just exhaustion, a scene appeared before me in the shower where missing children began stepping out, moving around the corners of buildings. They began to walk down the street toward me. Also, men rose up from the graves of “unknown soldiers,” and polar explorers with fur-lined parkas stepped onto the street. This strange crowd of dead, missing, and lost

Survival, cont. on page 13

people all responded to my declaration, “Awly, awly oxen free” and moved with me toward “home” and a chance to start again. My new start involved a definitive diagnosis and sophisticated technology. It required exotic chemotherapy drugs and a targeted antigen. It included a team of powerful minds analyzing my blood chemistry and performing recommended procedures. All of these activities, when observed from a short distance, are what many people call “battling cancer.” I will not call it that.

It wasn’t until the priest visited my hospital room a second time that I began to understand my relationship with this disease. It paralleled my relationship with nature and, in a significant way, reflected my experiences on Lake Superior.

The metaphor of combating a disease in a battle to the death is ubiquitous. I’ve never battled the lake, conquered a mountain, or defeated nature in any way. I was not prepared to fight now. What I knew from Lake Superior was that it could do great harm to me. It could change from calm to violent so fast that without preparation I would be destroyed. The lake is so cold that in minutes it could suck the warmth from my body and demolish my will to live. Its rocks, and waves, and fogs, and winds could all conspire to annihilate me, and yet I care more about Lake Superior than I do any other place I know. I treasure each minute I spend in my kayak on the water. When I am on Lake Superior I whoop like a cowboy and smile like a Hare Krishna. Lake Superior is never two times the same. It is a place in the wilderness where the ultimate rules of nature prevail, and every minute there is a session in what matters.

I couldn’t have known that the times I spent bouncing through big waves, or paddling into stiff winds, were the moments when I was learning the biggest lessons of my life. Lake Superior is the harshest environment I know. I’ve paddled through ice in January that without warning became too thick to move through; I’ve been caught in a sudden hailstorm, and struggled through fresh gales. Eventually I’ve always found a quiet bay or a sandy beach, a place of shelter and calm. I’ve seen magnificent double rainbows after a storm and completely relaxed as the lake’s huge rollers rose and fell beneath my kayak. I’ve admired the inexorable action that



Kayaker and Split Rock Lighthouse on Lake Superior - Photo by Nick Carlson

smoothed the stones on beaches and marveled at the power that carved caves from solid stone. It is nature undiminished by my presence. I think it must be as amazing today as it was to the earliest humans who knew it.

And most important to me now is the knowledge that it means me no harm. Lake Superior does not care about me. Its ferocity is benign, in it my respect has ripened. I must learn how to survive its indifference. I cannot battle its power but have learned to respect and honor its beauty and strength.

I do not deny the irony of my love for this place that has none for me. I fully appreciate the terms of our relationship. There exists in it a world of honesty and pleasure. It teaches me to be humble, to understand that the machinery of the planet is not concerned with me, that these are the conditions of life. I, without a doubt, intend to survive, but that survival cannot be guaranteed or granted.

Pushing the blade of my paddle through the shimmering glaze of the lake, I pull hard then dip the other blade on the opposite side and pull again, rhythmically, first one side then the other. Without haste, I urge my kayak across the water. Ripples swell and succeed one another as they fall away from the bow on my path across the lake.

All ye, all ye out, are in now free.



MEDICAL NEWS ROUNDUP

BY SUE HERMS, IWMF RESEARCH COMMITTEE MEMBER

Revised Prognostic Scoring System Proposed for WM –

An article published in the journal *Leukemia* by a group of international WM researchers concluded that the International Prognostic Scoring System for WM (IPSSWM), developed a decade ago, should be revised to better capture the prognosis of WM patients in the current era that includes the widespread use of rituximab-containing therapy regimens. Based on data from 492 symptomatic, untreated patients who were followed for a median of seven years, the researchers formulated a revised scoring system model: beta2-microglobulin equal to or greater than 4 mg/L, serum albumin less than 3.5 g/dL, lactate dehydrogenase (LDH) equal to or greater than 250 IU/L, and age 66-75 years are scored with 1 point each; age less than 66 is scored with 0 points, and age greater than 75 is scored with 2 points. The model resulted in scores of 0-5. There was no difference in prognosis with patients scoring 4 or 5, so for clinical applicability, the patients were divided into five groups with scores of 0, 1, 2, 3, and 4-5. Accordingly, the three-year WM-related death rates of these five groups were 0%, 10%, 14%, 38%, and 48%, respectively, while the overall ten-year survival rates were 84%, 59%, 37%, 19%, and 9%, respectively. The model was validated in another set of symptomatic, untreated WM patients.

*Oprozomib is an oral proteasome **inhibitor** with a structure similar to carfilzomib (Kyprolis).*

Results Reported for Clinical Trial of Oprozomib in Relapsed Multiple Myeloma and WM –

Researchers at Dana-Farber Cancer Institute presented data in the journal *Clinical Cancer Research* from a Phase 1b/2 study of single agent oprozomib in patients with relapsed multiple myeloma and WM. Oprozomib was administered once daily on days 1, 2, 8, and 9 (called the 2/7 schedule) or on days 1-5 (called the 5/14 schedule) of a 14-day cycle. Median duration of treatment was 34.6 weeks on the 2/7 schedule and 8.1 weeks on the 5/14 schedule. The overall response rates in 31 WM patients were 71.4% and 47.1% for the 2/7 and 5/14 schedule cohorts, respectively. The most common serious adverse events were gastrointestinal and hematologic. The maximum tolerated dose determined for WM was 300 mg/day on the 2/7 schedule and 240 mg/day on the 5/14 schedule. Oprozomib is an oral proteasome inhibitor with a structure similar to carfilzomib (Kyprolis).

Combination of Ibrutinib and Rituximab for WM Receives Approval by European Commission –

The European

Commission has approved the expanded use of ibrutinib (Imbruvica) to include the addition of rituximab (Rituxan) for the treatment of WM patients. The Commission based its approval on a positive opinion in June from the European Medicines Agency and on data from the Phase 3 iNNOVATE clinical trial of WM patients that evaluated ibrutinib in combination with rituximab versus rituximab with placebo and concluded that the combination significantly increased progression-free survival over rituximab. The US Food and Drug Administration approved the combination for patients with WM in August 2018.

New Phase 1 Trial to Open of Ibrutinib Combined with ERK Inhibitor –

Dana-Farber Cancer Institute is planning to open a Phase 1 clinical trial to study an investigational drug called LY3214996 in combination with ibrutinib (Imbruvica) in patients with chronic lymphocytic leukemia, mantle cell lymphoma, marginal zone lymphoma, and WM who have mutations that are thought to confer resistance to ibrutinib. LY3214996 is an oral inhibitor of ERK (extracellular signal-related kinase), part of an important pathway in cancer growth. The study anticipates enrolling 18 participants, all of whom must be actively receiving ibrutinib monotherapy, experiencing disease progression, and demonstrating a BTKCys481 and/or PLCy2 mutation. The identifier number on www.clinicaltrials.gov is NCT04043845.

New Phase 2 Trial Will Combine Daratumumab and Ibrutinib in WM –

Weill Cornell is planning to open a Phase 2 trial of daratumumab (Darzalex) plus ibrutinib (Imbruvica) in 24 WM patients. The trial will have two arms: Cohort A will consist of patients who are ibrutinib naïve and either untreated or relapsed from another therapy, and Cohort B will be comprised of patients who are currently receiving ibrutinib but whose response has plateaued. In Cohort B, daratumumab is being added in an attempt to deepen response. Daratumumab is a monoclonal antibody that targets the surface molecule CD38 and is administered intravenously. The identifier number on www.clinicaltrials.gov is NCT03679624.

French Trial to Study Mutations in WM and Improve Methods for Disease Monitoring –

A clinical trial in France is recruiting 40 participants with untreated WM to determine the best laboratory method for following the MYD88 L265P mutation over time as a marker of response to treatment, to assess the best type of sampling for the mutation (in particular whether this mutation is present in blood in order to limit invasive procedures for bone marrow sampling), and to evaluate the prognostic significance of other recurrent mutations and their feasibility as therapeutic targets. The trial is identified on www.clinicaltrials.gov as NCT03952052.

Medical News Roundup, cont. on page 15

Chinese Study to Begin Enrollment for Ibrutinib in Relapsed/Refractory WM Patients – Relapsed/refractory WM patients in China will soon be offered the opportunity to participate in a clinical trial of ibrutinib (Imbruvica). The study anticipates an enrollment of 17 patients, to begin November 2019. The identifier number on www.clinicaltrials.gov is NCT04042376.

Final Results Published for Phase 3 Trial of Maintenance Rituximab in Follicular Lymphoma – Final results were published in the *Journal of Clinical Oncology* for the international, randomized Phase 3 PRIMA study of 1,018 follicular lymphoma patients treated with two years of maintenance rituximab (Rituxan) versus observation alone following frontline chemoimmunotherapy. At nine years of follow-up, median progression-free survival was 10.5 years for the group that received maintenance compared with 4.1 years for the observation group. However, the improvement in progression-free survival did not lead to an improvement in overall survival, which was approximately 80% for both groups. In this trial, patients were initially treated with combination therapy that included rituximab; those who responded were then randomly assigned to either two years of observation or rituximab maintenance given every eight weeks. The authors noted that death due to second cancers was almost four times more frequent in the observation arm and speculated that earlier relapse in that arm may have led to the recurrent use of cytotoxic- and radiation-containing regimens that increase the frequency of second cancers. However, it was also noted that serious adverse events, primarily infections, were more common in the maintenance arm.

*Standard **pre-medications** (Benedryl and Tylenol) do not always **prevent** reactions.*

Canadian Study Reduces Incidence of Rituximab Infusion Reactions – Rituximab (Rituxan) is associated with frequent infusion reactions that can cause a significant burden to patients and health care practitioners. Standard pre-medications (Benadryl and Tylenol) do not always prevent reactions. A Canadian study presented at the American Society of Clinical Oncology 2019 Annual Meeting added the anti-inflammatory drug montelukast and the antihistamine drug rupatidine, alone and in combination, to standard pre-meds and compared them to standard pre-meds only in 87 patients with lymphoproliferative disorders who were receiving initial rituximab treatment. Infusion reactions occurred in 92% of patients on standard pre-meds only versus 38%, 45%, and 33%, respectively, in patients also on montelukast, rupatidine, and a combination of the two. Mean infusion times were shorter in those also receiving montelukast and rupatidine, particularly in combination.

The addition of these medications lowered the overall cost of rituximab administration by reducing the costs of rescue medications and nursing care.

Study Characterizes Gastrointestinal Toxicities of Rituximab Therapy – Gastrointestinal toxicities associated with rituximab (Rituxan) are not well understood. An article published in the *American Journal of Clinical Oncology* by researchers from Baylor University and MD Anderson Cancer Center described the features of rituximab-associated colitis (inflammation of the colon) in a retrospective study of 13,717 cancer patients who had received rituximab, 1660 of whom had undergone a colonoscopy between 2000 and 2018. Seventy (4%) of those who had a colonoscopy were diagnosed with colitis. The median time from treatment to onset of colitis was 181 days, and symptoms included diarrhea, abdominal pain, bleeding from the rectum, and concurrent fever. The median duration of symptoms was 21 days. In most cases, the colitis was mild, requiring supportive care only, although there were rare cases requiring intensive care unit admission.

Another Biosimilar for Rituximab Approved by FDA – The US Food and Drug Administration (FDA) has approved Ruxience, a biosimilar for rituximab (Rituxan) for the treatment of non-Hodgkin's lymphoma, chronic lymphocytic leukemia, and certain other indications. The approval was based on the review of data that compared its efficacy, safety, and pharmacokinetic profile to rituximab in patients with follicular lymphoma. Ruxience, manufactured by Pfizer Inc., has been filed for regulatory approval with the European Medicines Agency and is under review.

Acalabrutinib Receives Breakthrough Therapy Designation for CLL – AstraZeneca announced that the US Food and Drug Administration (FDA) has granted Breakthrough Therapy Designation for acalabrutinib (Calquence) as a monotherapy treatment for patients with chronic lymphocytic leukemia (CLL). This designation is for the purpose of accelerating the development and regulatory review of new medicines that are intended to treat a serious condition and that have shown encouraging early clinical results. Acalabrutinib is a second generation BTK inhibitor currently approved for the treatment of relapsed/refractory mantle cell lymphoma.

Interim Results Reported for Frontline Ibrutinib and Venetoclax Combination in High-Risk and Older CLL Patients – Interim results were reported in the *New England Journal of Medicine* for a Phase 2 trial combining ibrutinib (Imbruvica) and venetoclax (Venclexta) in previously untreated high-risk and older patients with chronic lymphocytic leukemia (CLL). Eighty patients were treated with ibrutinib (420 mg once daily) for three monthly cycles, followed by the addition of venetoclax (weekly dose escalation to 400 mg once

daily). The combined therapy was administered for 24 cycles. After 12 combined treatment cycles, 88% of the patients had complete remission or complete remission with incomplete blood count recovery, with 61% achieving undetectable minimal residual disease by flow cytometry. Three patients had laboratory evidence of tumor lysis syndrome, and the adverse event profile was similar to what has previously been reported with monotherapy of ibrutinib and venetoclax. At the time of this report, most patients were still receiving the combined cycles, so that data from the completed therapy are not yet available. This time-limited treatment strategy is anticipated to lead to deep remissions, prevent the emergence of drug resistance, and provide the potential for treatment-free intervals rather than continuous dosing.

Bi-Specific CAR T-Cell Therapy Used in Phase 1 Trial of NHL – A bi-specific anti-CD19, anti-CD20 chimeric antigen receptor (CAR) T-cell approach was safe and produced complete responses in the majority of patients with relapsed or refractory non-Hodgkin's lymphoma (NHL) in a Phase 1 study. The results were reported at the American Society of Clinical Oncology 2019 Annual Meeting and in *Hematology News*. Eleven of 17 patients had a response to treatment by day 28, and of those patients, nine had complete responses, all of which are ongoing. There were no deaths attributed to treatment, no serious grade cytokine release syndrome, and only two patients had neurotoxicity, which was reversible. Bi-specific targeting is being investigated because CAR T-cell therapy targeting only CD19 is resulting in some relapses due to down-regulation of CD19 on the tumor cells. Investigators plan to conduct Phase 2 studies in more cohorts, including patients who have relapsed after CD19 CAR T-cell therapy.

Interim Trial Results Reported for Bi-Specific CAR T-Cell Therapy in Multiple Myeloma – Meanwhile, a different

bi-specific CAR T-cell therapy was used in patients with relapsed or refractory multiple myeloma, this one targeting CD19 and BCMA (B-cell maturation antigen). At six months of follow-up in this Phase 2 trial, 20 of 21 patients had a response. Cytokine release syndrome occurred in 90% of patients but was mild or moderate. The most common serious adverse events were hematologic, including neutropenia (low neutrophil count), anemia, and thrombocytopenia (low platelet count). The study was conducted in China and published in the journal *Lancet Haematology*.

FDA Announces New Pilot Program to Help Physicians Get Access to Investigational Therapies for Their Cancer Patients – The US Food and Drug Administration (FDA) has announced a new pilot program called Project Facilitate to assist oncology health professionals through the process to submit Expanded Access requests for investigational (unapproved) therapies for their cancer patients when a clinical trial is not an option, as in cases where patients do not meet trial requirements or live too far from a trial site, and there are no satisfactory alternative therapies available. The Project Facilitate phone number is 240-402-0004, and the email address is OncProjectFacilitate@fda.hhs.gov.

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COOKS' HAPPY HOUR

EDITED BY PENNI WISNER

The first thing my mother taught me to cook was meringues. The first thing my French godmother taught me to make was vinaigrette. So it is no surprise that it was my French godmother who introduced me to cabbage as food. Until that time, for me, cabbage meant coleslaw (weepy, wet, and sweet). She changed my mind when she sautéed shredded green cabbage with ginger and garlic to serve alongside a simple flank steak topped with crumbled, dried oregano.

Some months later, I was introduced to a red cabbage salad with toasted walnuts and parsley. The chef heated red wine vinegar and poured it over the thinly shredded cabbage, causing it to wilt a bit. Then he dressed it with salt, pepper,

minced green herbs, minced red onion, and a mixture of walnut oil and olive oil. But I've always repeated the salad with just olive oil. If you happen to have walnut oil, this would be a time to use it.

Then, at a three-star restaurant in the south of France, I chose a dish of pigeon served on a bed of braised cabbage flavored with wine, apples, and bacon. Since bacon should probably not appear in a column touting healthy food, I tell you about that dish only to get your cooking juices flowing. An equally good accompaniment to chicken, sausage

Cooks' Happy Hour, cont. on page 17



Green, purple, and Napa cabbages

(chicken, turkey, or pork), or sautéed tofu marinated in turmeric would be shredded cabbage braised in one of the new fermented, dry apple ciders you can find these days. Add some apple chunks and minced fresh thyme. Cook it down until the liquid is syrupy. Season with salt and pepper.

In the fall, beautiful cabbages jump straight out of the fields and into farmers markets. There is the round, densely packed green cabbage, the stalwart of coleslaw. And its twin in a red dress, red cabbage. There is the more tender, crinkled Savoy cabbage, the elongated and frilly Napa cabbage, the pointed and pale green cone cabbage, as well as so many more... which is a good reason to go to the farmers market where you can ask the vendors for cabbage inspiration. But, if you simply choose to go to the store, you will still find crisp, dense cabbages as well as convenient packages of shredded cabbage. If you dislike the idea of pre-prepared ingredients, as I do, then invest in an inexpensive handheld mandoline. I use mine almost every day. In just a few moments, it can shred cabbage almost impossibly fine.

In October, when this issue of the *Torch* comes out, the weather is still warm (or warm-ish. Really, who knows these days?) and salads remain seasonally appropriate, but their ingredients morph. Some can star cabbage. Let's get one thing straight: you do not need to add sugar to shredded cabbage to get it to wilt. Salt will do the trick all on its own. If you want to make a coleslaw-type salad, toss your shredded cabbage in a large bowl with some salt and pepper and set it aside for about 15 minutes. Press down on the cabbage and pour off the liquid that will have gathered in the bottom of the bowl. Then add some shredded carrot, shredded radish for color and crunch, finely diced red onion or shallot, or thinly sliced green onions, apple cider vinegar, olive oil, a dash of honey (if you must), a sprinkling of poppy seeds, and a dusting of chopped parsley and dill. Voila, a healthy, crisp coleslaw. Add some roasted peanuts or toasted, chopped almonds and some shredded, roasted chicken or tofu, and you have a main dish.

One day, I'd made a sort of Asian-inspired main dish and wondered what to do for a vegetable. There in the fridge was a green cabbage. This is often the case and both the good news and the bad news about cabbage: You bring it home, and then it lurks in the back of the refrigerator, berating you every time you notice it and then ignore it. The good news is that when you finally do reach for it, it will be just fine. You might need to discard an outer leaf or two, but no more. I hope this little talk of ours will encourage you to bring home a cabbage and use it immediately.

That green cabbage, once shredded, inspired an Asian slaw that I often make. In a large bowl combine 1 pound or so of shredded green cabbage (a mix of red and green would be pretty); 1 or 2 two shredded carrots; about 4 very thinly sliced green onions (both the white and green parts); a handful or so of shredded daikon radish; a large handful of roughly chopped cilantro; 1 finely chopped, small serrano or jalapeno chile; a generous tablespoon of peeled and finely chopped ginger; 1 clove of garlic, minced or pressed; 1 tablespoon of freshly squeezed lemon juice; 2 tablespoons of rice vinegar; 1 tablespoon of fish sauce; and 3 tablespoons of canola oil or mildly flavored olive oil. Toss all that together very well and taste for seasoning. The fish sauce may provide all the salt needed. If not, season with salt and a pinch of *shichimi togarashi* (a Japanese seasoning blend that includes chile and black sesame seeds), or cayenne. Taste again and add more spice as desired.

The joy of salads is that they respond so well to whim and happenstance. Instead of fish sauce, you might try soy sauce and sesame oil, as well as a good sprinkling of toasted sesame seeds, white or black or both. Add shallot or red onion instead of green onion. Or skip the Asian aspect completely and dress the mixture with a balsamic vinaigrette or a mustard/red wine vinaigrette.

If you spend fine fall afternoons outside by the grill (or grill indoors on a grill pan or in the broiler), add cabbage to your mix of eggplant, onion, and squash. Cut a cabbage into wedges, keeping a bit of the core attached to each to hold it together, or use a sharp metal skewer to hold the wedges' shape. Season with salt and pepper and brush liberally with olive oil. Place over direct heat on a clean, oiled grate. Cook on all sides until slightly charred and then move to a cooler part of the grill and let cook until the wedges are crisp-tender. Serve warm and whole or cut them into strips and dress them with a tahini or miso dressing.

David Tanis, in his *New York Times* column, City Kitchen, advised this tahini dressing: mix $\frac{1}{4}$ cup tahini (the higher quality the brand, the better the result), 2 tablespoons freshly squeezed lemon juice, and 2 tablespoons olive oil into 1 cup whole milk yogurt (I like to use kefir for this type of dressing). Season with salt, pepper, 1 large clove pressed garlic, and 1

pinch of chile flakes (such as Aleppo) or 1 pinch of cayenne. For a miso dressing, combine equal amounts of white miso and soy sauce in a bowl. Add half as much rice vinegar and mirin. Whisk in seasonings: finely minced ginger and pressed garlic, 1 small splash of sesame oil, 1 pinch of chile flakes, and pepper. Depending on the sweetness of the mirin you use, you might want to add a little brown sugar as well. Both of these dressings will keep well in the refrigerator for several days.

For snacks, try briefly blanching Savoy cabbage leaves. Drain and dry them, then roll them around any finely chopped or shredded, well-seasoned filling (such as any of the salads above) and mix with a little rice, if desired, to make them more substantial.

Cabbage also lends itself well to quick pickles. Pack a clean jar with shredded cabbage, some carrot for color, and thinly sliced jalapeno for spice. Heat equal parts cider vinegar and water with a good dose of salt and seasonings to your liking, perhaps seeds such as fennel, dill, and coriander, and/or whole allspice, sliced ginger, whole cloves, and star anise. Bring to a boil and pour over the cabbage, making sure the vegetables are covered in the liquid. When cool, cover well, and refrigerate. You can use the pickles within an hour or so, and they keep refrigerated for a week or more.

Our motto: Eat Well to Stay Well

Join our Club!

Your legacy is important. That's why you take time to plan and provide for the people and causes that mean the most to you. If you've included our organization in your will, trust or other planned gift, please let us know. We want to honor you with membership in our legacy society, and more importantly, we want to make sure you're thanked today and your legacy is honored tomorrow.

QP-2015-197.1-cp



The Ben Rude Heritage Society for Legacy Gifts to the IWMF

The IWMF has a special club for those who name the IWMF as a beneficiary of their estate plan—the Ben Rude Heritage Society. No gift is too small for membership! If you have already made a provision for the IWMF in your will, trust, life insurance, or as a beneficiary of your IRA, please let us know and we'll enroll you in the Ben Rude Heritage Society. You can remain anonymous if you prefer. Either way, we would like to say thank you and keep you in the loop with all things IWMF-related. For more information on estate gifts or to join the Ben Rude Heritage Society, call or email the IWMF office or contact our **Individual Giving Director Jason Watkins at 517-974-9742 or JWatkins@IWMF.com**.

ENDING THE YEAR WELL

Get a head start now on your year-end tax planning. Do you own an IRA and/or a 401(k)? Are you age 70½ or older? Do you expect to be in a higher tax bracket?

There are several ways that you can shift tax dollars to charitable dollars and support the IWMF's mission at the same time. These include a zero tax gift and sale, a donor-advised fund, the outright gift of an asset, or an IRA charitable rollover. As you think about tax planning, this may also be an appropriate time to think longer-term about a legacy gift to the IWMF.

Imagine a Cure Campaign Progress Report as of September 3, 2019



SUPPORT GROUP NEWS

EDITED BY PENNI WISNER

PLEASE NOTE

Contact information for all support groups is available at:

<https://www.iwmf.com/get-support/us-and-international-support-groups>

Details of support group meetings and other upcoming events are posted on <https://www.iwmf.com/news-events/events-calendar>. Please check there to confirm details of future events.

CALIFORNIA

Monterey Bay

The Santa Cruz/Monterey Bay Support Group met for a sharing meeting towards the end of July. One member returned feeling strong after a scary re-occurrence over the winter. Plus, two new members attended who had never met anyone with this rare disease. The sharing continued for two hours, using up the time allotted to a planned video. All left feeling quite a bit better and glad they endured the summer tourist traffic to get here! The next meeting is planned for Sunday, October 20.

Orange and San Diego Counties

Everyone was very friendly and glad to be able to attend a meeting in Orange County. Last minute issues prevented one enthusiastic WMer from attending in person, but he did join us through the miracle of FaceTime. He greeted each person and repeated his dedication to being a part of the group, starting next meeting. IWMF Individual Giving Director Jason Watkins was in town, and he was a positive, engaging, and interesting participant-speaker for the new group. Members asked what kinds of things other groups are doing, what obstacles they face, and how he got interested in the IWMF. Other members then started speaking up more about what they liked about past meetings and how traffic has been an obstacle that has kept them from attending in LA as well as in San Diego.

CONNECTICUT

On June 29 the Connecticut WM Support Group held its meeting at the Westfarms Mall meeting room in Farmington, CT. We began our meeting at 1:30pm with a half hour informal “meet and greet.” We were fortunate to have a presentation on WM by Dr. M. Lia Palomba of Memorial Sloan Kettering Cancer Center, New York, NY. We were very impressed by her extensive knowledge of WM, treatment experience with Imbruvica, and potential upcoming WM treatment drugs. She spoke for an hour, followed by a lively



Dr. Lia Palomba speaks to the Connecticut Support Group, June 2019.



Connecticut Support Group members

Q&A session. Following her presentation and after a group picture and short break, we went around the room discussing our individual WM stories and treatments. We concluded our meeting at 4:30, and a small group of meeting attendees had a nice dinner afterward at a restaurant downstairs in the Mall. In total we had approximately 25 attendees.

EASTERN OHIO/ WESTERN PENNSYLVANIA/WEST VIRGINIA

The peak of the July heat wave could not deter a group of 21 dedicated members from venturing out to a support group meeting at the library in Parma, OH. Several members shared their positive thoughts about the recent Ed Forum, reflecting on the exceptional quality of the event: cutting-edge information, networking opportunities, friendly atmosphere, and great location. Support Group Leader Marcia Klepac

Support Group News, cont. on page 20

provided an overview of treatment advances presented at the Ed Forum, including new clinical trials—evidence of progress and hope. The sharing session engaged members in a discussion that highlighted the risks vs. benefits of various treatment choices, local options for good quality WM care, and personal experience in navigating the process of consulting WM experts. The appetizing potluck lunch greatly contributed to an enjoyable afternoon.

FLORIDA

Southern Florida

After meetings in January and March, group members attended the IWMF Educational Forum in Philadelphia in June. A September meeting took place too late for inclusion here, but the next meeting is planned for Saturday, December 7, from 11am to 2pm. The meetings are all held at Memorial Hospital West in the first floor GME classroom 1. The hospital is located at 701 N. Flamingo Road, Pembroke Pines, FL. Dr. Daren Grosman, hematologist-oncologist with Memorial Hospital, will be available at both meetings to answer any questions you have regarding WM. Lunch will be provided for attendees courtesy of LLS.



Chicago Support Group members

ILLINOIS

Chicago Area/SE Wisconsin

The eleventh annual summer gathering for fellowship and food was a great success for young and old. This year it was held for the first time at the home of Cyndi and Tom Royce, friends of group member Cheryl Sproul, a relatively new WM patient. The group thanks Cyndi and Tom for their friendship, for a great poolside venue, and for generously providing a catered dinner to supplement snacks brought by members. Several children and grandchildren enjoyed the summer sunshine and temperatures while participating in swimming and bean bag games.

The discussion period included newbies and veterans sharing stories. Don Brown, a 17-year survivor, shared parts of his strategy, which includes avoiding cancer drugs when reasonable and always being vigilant, especially when starting a new treatment. Karen Ferguson shared her experience with the Live Strong program at the YMCA, a free program that encourages physical activity for cancer patients. (Being active is also one of Don's strategies.) There was significant discussion regarding ibrutinib, which six patients in the group are currently taking—one for more than six years! All are experiencing good responses, but there was some discussion regarding reducing dosages and the consequences of stopping altogether. The fall meeting will take place on Saturday, October 19, 2019, at the LRF Educational Forum venue in downtown Chicago. The support group meeting is planned for 5:00pm on Saturday. Check the LRF website for details of the LRF program and WM speakers, including Dr. Jorge Castillo from Dana-Farber Cancer Institute in Boston.



Indiana Support Group members

INDIANA

A beautiful Indiana summer on July 20 provided the backdrop for a Saturday morning sharing meeting fueled by breakfast snacks from Panera Bread and coffee. A record 23 Waldenstrom patients, partners, and friends attended. Nine of those have been attending since the first meeting in July 2011. In addition, one new member joined our "elite" club. After introductions, announcements, and reports from the recent Ed Forum, group members shared their journeys and answered questions.

MINNESOTA/WESTERN WISCONSIN

Each year, the group winds down the summer by gathering for an informal get-together, and this year we had a beautiful day for a picnic. A total of 20 people joined Support Group Leaders Eunice Quast and Michelle Blazek at the home of Eunice's daughter in scenic Stillwater, MN. The group was diverse, with diagnoses as far back as 2003 and as recently as a few months ago. After sharing a meal and getting to know



The MN/Western Wisconsin group posed after meeting and sharing a potluck lunch.

each other better, Eunice covered upcoming educational opportunities and other WM-specific information. The next meeting is planned for Saturday, October 26.

NEW YORK

Eastern NY/Western New England

Four group members attended the IWMF Ed Forum in Philadelphia. They learned a great deal from the excellent presenters, appreciated the opportunity to have personal conversations with experts, and met WMers from all over the US and many other nations. A late fall meeting is planned based on information gleaned from the Forum. In September, at the invitation of the support group, Dr. Jorge Castillo of Dana-Farber presented a thorough update on Waldenstrom's followed by an enthusiastic and vigorous question-and-answer period. The meeting was held in the home of a group member and lunch for all preceded the program. The turnout was excellent and included members from throughout the group's region. The group also appreciated meeting Dr. Castillo's family who accompanied him to the Lake Placid area.

Rochester/Western and Central NY

In June, a small group met for lunch at the Casa Italiana on the beautiful campus of Nazareth College in Rochester, NY. They quickly engaged in lively conversation around topics featured at the 2019 IWMF Ed Forum. The members were eager to learn the new and exciting information from the world of WM. At this particular meeting, the subject of finding the right doctor dominated the conversation. (Trouble finding a physician well-versed in WM is a common issue for all patients.) Members exchanged doctor names and locations, hoping to help fellow WMers find the right fit in a physician.

NORTHERN VIRGINIA/WASHINGTON DC/ WESTERN MARYLAND

Dr. Jeffrey Matous, medical director of the Colorado Blood Cancer Institute, arrived in Washington, DC, in May to give a



Dr. Jeffrey Matous and Lu Kleppinger

presentation to the local group. His program was engaging for all, as he addressed topics for newly diagnosed Waldenstrom's patients and reviewed new developments for more experienced WM patients. He described WM, beginning with diagnosis and symptoms, then moved on to treatment guidelines and when to commence treatment. In addition, he delved into genetics, including a discussion of the genes MYD88 and CXCR4, and stated that more needs to be learned about mutations. Underscoring that Waldenstrom's is a rare cancer with only about 1500 new diagnoses per year in the United States, he explained that WM is different in everyone and thus is "unique to you." As many know, Dr. Matous is an excellent speaker, appearing at the IWMF Ed Forum on a yearly basis. Almost 60 participants attended and were rewarded when Dr. Matous kindly stayed on to address numerous individual questions after the program. The group is grateful for his expertise and attention and sincerely thanks him for making the trip.

OREGON/SOUTHWEST WASHINGTON

On a sunny June Sunday, a full complement of 18 WM patients and their caregivers met at Lake Oswego to discuss all things Waldenstrom. A surprise visitor, the IWMF's Individual Giving Director Jason Watkins, who was in the Pacific Northwest to meet with donors, also attended. He particularly enjoyed the cooler weather as compared to his home in coastal Georgia.



Oregon/SW Washington Support Group members

Support Group Leader Marie Navarra presented great feedback from the Philadelphia IWMF Ed Forum. She indicated that the presentations seemed less jargon-filled and more targeted to the patient layperson. She also reviewed the various markers on blood tests that are pertinent to WM patients. Jason brought news of pending changes at IWMF headquarters, not the least of which is the appointment of a paid executive director to oversee day-to-day operations. Up to this point, the IWMF has been an all-volunteer organization. Perhaps the best news discussed is the selection of the nearby Seattle area as the site of next year's Ed Forum. The proximity means that many locals can make plans to attend.

PENNSYLVANIA

Southeast PA/Harrisburg

The group celebrated summer and July with a potluck picnic. The event included a discussion of the recent Ed Forum in Philadelphia which Support Group Leader Teresa Eschelmann and husband Michael had attended. Future meetings are planned for Nov 2, 2019, and March 8, 2020, both on a Sunday from 2 to 4pm at Messiah Village's game room.

SOUTH CAROLINA

After taking the summer off, the group plans to meet at a new, and wonderful location: Leeza's Care Connection at the Michael J. and Mary Meech Mungo Home, 201 St. Andrew's Road, Columbia. The date will be November 2 from 1 to 3pm.

TEXAS

Dallas/Northern Texas

The group met twice this summer. In June the meeting featured a replay of Dr. Steven Treon's livestream presentation from the IWMF 2019 Ed Forum. The presentation was well received by all in attendance and sparked lively conversation. Dr. Treon's comments distinguishing between research targeted to control WM vs. research aimed at finding a cure for WM were also discussed. Members who had not attended the Ed Forum or viewed the livestream really appreciated the video being available so soon after the presentation. Links to the presentation and the Q&A that followed were sent to members via email so that everyone would have an opportunity to view or review the information. At the August meeting, Angela Robertson, a support group member, gave a presentation about her 10-year journey with WM. This was the second of occasional presentations by members to share a detailed look from symptoms and diagnosis to the present. As always, after the educational presentations, the group enjoyed lunch, courtesy of the Cvetko Patient Education and Support Center at Baylor Charles A. Sammons Cancer Center Dallas, where meetings are held.

The second part of both meetings comprised a "caring and sharing" session, giving all members in attendance an opportunity to update the group on treatments, progress of their health, current life events, and concerns. Email

updates from members not in attendance were read. The Dallas WM Support Group meets on the third Saturday of even months at the Cvetko Patient Education and Support Center at the Baylor Scott & White campus in Dallas. The final meeting for 2019 will be Saturday, October 19.

Denton

Cathy Hartman has stepped up to form a support group in Denton, TX. She became involved with IWMF after being diagnosed with WM in 2015. She discovered that most medical

*"The great resources on the **IWMF website** helped so much in that first year."*

professionals knew very little about WM, and she needed to know more than she could learn from her doctor. When she searched the web, she discovered the IWMF. She continues: "The great resources on the IWMF website helped so much in that first year. Then I went to the Educational Forum in 2017 and haven't missed one since. I decided to start this group because I wanted to meet and learn from other, local WMs. I have been married for 50+ years and have a daughter. My career was in large academic libraries specializing in digital libraries. I first retired at the end of 2015, then was asked to return in 2017 for another year, retiring again in 2018. Now, some favorite pastimes are walking (The Walk and walk!), and I am just beginning yoga classes. Plus, I register people to vote, and I love reading hard SciFi books."

The group's first meeting went well. Ten people attended and filled the allotted two hours with lively conversations. Members decided to meet every other month (the odd-numbered months, so that people can also attend the Dallas group meeting on even-numbered months). The second meeting was planned for September. So far, meetings have been held in the local public library which works well. One discussion was a brainstorming session to come up with program ideas. Steve Pine, leader of the Dallas group, attended the meeting, which was great.

Houston

In mid-September, the group hosted Dr. Scott Creighton, a Harvard psychologist, who spoke on "The Creative Dynamics of Illness and Aging." Dr. Barbara and John Manoussos hosted the group at their home and served a luncheon of pastitio (Greek lasagna) and salad.

WASHINGTON/SEATTLE AREA

Fourteen members, including two new attendees, met at the Shoreline Library on the beautiful Sunday afternoon of

Support Group News, cont. on page 23



Washington/Seattle Area Support Group members

August 18. We always seem to be happiest when sharing information and providing an upbeat and inclusive setting for all, and this time was no exception. Our discussions about local providers and second opinions were particularly useful, and many continued conversations during a break when we enjoyed ample refreshments, thanks to Linda Pochmerski. We look forward to our big November meeting in Seattle, when we often have 60 to 70 people attend for a WM specialist speaker. Details to come later on www.iwmf.com.

INTERNATIONAL SCENE

EDITED BY ANNETTE ABURDENE

CANADA

After 20 years of dedication, service, and commitment to WM patients, Arlene Hinchcliffe has resigned as president of the Waldenstrom's Macroglobulinemia Foundation of Canada (WMFC). She will continue to serve as the Oakville Support Group leader. The new WMFC Board consists of Paul Kitchen, chair; Betty McPhee, vice chair; J.A. Clancy, treasurer; David Johnston, secretary; Raffaella Mercurio; and Cam Fraser. The Board has a huge task ahead of it to carry on Arlene's legacy and to implement a new strategic plan, which is available for everyone to see on our website at www.wmfc.ca.

Thanks to the generosity of our members and special donors, we are proud to invest in three significant research projects. First, we are continuing to fund a project in which Dr. Ruben Carrasco from Dana-Farber Cancer Institute (DFCI) is the lead investigator. This project is to develop a mouse genetic model of WM. Second, we are funding another DFCI project, "The Development of a Comprehensive Epigenetic Roadmap of WM," with Dr. Steven Treon as the lead investigator. The third project is "The Use of Peripheral Blood Cell-Free DNA for Genetic Profiling in Patients with WM." This will potentially lead to a non-invasive platform for mutation detection at the time of diagnosis, replacing the bone marrow test. The lead investigator is Dr. Christine Chen at Princess Margaret Hospital, University Health Network, in Toronto. The total amount of these three projects is CN \$402,847.

This fall our support groups are continuing to run in several major cities across Canada. We invite you to check out our website for specific times and locations. Go to www.wmfc.ca and click on the support link.

Betty McPhee, WMFC, reporting



Dr. Jorge Castillo (back row, center), Dr. Hou Jian (on his right), and Dr. Wan Yi Ke (front row, second from right) in Shanghai

CHINA

On July 1, 2019, Dr. Jorge J. Castillo from Dana-Farber Cancer Institute lectured at Shanghai Renji Hospital. Doctors from the Hematology Department of Renji attended the lecture.

The head of the Hematology Department, Dr. Hou Jian, welcomed Dr. Castillo for his first visit to Renji Hospital. In his lecture, Dr. Castillo introduced WM treatments, talked about clinical experiences at Dana-Farber, and shared information about recent WM research in the US. He then commented on some knotty problems which Renji's hematologists have been

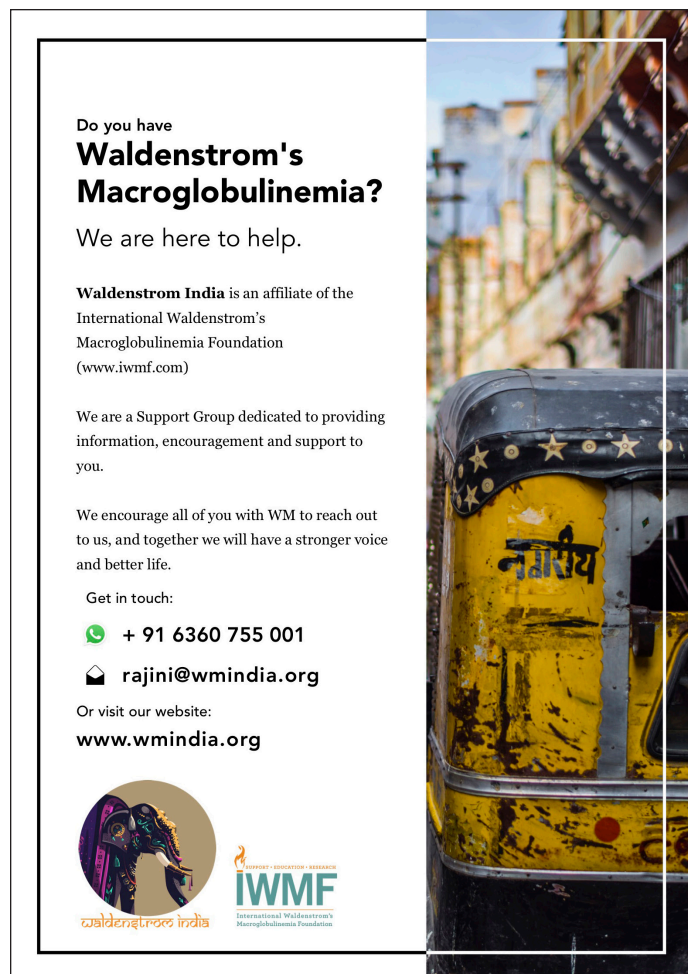
International Scene, cont. on page 24

facing with WM diagnosis and treatment. After Dr. Castillo's lecture, Dr. Wan Yi Ke from Renji gave her case report on a gene study of twin brothers who both had WM.

Dr. Castillo appreciated all the efforts by Renji hematologists to add to our knowledge of WM and invited the Chinese researchers to cooperate with US research institutions.

WM-China support group leader, Roger Yao, also attended the lecture. He shared with Dr. Castillo the progress of the WM-China support group and discussed with Dr. Hou plans for the next WM educational meeting.

Roger Yao, WM-China, reporting



INDIA

Poster by Waldenstrom India advertising the organization

Waldenstrom India is proud to announce the completion of our new website, <https://wmindia.org>, and the start of a dedicated WhatsApp channel at +91 6360 755 001 for patients, doctors, and supporters in India. We request those of you who are familiar with patients and supporters in India to encourage them to get in touch with us!

This quarter also saw us meet doctors at a large hospital in Bangalore and bring them on board with our support group efforts for India. We also successfully put up posters for our support group at the hospital, which is well-known for its hematology and oncology practice and attracts thousands of patients from across the country.

Influenced by the startup spirit of Bangalore and public service spirit of the IWmf, we worked with the lead designer at Swiggy, an Indian unicorn startup, to incorporate best-practice design principles and create the poster for our affiliate on a pro-bono basis. We hope that you find this poster helpful and can use it as a guide for your own support groups. Please reach out to us for the soft copy.

Saurabh Seroo, WM India, reporting

UNITED KINGDOM

WMUK at IWmf Educational Forum, Philadelphia

Lindsey Bennister, WMUK's new chief executive, joined international group leaders and delegates at the IWmf Educational Forum in Philadelphia. Lindsey said, "I learnt so much about WM and came away greatly inspired by the work of the IWmf. It was a hugely informative trip, and I met some wonderful delegates who shared their experiences with me and made me feel very welcome. I look forward to seeing everyone again next year and to continuing our close working relationship with the IWmf."



Dr. Shirley D'Sa (WMUK founder and WM specialist doctor) presents data from the WMUK Rory Morrison Registry.

WMUK Patient – Doctor Summit

WMUK held another successful national event for WM patients, caregivers, and health professionals in July. This year's event exceeded all expectations. Over 150 delegates travelled to London to meet others, hear presentations from expert doctors and patients, and take part in smaller workshop sessions especially for patients and care givers.

International Scene, cont. on page 25



Delegates during the question and answer session

Highlights of the day included an early-bird session on understanding WM by Dr. Shirley D'Sa from University College London Hospital, which hosts the largest WM clinic in the UK. Delegates then enjoyed a session focused on the psychological aspects of living with WM, with an entertaining, inspiring, and upbeat presentation from WMer Bob Perry about how setting up a WM support group helped him cope with his diagnosis.



Delegates in the exhibition area viewing posters

short session with one of the WM expert doctors who were present throughout the day.

Feedback has been excellent, with lots of suggestions for future events, including regional meetings between the larger national events. We were delighted to welcome a significant number of new people who were recently diagnosed and attending the summit for the first time—almost 40% of those who provided feedback were first-time attendees.

Regional Support Groups

The BAD WMers (Bournemouth and District) Support Group is following its successful inaugural meeting in May with another meeting in November. Group leader Bob Perry has decided to take his support group on the road to make it



Support Group Leader Bob Perry of BAD WMers

more accessible to other patients in the region. He will hold this meeting in a community centre on a farm in Winchester, to attract people who live in the Surrey, Hampshire, Sussex, Dorset, and Wiltshire areas.

WMUK Rory Morrison Registry

The WMUK Rory Morrison Registry has said a sad farewell to Dr. Joshua Bomsztyk, who has been leading the Registry project since its conception. Josh remains involved in an advisory capacity, and has been succeeded by two new clinical fellows, Oliver Tomkins and Suzanne Arulogan, who will be working with the WMUK Registry Committee to further develop our work in this area. A current priority for the Registry is the collection of data from patients being treated with ibrutinib in England, to help inform a future appraisal of the drug by NICE, the institution that assesses the clinical and cost effectiveness of new treatments in England and Wales. Ibrutinib is currently funded on the National Health Service via the Cancer Drugs Fund whilst more evidence is gathered. WMUK is working hard to provide evidence from patients about the impact of ibrutinib to support its continued funding.



Eric Low, WMUK Trustee, opens the plenary session on the WMUK RORY MORRISON REGISTRY.

WMUK Future Plans

In July, WMUK's Board of Trustees met and approved a new strategy for the next five years. First up will be the development of a new website, to be launched at the end of this year.

Lindsey Bennister, WMUK, reporting

European Hematology Association Congress Featured Educational Sessions on WM

The 24th Congress of the European Hematology Association (EHA) took place at the RAI Amsterdam Convention Centre on June 13-16, 2019, in the Netherlands. With 12,000 attendees from 123 countries, the EHA Congress represents the largest meeting devoted to hematology in Europe. Over 2,000 of the attendees were present at the two back-to-back educational sessions devoted to Waldenström's macroglobulinemia (WM).

Chairing both sessions was Dr. Monique Minnema, an active member of the Haemato Oncology Foundation for Adults in the Netherlands (HOVON) working parties for multiple myeloma and professor of medicine at the Academic Medical Center, Amsterdam, and the University Medical Center, Utrecht.

Dr. Steven Treon, professor of medicine at Harvard University Medical Center, provided an overview of the rapid translation of genomic advances into new treatment options for WM, including the role of MYD88 and CXCR4 in predicting treatment response to ibrutinib.



Dr. Alessandra Tedeschi, a clinical trialist in the Department of Hematology, Azienda Ospedaliera Niguarda Ca' Granda in Milan, Italy, discussed frontline treatments for WM, including chemo-immunotherapy and the use of novel treatments such as ibrutinib. Dr. Christian Buske, professor of medicine and medical director at the Comprehensive Cancer Center and the Institute of Experimental Cancer Research at the University Ulm, Germany, reviewed treatment of relapsed and refractory WM and the importance of findings from the Phase 3 iNNOVATE study that randomized ibrutinib and rituximab against rituximab in symptomatic WM patients. The combination of ibrutinib and rituximab showed significantly higher response rates, including depth of response, and longer progression free survival than rituximab.

BETWEEN JUNE 1 AND AUGUST 31, 2019, THE FOLLOWING CONTRIBUTIONS TO THE INTERNATIONAL WALDENSTROM'S MACROGLOBULINEMIA FOUNDATION WERE MADE IN MEMORY OF:

Nanette Dobin Cronan

Dixie Arnold
Jennifer Brinkley
Kemp Cook
James Duffy
Danielle Gletow
Lisa Hawes
Jeffrey and Phyllis Lavine
Kelly and Michael LaVine
Anne and Abe Rosenthal
Olive Schiff
Eric Weiner

Richard Fleischer

Kristin Rejent

Michael Gabridge

Mary Assink

Michael Gabridge (cont.)

Harris and Beth Kiekover
Courtney O'Connor
Leendert Roos
Jim and Louise Staple

William A. Gagliardi

Debra Weiner

Mary Jo Haffner

Anonymous
Anonymous
John Bayne
Patti Carr
Diane Charles-Murphy
Dolores "Dee" Dugan
Ron and Hillary Fayle
Ron and Pam Gruber

Mary Jo Haffner (cont.)

Jill Henderson
Patricia and Dave Koch
John and Patricia McDonough
Steve and Kathy Schultz

Laura M. Elashewich

Susanne Tilp
TOPS Club VA0056, Winchester
Mark Zimmerman

Carl Roeder

Robert and Teresa Roeder

Michael J. Smith

Samantha Rosenberg

**BETWEEN JUNE 1 AND AUGUST 31, 2019, THE FOLLOWING CONTRIBUTIONS TO THE
INTERNATIONAL WALDENSTROM'S MACROGLOBULINEMIA FOUNDATION WERE MADE IN HONOR OF:**

Mady Bay's Birthday

Suzanne Barg
Diane Bonawitz
Jean Capuano
Gianny Huber Stever
Jennifer Keegin
Judi Kelly
Gavin Lane
Bex Marie
Theresa Molick Ugenti
Nosinauq Wright

David Bethel's Birthday

Don Bethel

Lawrence Bonney's Birthday

Suzanne Coleman
Robert Dickson

**Marcia Bradberry's Fundraiser for
Waldenstrom's**

Lisa and Robert Brauch
Laurie and Larry Mulligan
Debra Pollard
Pat and Debbie Pollard
Megan Turner

**Ron Branscome's Walk for
Waldenstrom's**

Linda Branscome
Scott Branscome
Sandra Brooks
Debbie Cartwright
Laura Moyer
Dennis Parsons
Susan Sargeant
Craig Schulin

Mark Davidson's Birthday

Lolita Campbell
John Fletcher
Renae Graczyk
Patricia Konomos
Greg Olson
Jan Piaskowski
Dominique Provost

**Karen Fiorello's Walk for
Waldenstrom's**

David Cody
Edward Derkun
Frank Fiorello
Arthur Geoffrion
Joshua George
Robert Hughes
Eliana Jimenez
Tim Lopian
Olivia Milholland
Al and Judy Mouns
John Rutledge
Carol Stanley
Susan Torok
Dar and Celeste Vega

Katie Fitzgibbon's Birthday

Siehpwahle Butterquist
Taja Costigan
Barry Gage
Sophie Gage
Louis Gage
Ciara Joyce
Susan Tate
Leon Thomas

**Julianne Flora-Tostado's Walk
With Us!**

Lou and Kathy Ceppi
Sam George
Jose and Arlene Pineda

Katherine Fowler's Birthday

Deborah Hockenberry
Greg Mias
Holly Olmstead
Judith Ramsdell

Bruce Fox's Birthday

Debbie Blick
Michael Blick
Stephen Dobkin
Daniel Layish
Donna Mosley
Joff Samuel
David Weingast

**Cheryl Frustieri's Walk for
Waldenstrom's**

Jane and Dan Brannegan
Linda Francis
Douglas Muir
Marko Rankovi
Peter Thompson
Wayne and Deborah Tiusanen

Shirley Ganse's Walk for WM!

Terri Morin-Dilts
Robert Stanley
Margaret Woltjer

Kathy Gregory Loller's Birthday

Connie Aguirre

IWMF

William Flora
Aaron Wesq

Michael Joyeux's Birthday

Margaret Ann
Jonathan Gilroy
Brian Martin
Chris Minto
Nic Wendy
Darren Wright

Randi Koch's Birthday

Dawn King
Lindsey Kjoller
Tristin Koch
Pat Koch
Randi Koch
Elaine Koch Mercier
Victoria Longo

Randi Koch's Birthday (cont.)

Lucille Maddalena
Gary Seminarra
Britt Thomas
Dana Wotruba

**Randi Koch's Kicking Butt and
Taking Names Fundraiser**

Karen Kerwin

Virginia Lansdale's Birthday

Joyce Deschamps
Anna Eichel
Ann Frances
Debra Kuszewski
Virginia Lansdale
Maddy O'Connell
Patty Pirk
Mary Rider
Stephanie Smith
Aimee Van ausdall
Kate Willaert Lobbereg

Anita Lawson's Walking for a Cure

Karen Ciampa
Alice Gill
Ruslana Midway
Eleanor Pascale
Christine Weaver

Katie Parson's Birthday

Anne Helms
Jill Johnson Williams
Tom Parsons
Roxanne Parsons

**Angela Perry Barrett's Raising
Money for a Cause**

Angela Barrett

**Raising Money for Cancer
Research**

Mark Aloway
Valerie Cox
Judy Frederick
Johnetta Gray

Barbara Renico

Laurene Peterson

Bob Ulkus - CT for a Cure 2019

Nicole Chiravuri

Aaron Wesq's Birthday

Carolanne Curry
Kaitlin Dagostino
Nancy Hadley
Aaron Wesq

Lisa Wise

Delores Federico
Jill Parrish



International Waldenström's
Macroglobulinemia Foundation

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