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INTERNATIONAL WALDENSTROM'S MACROGLOBULINEMIA FOUNDATION

INSIDE THIS ISSUE

EIGHTH INTERNATIONAL WORKSHOP ON WALDENSTROM'S MACROGLOBULINEMIA IWWM8: SUMMARY II

BY GUY SHERWOOD, MD, VICE PRESIDENT FOR RESEARCH

The IWWM-8 Class Photo of attendees at the 2014 Workshop gathered in the halls of Parliament. In the front row, from left to right: Dr. Steven Treon, Dr. Shirley D'Sa, Miss Owen, Dr. Roger Owen, Dr. Morie Gertz, Dr. Enrica Morra, Dr. Robert Kyle, Lady Tricia Cohen, Sir Philip Cohen, and the spirit of Sir Winston Churchill.

Photo by Boyd Photography and Phil Brodsky, courtesy of the Bing Center of the Dana-Farber Cancer Institute.

The Eighth International Workshop on Waldenstrom's Macroglobulinemia (IWWM8) was held August 14-16 in London, United Kingdom. In the last issue of the *Torch*, I summarized the lecture sessions that dealt primarily with WM pathophysiology, genetics, cell to cell signaling, WM cell origin, characteristics of the WM cell, diagnosis of WM, and predisposition to developing WM. In this January issue of the *Torch*, I shall review the lectures that treat the clinical aspects of WM, including the currently recommended treatment options as well as the existing new drugs that are soon to be in clinical trials and the newer agents being developed.

First, however, we must begin with the interesting and often controversial session "Great Debates in Waldenstrom's Macroglobulinemia." Moderated by Dr. Véronique Leblond of France and Dr. Shirley D'Sa of the UK, a series of four debates was held whereby two expert clinicians discussed the pros and cons of hotly contested viewpoints regarding treatment controversies in WM.

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GREAT DEBATES IN WALDENSTROM'S MACROGLOBULINEMIA

"Should the MYD88 and CXCR4 mutations be tested in all WM patients?" was the question posed in the first debate. **Dr. Xavier Leleu** of Lille, France, took up the affirmative side of the debate. Referencing the seminal work by Dr. Treon et al. as well as other studies demonstrating that the MYD88 L265P mutation is present in approximately 90% of WM patients, and noting that this mutation appears to be highly specific for WM, Dr. Leleu suggested that this mutation can indeed be labeled a molecular signature and should be considered a part of the diagnostic workup for WM. Dr. Leleu went on to suggest that the CXCR4 mutation, the second most common mutation (found in approximately 20-30% of WM patients), was associated with significant tumor proliferation and dissemination to extramedullary organs and to drug resistance – thus leading to disease progression and decreased survival in WM – and therefore holds valuable prognostic information. In summary, genetics, in the view of Dr. Leleu, dictates the clinical course in WM.

Dr. Eva Kimby of Sweden had the unenviable task to counter Dr. Leleu's arguments and, in fact, to attempt to dampen the enthusiasm of the conference participants with respect to the significance of MYD88 and CXCR4 mutations that have been such a centerpiece at this conference. Dr. Kimby cautioned that although the MYD88 mutational status may help to discriminate WM from marginal zone lymphomas and other closely related diseases, the mutation cannot be considered exclusively diagnostic of WM as it has also been found in some MALT lymphomas, CLL, and in splenic marginal zone lymphomas as well. Furthermore, the MYD88 L265P mutation is common in Primary Cutaneous Diffuse Large B-Cell Lymphoma and in the "activated B-cell" subgroup of DLBCL. Although the MYD88 L265P mutation has been found in WM and IgM MGUS (considered a precursor to WM), further studies are needed before testing all IgM MGUS patients. Dr. Kimby acknowledges the importance of the CXCR4 mutation as well, potentially as a marker of prognosis, but once again cited the paucity of data and the need for further studies. Dr. Kimby quite simply sought to caution the conference participants not to be too hasty to adopt the testing of MYD88 and CXCR4 mutations on all WM patients (and possibly IgM MGUS patients) until further research and validation studies are complete.

"Should bendamustine or ibrutinib be the first salvage in WM?" was the debate question next proposed. **Dr. Mathias Rummel**, of Giessen, Germany, was clearly in his element here vouching for bendamustine as the first salvage option for WM, given the fact that he was involved in a large prospective, multicenter, randomized clinical trial in Germany between September 1, 2003, and August 31, 2008.

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Dr. Rummel and his collaborators compared bendamustine plus rituximab versus CHOP plus rituximab (R-CHOP) as first-line treatment for patients with mantle-cell and indolent lymphomas (including 41 WM patients). The results were overwhelmingly in favor of the bendamustine plus rituximab arm: The median progression-free survival was significantly longer (69.5 months) for WM patients in the bendamustine plus rituximab group compared to the R-CHOP group (28.1 months); bendamustine plus rituximab was better tolerated than R-CHOP. Dr. Rummel concluded without fanfare that bendamustine plus rituximab is an active and well tolerated regimen in patients with indolent lymphomas including LPL/WM and therefore effective for relapsed or refractory disease.

Not to be outdone, **Dr. Lia Palomba** of the Memorial Sloan-Kettering Cancer Center in New York cited a study of her own whereby she and her colleagues evaluated the activity of monotherapy with ibrutinib (Imbruvica) in patients who had failed or progressed after at least one prior therapy. Out of 63 patients enrolled, they observed an overall response rate of 87.3%, including 68.3% major responses. The treatment was apparently well tolerated, and at a median follow up of 48 weeks, 80% of the patients remained on treatment – quite remarkable. Side effects were usually noted in the first few weeks of treatment and resolved or diminished over time even with continuation of treatment. As an added bonus, the responses to ibrutinib treatment generally improved over time as well. Dr. Palomba feels that in this era of personalized medicine where genetics plays an increasingly important prognostic role, and, given the ease of taking the oral pill ibrutinib, the use of targeted therapies such as ibrutinib should be encouraged, compared to the more traditional chemotherapeutic agents.

"Should carfilzomib be given instead of bortezomib for WM?" was the topic for the third debate. **Dr. Irene M. Ghobrial** from the Dana-Farber Cancer Institute argued that, given the high level of debilitating peripheral neuropathy (PN) with bortezomib (Velcade) in WM patients, new second generation agents are needed. Dr. Ghobrial stated that carfilzomib, a second-generation selective proteasome inhibitor, has demonstrated a favorable toxicity profile and clinical efficacy in a clinical trial by Dr. Steven Treon and colleagues. The combination of carfilzomib, rituximab, and dexamethasone (CaRD) in 31 patients with symptomatic WM produced some very encouraging results: overall response rate (ORR) was 87.1%. One patient attained a molecular complete response or CR (the first molecular CR in WM). Dr. Ghobrial also noted that the response to CaRD was independent of the presence of the CXCR4 mutation (implicated in drug resistance and poor prognosis). Treatment-related PN with carfilzomib was very low: only 1 patient suffered grade 2 PN, and no patient discontinued the CaRD trial because of neuropathy. Dr. Ghobrial concluded by stating that the carfilzomib-based CaRD combination represented an important advancement in the treatment of WM patients requiring proteasome inhibitor-based therapies.

Dr. Meletios A. Dimopoulos of the University of Athens, Greece, was essentially succinct in his rebuttal. Quite simply, as is often the case in these debates regarding new emerging therapies, Dr. Dimopoulos argued for more data before the next generation proteasome inhibitors (such as carfilzomib) are recommended over bortezomib. The concern over potential cardiotoxicity of carfilzomib and the relatively low numbers of participants in the CaRD trial mentioned above by Dr. Ghobrial, were noted by Dr. Dimopoulos as reasons enough to proceed with caution before espousing the newer second generation proteasome inhibitors.

"Are response criteria for WM adequate?" was the question posed for the last debate. **Dr. Roger G. Owen** of the St. James's Institute of Oncology, Leeds, UK, argued that the current response criteria represented a consensus achieved at the Sixth International Workshop on Waldenstrom's Macroglobulinemia and were subsequently updated in 2013. Dr. Owen reminded the audience that the principal role of these response criteria was to enable consistent reporting of clinical trial data. He went on to state that unified response criteria are of critical importance in WM as there have been few randomized, controlled trials. The response criteria should predict overall outcome in terms of progression free survival (PFS) and overall survival (OS), correspond with clinical benefit, and allow retrospective comparison of historical data. Dr. Owen did note that several challenging factors remain, namely: clinical heterogeneity (no two people are the same), the variable kinetics of IgM response, and the now frequently observed (and increasingly acknowledged as important) discordance between response to treatment in IgM level and response in bone marrow and tissue (hence the need for planned bone marrow assessments and imaging studies regardless of IgM response).

Dr. Enrica Morra of the Niguarda Ca' Granda Hospital, Milano, Italy, countered by stating that the current consensus-based response criteria are mainly based on the degree of reduction of the serum IgM. The introduction of new drugs and new combination regimens are leading to progressively improving responses with deeper reduction of the IgM component. There is therefore now a need to further refine the criteria for response assessment in WM: a new category of Very Good Partial Response (VGPR) has been proposed. Several key points need to be considered as well when redefining response criteria: "Is the reduction of the M component correctly analyzed?" The variability of the IgM kinetics with different treatments, such as rapid decline with some treatments and not with others, may lead to some difficulty when assessing response. The "IgM flare" phenomenon, for example, requires an adjustment of the proper timing of response evaluation. Dr. Morra also

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asks: "Are bone marrow aspiration and biopsy indicated at restaging for all patients? Given the discrepancy between serum IgM and bone marrow response observed with newer treatments (e.g. bortezomib), a simultaneous serum and bone marrow assessment should be part of restaging in all cases. The bone marrow biopsy needs to be further evaluated by flow cytometry and immunohistochemistry studies. When is molecular evaluation indicated?" Once again the development of newer targeted therapies has led to improved clinical responses, and particularly when complete responses are observed should assays for the MYD88 mutation in CD19-selected bone marrow cells and peripheral white blood cells be instituted. It appears that Dr. Morra is simply telling us that the response criteria need to continuously evolve with the rapidly changing landscape of WM treatment.

NOVEL DRUG DEVELOPMENT FOR WM

Resumption of lectures began at the conclusion of the great debates with the very interesting session on the development of novel drugs.

Dr. Xia Liu, a colleague of Dr. Steven Treon at the Bing Center for Waldenstrom's Macroglobulinemia, Dana-Farber Cancer Institute, presented a lecture on the direct targeting of the MYD88 structure in WM. Dr. Liu reminded us that the MYD88 L265P mutation is present in greater than 90% of WM patients. MYD88 L265P can activate multiple downstream signaling pathways which support malignant cell growth and survival. MYD88 homodimerization (the joining of two identical proteins to form a single molecule) is required to initiate the Myddosome signaling complex and trigger the downstream signaling pathways. The previous work of Dr. Liu and colleagues demonstrated that WM cell growth and survival could be reduced by inhibiting MYD88 homodimerization, providing a rationale to directly target the MYD88 complex in WM. Using lab-generated MYD88 mini-peptides, they were in effect able to disrupt MYD88 homodimerization, resulting in apoptosis and reduced cell survival in WM cell lines. These elegant and complex studies may lead to the development of inhibitors directly targeting MYD88 homodimerization in WM.

Dr. Sara Buhrlage, of the Dana-Farber Cancer Institute, measured the anti-proliferative effect on WM cell lines by molecular inhibitors that target enzymes downstream of the MYD88 complex. These inhibitors were used both alone and in combination with the BTK inhibitor ibrutinib. Dr. Buhrlage's experiments successfully identified new inhibitors of BTK, IRAK1/4, PI3K, TAK1 and MALT1 (known to effect NFκB signaling). The identification of these new inhibitors may lead to new treatments for WM.

Dr. Steven T. Pals of the University of Amsterdam, The Netherlands, presented a very interesting talk on targeting adhesion and migration of cells in WM. Dr. Pals prefaced his presentation by reminding the conference attendees that WM growth and survival relies on signaling by the B-cell antigen receptor (BCR) as well as growth and survival signals provided by the tumor microenvironment. Dr. Pals and colleagues subsequently evaluated the signal inhibitors ibrutinib and idelalisib in WM. Their studies revealed that inhibition of the BCR signaling pathways BTK and PI3Kδ by ibrutinib and idelalisib resulted in decreased retention of WM cells in the bone marrow microenvironment, which in turn led to clinically important WM tumor regression.

Dr. Aldo M. Roccaro of the Dana-Farber Cancer Institute, Boston, discussed targeted therapy of the mutated CXCR4 gene (found in approximately 20-30% of WM patients) which is now known to support disease progression in WM. Dr. Roccaro presented data that demonstrated anti-WM activity of a novel monoclonal antibody anti-CXCR4 (BMS-936564). Importantly for all WM patients, BMS-936564 was able to target both wild type (i.e. non-mutated) and CXCR4-mutated WM cells, suggesting that novel CXCR4-targeted therapies in WM may be of clinical benefit.

PROGNOSTICATION AND SURVIVAL IN WM

Dr. Pierre Morel of the Centre Hospitalier Schaffner de Lens, Lens, France, discussed prognostication in the era of molecular markers. There has been a veritable explosion of recent discoveries in the genetics of WM. Among such discoveries are the following:

- WM patients with the MYD88 L265P mutation (found in 90% of WM patients) have improved prognosis
- The CXCR4 mutation found in approximately 20-30% of WM patients confers decreased survival.
- CXCR4 mutated WM patients treated with ibrutinib had lower major response rates.
- Polymorphisms (genetic variations within a population) of the FcγRIIIA receptor (rituximab target) can result in dramatically improved responses to rituximab-based therapy.
- WM patients with the FcγRIIIA-158V/V polymorphism (homozygous for valine) had higher response rates than patients with the FcγRIIIA-158F/F polymorphism (homozygous for phenylalanine).

Currently WM patients are placed in prognostic categories based on the identification of asymptomatic and symptomatic patients and the *International Prognostic Scoring System for Waldenström Macroglobulinemia* (ISSWM). The new genetic markers, biological prognostic factors, as well as continued assessment of conventional clinical characteristics represent a series of dynamic challenges for the update in prognostication for WM patients.

Dr. Efstathios Kastritis of the Greek Myeloma Study Group discussed the competing risk factors for survival in WM. Since many WM patients are elderly, many patients will die from

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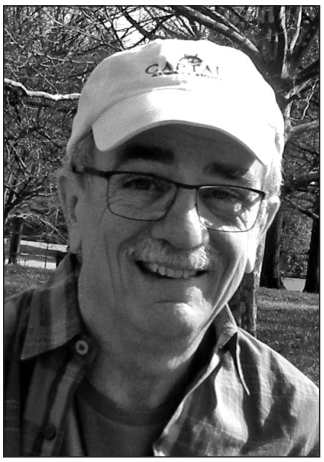
PRESIDENT'S CORNER



Happy New Year! Welcome to 2015!

In my personal life, this new year is a turning point. My mother almost made it to 2015. She would have turned 100. Unfortunately she passed away in mid-September shortly after her 99th birthday party. My mother was born during World War I. She remembered heating homes with wood, having babies at home, outhouses, water pumps, and driving through the night with your feet on hot water bottles and arriving with your feet on ice packs. Whenever asked what was the secret to her longevity, she would answer, "Hard work."

Besides the value of hard work, she taught my brother and me some very important life lessons including:

- If you open it, close it.
- If you get it out, put it back.
- If it's worth doing, it's worth doing right.
- Thriftiness and cleanliness are next to godliness.
- There's tremendous value in being a part of a tight-knit community.

My parents were both very proud that their sons graduated from college and were successful, independent, hard-working members of society. My father died at 53 from lung cancer. Consequently my mother viewed cancer as a death sentence. So I spared her, and she was the only person in my private life who did not know I had WM.

I am my mother's son, and so as we enter 2015, leaving behind us the very busy and productive 2014, I'm delighted to share with our WM community all the results of hard work done right and what's on the horizon.

In the twilight of 2014 we can see sure progress down the road to better treatments:

- In Europe, the application made to the European Medicines Agency (EMA) by Pharmacyclics, the manufacturer of Imbruvica (ibrutinib), has been accepted, specifically providing approval for the use of this drug in the treatment of WM for patients throughout the EU. For patients in the US, the FDA Food and Drug Administration (FDA) will soon approve Imbruvica (ibrutinib) as a treatment for WM. This approval marks the very first time a drug has been approved for our orphan disease and a moment WMers have been waiting for since our disease was first diagnosed in 1944. Approval by the FDA will make it easier for WMers to obtain Imbruvica and to receive reimbursement for it.

  While recognition by the FDA will be an historic step, we are still far from the goal of finding a cure for our disease. Imbruvica is not a cure. Imbruvica does not work for everyone, and it will not replace all the other treatments we've come to rely upon. But the approval by the FDA will be tangible proof that we are making progress in getting time and attention devoted to our orphan disease.
- The record number of clinical trials open to WMers also demonstrates the time and attention WM is receiving. While the *Torch* column Medical News Roundup regularly includes information about the most recent trials (see page 11 of this issue), you must check *clinicaltrials.gov/* for a complete listing. This is a US-based site, covering clinical trials in all 50 states and in 187 countries worldwide. Just type in Waldenstrom's macroglobulinemia and click. Then check open studies and next click the map to see the clinical trials that are available where you live.

  Remember, clinical trials are essential to finding a cure, but they are of value only if enough WMers sign-up. So please discuss clinical trial options with your doctor.
- I just returned from the ASH (American Society of Hematology) meeting in San Francisco where the rate of progress continues to accelerate for our disease. Look for an article on the key news from ASH in our next *Torch*.

As 2015 dawns, the IWMF is stronger than ever with:

- A new website. We are replacing our old website because it was written in outdated software and was difficult and expensive to update. The new website will feature pictures of real WMers. If you want to volunteer your photos, please contact the IWMF Webmaster, Barry Nelson, at *BarryNelson@alum.MIT.edu*. The new website is designed to work well on mobile phones and and tablets, devices that were not in use when our previous website was built. You should also find it easier to locate the information you need.
- Three new Board of Trustee members: Gayle Backmeyer, Eileen Frishman, and Barry Nelson. See the next issue of the *Torch* for a brief profile of each of these talented folks. Join me in saying thank you to each of them for volunteering their time and talents.

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- A new Office database. Like our website, our old database was just too old and inefficient. It was costing us time and money that we'd rather use for better purposes. The new database will enable us to work more efficiently. To improve our efficiency even more, please make sure we have your e-mail address, date of birth, and date of diagnosis (month and year or just the year). If you're not sure we have that information for you, please e-mail it, mail it, or call it in to Lisa Abbott at *office@iwmf.com* or IWMF, 6144 Clark Center Ave., Sarasota FL 34238 or (941) 927-4963. As with all of your data, it will remain confidential.

On the Horizon

2015 will be a momentous year for the IWMF:

We will hold our **Twentieth Educational Forum** in Dallas, TX, on May 1-3, 2015. See the articles below and on page 7. Use the brochure that is enclosed to sign up or sign up at the new website. We have a great hotel rate at a beautiful hotel, the Hilton DFW Lakes Executive Conference Center. Once again this rate is good for the 3 days before and after the Educational Forum, so why not make a vacation of it? My wife and I will be heading down to Austin afterwards to check out the music scene there. The line-up of speakers is incredible. Our keynote speaker, Dr. Kenneth Anderson, is chief of the Division of Hematologic Neoplasia at the Dana-Farber Cancer Institute. Dr. Lee Greenberger, the Chief Science Officer at the Leukemia & Lymphoma Society (LLS), will be speaking about the new IWMF/LLS Strategic Research Roadmap for WM.

This IWMF Strategic Research Roadmap will guide our research thinking and investments for the next several years. It will be mapped at a think tank near the end of March by fifteen of the leading minds in WM, lymphoma, genetics, and cancer research. We are working out the final details of this two-day meeting now. The end result will be a strategy that points to where we should best invest your money to push us closer to the cure we all want to see.

There's a lot of good news and promising directions as we head into 2015. My mother would be proud of all of us.

Have a healthy and happy new year!

Carl

IT'S TIME TO MAKE YOUR PLANS FOR THE 2015 ED FORUM!

This year marks the twentieth anniversary of the IWMF Educational Forum, and we want you to join us for this very special occasion on May 1-3 in Dallas, Texas. Our theme for this year's Forum will be *Imagine a Cure – Parade of Hope*, and the IWMF is planning several events to celebrate this anniversary.

In addition to the educational and social activities offered at the Forum, we hope that you will take advantage of all there is to see and do in the Dallas-Fort Worth area. See the accompanying article "Dallas-Ft. Worth (DFW) Says 'Welcome, IWMF!'" to help you get started on your plans!

We have negotiated a special room rate of $127 per night at the Hilton DFW Lakes Executive Conference Center in Grapevine, TX, which is conveniently located near the Dallas-Fort Worth Airport. The hotel is in a resort-like setting, with trails for walking, jogging, and horseback riding; indoor and outdoor pools; facilities for fishing, tennis, and golf; and a spa and fitness center. To make your reservations, call 817-410-6795 or Toll-Free 800-984-1344 and be sure to mention "IWMF" to receive the special rate. Or go to *www.hilton.com/en/hi/groups/personalized/D/DFWAHHF-4WM-20150430/index.jhtml?WT.mc_id=POG* for general information about the hotel and online reservations.

We are pleased to have Dr. Kenneth Anderson from Dana-Farber Cancer Institute deliver our keynote address for the Friday evening Welcome Dinner. Dr. Lee Greenberger of the Leukemia & Lymphoma Society will be a special guest on Sunday to talk about the new strategic roadmap for WM research. Our other agenda topics and speakers include the following:

- I've Been Diagnosed with WM – What Happens Now? – Dr. Joseph Mikhael, Mayo Clinic
- Familial WM – Dr. Mary Lou McMaster, National Institutes of Health
- I Need Treatment – First-Line Treatments and Side Effects – Dr. Larry Anderson, University of Texas Southwestern Medical Center
- My WM Is Back – Relapsed/Refractory Treatments – Dr. Sheeba Thomas, MD Anderson Cancer Center
- "The Garden Talk" Updated – Dr. Morie Gertz, Mayo Clinic
- How B-Cells Work and Talk to Each Other – Dr. Stephen Ansell, Mayo Clinic
- Harnessing Killer T-Cells – Dr. Julie Nielsen, Deeley Research Centre, Canada
- Integrative Oncology – Dr. Claudia Harsh, Baylor Charles A. Sammons Cancer Center
- Genomic Landscape of WM – Dr. Zachary Hunter, Dana-Farber Cancer Institute

It's Time to Make Your Plans, cont. on page 7

It's Time to Make Your Plans, cont. from page 6

- Targeted Therapies for WM – Dr. Steven Treon, Dana-Farber Cancer Institute
- The "Burning Questions" about WM – Dr. Morie Gertz, Mayo Clinic

We are again offering several breakout sessions on treatments and other topics of interest so that you have the opportunity to network with your fellow WMers in an informal setting. The Forum is also your chance to meet and ask questions of the experts in WM. As always, our popular Ask the Doctor Panel, moderated by Dr. Robert Kyle, will take place on Sunday morning.

Support Group Leaders will have the opportunity to attend a half-day workshop at the hotel on Thursday, April 30, organized by Marcia Klepac, IWMF Support Group Coordinator.

Traditionally, Saturday evening dinner at the Forum has been "on your own." While this will not change, we are offering you the option of making reservations for a Saturday Night Texas Barbecue Buffet from 7-9 PM at the Bonnie & Clyde's Restaurant in the hotel. The cost is $18 per person, including beverage, tax, and service charge, and a cash bar will be available.

See our website at *www.iwmf.com* or use the enclosed brochure in the *Torch* to register for the Educational Forum and sign up for the optional buffet. Take advantage of our special early registration rate of $199, available until April 1, 2015. We can't wait to see you in Dallas!

DALLAS-FORT WORTH (DFW) SAYS "WELCOME, IWMF!"

BY DR. LAWRENCE COTTLE

"Howdy, Y'All!" Yes, Texas is known for its friendliness and welcoming spirit Indeed, Texas comes from the Caddo Indian word "tejas" meaning "friends" or "allies," and you will experience just that when you come here!

The Dallas-Ft. Worth area is the fourth largest metropolitan area in the U.S., home to over 6.6 million people and growing at a rate of over 2,000 per week. "Big, bustling, and business-like" are appropriate adjectives to describe the area and its people and their spirit. Let's take a brief look at the welcoming, fun environment which will surround you during your stay.

DALLAS

Boasting the largest urban arts district in the U.S., Dallas also has the country's largest light-rail network, DART (Dallas Area Rapid Transit). One of the newest gems in this gleaming city of the Southwest is the Klyde Warren Park, a scenic downtown park that opened in 2013 adjacent to the Arts District. The park is shown in the background of *"SITES & ATTRACTIONS"* under "Things To Do" on *www.visitdallas.com*, and you can view several eye-opening videos if you click the website's "About" button. Also opening in 2013 were the Perot Museum of Nature and Science and the George Bush Presidential Museum.

So much to see and do – let's look at just a few. Visit the Dallas World Aquarium and the Dallas Arboretum for a varied and thoughtful look at nature. In contrast, Dallas is also the home of the Sixth Floor Museum at Dealey Plaza downtown in the heart of the West End Historic District. This area was, of course, the scene of the assassination of President Kennedy and preserves the history of events of that tragic day and week.

In the Arts District are the very spacious Dallas Museum of Art and adjacent Nasher Sculpture Center. The arts flourish in Dallas with the beautiful Morton H. Meyerson Symphony Center, the AT & T Performing Arts Center, and Dallas City Performance Hall. A most unique and enticing collection is featured in the Trammel and Margaret Crow Collection of Asian Art. You won't want to miss seeing as many of these venues as possible!

Downtown also features the Reunion Tower Geo-Deck and Underground Tunnel and Sky Bridge System, all displaying truly unique views above and below ground. The Dallas Holocaust Museum is close by.

On the edge of downtown is something different – the Medieval Times Dinner and Tournament venue offers an experience back in time. And if you *really* want more "moving excitement" and variety, visit Six Flags over Texas in nearby Arlington.

FORT WORTH

The "City of Cowboys and Culture," Fort Worth's dazzling downtown was recently named "best downtown in the nation." At the heart of one of the safest, cleanest urban areas in the US is Sundance Square. This 35-block area features a variety of galleries, restaurants, shops, and performance venues. Nearby is the Bass Performance Hall, home to classical music and the arts and many other entertainment programs.

But this is only a start. "Things To Do" at *www.fortworth.com* showcases historic sites, museums and galleries, shopping, the arts and more. Some of the finest art museums anywhere are the Amon Carter Museum of American Art and the Kimbell Art Museum (called by some the "American Prado Museum").

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Dallas-Fort Worth (DFW), cont. from page 7

Explore the "Western experience" through the Stockyards National Historic District and Cowtown Coliseum. And the Ft. Worth Museum of Science and History has an excellent variety of exhibitions from Energy Blast to the Cattle Raisers Museum to Omni Theatre IMAX Dome, unique for its kind.

Descriptions of these and so many more places to go and things to see and do can be found on the respective websites of both these great Texas cities!

GRAPEVINE

Maybe you don't want to venture too far from the Hilton DFW Lakes Executive Conference Center but would like to see something different? How about Grapevine Mills Mall, a huge shopping mall only about a 10- to 12-minute walk from the hotel? See *www.grapevinetxonline.com/grapevine-mills-mall* for details.

Want more? Then visit the Gaylord Texan Resort and Convention Center, a 5-minute ride from the hotel. The Atrium is huge, with several restaurants, shops, and other venues. You will be awestruck by the sheer size of this place, an unforgettable experience! For a preview, go to *www.gaylordtexan.com*

Or visit *www.grapevinetexasusa.com* for a broad overview of Grapevine.

Y'All come! Wherever you visit during your stay, you'll be welcomed Texas-style.

Dr. Cottle was the co-founder of the North Texas WM Support Group (Dallas-Ft. Worth area) in early 2004, along with the late Jerry Fleming. He has lived in Dallas for over 20 years and continues to work part-time through his Doctor of Chiropractic education as a B.E.S.T. practitioner (bioenergetic synchronization technique). He credits this particular training and nutritional support, along with earlier conventional care, as helping him "significantly ameliorate an aggressive WM state," and his current health is "very near normal."

IWMF INAUGURATES THE YOUNG INVESTIGATOR AWARD

A program recently established by the IWMF offers younger researchers the opportunity to participate in the International Workshops on Waldenstrom's Macroglobulinemia that are organized by the Bing Center of the Dana-Farber Cancer Institute on alternate years and in different locations. Known as the Young Investigator Award (YIA), this program provides travel expenses and lodging for the duration of the Workshop. The YIA is open to younger researchers already engaged in projects concerning WM. The program will continue to coincide with future Workshops in the expectation that support for the WM experts of tomorrow ensures that the recent progress made in WM research is carried forward for years to come.

In this first year of the program, four Young Investigator Awardees (YIAs), selected on the basis of abstracts submitted to and ranked by the IWWM8 Scientific Committee, traveled to London and participated in IWWM8. The YIAs for 2014 were: Julie Nielsen, PhD (Canada); Eric L. Smith, MD, PhD (USA); Jaimal Kothari, MD (UK); and Jonas Paludo, MD (USA). Funding was provided by the IWMF together with our affiliated organizations in Canada (WMFC) and the United Kingdom (WMUK). Thanks are due to members of the IWWM8 Scientific Committee for their participation and to Christopher Patterson of the Bing Center who organized travel arrangements for the awardees.

This issue of the *Torch* begins a series of articles introducing each of the YIAs. Read on to meet Dr. Julie Nielsen and learn about the innovative T-cell research she is conducting at the Trev and Joyce Deeley Research Centre of the British Columbia Cancer Agency in Victoria, British Columbia, Canada.

INTRODUCING YOUNG INVESTIGATOR AWARDEE JULIE S. NIELSEN, PHD

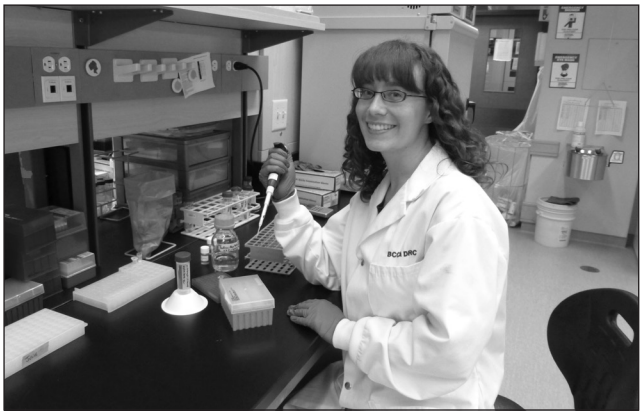
AS TOLD TO PENNI WISNER

Dr. Julie Nielsen was one of four younger researchers granted a Young Investigator Award to attend IWWM8, the International Workshop on Waldenstrom's Macroglobulinemia held in London, August 2014. Her award was sponsored by the IWMF and the WMFC, the Waldenstrom Macroglobulinemia Foundation of Canada. Currently Dr. Nielsen holds the position of Research Associate at the Trev and Joyce Deeley Research Centre of the British Columbia Cancer Agency in Victoria, British Columbia.

"My high school biology teacher got me excited about cells and genetics," says Dr. Nielsen, reflecting on the experience that led to her career as a medical geneticist. "In university, I found that genetics held the most interest for me." That early interest led to a PhD in medical genetics from the University of British Columbia in 2006: "My PhD work focused on how the blood system develops, and I worked on breast cancer research as well."

When it came time to look for a position, Dr. Nielsen combined her interest in the blood system with her longstanding interests in genetics and cancer, a combination that made her a great fit for the laboratory of Dr. Brad H. Nelson at the Trev and Joyce Deeley Research Centre. Dr. Nelson's research specialty is the role of the immune system in ovarian cancer; specifically he uses cells of the immune system called T-cells to identify and then destroy the cancer cells. He has also extended his research to ascertain if T-cells can be directed to kill cancer cells in lymphoma. As Dr. Nielsen comments today, "When I heard about Dr. Nelson's work, using the immune system sounded like a really good strategy, a very promising strategy."

She landed in just the right place at the right time. "Right at the beginning of my time at the lab, a new project was being considered. Dr. Nicol MacPherson, the oncologist for Waldenstrom's patient Bruce Shepp, had approached Dr. Nelson to suggest researching the potential role of the immune system's T-cells in Waldenstrom's." Dr. Nielsen was given the choice of various other projects in the lab or leading this new WM work. "I liked the idea of starting from the beginning: recruiting patients, gathering tissue samples, spreading the word among doctors to encourage referrals." For the past seven years she has led the laboratory's lymphoma research (with a special focus on WM) under Dr. Nelson's supervision. Mr. Shepp, the WM patient, provided the initial funding, and in 2014 Dr. Julie Nielsen was awarded a research grant from the IWMF to further her investigation of immune system-based therapy for WM.



Dr. Julie S. Nielsen in her laboratory at the Deeley Research Centre of the British Columbia Cancer Agency.

The placement of the lymphoma research center on the top floor of the British Columbia Cancer Agency gives Dr. Nielsen many opportunities to interact with patients as well as to recruit new patients for her research projects. "We have over 100 patients in our study. Every year they come in to give a blood sample. I talk to them whenever they have questions and want to know more about our research. Talking to them motivates me to continue the work."

When asked how she relaxes in her spare time, Dr. Nielsen replies, "The reality is that I love my job, so I work too much! I don't get very stressed by the work because I have been doing research for about 14 years now and know that experiments do not always work out. But I love to hike. There are lots of mountains nearby and the coast is right here, too. And I enjoy live music, all kinds.

Introducing Young Investor Awardee, cont. on page 10

"Traveling is a big passion. I do not like to sit still, so I never stay home when I have more than two or three days off." Dr. Nielsen's parents and grandparents (all Canadian) inspired her wanderlust. "When I was a child, our family took a lot of road trips. My grandparents joined us for some of those as well as frequently visiting friends in Australia. My dad was a teacher, and he spent one year teaching in Australia. My brother and I went to school there that year, and we all traveled extensively while there.

"Because my husband works as a pilot, we have been able to do a lot of overseas traveling. And we have been able to take my parents along several times, which has been a lot of fun. My favorite places have been Iceland, Italy, and Greece. We have not gone to any particular country specifically to hike, but we have done some hiking while travelling. There are so many beautiful coastlines, waterfalls, glaciers, and mountains that you would miss if you didn't hike to them!" Another interest of Dr. Nielsen's is photography. She can then indulge in the best kind of multi-tasking: taking photographs while traveling and hiking.

To summarize her research in simple terms, the laboratory work of both Dr. Nielsen and Dr. Nelson focuses on T-cells, cells of the immune system that have the ability to identify and destroy abnormal cells. Each of the billions of T-cells in every person's immune system carries a receptor on its surface to identify specific cells that are foreign to the body and to target them for destruction, whether they are bacteria, viruses, or mutated cells that have "gone wrong."

Two huge breakthroughs occurred to spur Dr. Nielsen's current research strategy. "The first was to find something shared by WM cells in all or most patients that might be used as a target for the T-cells," she said. "In the past five years, it has become possible to identify the genetic mutations frequently associated with WM. In 2011 the team led by Dr. Steven Treon of the Bing Center at the Dana-Farber Cancer Institute identified the MYD88 mutation that is found in a large majority, perhaps 90%, of WM patients. That gave us our target. The second breakthrough needed was to discover T-cells that could recognize the MYD88 mutation. This is exactly the type of analysis that our laboratory does, and we did find those cells. Now we have our target, the MYD88 mutation, and something that can detect it, a T-cell receptor that recognizes and targets the MYD88 mutation."

The breakthroughs described by Dr. Nielsen are the first steps in the development of a new treatment strategy that is known as "adoptive T-cell therapy." In this strategy, T-cells taken from WM patients will be engineered to express the T-cell receptor that targets the MYD88 mutation. Patients will subsequently be infused with large numbers of these engineered T-cells, familiarly known as "killer T-cells," that are intended to recognize and destroy WM cells throughout their bodies.

Looking back on her experience in London at IWWM8 supported by the YIA travel award, Dr. Nielsen says, "The Workshop gave me a great overview of the research going on internationally. It also allowed me to meet colleagues I'd not met face-to-face as well as potential collaborators. I had a poster in the Workshop and gave a brief oral presentation on the preliminary research data that won us the new co-funded IWMF/WMFC grant.

"The grant will fund all the lab work needed before testing the strategy in human trials. We estimate these experiments required by the FDA will take about two years. We are very excited about this. This gives us hope that we really can now move forward with this strategy."

"Harnessing Killer T-Cells" is the title of the presentation Dr. Julie Nielsen will deliver at the 2015 IWMF Ed Forum in Dallas-Fort Worth, May 1-3.

What is the IWMF Telephone & E-mail Network?

When you were newly diagnosed and first made contact with IWMF, you may have noticed an option to participate in this program by checking a box on the membership/giving form which was included with your new patient information packet. The opportunity to participate is also available when you donate online at *iwmf.com*. The Telephone & E-mail Network is a valuable resource, providing comfort and reassurance by connecting you with other WM survivors and caregivers in your area. Participation means you are willing to share your contact information with other WMers nearby. If you do not indicate that you wish to participate in the Telephone & E-mail Network, your telephone number and e-mail address will not be released to other members. Your *Torch* newsletter has a membership/giving form enclosed should you wish to participate.

IN THE TORCHLIGHT
WMER COMPLETES 2014 MARINE CORPS MARATHON

BY NICK STINSON

On March 27, 2013, 43-year old Konnie Stinson successfully registered for the 2013 Marine Corps Marathon to be held the following October, setting her on the path to achieve a goal that she had held for several years. There was, however, one small wrinkle: Konnie had not been feeling well for several weeks, experiencing shortness of breath, headaches, and light-headedness. Within a few weeks – and just prior to her son's second birthday – she would be diagnosed with Waldenstrom's macroglobulinemia.

Konnie Stinson looking strong 11 miles into the Marine Corps Marathon in Washington DC, October 26, 2014.

With an IgM level topping 4000 and a bone marrow biopsy showing 90% bone marrow infiltration, her doctors started treating her immediately with plasmapheresis and chemotherapy. The summer of 2013 held many challenges as she dealt with the combination of Waldenstrom's symptoms and the side effects of chemotherapy. Yet Konnie remained hopeful that she would be able to run the marathon in October. By early August, however, she finally had to admit to herself that this would not be possible. Asked to recall this moment of truth, Konnie says, "It was awful – I thought I had collected myself, but I broke down and cried on the phone with the woman from the marathon. She offered the following encouragement, 'Hey, look at it this way – you'll have an extra year to train.'"

Konnie wrapped up her treatments in November of 2013, achieving a partial response but of short duration. The next move was to pursue a maintenance regimen, first with rituximab and then with the newly introduced ibrutinib. Her response to ibrutinib was excellent, but she experienced serious side effects that led her to discontinue the drug in April of 2014. Again, her blood numbers quickly headed in the wrong direction.

With her husband Nick, Konnie attended the Tampa IWMF Ed Forum in late May. It was a rare chance for them to unplug from their hectic life, and they found time to discuss how she might remove some of the roadblocks standing in the way of the marathon. "I was concerned that she was taking a huge emotional risk – she would be devastated if she couldn't run that race," says Nick looking back to those days. "And the complications from her WM had the deck stacked against her, but I was ready to support her no matter what she chose to do."

Shortly after returning home from the Tampa Forum and after consulting with her doctors, Konnie decided in early June to resume the therapy once again. Of this decision and what it meant for her marathon aspirations, she now says, "I was going to run it no matter what – there were no other options. My deferral in 2013 was for one year only and now registration is by lottery, which meant I might not get in next time. In 2014 I was running it."

It was at this point in her journey where her toughness and dedication came into full display. She joined a training group that would train on Wednesday nights and Sunday mornings. Starting in early July, she would receive her chemotherapy every Friday, and be out running in the hot Maine summer weather less than 48 hours later. Every week she ratcheted up the distance, culminating with a 22 mile run in mid-October. Reflecting on what it was like to train while concurrently receiving chemotherapy, Konnie says, "It was good to have something else to focus on, I was happy to be outside running even though I felt terrible – I was happy that I wasn't inside hooked to a pheresis machine. Some days were slow, but I had come so far from the previous spring when I could not ascend a flight of stairs without being short of breath."

Konnie at the finish line: "I could have kept running."

The hard work over the summer paid off, and she was ready for the marathon as October arrived. However, she would face one final and significant challenge. On her last long run, exactly one week before the race, a severe bout of plantar fasciitis flared up in her foot. "I have had plantar fasciitis on and off for ten years, but this was by far the worst ever – I literally couldn't walk on it. I was so angry, but had to figure out how I was going to do the race." An orthopedic specialist reluctantly agreed to give her a shot of hydrocortisone in her foot. He couldn't say no when she told him about the journey she had been on over the last several months.

In the Torchlight, cont. on page 12

In the Torchlight, cont. from page 11

On October 26, 2014, with eight close friends and family members in attendance, Konnie ran the 26.2 miles of the Marine Corps Marathon in Washington DC. Konnie had this to say when asked about the significance of the accomplishment, "Finishing was bigger than running the 26.2 miles. Running used to be a solo activity for exercise and therapy, but this journey was not a solo one. Prayers came from around the country, I had unconditional support from so many people – my coach, dietician, people helping to watch my 3-year old when needed, peers in my running group, and my family. I saw that community is huge in overcoming any obstacle."

Concerning Konnie's achievement, her admiring husband Nick has this to say, "I got her a card a few days before the race to give her a final shot of encouragement. It had a picture of a chocolate chip cookie with the following words:

Tough Cookie (tuf kook-e) noun:

1. *A person with the right mix of sweetness and strength.*
2. *One who doesn't crumble under pressure.*
3. *A fighter who's too busy kicking butt to sit down and cry, but knows it's okay to do both.*
4. *A person who doesn't always ask for support, but has lots of friends who would do anything to help.*

I can't think of a better way to sum up Konnie's persona and spirit – this description "fits to a tee."

Konnie Stinson is the co-leader of the new IWMF support group in Maine.

In the Torchlight *is a column for sharing the personal stories of Wallies of all ages to illustrate spirit and strength in the face of adversity. Our pages are full of stories of awards, accomplishments, successful treatments, new adventures, strength of character. Won't you share yours with the* Torch*? Let us hear from you at:* ariginos@me.com

SOMETIMES

BY ARMAND THOMAS

Sometimes, I forget. That's not a bad thing.
I just go about my eclectic life, flaunting gravity, mapping horizons, staying in motion, limits be damned.
The world has long been my oyster, albeit I never really liked that idiom, being a vegetarian since the age of eleven.
I've worked in the arts, as an actor and stage-hand. I gravitated to filmmaking and became a set prop-man on many high-profile productions.
I later returned to the live stage, climbing the ranks to become a key player in several Cirque du Soleil creations.
My schooling was in journalism. I slotted the editorial desk and chased stories as a reporter – even fulfilling a childhood fantasy as a Major League Baseball beat-writer for more than 3 seasons.
Pinch me, I'm Mr Ripley!
Mostly, of all things I've somehow managed to accomplish over my 55 years, the art of travel is undeniably my most identifying marker.
I wander the world to reap knowledge, fuel my senses, and to find purpose in capturing photographs that tell good stories.
I'm not always successful, but I try – perhaps too much, and for too long – not noticing the years zip by, or how this solitary passion keeps one single.
But I digress.
As I said, sometimes, I forget, and merrily keep on like this.

And then, there are times I stop, and remember.
Times when blissful fancy turns into lousy reality.
Times when I can't lift my foot off the ground, or my spirit out of the dumpster.

Armand Thomas in the Window, the Las Vegas venue displaying his photographs taken during thirty years of travels around the world.

I remember how my life changed so drastically since 2008, when I took the proverbial left turn at Albuquerque and landed in downtown Lymphomaville.

Just last January, for instance, I hopped the Pacific for Southeast Asia, longing to get a little lost in Vietnam and Cambodia.
It was wonderful.
I felt robust and nearly euphoric dodging infernal traffic and bounding up ancient ruins.
I mixed with locals as always, but stayed inside my hygiene bubble – utterly careful with food, water, and any sign of filthiness.

Sometimes, cont. on page 13

Sometimes, cont. from page 12

Even before I was declared immunodeficient, seven years ago, I practiced strict cleanliness. My new world order merely kicked up the habit a few notches.

All good until…
On my return Stateside, I happened to have smuggled home a most unwanted souvenir.
At first, it had the makings of jet lag – weakness, sluggishness, disorientation. I've often joked that my type of vacation is so grueling, the demands I place on myself so physically taxing, that I need time off to rest once it's over.
But this was no ordinary fatigue.
With each day, my ability to walk diminished. I could barely raise a foot to put on a sock. I felt numbing from my toes rising into my legs.
I've known neuropathy before, after chemo, but this was much more debilitating. Not just ants and pins and needles, but dying limbs.

I learned early on that Waldenström is no ordinary cancer. It's a devious prankster, dodging conformity, skewing predictability.
"You'll die with it, not from it," the expression goes.
But between those reassuring lines, there's the stark fact that WM has goonies imbedded within the walls of its haunted house.
It's indolent alright – you can play whack-a-mole when its ugly head rears up – usually, hopefully.
And at the best of times, daily life is somewhat normal, and we are oblivious to having defective blood cells. I mean, who doesn't have some defect or other.
Nobody's perfect, after all.

And that's how Guillain-Barré syndrome snuck up on me.

Did I pick up a bug in Saigon? Was the recycled air on the flight back a little, um, mucky? We'll never know.
But my immune system, being jumpy and somewhat stupid, detected an infection, or maybe a bacteria, a virus? something ... (no one could tell precisely).
And it went on the attack, to defend me, understand.
Trouble is, my immune system never stopped attacking, even after the bug or whatever made haste.

What ensues is a systematic paralysis of the nervous system, attacking bottom-up, first shutting down motors of the legs, then working above the waist, into the organs, the diaphragm, sometimes the brain ...
That, in a nutshell, is GBS: my own system wreaking havoc on itself.
It's incurable, but mercifully reversible, unless it kills you first.

By the time I checked myself into the ER, I could barely walk and my arms and neck tingled.
I'm not a religious man, but thank God for modern medicine.
I received 5 rounds of plasmapheresis in the hospital, followed by 7 day-long infusions of IVIG at the oncology clinic, and lots and lots of physical therapy.
At first, I needed a walker to get out of bed; exercise consisted of 2 laps around the nurses' station. Then came a cane, and eventually, gingerly, enough strength to wobble back on my own two feet.
I coped well with three months off work and hours of mindless television - but the mental anguish was another thing.
For many days, I was waiting for test results, word from my newest of doctors, a neurologist, that what I had suffered was indeed classic Guillain-Barré syndrome, period.
And not GBS wrapped into another illness – there was talk of ALS, MS, and other horrifying bunch of letters.
Whenever doctors tell me they want to rule out something very rare, I brace myself.
My life has been filled with rarities – for better or worse.
Honestly, I could deal with another setback that takes time to resolve. But I broke down awaiting the verdict as if it was a death sentence or a governor's reprieve.
That was the craziest, scariest of times. How can we ever get used to that, the next bad thing, the unexpected twist in the tale, even as survivors of our fuzzy, incurable blood cancer?

When the call finally came, and I was told I "only" had Guillain-Barré, it was like a new lease on life. Tears of joy ran down my face, elation like none other, a cocktail of pure relief and profound sadness.
Oh, how we marvel at the things taken so for granted – like sitting and standing without a yelp, or going outside to get the mail. Small silly things.
Such stark contrasts: one moment I was in spin class, sweating buckets on the stationary bike, my mind formulating plans about my impending trip to the Far East; the next I'm staring at a dropped quarter, wondering if the effort to bend down and pick it up is entirely worth 25 cents.

Since my diagnosis in 2008, I've danced to many medical tunes:

- At DX, IgM topped 10K, HgB at 5 – severe anemia, blood transfusions, lots of R-CHOP
- At stem cell collection at MD Anderson, developed bladder infection caused by outpatient chemo, self-administered from a backpack unit connected to my bloodstream – I peed blood so badly that I received a rather big catheter up my wazoo for eight excruciatingly agonizing days

Sometimes, cont. on page 14

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 *Torch* editor Alice Riginos at *ariginos@me.com*

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- Pain in my right knee? No, not too much tennis, but a colony of WM cells on the bone. Radiation
- Itchy lump on my left shoulder? No, not lipoma (fatty tissue), but another blister of WM cells. Radiation
- Zero dental crowns pre-DX; thirteen as of 2014 - due mostly to dry mouth, calcium and immunity issues
- Chronic fatigue. Low testosterone levels. Bouts of depression. Oh, and did I mention bouts of depression?
- And then, Guillain-Barré

Life is as precious as it is fickle.
I've learned that over and over in my WM years - often cursing those words, but sometimes, speaking them with an odd sense of gratitude.
Because even if Waldenström is arbitrary, it doesn't have to be meaningless.
As I struggle to overcome my latest setback, I'm reminded that there's still things to do, and hope to embrace.

It's easy to become worn down, to live in fear of the next unwanted adventure, to surrender to mediocrity and a sedentary existence.
As the saying goes: it's in the darkest nights that the brightest stars shine; or, it's in the face of adversity that one's true grit is revealed.

Sure, pithy aphorisms, granted. But hey, I need something after giving up Effexor.

If nothing else, Waldenström has made me more appreciative of the moment.
Nothing hones perspective more than reflecting on one's own expiration date.
I don't dwell on the morbid, but neither do I proceed blithely into the good night.

Ironically, that's what compelled me to continue traveling – despite the perils of infections, microbes, fatigue and sudden loss of health.
Of course, I won't invite catastrophe; I'm careful where and when to stroll about. I won't eat street food. I won't pet a stray cat regardless of how cute.

But neither will I define myself by the inevitable prospect of relapse. I know the boogieman is stalking; in the meantime, keep moving forward wisely.
I love to ride my Triumph motorbike; I enjoy playing Hold'em Poker (hey, when in Vegas!); I work out hard and as often as I can at the gym, and yes, I plan to take more trips abroad.
And I do nag at myself: what more can you do? Help feed the homeless? Advocate to save the elephants from poaching? Champion women's rights in the Middle East? Orate about the dangers of texting while driving? Donate to the IWMF and other agencies in our ongoing fight against cancer? Yes and yes and all yes. Living on the edge can be liberating; it gives license to act and power to succeed.

Waldenström may have tripped me up, but I'm still on the move, and with greater purpose.

A few weeks after being released from the hospital, and still recuperating by and large, I opened an exhibit at the West Las Vegas Library Gallery, entitled "Egypt - Photographs of Everyday Life".
It was a long overdue tribute to my native land, with pictures I took during two visits in 1994 and 2010. I was born in Cairo, my family moved to Canada when I was 6, and now I reaped such inner reward, displaying my work from my old ancestral desert home at my new adopted one.

In August came another fortunate invitation, to become a 3-month artist-in-residence at an arts and community space in Downtown Las Vegas – called the Window.
There, I displayed photographs from around the world, and conducted themed slideshows accompanied by live music.
A show "30 years in the making," I quipped at my presentations.
The experience was as flattering as it was cathartic - making me remember and forget all at once.

visit my photo galleries and blog at:
armandthomas.com

November 2014

FROM IWMF-TALK

BY JACOB WEINTRAUB, MD

As fall and winter approached, the discussions on IWMF-Talk continued to focus on familiar topics, especially newer treatments and drug combinations. Frequent discussions concerned seeking second opinions once WM has been diagnosed. Many new participants joined and were welcomed by the group with replies that answered questions, made observations about laboratory tests, and offered suggestions about obtaining second opinions from WM experts around the country.

HUMAN INTEREST ITEMS

Many posts made to IWMF-Talk do not relate directly to medical news and research concerning WM but instead are

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From IWMF-Talk, cont. from page 14

links to other medical topics or items of human interest. Included are patient experiences with cancer or treatments in general, articles about caregivers, fundraising events, and other media-related items. IWMF-Talk Manager and IWMF Trustee **Peter (Pete) DeNardis** and others posted several such links.

Pete shared an article from a blog posting with the title "Surviving Cancer and Wrinkles" written by a breast cancer survivor. She writes: "We should be no more ashamed of our age than a tree should be embarrassed by its many rings." We should instead "celebrate" the lines. *huffingtonpost.com/sarah-thebarge/what-surviving-breast-cancer-at-27-taught-me-about-wrinkles_b_5997756.html*

Pete posted a link to the Tuesday, October 14, airing of the Today Show with a discussion of the do's and don'ts about what to say when a friend or loved one has cancer. Also included is advice from a psychologist about various aspects of providing support. *nbcnews.com/id/36090945?launch=56232065&config=26185044*

A link to an MD's blog records a brief history of the major classes of drugs that have been used to treat low-grade lymphomas since the 1940s. Given the early trials of radiation with dreadful results, it is impressive to see how far we have come, yet frustrating to realize how far we have yet to go. *cll-nhl.com/2014/09/immunotherapy-for-indolent-low-grade.html#.VClaYPldXTQ*

Wanda H posted a link to an article on *KevinMD.com* titled "7 Ways to Help Your Caregiver." These recommendations include being honest with your caregiver about what he or she can reasonably do for you and then asking for help accordingly, encouraging your caregiver to do some things independently without you, and letting your caregiver know how much he or she is valued. This article is very valuable for all of us. *kevinmd.com/blog/2014/11/7-ways-help-caregiver.html*

Wanda also posted a link to a study out of Germany that found a high prevalence of mental health issues, mainly depression and anxiety, arising from the adjustment to a cancer diagnosis. Results of this study were published in a newsletter from the American Society of Clinical Oncology which also includes helpful links on ASCO's cancer information website about finding help and support. *asco.org/press-center/one-three-people-cancer-has-anxiety-or-other-mental-health-challenges*

Pete posted a link to an abstract of an article concerning perceived quality of life among patients with NHL, most of them actually WM patients and members of IWMF-Talk. The article discusses "mindfulness," the stress of being diagnosed with cancer, and the experience of depression and anxiety and quality of life in people with NHL. *http://www.scirp.org/journal/jct/*

Dr. Jacob Weintraub posted an article from *Cure Magazine*, "The Art of Breaking Bad News," which deals with all the emotions that a person experiences when a cancer diagnosis is received. One point the article makes is that there are not many doctors trained in this area, and it provides a model for training medical professionals in ways to present sensitive news to patients. *curetoday.com/articles/The-Art-of-Breaking-Bad-News*

Dr. Jacob also posted an article about the rising cost of generic medicine as reported in the AMA "Morning Rounds" in a recent issue of the *New England Journal of Medicine*. The study points to the impact of less competition in the generic drug industry. Prices have been low because of competition in the industry, and when the competition lessens, the prices do not stay low. *nejm.org/doi/full/10.1056/NEJMp1408376?query=TOC*

IMBRUVICA (IBRUTINIB)

Atrial fibrillation

Atrial fibrillation appears to be an issue for several people who are receiving Imbruvica, although it is not well documented that "afib" is directly caused by the treatment itself.

John E reported that he has been taking Imbruvica and that his WM was showing improvement. However, he developed atrial fibrillation, for which his cardiologist prescribed Xarelto and flecainide. But when his hematologist/oncologist heard that John was being treated with the anticoagulant Xarelto, he stopped the Imbruvica. It has been shown that Imbruvica can decrease a person's platelets; this may be one reason for a patient not to be on both Xarelto and Imbruvica at the same time.

Michael L posted that he could find no evidence of a causal link between Imbruvica and atrial fibrillation. He reports that about 5% of patients taking Imbruvica develop this condition. He also notes atrial fibrillation is rather common among older

From IWMF-Talk, cont. on page 16

HOW TO JOIN IWMF-TALK

Here are two ways to join:

1. Send a blank e-mail to: *iwmf-talk-subscribe-request@lists.psu.edu*

   Make sure to enter the word "subscribe" as your subject, and do not sign or put anything in the message area (make sure you do not have any signature information in there). Also, do not put a "period" after "edu" or it will reject. Once approved you can post by sending e-mail to *iwmf-talk@lists.psu.edu*
2. Contact Peter DeNardis at *pdenardis@comcast.net* and provide your full name

From IWMF-Talk, cont. from page 15

patients, so its appearance may be a chance occurrence, given the age of many WM patients.

Decrease in pulse rate

Several people reported a decrease in pulse rate when taking Imbruvica. **John P** reported a decrease in both IgM and also in platelets, which was not unexpected. However, he also reported that his pulse decreased to the mid-50s where it remained, up to the time of his post to IWMF-Talk. John asked if anyone else had experienced the same drop.

Colin P reported that Imbruvica inhibits BTK and BMX/ETK. BMX/ETK is another member of the same tyrosine kinase family as BTK and is highly expressed in the human heart. He cited an FDA Pharmacology Review of Imbruvica that included a report of pulse rate reduction in laboratory animals. The reduction in pulse rate depended on the dose and the time after dosing. A reduction in heart rate of as much as 30%, comparable to that reported by John P, was noted.

Use of other medications with Imbruvica

More discussion followed about Imbruvica and concurrent use of other meds that can affect platelet function. **Bob K** asked if Advil and other nonsteroidal anti-inflammatory drugs (NSAIDS) are permitted with Imbruvica. Several others, including **Anita L,** indicated that their oncologists told them that these meds are not permitted when taking Imbruvica because of the bleeding risk. **Pavel I** reported that he has been discouraged from taking fish oil and even the low dose "baby" aspirin.

Food intake in relation to dosing

The issue of food intake in relation to dosing of Imbruvica, a recurring topic as more and more people are started on this new oral treatment, was discussed again.

Sue B reported that she has not received any directions from her oncologist or pharmacologist regarding eating before or after taking the med. She asked if there are any food restrictions. **John P** stated that the package insert he received with the capsules indicates that taking Imbruvica with food increases the exposure approximately two-fold compared with taking the med after overnight fasting. John has chosen to take the pills when he gets up in the morning, and then he eats breakfast two hours later. He also checked with the pharmaceutical company's call-in line and was told that consuming grapefruit or grapefruit juice can increase the "exposure" by as much as 20 times. "Exposure" in this context appears to refer to the level of the drug in the blood.

On the other hand, **Robert K** stated he received no restrictions related to eating concerning either time or food, including grapefruit. **John E** reported the guidance he was given was to take Imbruvica two hours after a meal or a half hour before a meal. **Reggie A** also stated that his WM specialist told him that the med may be taken with or without food, excluding grapefruit and Seville oranges, but that he should take the pills at the same time every day. Reggie is responding well to the treatment, getting a great response.

FLUDARABINE

While fludarabine is a treatment not used as often now as it was even five years ago, it remains a topic still discussed periodically. **Kevin B** posted that he has IgM monoclonal gammopathy with neuropathy in his feet and with very significant symptoms. He had Rituxan infusions in 2014 and has had subsequent IVIG infusions without much benefit. His doctors have recommended fludarabine, either alone or combined with Rituxan. Kevin asked about the experiences of others with fludarabine, especially the effect on WM and side effects from the medication. **Hank S** suggested that Kevin obtain a second opinion, since fludarabine has potentially significant adverse effects.

Dr. Tom Hoffman stated that lowering the IgM helps improve neuropathy and that a severe neuropathy should be treated aggressively. Fludarabine is a great drug for inducing significant improvement in WM, but it also can have severe side effects. In addition, in people treated with fludarabine there is a higher incidence of transformation from WM to a more aggressive lymphoma. Fludarabine is no longer used routinely in second-line treatment after only one treatment failure. Dr. Tom also recommended a second opinion.

Julie D reported she has started treatment with fludarabine and Rituxan, following consultation with Dr. Treon at Dana-Farber. Her indications included bulky lymphadenopathy, a lytic lesion in her jaw, and a kidney lesion. Given her situation and the consultation with Dr. Treon, Julie was comfortable with this drug combination. After five months of treatment, her adenopathy has been significantly reduced while the lytic lesion was unchanged. Her IgM also declined, her hemoglobin increased, and she did not report significant side effects.

Tim B indicated a similar response to the fludarabine-Rituxan combination. The fludarabine made him slightly nauseous and gave him flu-like symptoms for a few days. His IgM dropped, as did his M spike, and his hemoglobin increased to the normal range. His response has continued for five years. However, Tim also suggested a second opinion for a more informed decision about further treatment with fludarabine.

BENDAMUSTINE

Finally, there was discussion about bendamustine. **Leon M** posted a question about an item he found in the previous *Torch*: The National Comprehensive Cancer Network (NCCN) Diagnostic and Treatment Guidelines for WM have changed to include bendamustine as a regimen potentially toxic to stem cells. Leon was looking for more information about this. List Manager and IWMF Trustee **Peter DeNardis** reported that a person would have to go directly to the NCCN website (*http://www.nccn.org*) and create an account in order

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From IWMF-Talk, cont. from page 16

to get that information. It is a fairly easy process and does not result in an increase in unwanted e-mails.

Another question about bendamustine came from **Donna O.** She has completed six months of treatment with bendamustine and Rituxan. However, four months after completing the treatment, she had a significant decrease in her hemoglobin and was diagnosed with autoimmune hemolytic anemia. Donna wondered if this could have been triggered by the bendamustine.

Ron T responded that he had developed warm autoimmune hemolytic anemia after a second course of fludarabine and noted that fludarabine shares some molecular characteristics with bendamustine. Since autoimmune hemolytic anemia resulting from fludarabine is well documented in the literature, it is possible Donna's hemolytic anemia was triggered by her treatment with bendamustine.

HAPPY NEW YEAR TO ALL

There are sure to be ongoing discussions on IWMF-Talk throughout 2015. New members will join, new information will be published and shared, and experiences regarding every aspect of WM will be introduced and discussed. Join us! Everyone is welcome!

MEDICAL NEWS ROUNDUP

BY SUE HERMS, IWMF BOARD MEMBER

Ibrutinib (Imbruvica) Under Consideration by the FDA for Approval in WM – Janssen Research & Development and its strategic partner, Pharmacyclics, Inc., announced the submission of a supplemental New Drug Application for ibrutinib (Imbruvica) to the U.S. Food and Drug Administration for the treatment of WM. If accepted, this will be the first approved treatment for WM. Janssen and Pharmacyclics are continuing clinical development for Imbruvica, including Phase III study commitments for several patient populations that include WM.

Pharmacyclics Applies for Expansion of Ibrutinib (Imbruvica) to WM Patients in Europe – Meanwhile, Pharmacyclics announced the acceptance of a Type II variation application for ibrutinib (Imbruvica) by the European Medicines Agency (EMA) to expand the drug's use to the treatment of WM patients in Europe. If the application is approved, ibrutinib would be the first drug specifically approved there for WM. The EMA is roughly comparable to the Food and Drug Administration in the U.S., although it operates as a decentralized scientific agency (not a regulatory authority) of the European Union.

Novel Flu Vaccine Strategy Investigated in WM and Similar Disorders – Yale Cancer Center has opened a trial to investigate a novel flu vaccination strategy in patients with WM and other plasma cell disorders. The study is called SHIVERING (Study of High-dose Influenza Vaccine Efficacy by Repeated dosing IN Gammopathy patients). In this study, the first high-dose flu vaccine will be administered followed by a second high-dose flu vaccine booster after one month. The high-dose flu vaccine was approved in 2009 by the FDA for use in individuals age 65 and older. The goal of the study is to enroll 100 patients, regardless of age, who have not yet received this season's flu vaccine and to identify the efficacy of repeat flu vaccinations. The clinical trial identifier number is NCT02267733.

British Study Reports Results of BEAM Conditioning Regimen for Autologous Transplantation in WM Patients – The Department of Haematology at University College London Hospitals NHS Foundation Trust reported its experience with the BEAM conditioning regimen prior to autologous stem cell transplantation in WM patients. BEAM consists of four drugs, carmustine, etoposide, cytarabine, and melphalan. The study reported an overall survival rate of 88% at one year post-transplant, with a low level of toxicity and no reported secondary malignancies.

Study Looks at WM and Associated Autoimmune Conditions – The Department of Internal Medicine at the University of Connecticut studied inflammatory and immune-related conditions associated with WM. This small study looked at 12 WM patients, 58% of whom had documented autoimmune conditions. Of these patients, 57% had more than one autoimmune disorder. Identified disorders included Hashimoto's thyroiditis, pernicious anemia, immune thrombocytopenia, cold agglutinin autoimmune hemolytic anemia, chronic inflammatory demyelinating polyneuropathy, polymyalgia rheumatica, temporal arteritis, and antinuclear antibody positivity.

Dana-Farber Cancer Institute Examines Incidence of Extramedullary Involvement in WM Patients – A study presented by Dana-Farber Cancer Institute examined WM patients for extramedullary involvement (EMD), which is the presence of WM cells in tissues outside the bone marrow. Of 985 WM patients evaluated, 4.4% were identified to have EMD. Of this subset of patients, 21% presented with EMD at diagnosis, while 79% developed EMD post-therapy. The most frequent EMD sites involved were pulmonary, soft tissue, cerebrospinal fluid, renal, and bone. The median overall survival at 10 years was 79%.

Medical News Roundup, cont. on page 18

Idelalisib (Zydelig) Receives Marketing Approval in Europe for Chronic Lymphocytic Leukemia and Follicular Lymphoma – Gilead Sciences announced that the European Commission has granted marketing authorization for its oral drug idelalisib (Zydelig) for chronic lymphocytic leukemia (CLL) and follicular lymphoma (FL). In CLL, the drug has been approved in combination with rituximab for patients who have received at least one prior therapy or as first-line treatment in certain patients unsuitable for chemo-immunotherapy; in FL, the drug has been approved as single-agent therapy for patients who are refractory to two prior treatments. Adverse drug reactions reported in clinical studies included infections, neutropenia (reduced neutrophils), pneumonitis, diarrhea/colitis, increased transaminase (an indicator of liver function), rash, and fever. Idelalisib inhibits PI3K-delta, a protein that is over-expressed in many B-cell malignancies.

Phase I Study Presents Results of Bortezomib (Velcade) and Alvocidib in Indolent Lymphomas and Multiple Myeloma – A multi-center U.S. Phase I study reported the use of bortezomib (Velcade) in combination with intravenous alvocidib (flavopiridol) in patients with recurrent or refractory multiple myeloma, WM, mantle cell lymphoma, and other indolent lymphomas. The study was designed to determine the dose-limiting toxicities and maximum tolerated dose. A total of 44 patients were enrolled, with 39 patients assessed for response. The maximum tolerated dose was 1.3 mg/m^2 for bortezomib and 40 mg/m^2 for alvocidib. The total response rate was 33%, and the most common toxicities included lymphopenia (reduced lymphocytes), neutropenia (reduced neutrophils), thrombocytopenia (reduced platelets), diarrhea, fatigue, and sensory neuropathy. Alvocidib is a CDK (Cyclin-dependent kinase) inhibitor.

Ibrutinib (Imbruvica) and ABT-199 Identified as Potential New Combination Therapy – Preclinical data presented at the American Association for Cancer Research conference on hematologic malignancies indicated that the combination of ibrutinib (Imbruvica) with the new investigational agent ABT-199 may improve outcomes for patients with mantle cell lymphoma and chronic lymphocytic leukemia. This presentation was made by researchers at the University of Virginia School of Medicine who undertook a systematic approach to identify combinations of drugs that might improve the ability of ibrutinib to kill cancer cells, and this particular combination was the most effective. Ibrutinib and ABT-199 affect different pathways involved in promoting cancer cell survival and growth – ibrutinib targets Bruton's tyrosine kinase (BTK) while ABT-199 targets BCL-2.

New Oral PI3K Inhibitor to Be Tested in Hematological Malignancies – Infinity Pharmaceuticals is entering into agreements with Roche and AbbVie to develop and commercialize duvelisib, an oral inhibitor of P13K-delta and P13K-gamma, for treating patients with hematological malignancies. The agreement with Roche will use duvelisib with the anti-CD20 monoclonal antibody obinutuzumab (Gazyva) in three separate trials, including one for treatment-naïve patients with indolent non-Hodgkin's lymphoma. Infinity and AbbVie will jointly commercialize duvelisib.

Phase I/II Trial Will Look at Novel Proteasome Inhibitor for Multiple Myeloma – The U.S. Food and Drug Administration has granted clearance to proceed with a Phase I/II trial of VLX1570 for relapsed and/or refractory multiple myeloma. The clinical study will be conducted in collaboration with the Memorial Sloan-Kettering Cancer Center and the Dana-Farber Cancer Institute. VLX1570, manufactured by the Swedish company Vivolux, acts on the proteasome through a different mechanism of action than bortezomib (Velcade) by inhibiting the initiation process that regulates the breakdown of defective proteins.

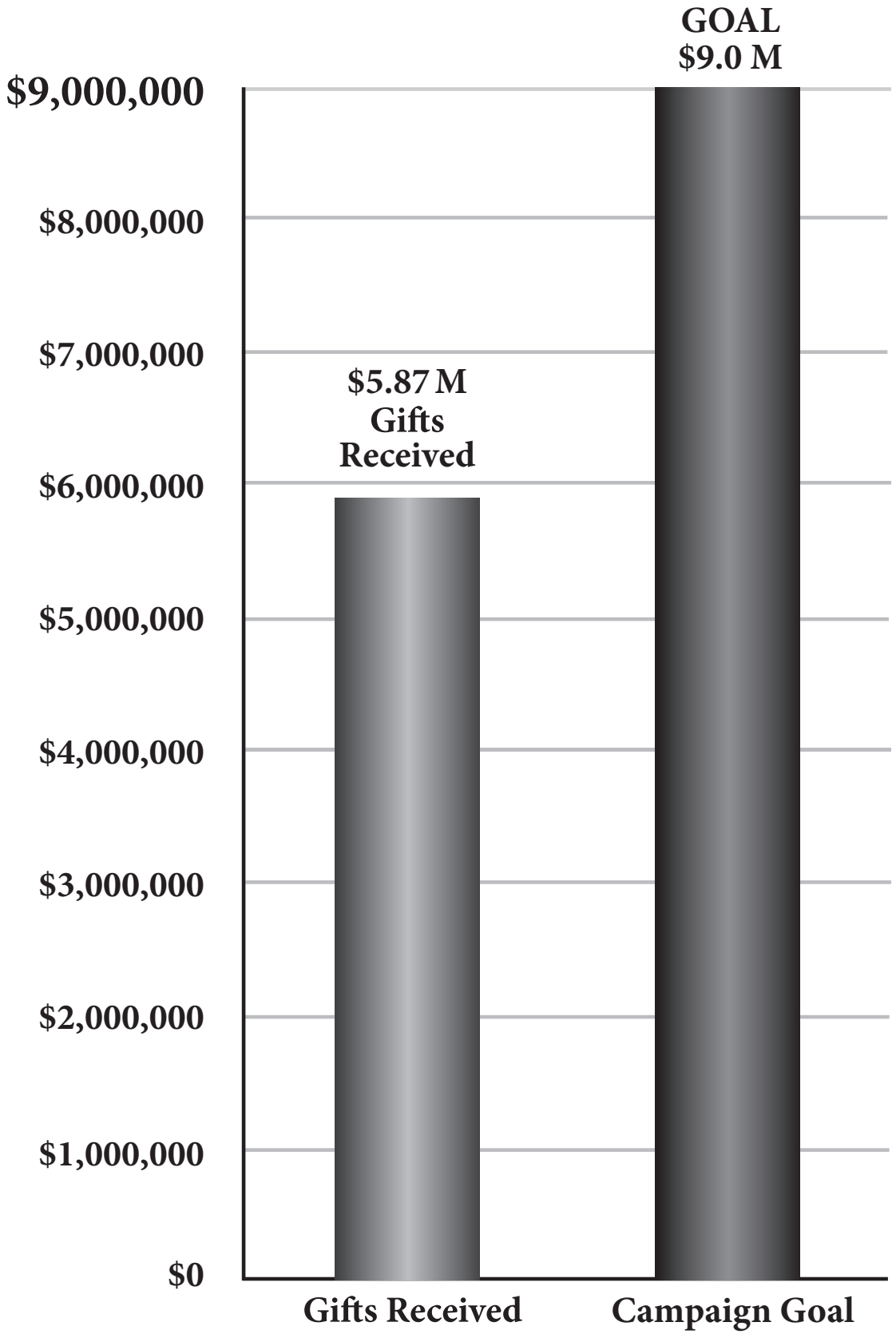
Phase I Trial Will Study Marqibo (Vincristine) Injection with Bendamustine and Rituximab for Indolent Lymphoma – A new Phase I clinical study will evaluate the use of vincristine sulfate liposome injection (Marqibo) with bendamustine and rituximab in indolent B-cell lymphoma (BRiM therapy). Bendamustine-rituximab is a standard chemotherapy regimen for treatment of many such lymphomas, and vincristine sulfate has been a traditional component of chemotherapy regimens. This trial will assess the safety of this combination by establishing the maximum tolerated dose of Marqibo in the combination. The clinical trial identifier number is NCT02257242.

Clinical Trial Collaboration Will Evaluate New PD-1 Inhibitor in Combination with Ibrutinib (Imbruvica) – Bristol-Myers Squibb has entered into a clinical trial collaboration agreement with Janssen Research & Development and Pharmacyclics, Inc., to evaluate the safety, tolerability, and preliminary efficacy of its investigational PD-1 immune checkpoint inhibitor nivolumab (Opdivo) in combination with ibrutinib (Imbruvica). The Phase I/II study will focus on patients with non-Hodgkin's lymphoma, including diffuse large B-cell lymphoma, follicular lymphoma, and chronic lymphocytic leukemia.

New Kinase Inhibitor in Several Trials for Relapsed/Refractory B-Cell Non-Hodgkin's Lymphoma – The novel aurora A kinase inhibitor alisertib (MLN8237) is being evaluated in several Phase I and Phase II clinical trials in combination with other therapies for the treatment of patients with relapsed or refractory B-cell non-Hodgkin's lymphoma. Alisertib is an oral medication developed by Millennium Pharmaceuticals.

The author gratefully acknowledges the efforts of Peter DeNardis, Charles Schafer, John Paasch, Wanda Huskins, and others in disseminating news of interest to the IWMF-Talk community. The author can be contacted at suenchas@bellsouth.net *for questions or additional information.*

Imagine a Cure Campaign Progress Report as of October 31, 2014



The total amount for Gifts Received includes all gifts to the Member Services and Research Funds, pledges made over a five year period, and planned legacy gifts.

WHAT DO YOU GIVE SOMEONE WHO HAS "EVERYTHING," INCLUDING WM?

Tom and Jeanie Myers

If you are the sister of former IWMF Board Member Tom Myers, you establish the *W. Thomas Myers Research Fund of the IWMF* in your brother's honor as a surprise for his birthday.

Jeanie Myers decided, "My gift was made now because Tom and I are the only ones left in the immediate family. He has had this terrible disease for such a long time. I fear for his ability to beat it, as he has also had some heart problems. I wanted the IWMF to continue to find answers and treatments as long as funds hold out. After I am gone is not when Tom needs the support!" Like so many others, Jeanie realized that the only hope for a cure was to increase IWMF-supported research.

Tom Myers became involved with the IWMF when he attended a support group in 1999 in Washington, DC, about 3 hours from where he and his wife Karen now live. In 2000 Tom joined the Board of Trustees, initially working on publications. When Judith May became President of the IWMF, Tom stepped into her position as Vice President for Research. He also developed the Ed Forum programs from 1995 to about 2010. With a PhD in paper chemistry and about 35 years in the paper industry, Tom retired from his career in 1997. That left him lots of time and energy to volunteer for various things for the IWMF. It also gave him time to do the other activities that he loves: biking, sailing, golf, and skiing. Tom retired as Board Member and Vice President for Research at the end of 2013 but remains active as a member of the Research Committee.

Meanwhile, Tom's sister Jeanie moved to western Maryland to be closer and to "get to know Tom as an adult" after she finished a 43-year-long career at IBM and private contract work at the National Institutes of Health (NIH) in Bethesda. Upon retirement, she moved into the 1870 brick house that has been in the family since her great grandfather lived there. Most recently her grandmother and aunt had inhabited it, and it needed renovating. So this energetic retiree went to work and is now happiest in its large and verdant gardens where she grows berries, vegetables, and flowers. Her other passions include programming and music, and she participates in two recorder groups and two choirs.

Jeanie says that her brother Tom is a "terrific guy" and has done so much good in the world, volunteering on numerous boards and putting all of his children and grandchildren through college, just to name a few of his good works. She says that he has remained active and that he feels well. In fact, after recent heart valve surgery Tom resumed bicycling a mere two weeks later! Clearly, "he has his energy back!" Longevity runs deep in the Myers family. Tom and Jeanie's mother lived to be 98, their aunt lived until 101, and their grandmother reached 104. But Jeanie did not want to postpone offering a very sizable and generous donation to the IWMF any longer. She decided, "I have to do it NOW!"

Jeanie Myers gave her brother a wonderful birthday surprise when she established the W. Thomas Myers Research Fund of the IWMF *in his honor.*

With money coming from the sale of her Washington home, Jeanie talked things over with Dave Benson, the Senior Development Officer for the IWMF, and decided that she would establish the *W. Thomas Myers Research Fund of the IWMF*, designating her $100,000 research gift to Dr. Stephen Ansell at Mayo Clinic. The Research Partners Program is for donors who give $50,000 or more per year for two or more years to fund a specific research proposal that has been vetted and approved by the IWMF Scientific Advisory Committee and the IWMF Research Committee. Jeanie determined that, "The need is now; the people you love and care for need this now." She stated adamantly that, "You simply don't put this off."

So when you or your loved ones want to figure out what to give to your family member or friend with WM for a birthday, anniversary, retirement – or any other occasion – give the gift that he or she is sure to benefit from, a gift to the IWMF. Those of you who choose to establish either a Named Gift Fund with a $50,000 pledge payable for up to 5 years or a Research Partners Fund, as Jeanie Myers did, can designate where your funds are used. However, if giving $50,000 or more is out of your reach, please honor your friends and family with a gift of any size. It's a thoughtful and generous way to celebrate them and to help the IWMF continue to fund a search for a cure.

If you would like to learn more about how you too can establish an IWMF Named Gift Fund or a Research Partners Fund, feel free to contact Dave Benson at *Dave@dbenson.com* or by telephone at 952-837-9980.

RYAN'S JOURNEY TO THE 2014 BANK OF AMERICA CHICAGO MARATHON FINISHING THE RACE IN COMMUNITY

BY RYAN SCOFIELD, IWMF MEMBER, AND DON BROWN, SUPPORT GROUP LEADER, CHICAGO

Two of Ryan's supporters were there to cheer him on: on the left, Don Brown, leader of the Chicago area support group, and on the right, Dave Perrin, support group member.

Don Brown speaks first, reflecting on his first contact with Ryan.

My introduction to Ryan Scofield began with a phone call in 2010 from a young man – only 35 years old, married and the father of a small son – who had been recently diagnosed with Waldenstrom's macroglobulinemia. Ryan was calling me because I am the support group leader of the Chicago area. I am also a fellow WM patient. He had been advised that he needed treatment for his Waldenstrom's, and he wanted to understand his disease and to connect with our wonderful organization. We met in person when, as a family, Ryan and his wife, Krista, and little Arthur visited our home. Mary and I were very moved to meet the Scofield family and share helpful insights to living with WM. Since that time Ryan has become an informed patient, participating in his treatment decisions, and he has become an active supporter of the IWMF in the Chicago community. Our relationship has grown into a personal friendship. Not too long after his first treatment, Ryan sent me a note with his picture climbing a mountain with Arthur on his back. I still keep that note and photo, together with a graph of his improved IgM and hemoglobin, hanging above my desk.

Ryan has since run the Allstate Chicago Half Marathon in 2012 and, most recently, the prestigious Bank of America Chicago Full Marathon in the fall of 2014. Donations made in support of Ryan and his friends were designated for the IWMF Research Fund and totaled $7,000 in 2012 and $15,000 in 2014. Ryan may not have finished the last race himself, but his community of three other racers did it for him.

Ryan Scofield comments on his role as fundraiser:

Following successful treatment for WM, I knew that I had to go further and become part of the solution. Taking treatment and just hoping for the best didn't suit me. So I wanted to do something to help, to be part of the cure for myself and for the people who will be diagnosed in the future. My thought was simple: If I could raise some money for research, I would be supporting my own cure.

I ran the Allstate Half Marathon with some friends and raised almost $7,000 for the IWMF, the organization that has helped me as it has so many others. I was struck by how many people wanted to donate. The donations made in my name didn't end up in a huge pool of money, they went directly to funding research for Waldenstrom's macroglobulinemia through the IWMF Research Fund.

After my success in putting together the Half Marathon fundraiser all by myself, I realized that I might do even better if I registered as an official charity at a more prestigious event. So, for my second time around I built a small team including Billy McMillin, Jarad Bingham, Terry Bingham, Nadia Burke, and myself. We were shooting for a full marathon in one of the world's biggest, the Bank of America Chicago Marathon, and the team ran it. As an official charity, we raised even more money! Again people were "falling over themselves" to donate money going to the IWMF.

My takeaway from this experience is that we can all be a part of the cure. Anyone can set up a fundraiser and ask their friends for money. You'll get it and your friends will be happy to help. And you will know that you did something to fight back against this disease and give real exposure to Waldenstrom's macroglobulinemia, a disease known to relatively few people.

Waldenstrom Runner Ryan Scofield ran the Bank of America Chicago Full Marathon on October 12, 2014. Contributions in support of Ryan and his team totaled $15,000.

COOKS' HAPPY HOUR

BY PENNI WISNER

For some years now, I've prepared a vegan, buffet-style lunch for the Cancer Survivors' Retreat Day put on by the Cancer Resource Center located at UCSF's Mt. Zion campus. For the very first event, I found a quinoa salad recipe on Rebecca Katz's blog *rebeccakatz.com/recipe-box/*. Rebecca, author of several cookbooks including *The Cancer Fighting Kitchen*, gets my highest recommendation for colorful, healthy, tasty recipe inspiration.

That quinoa salad has been on each menu since. I never tire of it and it has the distinct advantage of lasting many days in the refrigerator. It tastes just as good in the summer as in the winter. And thus, it forms the framework for our subject: grain salads. You made a New Year's resolution to eat more whole grains, yes? And there are so many these days: quinoa in all sorts of colors, farro (an ancient type of wheat), bulgur, buckwheat, barley (have you tried the purple barley yet?), rice, etcetera.

Here are a few ground rules for composing your grain salads. 1. You want a dressing that packs a lot of punch to flavor the more neutral-tasting grains. 2. You might choose a blend of grains, cooked separately so they cook up fluffy and separate. Or choose the same grain but in a surprising color, such as black rice. 3. Think texture and add vegetables such as jicama, radish, fennel, cabbage, celery, carrot, and cucumber and/or toasted nuts for crunch. 4. Think seasonally. Change your add-ins to reflect what is available. In spring perhaps add watercress, later in the summer, line bowls with butter lettuce, and in the fall and winter, try chicories and frisée. 5. Balance sweet and tart. Keep the dressing on the tart side and balance it with dried or fresh fruit such as raisins of any and all colors, dried cranberries, tart dried cherries, dried pears, pomegranate seeds, sliced persimmons. 6. Add herbs and a member of the onion family. In my opinion, mint always belongs in the mix because it adds such a fresh flavor. Diced red onion, shallot, or thinly sliced scallions also perk up the flavors. 7. In my book, some kind of chile is always a welcome addition. You could whisk a chili paste or ground chili into your dressing, or add thinly sliced jalapeño or Serrano chilies. 8. Keep your salad vegan or add a cheese such as little cubes of feta or ricotta salata.

If you make up a batch of a grain salad, you can pack it for lunch all week. Or serve it as a side dish or appetizer; top it with cooked meat, poultry, fish, or coddled or hard-boiled eggs; or add cooked legumes such as lentils (Choose the small French lentils or the black lentils sometimes called "caviar" or "beluga" lentils. These keep their shape when cooked.), chick peas, or edamame.

Rebecca was the first cook I encountered who dispensed with the two-parts-boiling–liquid-to-one-part-grain cooking instructions still found on quinoa packages today. Instead, she recommends one part quinoa to one and one-quarter parts water or broth. That translates to 1 cup quinoa to 1 1/4 cups water (to serve about six), cooked in a covered pot until the little white tails on each grain unfurl. Then spread the quinoa on a baking sheet and comb through it with a fork or your fingers to remove lumps and let the grain cool. The result: fluffy, separate grains. One year, we cooked the quinoa according to package directions and had quinoa mush. We froze it all and started over for the salad. (The frozen grain eventually became a favorite dish – quinoa pumpkin risotto: the grain mixed with a little broth, herbs, roasted winter squash, freshly grated Parmesan, toasted pumpkin seeds, and a drizzle of white truffle oil. But I digress. As usual.)

To make Rebecca's quinoa salad, cook the grain according to Rebecca's method above adding a little salt to the water. While the quinoa cooks and cools, make the dressing: Whisk together equal parts lemon and orange juice, a hefty amount of freshly grated orange zest (for a quarter cup of juice use at least the zest of one large orange), plus ground cumin, ground coriander, sea salt and freshly ground pepper to taste. Add enough extra-virgin olive oil to give you a light, flavorful dressing. Do not be shy with your seasonings; remember that the dressing needs to flavor the quinoa. As for amounts of cumin and coriander: Start with twice as much cumin as coriander, say 1 teaspoon of cumin to 1/2 teaspoon coriander. Toss the quinoa with the dressing. Taste and add more dressing as needed. Just before serving, add large handfuls of dried fruit such as raisins, dried cranberries, and/or dried, tart cherries, plus toasted, unsalted pistachios, and fresh mint. Do not skip the mint; it gives the salad its bright, fresh taste.

Just the other day, I enjoyed a dinner at Bouli Bar where a Mediterranean salad has been on the menu since the restaurant opened. The chef, Amaryll Schwertner, has a real talent creating dishes with unusual and stand-out flavors. Her salad is a great exemplar of all the rules above. The base of the salad is farro and bulgur. It was late fall, so the greens included purslane (a wild, thick-leafed green usually called a weed but delicious nonetheless) and frisée, plus mint and parsley. Pomegranate seeds and toasted pistachios sparkled in the mix; a pomegranate juice reduction (Heard of pomegranate syrup? It is pomegranate juice boiled down until thick.) mixed with a red wine vinaigrette dressed the salad. Barberries (another wild plant with deep red berries with a tart citrus flavor), and za'tar, also Middle Eastern, a blend of wild thyme, sumac (also tart and citrusy), and sesame added surprising and delicious flavors.

In the midst of the winter doldrums, let grain salads lift your spirits.

Our motto: Eat Well to Stay Well

INTERNATIONAL SCENE

EDITED BY ANNETTE ABURDENE

AUSTRALIA

AUSTRALIAN ADVISORY GROUP

The Australian Advisory Group continues to focus on initiatives that enhance Australian WM patient treatment and funding. Strong support in education, advocacy, and organisation from IWMF and the Australian Leukaemia Foundation continues to be of great benefit.

PATIENT EDUCATIONAL MEETINGS

Patient education and support meetings are now being held in three states. The organisational support by the Leukaemia Foundation and provision of meeting venues is highly valued. Regular meetings in Brisbane are continuing. The first meeting in Melbourne was held in October. Meetings will be continuing in 2015. In Sydney the November meeting had a record attendance of thirty. **Janelle Sullivan's** presentation giving a patient's perspective of Waldenström's was enthusiastically received. A follow-up session is planned in early 2015 to allow more time for discussion and questions.

Janelle Sullivan and Bob Lallamat following Janelle's presentation to Sydney Support which included stories of the challenges faced by WM patients to receive a therapy which had not been approved by the relevant Australian Health authorities. Janelle and Bob are both Australian pioneers in receiving bendamustine.

TELEPHONE FORUMS

For WMozzies, the Leukaemia Foundation hosted a telephone forum on November 20. It featured a presentation by Dr. Constantine Tam on the ABT-199 clinical trial involving WM patients. Victorian WMozzies **Colin Parrish** is one of four WM patients in this trial. Colin's story as a WM patient is to be included on the new IWMF website as well as in the Patient Stories posted at the IWMF 2015 Educational Forum. Dr. Tam also talked about his abstract given at IWWM8 and the development of Australian clinical practice guidelines for WM.

LYMPHOMA PATIENTS EDUCATIONAL MEETING

A Patient Educational Day is to be held on 27 February at Concord Hospital, University of Sydney. Bendamustine expert Professor Mathias Rummel will be available to do the first breakout session for WM. Some 10% of WMozzies have received treatment with bendamustine – even though there is no Pharmaceutical Benefit Scheme (PBS) funding yet available. Professor Gilles Salles is doing a follow up session. Professor Salles is an acknowledged specialist in haematological oncology, notably lymphomas, and has done WM patient clinical trials. Sessions specific to the needs of WM patients are also planned.

IWMF DIRECTORY OF AUSTRALIAN WM DOCTORS

Dr. Constantine Tam and Associate Professor Judith Trotman were added to the IWMF Directory of Australian WM Doctors posted on *iwmf.com*. Australia does not publish a local directory. The Australian haematology profession prefers, for referrals, that haematologists and patients contact multidisciplinary haematology centres to identify a WM haematologist willing and able to provide a consultation for a patient with WM.

WORLD LYMPHOMA AWARENESS DAY (WLAD)

September was World Lymphoma Awareness month and on Sunday September 14 WMozzies were there when Australia kicked off the global World Lymphoma Awareness Day celebrations. Even the Sydney Opera House was part of the fun, lighting up lime green to raise awareness for lymphoma. For WLAD 2014, WM patients also participated in the 27 educational events for patients held by the Leukaemia Foundation. The theme for the WLAD events was lymphoma treatment focusing on new therapies emerging for lymphoma and the issues Australians face accessing new therapies before they become available on the PBS.

AUSTRALIAN WM CLINICAL TRIALS

Regarding Imbruvica (ibrutinib), Australia is a participant in the first ever WM clinical trial with four of the 59 international clinical trial locations. The first Australian enrolled in this trial is a WMozzies member, **Michael Van Ewijk**. The principal investigator of this trial in Sydney is Associate Professor Judith Trotman, while in Victoria the principal investigator is Dr. Constantine Tam.

It is encouraging for Australia that Pharmacyclics & Janssen Pharmaceuticals have filed an application with the U.S. Food & Drug Administration (FDA) for approval of ibrutinib in the treatment of Waldenström's macroglobulinemia. It is hoped that approval by the FDA will assist to pave the way for Australian PBS funding.

AUSTRALIAN WM MANAGEMENT GUIDELINES

Dr. Constantine Tam is leading the development of the Australian WM management guidelines. Others helping in the development are clinicians, researchers, and people living with WM. Recent publications of international guidelines are being used as a backbone. The Australian guideline is in the context of our unique PBS system, accounting for differences

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in drug access and diagnostic technology. Dr. Tam attended IWWM8 in London in August and is a member of the International Panel developing the IWWM8 consensus on international WM clinical practices.

WMOZZIES WEBSITE

Planning of the development of the WMozzies website is continuing. The aim is to improve the Web content and presentation. Two WMozzies have responded to the talk list invitation for expression of interest in participating in Web developments. Currently the WMozzies domain is based in the US and options for transfer to Australia are being explored. A telephone conference with Barry Nelson, the newly appointed IWMF Webmaster, has been arranged for January. This will assist linking the WMozzies website to the enhanced features in the new *iwmf.com* website.

WMOZZIES CART-WHEEL DATABASE

The project feasibility study has been completed, confirming that the CART-WHEEL BioGrid database is fit for purpose. We are currently revising the content of the database following a review by local WM haematologists from a clinical perspective. A cross check is planned of our data elements with those in the WMUK clinical registry. We are also conferring on the UK approach to data collection and tissue bank links.

IWMF-DFCI WM EPIDEMIOLOGY STUDY

WMozzies are keen to link in with Dr. Irene Ghobrial's questionnaire and tissue bank study supported by the IWMF and the Dana-Farber Cancer Institute (DFCI). Possibilities for including bone marrow samples from WMozzies in the IWMF-DFCI epidemiology study of patients with Waldenström's are under discussion. Dialogue is advancing to allow WMozzies to join the more than 1,000 WM patients already part of this vital research to examine further the genomic and epigenetic regulators of tumour progression in Waldenström's.

AUSTRALIAN CANCER CONSUMER NETWORK (ACCN)

Australia's first national Who's Who Directory of cancer consumer organizations was launched for ACCN in Canberra at Parliament House. WMozzies is listed in the Directory to enable Parliamentarians to provide information to people about cancer organisations. The Directory was launched on 26 November by the Co-chairs of Parliamentarians Supporting Cancer Causes, Dan Tehan, MP, and Senator Deborah O'Neill. WMozzies Andrew Warden attended the launch with other representatives of cancer consumer groups.

Andrew Warden, WMOZZIES, reporting.

BELGIUM (FLANDERS)

CMP VLAANDEREN

The Flemish contact group, CMP Vlaanderen, is a support group for two disorders, WM and MM. Needless to say, the WM patients are in the minority: WM is a very rare cancer and consequently the WM patients form just a small community. Nevertheless, we report with pleasure that the list of our members is increasing every year. This is due to the greater attention that physicians give to the disorder and the information given to newly diagnosed patients about the existence of CMP. Meanwhile we have passed the milestone of one hundred members. Not so bad for half of a small country! But it could be better. According to the Belgian cancer registry, every year about seventy new WM patients are registered. There is still work to be done!

CMP Vlaanderen had not only a busy year in 2014 but also a successful one starting with the marvelous jubilee symposium in January, of which a full report was previously published the *Torch*, issue 15.2 (April 2014) pages 16-17.

REGIONAL MEETINGS AND LONDON FORUM

In the course of the year, regional meetings were held in different parts of Flanders. In Leuven, Aalst, and Brugge en Houthalen (Limburg) groups (of at least thirty participants each) met to hear a representative of the Vlaams Patiënten Platform, (the Flemish Patients Platform or VPP) present a lecture on "Know your Patient Rights!" Following the introduction of the law on patients' rights in 2002, patients have the right to informed consent and the right to information about their health condition. Many patients do not know that law and consequently are ignorant of their rights.

In Antwerp, Dr. Zachée, a hematologist, explained to an audience of fifty interested listeners the "Acquired Immune Deficiency in WM and MM and How to Treat It." Later in

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NEW IWMF AFFILIATE/SUPPORT GROUP ESTABLISHED IN ITALY

We are pleased to announce the establishment in Italy of an IWMF Affiliate/Support Group under the sponsorship of Dr. Enrica Morra, President of Associazione Malattie del Sangue ONLUS, Scientific Director of the Lombardy Hematology Network.

This is the first such group in Italy and we hope for its success in reaching out to and welcoming those in Italy touched by Waldenstrom's macroglobulinemia (WM).

Anyone interested in joining this support group should contact Flavia Mammoliti (*associazione@malattiedelsangue.org*)

the autumn, a second meeting took place in Houthalen on the topic "Participation in Clinical Trials and Scientific Research."

Both meetings were followed by interactions with fellow sufferers, giving them the chance to exchange experiences. This is actually the part of the meetings that is very much appreciated by the patients. A suggestion for future topics came from the healthy participants: a session for those who day after day take care of a sick partner. This is a proposal that we certainly will take into account for future regional meetings.

Unfortunately I could not attend the London Forum in August. The after-effects of a treatment earlier this year made that trip impossible. Jeannot Poelman represented CMP at the meeting of the EWMn and at the workshop.

ANNUAL SYMPOSIUM

Leuven, November 8: More than two hundred participants attended the yearly symposium. In the morning both WM and MM patients assembled in the auditorium of the university hospital for clarification on three issues that could interest patients of both diseases. Professor Peter Vandenberghe of the Molecular Diagnostic Center started with a speech on the role of genetic research in WM and MM. He was followed by Mrs. Saskia Cremers, chair of data management, Department of Hematology, who, accompanied by her assistant, Mrs. Eveline Thomis, revealed all the secrets of clinical studies. To Dr. Steven Pans, Department of Radiology, and to Prof. Olivier Gheysens, Department of Nuclear Medicine, fell the honor to conclude the instructive morning with a discussion of the latest imaging techniques in MM and WM.

After our minds were richly nourished by science, our bodies were refreshed with a lunch served in the *Alma*, the student restaurant. And refreshment was necessary because in the afternoon we got the "main course." Prof. Michel Delforge discussed the current and future treatments for MM, while Professor Ann Janssens spoke on the same topic for the WM patients. The audience was very interested and Professor Janssens had to answer many of our questions. It was a tiring day, and people not able to attend missed a lot. Fortunately the program is available to them.

LOOKING AHEAD

Taking a look forward, we see a new year with many challenges. In January the Belgian Hematological Society (BHS) will be hosting the Belgian contact groups for hematological diseases to negotiate the creation of an umbrella organization. We want to follow up on our meeting of last November with Dr. Alain Thibault, the Chief Medical Officer of arGEN-X. We had a very interesting conversation about the clinical study of ARGX-110 and how CMP Vlaanderen can contribute to the advancement of this program. One of the visitors to our past symposium was a representative of Janssen Pharmaceuticals. And of course we could have a talk about Imbruvica, that new drug admitted in the 28 member states of the European Union for CLL and MCL, but not for WM. I think that acceptance at the European level for the use of Imbruvica in the treatment of WM would be a challenge worth taking up for European WM patients.

At the WMFC fundraiser, from left to right: board member Betty McPhee, Indycar driver James Hinchcliffe, and Linda Atlin, wife of board member Jeff Atlin who passed away this year.

In 2015 we again plan to organize a yearly symposium, to arrange regional contact meetings, to follow up on what is going on with orphan drugs and orphan diseases – in Flanders, in Belgium, in Europe, in the world – and to do so much more to keep our fellow sufferers informed, confident, hopeful.

Joanna Van Reyn, CMP Vlaanderen, reporting.

CANADA

TORONTO: FOURTH FUNDRAISER

On Saturday October 25 the Waldenstrom's Macroglobulinemia Foundation of Canada held its fourth fundraiser, for a second time at the Bata Shoe Museum in Toronto. The event was a

Kirsten Johnston, wife of board member David Johnston, and WM support group member George Cram stand beside the handmade quilt which Kirsten, a renowned quilter, generously donated to the silent auction.

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James Hinchcliffe with "Ray's girls"– the close friends of Toronto support group member Raffaela Mercurio who turned out in support of Ray and the WMFC fundraiser. From left to right, "Ray's girls" are: Pina Bevilacqua, Mary Trozzo, Raffaela Mercurio, Carla Nikolovski, Grace Decandia and Vera Mercurio.

Charles Schafer, a founding member of the Nova Scotia WM support group, presents In Honour gift to Susan Gagnon in recognition and appreciation as she steps down after ten years as support group leader.

great success, and a good time was had by all. Our guests were able to roam throughout the three levels of the museum (which documents the evolution of shoes and fashion footwear throughout the centuries), dance the evening away, and nibble on some scrumptious food.

Add in some amazing auction items. A total of 46 items were generously donated this year, such as IndyCar Driver James Hinchcliffe's Indy 500 race suit, a lady's Philip Stein watch, beautiful artwork by local artists, handmade quilts, Spyder ski wear, and a week at the Regent Grand Resort in the Turks & Caicos Islands – just some of the exciting offerings. Everything was bid on and taken home by their delighted new owners.

James Hinchcliffe was on hand to lend his support for the WMFC. Waldenstrom's macroglobulinemia has touched our family and he hopes he can help bring awareness to this rare cancer. We thank everyone who volunteered or sponsored this fundraiser in support of the "Imagine a Cure" campaign.

Arlene Hinchcliffe, President, WMFC, reporting.

NOVA SCOTIA WM (NSWM) SUPPORT GROUP NEWS

Since the Queen Elizabeth II Health Sciences Centre hematology clinic treats most WM patients in the four provinces of Atlantic Canada – Nova Scotia, Prince Edward Island, New Brunswick, and Newfoundland and Labrador – our group has spent the last year reaching out to Wallies in this geographic area of about 2.5 million people. We now have 21 patients in our support group.

NSWM last met in October 2014 with 19 patients and caregivers in attendance. Thanks to tips from other support group leaders I received in Tampa last May, the Leukemia & Lymphoma Society of Canada has become a strong supporter of our group, with the local LLS Patient Education and Support Manager facilitating our caregiver session and treating us all to lunch. Thank you, Tanya Hastings! At our October meeting, Susan Pleasance, Associate Director, Hematology Research at the QEII, explained the clinical trial process and the current WM clinical trials available in Halifax. One of our group members is already enrolled in NCT02165397, and there was much interest from the rest of us. Of particular note: MYD88 L265P and CXCR4 genetic testing will be done as part of this trial, and results will be available to participants after the trial. While Imbruvica (ibrutinib) is now widely available in America and recently approved in Europe, it has no such status in Canada. Halifax is one of the first locations to start recruiting WM patients for a Phase III clinical trial (NCT02165397) that pits Rituxan and Imbruvica against Rituxan and placebo, with an Arm C for those refractory to Rituxan to receive Imbruvica only.

Susan Gagnon has stepped down as support group leader after ten dedicated years, and the group recognized her contribution with an 'in honour' donation to the WM Foundation of Canada.

Ron Ternoway, NSWM support group leader, reporting.

FINLAND

ANNUAL SUPPORT GROUP MEETING

The annual support group meeting took place in Finland on September 20 in Tikkurila, close to Helsinki. The meeting was held at the SOKOS Hotel. As in prior years, the Finnish Association of Cancer Patients took care of all practical arrangements, arranging for the visiting doctor, providing all meals and coffee breaks. Twenty-five participants attended, mainly from South and Central Finland. After the welcoming coffee, our presenting physician, Dr. Pekka Anttila, gave a very up-to-date and practical overview of WM and naturally answered many questions. Following a tasty lunch **Juha Wirekoski** from Eastern Finland described in a touching, but also humorous, way his four years' journey with WM. The meeting was finished with the traditional "round table" discussion. Each of us told his or her story about life with WM, diagnosis, symptoms before and after diagnosis, and

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International Scene, cont. from page 26

Attendees at the fourth German Waldenström meeting, organized by the Leukaemia Patient Support Group Rhein-Main (LHRM) which took place in Darmstadt.

treatment. This part of our meetings has always been very useful and informative.

Veikko Hoikkala, Finnish Support Group, reporting.

GERMANY

OCTOBER MEETING

The fourth German Waldenström meeting was again very much appreciated by patients, family members, and speakers. The meeting took place October 4-5 at the Commundo Hotel in Darmstadt and was organized by the Leukaemia Patient Support Group Rhein-Main (LHRM). There were 56 attendees with more unable to attend due to unforeseen circumstances. Prof. Christian Buske, Director of the Institute for Experimental Cancer Research, University Hospital Ulm, was fantastic: He explained his very scientific slides in perfect lay language to the satisfaction of all participants. Most patients had sent their questions in advance, so that the next presenter, Dr. Georg Hess of University Clinic, Mainz, came prepared and was terrific, too. Dr. Hess managed to answer more than one hundred questions and fielded additional ones from the audience. All in all it was a truly interactive event. On Saturday evening most of the participants met at the hotel's lavish buffet and shared both experiences of their disease journeys and lots of jokes and laughter.

Manfred Grimme, the Orlando FL to San Francisco CA cyclist, at the Golden Gate Bridge, the conclusion of his trip.

On Sunday before lunch, **Manfred Grimme**, a WM patient, gave a very touching talk about his January to April 2013 cycling trip from Orlando, Florida, to San Francisco, California, covering 6,230 kilometers!

The group consensus on Sunday afternoon was positive. It was good see many familiar faces again, and we will come back again. Our next meeting is planned for the fall of 2016 in Darmstadt.

MORE NEWS FROM GERMANY

Leukaemiehilfe Rhein-Main (LHRM) has published the German Waldenström patient guide. The scientific co-authors are Drs. Buske and Hess. At the October 2014 annual meeting of the German, Swiss, Austrian Hematology Association (DGHO) in Hamburg, the booklet was the highlight at the LHRM booth, together with LHRM's new project *blog4blood.de*. The guide is posted on the IWMF website, *iwmf.com*.

The German Society for Hematology and Oncology will hold a 90 minute session on Waldenström during their June 2015 meeting in Bonn.

Anita Waldman, chairwoman LHRM, reporting.

IRELAND

ANNUAL MEETING

The WM Support Group Ireland held its annual general meeting on Saturday, April 12, in the Stillorgan Park Hotel,

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International Scene, cont. from page 27

Dublin. Five out of the 13 members attended. After reporting on our WM stories to date, we discussed the new drugs becoming available, the meetings to be held in London in August 2014, and the knowledge of WM (or the lack of it) that doctors in Ireland have. For one new member, who was diagnosed in July 2013, it was the first time meeting anyone else with WM. I think we gave her plenty to think about!

I would love to hear from anyone who has recently been diagnosed with WM and, of course, from anyone else who has WM or is interested in it. I currently know of 12 WM'ers in Ireland. There must be more!

Sheila Thomson, WM Support Group Ireland, reporting.

UNITED KINGDOM: WMUK

THE UK REGISTRY AND BIOBANK

Following the huge success of the appeal led by Patron Charlotte Green and the award of a research grant by the IWMF, we were able to announce at the London Forum the go-ahead of both the WM UK Registry led by Dr. Helen McCarthy and the linked WM Biobank (tissue bank) at University College Hospital London (UCLH) led by Dr. Shirley D'Sa. Both are now in construction. WM medical specialists will enter patients' data in the Registry. We warmly thank Idera Pharma, Janssen UK, Gilead, The Binding Site, and the IWMF for their sponsorship of the WM UK Registry.

Subject to funding, the aim is that the central UCLH Biobank (tissue bank) will be linked to other centres interested in storing WM tissue for data analysis to improve understanding and treatment.

The Registry has generated considerable excitement in the WM community, particularly from Australia, and our partner, Dr. Peter Walton of Dendrite Clinical Services, is visiting Australia in 2015 to discuss possible co-operation with Andrew Warden of the WMOzzies.

BIRMINGHAM FORUM

WMUK is holding a regional forum in Birmingham on April 1 led by Dr. Guy Pratt of Birmingham Heartland Hospital. It will be in the iconic new Library of Birmingham, a tourist destination in its own right. The aim is to develop a rolling programme of regional meetings throughout the UK where there is demand and in each case to encourage the formation of a self-sustaining local group. Bookings are being taken on the WMUK website *wmuk.org.uk*

FUTURE DEVELOPMENTS

As WMUK expands it aims to offer more services to support patients, doctors, carers, and nurses, either in house or working with partners. It already has a very effective working relationship with the IWMF, and WMUK has now also established an excellent relationship with the Lymphoma Association, attending each other's meetings and recently sharing information in response to the government's consultation on the future of the English Cancer Drugs Fund. The Lymphoma Association has a particularly good programme of Clinical Nurse Specialist Education where working together will be a cost effective way of giving WM information at the point of diagnosis. WMUK also hopes to extend its range of publications, the next in line being a guide to neuropathy.

NEW THERAPIES

To date the UK has been relatively slow to adopt emerging therapies and also has a poor record of participation in trials compared with other European countries. With the arrival of novel small molecule agents such as ibrutinib and idealalisib, the position is unlikely to improve, as the high cost and lifelong use of these drugs present particular financial challenges to the National Institute for Health and Care Excellence (NICE), the gatekeeper to NHS funding. WMUK is thus committed to promote UK trials, encourage further updating of treatment guidelines, and encourage the generation of more quality of life data from WM patients which may, in part, justify the high cost of new drugs.

Roger Brown, WMUK, reporting.

SUPPORT GROUP NEWS

EDITED BY PENNI WISNER

Contact information for all support groups can be found at *iwmf.com* under MEMBER SERVICES

CALIFORNIA

Sacramento and Bay Area

The group gathered in September at the Roseville Kaiser to watch the DVD presentation by Dr. Steven Treon recorded at the May 2014 IWMF Forum in Tampa. The section devoted to a discussion of the new treatment Imbruvica (ibrutinib) was of particular interest. After refreshments, the meeting continued with a circle discussion of personal progress with WM. The next meeting, January 25, will take place in the San Jose area, a new meeting location for the group. Plans include a local oncologist as the speaker. It is hoped that the new location will be more convenient for some members than the usual Vallejo and Roseville locations.

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Support Group News, cont. from page 28

Members of the Connecticut support group gathered in Cromwell for their fall meeting.

COLORADO & WYOMING

On a gorgeous 80°F day in late October, 44 group members met in Denver. The large group turned out for detailed presentations from nurse practitioner **Megan Andersen** and **Dr. Jeff Matous**, both of the Colorado Blood Cancer Institute. Megan reviewed WM basics from diagnostic parameters to symptoms that indicate treatment is required. Dr. Matous, who had attended the Eighth International Waldenström's Workshop in London, shared many of the funny stories from London and gave key slides from researchers from many countries, as well as information on new clinical trials and drugs that can now be obtained in Denver. When Dr. Matous mentioned the East German interest and research on bendamustine, co-leader **Cindy Furst** pricked up her ears. She has been treated with the drug and hopes her results match those of the patients in the study who averaged nine years before retreatment was needed. He also discussed pros and cons in the newest WM diagnostic debate: should a MYD88 test now be a requirement for a WM diagnosis. Dr. Matous is of the opinion that, at the moment, it is not worth getting tested because treatment decisions would not be affected. This, of course, could change in the future, depending on results from more research. The pharmaceutical company TEVA sponsored the generous breakfast from Panera Bread before the meeting. All this support was thanks to the Leukemia & Lymphoma Society (LLS) winning a grant for support groups. **Julie Jakicic**, former IWMF staffer and now LLS staffer and local WM champion, attended the meeting as well. Caribou coffee and Light the Night Survivor T-shirts were also available to group members. Megan and Dr. Matous are frequent support group guests. Members were especially delighted to reconnect with Megan, who has been on maternity leave for most of the year. While she did leave her newborn at home, she highlighted her presentation with darling pictures of her baby daughter, Ellie, who is now eight months old. In fact, both Megan and Dr. Matous pepper their presentations with fun slides that enliven their talks.

CONNECTICUT

In the fall, 17 group members gathered in Cromwell, CT. Co-leaders **Gail Arcari** and **Bob Hammond** led the discussion on a wide range of topics, including a review of programs offered by the LLS and the IWMF and the continued need to support these programs through both individual outreach efforts and financial contributions. The group took a moment to reflect on the memory of **Pat Matrick** and her message: "enjoy living." She was a support group member who recently passed from "another" cancer, not WM. During the meeting, members shared personal stories about their WM journeys and treatment options. The group heard encouraging news: Major cancer treatment centers have begun to collaborate with local Connecticut hospitals regarding treatment protocols and to include WMers in clinical trials. The support group plans to meet twice yearly, with the next meeting to be scheduled in the spring of 2015 in southwestern Connecticut. Members will continue to share news through the group's new quarterly CT WM newsletter, *The B-Cell*. At the conclusion of the meeting, members enjoyed a meal together in the dining room of the Covenant Village of Cromwell.

ILLINOIS

Chicago Area/SE Wisconsin

In August, **Karl** and **Kathy Coyners** hosted the group's sixth annual picnic at their house in St. Charles, IL, a western suburb of Chicago. The shady, wooded yard and fishpond (even the fish got fed!) set the scene for a very successful coming together of more than 40 "new and old timers" for fellowship and food. The event gives members an opportunity to remember those who have passed away, especially

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Support Group News, cont. from page 29

Ron Draftz (his daughter Angelique attended once again) and **Brian Schaefer**, whose wife, Melissa, brought two of her four children, Robert and Laura. One "newbie" arrived as well as several who had been diagnosed in early 2014. Everyone seemed to enjoy the "beer brats" from leader **Don Brown** and the fried chicken and countless other dishes brought by others. The **Wyatt family** was well represented with children playing beanbag throw and sleeping on their father's shoulder. At the picnic, Don announced that **Ryan Scofield's** team of five runners would participate for the IWMF in this year's October 12 Bank of America Chicago Marathon. Ryan is a young WMer, father of two young children. At the picnic, Don and **Mary Brown** modeled newly designed T-shirts promoting the run (see also page 21 of this issue where Ryan, Don, and Dave Perrin wear the Waldenstrom Runner T-shirt). Fifteen T-shirts were purchased by picnic attendees to raise even more money as well as awareness of the disease. 2014 was the first year that the IWMF became an official registered charity with this well-known marathon. See more about Ryan's effort to raise money for Waldenstrom's research on page 21.

Linda Van Horn, PhD, RD, and Professor of Preventive Medicine at Northwestern University, spoke at the October meeting. Her topic, "The Role of Diet in Cancer Risk and Prevention," elicited many questions and was very well received by the large group. The next meeting is planned for April; the topic and speaker will be announced in early 2015 through the e-mail distribution list.

INDIANA

Dr. Guy Sherwood, Vice President for Research and local group member (that was then, Fall 2014; since then Guy and his family have moved back to Canada), drew a large crowd to hear his report on the London IWWM8 Workshop. Guy did an outstanding job making complex information understandable. Many questions and discussion followed and everyone expressed gratitude for the opportunity. The LLS provided coffee and breakfast snacks and a comfortable room for the meeting. Following Guy's talk, the participants shared their experiences and treatment regimens. There were questions, comments, and even applause for one member when he shared his story of improvement. Stacey Koleszar, LLS director of patient services, announced that Dr. Treon would be the speaker at the March 6 Ask the Doctor Conference sponsored by the Indiana LLS. Save the date! More information will follow. Please make sure that group leader **Gayle Backmeyer** (*divagayle@comcast.net*) has your e-mail address so that you receive further information. Due to the frequency of winter storms, the group does not meet in the winter months.

MICHIGAN

Susan and **Carl Stoel** held their first support group meeting in the summer of 2014. Thirteen patients attended and agreed they enjoyed the small group as it allows freer interactions. Carl started the meeting by placing pins, each representing a WM patient, in a map of Michigan. Then he told his own story of diagnosis and treatment. This opening prompted attendees to list their own treatments, and a general discussion of symptoms, complications, and treatment side effects followed. The afternoon included a social hour and refreshments before the general meeting began.

NEW YORK

New York City

The turnout for the last meeting of the year was excellent. Even better, there were several "newbies" attending who, it would seem, left the meeting feeling a lot more confident and hopeful about their future than when they arrived. The discussion was wide-ranging, although with an emphasis on treatments that balance effectiveness and toxicity. Several of the group's members are exceptionally well versed in the science of Waldenstrom's, and their ability to communicate was icing on the cake.

Rochester, Western and Central NY

Due to ill health – not WM-related – on the part of local leader **Stephen French**, the group has been inactive for several months. In the meanwhile, members are encouraged to attend the monthly support group meetings at the Rochester Gilda's Club sponsored by the regional LLS chapter. True to form, the meeting leader is a popular and knowledgeable nurse from Strong Memorial Hospital Oncology Clinic (owned and operated by the University of Rochester).

EASTERN OHIO, WESTERN PENNSYLVANIA, & WEST VIRGINIA

A great crowd of WMers and caregivers, some traveling several hours, met in Bedford, Ohio (near Cleveland), in June to hear Mitchell Smith, MD, PhD, Director of the Lymphoid Malignancy Program, Cleveland Clinic, speak on Waldenstrom's macroglobulinemia. Dr. Smith presented an excellent overview of WM and its uniqueness within the lymphoma spectrum. For over an hour, the participants enjoyed a very interactive Q&A session in which Dr. Smith addressed questions with sincere interest and expertise. All WM-related and survivorship questions were fair game. Members had an opportunity to get to know one another during the informal social period where all enjoyed sampling delicious culinary contributions. After a summer hiatus, the group re-convened in October at the Pittsburgh home of **Marcia** and **Glenn Klepac** for an informal get-together and potluck. Members participated enthusiastically, vividly sharing their unique experiences. It became clear that to live with WM is to experience many twists and turns. The group warmly welcomed a new member from Pittsburgh who joined in the spirit of the group. All enjoyed watching the video of the Mayo Clinic's Dr. Morie Gertz: "The Burning Questions

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about WM." The afternoon continued with a potluck topped off by **Shari Hall's** outstanding pumpkin cheesecake! The group then closed out the year with another preholiday get-together in December.

WESTERN OHIO, EASTERN INDIANA, & NORTHERN KENTUCKY

The West Ohio support group has been dormant for a couple of years but an old-timer is waking it up. **Ron Payne** has re-enlisted as the group leader and the group calls itself the WOWMERS. With more than 100 persons in the local database, the group has two meeting sites: central Ohio and Cincinnati. Attendance at the first of the paired-site gatherings, held a week apart, shows promise for a reinvigorated group. **Nancy Hess** has graciously agreed to be the co-coordinator of the group. She was diagnosed with WM in December 2011 and has remained well so far. Nancy worked in several areas of the medical field and still does some practice management. She is a Master Gardener and volunteer naturalist in Ohio. For many years she has enjoyed globetrotting and currently writes stories about adventures in faraway places. She also enjoys various types of needlework and loves to cook and bake.

PENNSYLVANIA

Harrisburg Area, Central and Southeast

Two kinds of pumpkin cake and a round-table discussion of personal WM journeys centered the group's November meeting at Messiah Village. The next meeting is planned for March, followed by the annual picnic in the summer.

SOUTH CAROLINA

The beautiful new cancer center at Self Regional Hospital in Greenwood, western South Carolina, was the site of the group's fall meeting. The center provided a platter of cut fruit and vegetables to fuel the informal, round-table discussion. Afterwards, several members continued together to dinner and a musical at the local theater. Thanks go to **Roger** and **Barbara Robinette** for making it all happen. Last spring, at the meeting held in Charleston, **Sue Herms**, IWMF Trustee and editor of Medical News Roundup for the *Torch*, presented an informative update of the latest advances in treatments. The spring 2015 meeting is planned for a March or April time frame in Beaufort, SC, on the east coast.

VIRGINIA

Dr. Mary L. McMaster gave a superb talk, "Waldenstrom's and MGUS in Families – Your Questions Answered," at the first Northern Virginia support group meeting in Fairfax, VA, in October. Dr. McMaster is the Senior Clinical Specialist in Familial Waldenstrom's, National Cancer Institute, National Institute of Health in Bethesda, MD. She has been working on Waldenstrom's as a clinician and researcher for decades and is a frequent speaker at the IWMF's Educational Forums. Dr. McMaster prepared her talk to cover the sixty questions sent in advance by group members – who also peppered her with even more questions following her ninety-minute presentation. Dr. McMaster made many memorable points. Among them was that while in 2014 WM is still not curable, it is "highly manageable." She added that the "goals of treatment are to reduce symptoms, ideally to improve bone marrow functioning, and to prolong the time a patient is off treatment." Several volunteer WMers and caregivers generously donated their time to help execute our inaugural event, and this made a significant difference in our experience of the day. **Marcia Klepac**, IWMF Trustee and current Support Group Coordinator, was an invaluable advisor to our planning.

causes other than WM. Treatment toxicity considerations and goals of therapy will likely differ when increasing numbers of elderly patients are enrolled in clinical studies. Dr. Kastritis and colleagues analyzed the survival of 408 patients with symptomatic WM. The median age of patients was 68 years; median follow up was 5.5 years; 52% of the patients died in the interval, but 23% of deaths were considered unrelated to WM. The median survival of patients greater than 75 years of age was 5.3 vs. 9.7 years for patients younger than 75 years. In patients greater than 75 years of age, approximately 40% of deaths were unrelated to WM. Dr. Kastritis suggested the design of clinical trials should take into account these age-related mortality statistics since many WM patients are of relatively advanced age when diagnosed and treated.

Dr. Jorge Castillo of the Bing Center DFCI presented data on a study evaluating the survival trends in patients with WM based on the United States Surveillance, Epidemiology and End Results (SEER) database. The study's primary objective was to describe the trends in relative survival (RS) and overall survival (OS) in patients with WM from the United States. Relative survival represents cancer survival in the absence of other causes of death and is defined as the ratio of the proportion of observed survivors in a set of cancer patients to the proportion of expected survivors in a comparable set of cancer-free individuals. A total of 6,231 patients diagnosed with WM between 1980 and 2010 were reviewed. The median OS times were 5.6 and 7.3 years for the 1980-2000 and the 2001-2010 cohorts. The 5-year RS rates for the 1980-2000 and 2001-2010 cohorts were 67% and 78%, and the 5-year OS rates were 56% and 65%, respectively. Older patients, men, and African Americans had worse outcomes than younger patients, women, and Caucasians. Dr. Castillo concluded that the results of the analysis demonstrated the significant improvements in the outcomes of US patients with WM in the last decade. This is largely felt to be attributable to the development of less toxic and more efficacious treatments as well as an increased focus on improved supportive therapies.

POSTER DISCUSSION SESSION OF INVITED ABSTRACTS

The conference attendees next took a break from the standard lecture format and were treated to a poster session where the invited researchers discussed their results in poster format. In the interest of space I have selected the abstracts that were presented by the four recipients of the IWMF Young Investigator Awards (see page 8 in this issue) as well as the awardee of the European Waldenstrom Macroglobulinemia Network (EWMn) Young Investigator Award.

Dr. Julie S. Nielsen of the Deeley Research Centre, British Columbia Cancer Agency, British Columbia, Canada, presented an interesting talk on her poster **"MYD88 L265P: A target for T-cell based therapy of WM."** T-cell receptors recognize small fragments of surface proteins (epitopes) that are presented to them by HLA class 1 molecules. The immune system's design permits proteins from healthy cells to be recognized as "self" and ignored, while cells containing foreign proteins will be attacked. The T-cell receptors are very sensitive – they can recognize even a single amino acid change in a surface protein that may contain hundreds of amino acids. Dr. Nielsen and colleagues were able to identify an epitope that was naturally processed and presented in MYD88 L265P B-cells. The CD8+ T-cell immune response was specific and robust for the L265P substitution, demonstrating that the MYD88 L265P mutation found in 90% of WM patients is a valued immunotherapy target in WM. Dr. Nielsen and team are developing a novel, highly targeted treatment for WM involving genetically modified T-cells. This work is supported by a research grant from the IWMF and WMF Canada. (See also page 9 of this issue)

Dr. E.L. Smith of the Memorial Sloan-Kettering Cancer Center presented a talk on his poster **"CD19 targeted chimeric antigen receptor modified T-cells for the treatment of Waldenström's Macroglobulinemia."** Chimeric antigen receptor (CAR) modified T-cell therapy consists of genetic manipulation of autologous lymphocytes and development of effective T-cell mediated anti-tumor immunity. Dr. Smith and colleagues were able to design and evaluate CARs that target the B-cell antigen CD19. They have tested the safety and efficacy of CAR T-cells in patients with chronic lymphocytic leukemia (CLL) and acute lymphoblastic leukemia (ALL) using second generation CAR T-cells that target the CD19 receptor on B-cells. They observed rapid complete molecular remissions in the first 14/16 patients treated with relapsed/refractory ALL! Since WM is a bone marrow predominant disease, as is ALL, WM is also considered an ideal disease to test CAR-modified T-cell therapy. In fact a clinical trial is now open for patients with relapsed or refractory WM, in which chemotherapy preconditioning is followed by a single dose of 19-28z CAR modified autologous T-cells. The future has arrived.

Dr. Jaimal Kothari of the Department of Haematology, University College Hospital, London, presented a talk on his poster **"Initial experience and clinical utility of a high resolution melting assay to detect the MYD88 L265P in peripheral blood and bone marrow aspirates in patients with lymphoplasmacytic lymphoma and related disorders."** Dr. Kothari and colleagues developed an assay that could detect the MYD88 L265P mutation in WM cells in both the bone marrow and the peripheral blood (PB). Pre-sorting CD19 B-cells with a magnetic activated cell sorting technique greatly improved sensitivity detecting the MYD88 L265P mutated PB WM cells. The researchers have found this MYD88 L265P mutation assay to have significant clinical utility and a useful diagnostic tool in patients with WM and related disorders.

Dr. Jonas Paludo of the Mayo Clinic, Rochester MN, discussed his poster **"Clinical features and survival outcome**

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of young patients with WM." There are relatively few WM patients under the age of 50. Dr. Paludo and colleagues analyzed data from 69 patients seen at Mayo Clinic from January 2000 to December 2013. Median age at diagnosis was 45 years (range 31-50 years); males constituted 65% of patients; 9 (14%) patients had familial WM; approximately 21% of the cases at diagnosis were in the smoldering stage. Constitutional symptoms were the most common clinical symptoms (43%), followed by hyperviscosity-related (23%) and paresthesia and neuropathy (17%) symptoms. Splenomegaly and lymphadenopathy were seen in 14% and 29% of the patients, respectively. The median hemoglobin at diagnosis was 10 g/dL (range: 5.4-14.6); platelet count 220 $x10^9$/L (80-501); β2 Microglobulin 2.7 mcg/ml (1.3-7.8); IgM level 4501 mg/dL (68-14400). Stem cells were harvested from 10 of the 12 attempted cases and 5 (8%) patients underwent autologous stem cell transplantation (ASCT); one patient who had an ASCT transformed to a higher grade lymphoma. ASCT was used as salvage therapy after a median of 6.5 regimens (range: 4-10). Of 67 patients treated, rituximab monotherapy (24%) was the most common initial treatment followed by the regimens of dexamethasone, rituximab, and cyclophosphamide (DRC; 15%), nucleoside analog-based (NA; 22%), chlorambucil-based (10%) and other therapies (28%). Sixty-five patients (97%) received rituximab during their disease course. Twenty-four percent of patients who received NA, as opposed to 2% of patients who received non NA-based therapy, developed therapy-related myelodysplastic syndrome or transformed lymphoma (occurring at a median of 7.6 years from NA therapy). Eight-year overall survival (OS) was 84% from frontline therapy (median 14.8 years). Of all deaths (n=18), only 1 was not WM-related. Dr. Paludo concluded that NA-based therapy is best avoided in young WM patients due to the high risk of developing myelodysplastic syndrome or transformation and, although effective, ASCT appears to be an underutilized approach in the treatment of selected young patients with WM.

Dr. Vilhjalmur Steingrimsson from the Department of Hematology, University of Iceland, Reykjavík, Iceland, presented a talk summarizing his poster **"Population-based study on the impact of familial form of Waldenström's macroglobulinemia on overall survival".** Strong familial clustering is observed in lymphoplasmacytic lymphomas (LPL) and WM. First-degree relatives of LPL/WM patients have an increased risk of lymphoproliferative disorders, in particular LPL/WM, non-Hodgkin lymphoma (NHL), chronic lymphocytic leukemia (CLL), and MGUS. WM patients with a family history of a B-cell malignancy had worse response and shorter progression-free survival when treated with rituximab. They did, however, obtain better responses to bortezomib-containing therapy. Dr. Steingrimsson and colleagues performed a large population-based study on LPL/WM patients, addressing whether familial LPL/WM is associated with worse overall survival. By using the Swedish Cancer Registry, the Swedish Inpatient Registry, and a nationwide hospital network, they identified 2185 LPL/WM patients and 6460 first-degree relatives based on information from the Swedish Multigenerational Registry. This large study revealed that 4% of LPL/WM patients had a family history of lymphoproliferative disorders whereas 3.5% had a family history of the more closely WM-associated entities such as LPL/WM, NHL, or CLL. Dr. Steingrimsson observed that a family history of lymphoproliferative disorders was not significantly associated with worse prognosis; a family history of a WM-associated entity such as LPL/WM, NHL, or CLL, however, leads to a significantly worse prognosis. No recommendations could be made at this time regarding potentially different clinical management strategies between familial and sporadic LPL/WM patients.

CURRENT THERAPY OF WM

Dr. Véronique Leblond of the Hôpital Pitié-Salpêtrière in Paris opened the session on this always interesting topic with a discussion of the controversial role of nucleoside analogs (NA) in WM. Dr. Leblond noted that both cladribine and fludarabine, used alone or in combination, have a proven track record in WM and deliver very good response rates in both untreated and previously treated WM patients. The addition of rituximab to the NA treatment regimen significantly improves responses, and a fair number of complete responses have been observed. The combination of fludarabine plus cyclophosphamide and rituximab (FCR) is very effective with an overall response rate of 89%, while 14% of patients obtained a complete response in one study. However, the safety of nucleoside analogs continues to be of some concern. The principal toxicity is myelosuppression, and patients considering autologous stem cell transplantation must use NAs with caution as stem cell harvesting may be adversely affected. Transformation to a more aggressive lymphoma or myelodysplastic syndrome is a serious concern attributable to NA-based therapy, but debate is still ongoing regarding the extent of this particular risk.

Dr. Christian Buske of the Institute of Experimental Cancer Research, University Hospital, Ulm, Germany, discussed alkylator-based therapy in WM. Despite the emergence of newer targeted therapies for WM, conventional chemotherapy with alkylator compounds such as cyclophosphamide (Cytoxan) is still used as it offers patients a well-tolerated and highly efficient treatment option. When used in the more aggressive regimen R-CHOP, a high overall response rate of 91% and a long time-to-treatment failure (TTF), with a median of 63 months, have been seen in well-documented trials. Alkylator-based therapy can be used in milder chemotherapy regimens such as the DRC regimen (dexamethasone, rituximab, and cyclophosphamide) without any major myelosuppressive toxicity. This popular regimen induces high objective responses and is characterized by very good progression-free survival rates for both treatment

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naïve and pre-treated WM patients. Dr. Buske concludes that alkylator-based therapy is still an important part of the therapeutic armamentarium for the treatment of WM and should be considered in combination with other newer agents as well.

Dr. Mathias J. Rummel of the Department of Hematology and Oncology, Justus-Liebig Universität, Giessen, Germany, discussed the use of bendamustine followed by rituximab maintenance in the treatment of WM patients. Dr. Rummel has previously reported at earlier conferences that the combination bendamustine-rituximab (B-R) demonstrated high efficacy in the primary treatment of WM. As a follow-up, Dr. Rommel and colleagues initiated a multicenter prospective randomized trial to investigate the impact of adding rituximab maintenance following B-R first-line induction in patients with WM (and other indolent lymphomas). Treatment consisted of a maximum of 6 cycles of B-R administered every 28 days plus 2 cycles of rituximab every 4 weeks. Patients who responded favorably were eligible for further treatment and were randomized to observation or to two years of rituximab maintenance every two months. The overall response rate to the B-R and two additional cycles of rituximab was 86%. At the time of this presentation, Dr. Rommel was unable to give final specifics as to the role of rituximab maintenance in this trial but did suggest that early data were very promising.

Dr. Meletios A. Dimopoulos of the Department of Clinical Therapeutics, School of Medicine, University of Athens, Greece, reported on the use of proteasome inhibitors in the treatment of WM. Proteasome inhibitors (PIs) have demonstrated efficacy in patients with WM. Bortezomib (Velcade) is the first in class proteasome inhibitor and when used as single agent in patients with relapsed or refractory WM is associated with responses of approximately 40%. The combination of bortezomib with rituximab (with or without dexamethasone) is very active and has shown favorable response rates of 66% - 83% as well as rapid times to first response (2-3 months). This "rapid response" activity of bortezomib has been used to great effect to minimize the "IgM flare" phenomenon seen at times with initiation of rituximab. Neurotoxicity is the major concern with bortezomib; weekly dosing and subcutaneous administration may reduce rates and severity of neuropathy. Bortezomib is not stem cell toxic, and there appears to be low risk for secondary malignancies. Carfilzomib, a second generation PI, is associated with a lower risk of neurotoxicity and is therefore recommended as an alternative to bortezomib, particularly for WM patients. The overall response rate for the combination carfilzomib with rituximab and dexamethasone (CaRD) was 87%, with a very low incidence of severe PN. Some concern has been raised, however, regarding the potential cardiotoxicity of carfilzomib, and Dr. Dimopoulos strongly urges further studies of this drug in WM patients before it is added to the list of recommended treatments for WM. Newer generation PIs are currently being evaluated, and oprozomib is in fact being used in a clinical trial for WM.

Dr. Steven P. Treon of the Bing Center for Waldenstrom's Macroglobulinemia, Dana-Farber Cancer Institute, presented a highly anticipated lecture on ibrutinib in patients treated previously for WM. Dr. Treon began by discussing the well-known MYD88 L265P mutation that is seen in 90% of WM patients and triggers malignant cell growth via the Bruton's tyrosine kinase (BTK) pathway, the target of ibrutinib. He also added that CXCR4 mutations are common in WM (found in 30% of patients tested) and result in drug resistance to ibrutinib. Dr. Treon and colleagues evaluated ibrutinib monotherapy in 63 previously treated WM patients, and examined the status of the MYD88 L265P and CXCR4 mutations on response outcome. At best response, median serum IgM levels declined from 3,610 to 915 mg/dL, hemoglobin rose from 10.5 to 13.5 g/dL, and bone marrow involvement declined from 60% to 30%. Overall and major response rates were 87.3% and 68.3% respectively, and median time to response was four weeks. Responses to ibrutinib were adversely impacted in patients who do not have the MYD88 L265P mutation (referred to as unmutated MYD88 or MYD88 wild-type) and in patients who carry the CXCR4 mutation. At a median follow-up of 48 weeks, 80% of patients remained on treatment without progression. Neutropenia (25.4%) and thrombocytopenia (14.3%) were found more commonly in heavily pre-treated patients. Atrial fibrillation was seen in patients with a prior history (4.8%). Procedure-related bleeding (3.2%) and recurring epistaxis (nosebleed) associated with marine oil ("fish oil") supplements (3.2%) were noted as well. IgA and IgG levels remained stable, and no excess infections were observed. Dr. Treon concluded that ibrutinib treatment in previously treated WM patients is an active and well-tolerated treatment that is characterized by rapid improvements in serum IgM and hemoglobin. However, the status of MYD88 L265P and CXCR4 mutations impacts ibrutinib response in WM patients.

TREATMENT CONSIDERATIONS IN WM

Dr. Irene M. Ghobrial, Dana-Farber Cancer Institute, discussed the integration of signaling inhibitors in WM. The MYD88 downstream pathways IRAK, PI3K/Akt/mTOR, and NF-kB are now the subject of intense investigations both at the bench and bedside levels. Several new clinical trials are currently evaluating these pathway inhibitors. The important interplay between WM cells and the bone marrow environment is also targeted using compounds that seek to interfere with the molecular signaling of the cytokines and chemokines that regulate B-cell proliferation, adhesion, and cell trafficking. A number of preclinical and clinical studies have shown promising results in patients with WM. BTK inhibitors (such as ibrutinib), PI3K/Akt/mTOR inhibitors (such as everolimus), new generations of PI3K inhibitors,

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CXCR4 inhibitors, HDAC inhibitors (such as panobinostat), and the newer generation of proteasome inhibitors all have improved the response and progression-free survival of patients with WM. Combinations of these newer biological agents are sure to markedly improve the duration of responses for WM and lead to improved quality of life.

Sandra Kanan, NP, of the Bing Center, Dana-Farber Cancer Institute, reported on the clinical characteristics of rituximab intolerance in patients with WM. Rituximab is a well-known and often used treatment in WM, both alone and in combination. Unfortunately rituximab causes infusion-related reactions (IRR) and cytokine release syndrome seen most often during the first infusion. The depletion of immunoglobulins such as IgA and IgG is an unintended side effect of rituximab, and the resultant hypogammaglobulinemia is associated with frequent and symptomatic recurring infections in many WM patients. The team at the Bing Center undertook a chart review of the patients seen at DFCI between 1996 and 2013 who developed intolerance to rituximab (outside of the common infusion related first-cycle IRRs). Forty WM patients were identified who were considered intolerant to rituximab. Fifty percent of these patients had not been previously exposed to rituximab; 53% of patients became rituximab intolerant while receiving single agent rituximab, 18% while receiving bortezomib-based therapy, 15% while receiving cyclophosphamide-based therapy, and 8% while receiving bendamustine-based therapy. Forty percent of patients developed rituximab intolerance while undergoing initial therapy, and the remaining 60% became intolerant during the maintenance phase. The most common adverse effects resulting in discontinuation of rituximab therapy were fever, chills, facial swelling, shortness of breath, hypotension, back pain, hives, chest pain, and serum sickness-like symptoms. Sixty five percent of patients were responding at the time of intolerance; 20% of patients received ofatumumab after developing rituximab intolerance, and 87% of these patients tolerated ofatumumab without incident.

Dr. Giampaolo Merlini of the Amyloidosis Research and Treatment Center, Department of Molecular Medicine, University of Pavia, Italy, discussed the diagnosis and workup of the WM patient with amyloidosis. Dr. Merlini, a world expert on amyloidosis, stated that an underlying IgM clone is responsible for primary amyloidosis in 7% of patients. Amyloid-related organ dysfunction (heart, kidney, and other organs) results in challenges for diagnostic workup and requires treatment of these susceptible patients. The irreversible damage that may ensue from the amyloid deposits necessitates a prompt and accurate diagnosis. Dr. Merlini therefore presented a strategy for early detection. The characterization of the amyloid deposits is a key step in the diagnostic process. IgM-AL amyloidosis is a distinct clinical entity characterized by higher frequency of pulmonary and lymph node involvement and of neuropathy, both peripheral and autonomic. A standard prognostic staging system based on cardiac biomarkers can be applied to IgM-AL amyloidosis, but serum albumin is an additional independent prognostic factor. Higher concentration of circulating free light chains is predictive of poorer outcome. Patients with IgM-AL amyloidosis are usually treated with regimens developed for non-IgM AL amyloidosis or for WM. Higher response rates (70-80%) are reported with purine analogues, autologous stem cell transplant, and the combination regimen of bortezomib, rituximab, and dexamethasone. The combination of bendamustine, prednisone, and rituximab is also a promising rescue regimen. Dr. Merlini concludes that the advent of newer agents may lead to improved outcomes for patients with IgM-AL amyloidosis.

Dr. Charalampia Kyriakou, a well-respected transplant oncologist from the University College, London, reported on the optimal timing for stem cell transplantation in WM. Although stem cell transplants have been used extensively in a number of blood cancers, the place and timing of this approach in WM remains controversial in many respects. Dr. Kyriakou stated that to conduct a prospective clinical trial in order to directly compare the outcome of either an autologous stem cell transplant (ASCT) or allogeneic stem cell transplant (Allo-SCT) in WM is challenging, given the indolent nature of the disease, its rarity, and the typically advanced age of patients. The variables range from selection of appropriate patients to the actual timing of the transplant itself. Promising results have been observed mainly from retrospective studies. A recently updated European database on the role of ASCT and Allo-SCT in 615 and 267 WM patients, respectively, showed that progression-free survival and relapse rate were significantly superior for responding WM patients receiving the ASCT early after diagnosis and after maximum response from first line treatment was achieved. Allo-SCT was associated with high toxicity, mainly related to graft versus host disease complications. Dr. Kyriakou concludes that the use of stem cell transplantation in WM patients is a feasible strategy for younger patients and for patients who are high risk with dismal prognosis. She cautions that first line and salvage therapies should avoid stem cell toxicity (referring to nucleoside analogs in particular) to permit potential transplant candidates to harvest stem cells.

Dr. Enrica Morra, Niguarda Ca' Granda Hospital, Milan, Italy, presented the final lecture in this session on the important topic of long-term toxicity of therapy in WM. At the very outset Dr. Morra explained that the occurrence of second hematologic and non-hematologic cancers are the most frequently reported long-term toxicities of chemotherapy in WM. Chemotherapy agents associated with higher long-term toxicity are the alkylating agents (such as chlorambucil and cyclophosphamide) and the nucleoside analogs (such as fludarabine and cladribine). The synergistic effect in producing DNA damage by the combination of fludarabine with cyclophosphamide or other alkylators

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may increase the risk of transformation to myelodysplastic syndrome/acute myeloid leukemia (MDS/AML). The median time to MDS/AML is five years. The prognosis of MDS/AML is generally poor, with a median survival of five months. Transformation of WM to diffuse large B-cell lymphoma (DLBCL) is also seen with cytotoxic agents. Of particular interest is the high incidence of second solid tumors in treated WM patients, when compared with other lymphoproliferative disorders. This increased risk is again related to the use of alkylating agents. Some researchers have suggested that the disease-related immunodeficiency and the therapy-related DNA damage might be strong contributors to the marked predisposition of WM patients to second cancers. Reactivation of viral infections such as hepatitis B, cytomegalovirus, herpes simplex virus, varicella zoster virus, and JC virus infection are seen and reported more often after a combination of rituximab-nucleoside analog therapy. Rituximab maintenance appears relatively safe, but long-term hypogammaglobulinemia can be a serious issue for some WM patients.

SPECIAL TOPICS IN WM

The final lecture session addressed a number of lesser known complications seen with WM.

Dr. Jean-Paul Fermand of the Immuno-Hematology Unit, Saint Louis Hospital, Paris, described the etiology and interventions for renal failure in WM. Although renal failure is relatively uncommon in WM, it may nonetheless occur because of tumor infiltration of the kidney or because of large amounts of all or part of the monoclonal immunoglobulin M (IgM) that are deposited in the kidneys. Three types of renal manifestations of IgM gammopathies occur in the course of an IgM-secreting proliferation: light chain cast nephropathy which is characterized by massive precipitation of the light chains into the kidney's filtration tubules (less common by far than in multiple myeloma); deposition of monoclonal IgM in the small intra-capillary blood vessels of the kidney (a rare condition usually manifested by acute kidney failure and microscopic urinary bleeding; usually seen in cases of high IgM serum levels and corresponding elevated hyperviscosity), and direct infiltration of the kidney itself by malignant B-cells (more common and may cause moderate renal impairment). Dr. Fermand urges clinicians to be on the lookout for renal complications in WM as early intervention can spare further loss of kidney function. Since WM patients are often of advanced age, it is at times difficult to differentiate WM-caused renal damage versus the much more common damage from long-standing hypertension or diabetes.

Dr. Marvin J. Stone from Texas A&M College of Medicine, Dallas TX, spoke on the role and management of cryoglobulins in IgM monoclonal gammopathies. Dr. Stone reminded the conference attendees that cryoglobulins ("cryos") are immunoglobulins in plasma or serum which precipitate or gel at <37° C and re-dissolve when warmed. Patients may be asymptomatic while others have a variety of clinical manifestations including purpura, arthralgias, weakness, acrocyanosis, Raynaud's phenomenon, gangrene, and renal function impairment. Perhaps the most crucial step in the diagnosis of cryoglobulinemia is the proper collection procedure. The blood must be allowed to clot at 37°C and red cells centrifuged promptly. The quantity of cryoprecipitate will be underestimated or totally lost if the specimen is not collected at 37°C. Type I or II cryoglobulinemias can be seen in WM and can have a dramatic effect on serum viscosity and cause severe hyperviscosity syndrome. Type I cryoglobulinemias are caused by monoclonal IgM, and the severity of symptoms is often dependent on the IgM level. Type II cryoglobulinemias are composed of IgM–IgG antibody-antigen complexes; these complexes precipitate due to the insolubility of the antibody-antigen complex. The treatment for Type I cryoglobulinemia is reduction of the IgM by plasma exchange (plasmapheresis) and/or chemotherapy. Types II cryoglobulinemias usually respond to corticosteroids or cyclophosphamide chemotherapy. Dr. Stone pointed out that the use of rituximab in patients with mixed cryoglobulinemias may lead to the risk of complex formation between IgG and monoclonal IgM and should therefore be used with caution.

Dr. Sigbjorn Berentsen of the Department of Medicine, University of Bergen, Norway, recommended that hematologists and oncologists distinguish between primary cold agglutinin disease (CAD), which is a well-defined clinicopathologic entity, and secondary cold agglutinin syndrome (CAS), a syndrome occasionally complicating specific infections or aggressive lymphoma. Dr. Berentsen went on to observe that many patients with CAD are also classified as having WM, whereas 5% or less of patients with WM are diagnosed with CAD as well. A recent study in which bone marrow biopsy and aspirate samples from 54 patients with CAD were re-evaluated by a group of lymphoma pathologists revealed the presence of a disorder termed "primary cold agglutinin-associated LPD." This disorder is distinct from lymphoplasmacytic lymphoma, marginal zone lymphoma and other previously recognized lymphoma entities. CAD treatment has generally followed therapy directed at eliminating the pathogenic B-cell clone. Newer treatments are now targeting the complement aspect of this complement-mediated disorder.

Dr. M. Lunn of the National Hospital for Neurology and Neurosurgery, London, discussed the diagnosis and management of peripheral neuropathy in WM and other IgM-related disorders. IgM-related neuropathies are often difficult to diagnose and even more difficult to treat. The most common neuropathy in WM is caused by IgM that reacts and binds to anti-MAG antibodies on the myelin sheath that surrounds the affected nerves. This type of

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neuropathy is characterized primarily by variable degrees of sensory loss, ataxia (loss of control of bodily movements), and occasionally an associated tremor. Currently the best evidence supports the use of IVIG and rituximab as a single agent for the neuropathy alone. Plasmapheresis has been used as well as a temporary measure until treatment directed at the underlying problem (WM in other words) is undertaken. Dr. Lunn cautioned the conference attendees that neuropathies of other sorts can also be associated with WM, including small fiber neuropathy, vasculitis, and, rarely, direct infiltration of the nerve ("peripheral Bing-Neel Syndrome").

Dr. M. Minnema of the Department of Hematology, UMC Utrecht, Amsterdam, discussed the clinical pattern and treatment of Bing Neel syndrome. Bing Neel syndrome (BNS) has been recognized since 1936, although its association with WM was unknown at that time. Since then, newer diagnostic modalities have permitted a separation of BNS into group A patients (with evidence of malignant cell infiltration of the CNS; group A includes the majority of patients), and group B (with no evidence of tumor cell infiltration). It is virtually impossible to distinguish the two types at clinical presentation. Bing Neel syndrome can be a presenting symptom in WM or can be a symptom of disease progression without any signs of progression of bone marrow infiltration. There is no established treatment regimen, and prognosis is usually very poor. Aggressive treatments similar to protocols seen in primary central nervous system lymphomas are used and consist of chemotherapeutic drugs that cross the blood-brain barrier (for example, high dose cytarabin and methotrexate) and are often combined with whole brain radiation or followed by autologous stem cell transplantation. Dr. Minnema presented for the first time a study on four WM patients who presented with Bing Neel syndrome as a primary symptom and were treated with oral fludarabine combined with rituximab. All four patients responded to the treatment and are still alive and well. One patient relapsed after five years and responded again to re-treatment with fludarabine and rituximab. Dr. Minnema therefore proposed that fludarabine-based treatments should be considered as an option for BNS, particularly in elderly and frail patients.

Dr. Evangelos Terpos of the School of Medicine, the University of Athens, Athens, Greece, discussed the rare coagulopathies and acquired von Willebrand syndrome in WM. Many WM patients may experience bleeding problems. Acquired von Willebrand syndrome (AVWS), IgM-induced platelet function defects, factor X deficiency, abnormalities in the function of fibrin, circulating anticoagulants, and thrombocytopenia may all predispose WM patients to hemorrhage. Hyperviscosity syndrome further worsens the bleeding problems seen in WM. Von Willebrand factor (vWF) plays a key role in primary hemostasis (stoppage of bleeding). Dr. Terpos and colleagues evaluated the prognostic importance of vWF antigen levels in the serum of 42 previously untreated patients with symptomatic WM. The patients with elevated vWF antigen levels (vWF Ag ≥200 U/dL) had a median progression-free survival of 12 months compared to 63 months for the patients with lower vWF antigen levels (vWF Ag < 200 U/L). Dr. Terpos concluded that serum vWF antigen levels are potentially important prognostic markers in WM.

The final word at IWWM8 was reserved for **Dr. Morie Gertz** of the Division of Hematology, Department of Medicine, Mayo Clinic, Rochester MN, who discussed the role of the autologous stem cell transplantation in the WM patient with amyloidosis. IgM amyloidosis is seen in 5% of all patients with AL amyloidosis. In a review of 590 patients with amyloidosis, 30 (5.1%) had an IgM monoclonal protein with consistent bone marrow findings and received autologous stem cell transplantation. Patients with IgM amyloidosis were significantly older and had a higher frequency of neuropathy. There was a higher frequency of cardiac involvement in non-IgM amyloidosis. There was no difference in overall survival between IgM amyloidosis and non-IgM amyloidosis patients (113 vs. 117 months). Fifteen of the IgM amyloidosis patients have survived for 5 years, and 13 have survived for over 10 years. Dr. Gertz concluded that treatment with stem cell transplantation is effective and results in long median survival for IgM-amyloidosis patients.

CLOSING THOUGHTS

I would be remiss if I did not mention the incredible assistance I received in the preparation of my two articles about the IWWM8 conference from the good people at Dana-Farber Cancer Institute in Boston. Not only did Dr. Steven Treon and Christopher Patterson respond to my queries in a timely fashion, but I also owe many thanks to Phil Brodsky and Robert Manning for their cheerful dispositions and their hard work during the many IWWM symposia I have attended in the past. The official website for the International Workshop on Waldenstrom's Macroglobulinemia (*www.wmworkshop.org*) is a veritable treasure trove of information and a well-oiled machine that just keeps on giving. I encourage everyone to visit the site and dig a little deeper into the incredible progress that has been made in WM basic research and treatments.

As always I reserve my personal impressions for the last segment of these articles. To date I have attended five of the last eight IWWM conferences and always return home with a sense of renewed hope and optimism. The 2014 Workshop was especially fantastic and encouraging. We are gaining new insights into the basic biological functioning of WM, we are realizing the potential of the cells of the immune system, we have newer, less toxic, and more effective treatments, and we are often treated to a glimpse of what's to come on the horizon. The continued development of targeted therapies such as ibrutinib, oprozomib (and others), the identification of important genetic markers such as the MYD88 L265P and CXCR4 mutations, and the emergence of immunotherapy

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as an effective treatment option – all leave me feeling very confident indeed.

The IWMF is a key player in these important advances. Many of the top researchers in the field of WM are supported by research grants from the IWMF, and they are quick to point out how favorably impressed they are by WM patients as a group. It appears that these clinicians and researchers regard WMers as very well educated with respect to their disease and as significant contributors to the advancement of knowledge in WM, whether through participating in clinical trials or through donations to the IWMF Research Fund.

There is hope, much hope on the horizon.

Donate and Participate.

SINCE OCTOBER 2014, THE FOLLOWING CONTRIBUTIONS TO THE INTERNATIONAL WALDENSTROM'S MACROGLOBULINEMIA FOUNDATION AND SINCE AUGUST 2014, THE FOLLOWING CONTRIBUTIONS TO THE WALDENSTROM'S MACROGLOBULINEMIA FOUNDATION OF CANADA WERE MADE IN MEMORY OF:

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Warren & Janice Waltman

Joyce Mould
Geoffrey William Mould

Emily Renaud
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Malcolm & Judy Roseman

David Schick
Lorraine Schick

Ronald Shelffo
Tamara Woods Kiel
Carolyn Lisa & Justina Cacioppo
Christopher McGrath

SINCE OCTOBER 2014, THE FOLLOWING CONTRIBUTIONS TO THE INTERNATIONAL WALDENSTROM'S MACROGLOBULINEMIA FOUNDATION AND SINCE AUGUST OF 2014, THE FOLLOWING CONTRIBUTIONS TO THE WALDENSTROM'S MACROGLOBULINEMIA FOUNDATION OF CANADA WERE MADE IN HONOR OF:

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Josh & Brandi Kellett
Krista McKim
Giles Robinson

Terry Bingham
Josh & Brandi Kellett

Andy Ferraro
Paddie Ferraro

Susan Gagnon
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David Hill
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Glen and Judy Magee
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Will & Shirley DeMaiter
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Glen and Judy Magee (cont.)
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LAUNCHING SOON!

A new IWMF website is in its final stage of testing. Launch date will be early in 2015, perhaps even before this *Torch* reaches you.

A dedicated team of volunteers has been hard at work over many months to improve and streamline this important member service.

Accessible by computer, tablet, and smartphone and updated regularly, the new *iwmf.com* will be your direct transport to information concerning every aspect of Waldenstrom's macroglobulinemia and all services and activities of the IWMF.

News of the launch will come to you by e-mail. Be poised to go online and explore the new website!