NEWSLETTER

Bing Center for WALDENSTRÖM'S MACROGLOBULINEMIA

Research • Treatment • Care

October 2014

Dear Patients & Friends-

There has been alot of activity with the Bing Center for WM during this past year. In August, we conducted our 8th successful International Workshop on WM and expanded with a Symposium on Multiple myeloma; www.wmworkshop.org , a multitude of global publications were produced including many aspects of MYD88 and CXCR4, the rapid growth of our DFCI web community chat room for Wm'ers brought to you by Dana Farber Cancer Institute and *Cancer Connect*, new clinical trials being produced, and a summarization on Ibrutinib.

Aside from our spotlight topics, constant updated information on our **9** dedicated website updates, forthcoming WM meetings, and [add special topic] have been included.

Below are Highlighted events listed for the next couple of months. For further information regarding any of these events, please contact Chris Patterson at cpatterson1@partners.org or any of the referenced contacts listed after the announcements.

November (SAVE THE DATES)

16th, November, Boston, MA The NESGM will be holding a physician-patient meeting at the Dana Farber Cancer Institute in Boston, MA, where our guest speaker, Zachary Hunter will lecture on an updated of genomics and genetics of WM; MYD88 and CXCR4. Afterwards, break-out sessions guided by the NESGM leader, Jack Whelan, will be initiated for patients and care-givers. Additional information and the agenda can be found on www.bingcenterforwm.org or you can contact Jack Whelan for registration or questions.

December (SAVE THE DATES)

6th thru the 9th, San Francisco, CA The 2014 ASH Physician Conference will be held from December 6th thru December 9th, 2014 in San Francisco, California. The American Society of Hematology (ASH), www.ash.org, is an annual conference for hematologists and oncologists that offer invaluable benefits, including up-to-date research, therapies, and networking events that allow physicians to connect with colleagues and interact with leaders in the field in all branches of hematology and oncology. Overall, the conference is always a great success for the Bing Center for WM. This year, we have our NP, Sandra Kanan presenting a poster discussion on "***rituximab intolerance in WM: A retrospective study of 40 patients***" and our clinician, Jorge Castillo, MD, giving an oral presentation on ***"incidence and survival outcomes of secondary malignancies [SM] among survivors of WM***, where patients with WM have a 49% higher risk of a SM than the general population" Both the poster presentation and oral presentation will be released in December for everyone.

In order for many of our WMer's to see our Bing Center's updated lectures that have been performed around the world, current and past videos are posted on our You Tube site. Each video can be found by accessing the link below or by going to the (www.bingcenterforwm.org) website where you will find a YouTube link at the top of the webpage. The most current events are those patient-specific lectures from the IWWM8 this past August in London, UK on Dr Treon, NP Kanan, and Zachary Hunter.

Dr Treon: "***Genomic and Treatment Advances in WM"***
NP Sandra Kanan: ***"Personal Survival Strategies***"
Zachary Hunter: "***Key Information About Your WM***"

http://www.youtube.com/user/BingCenterForWM?feature=plcp

NEW Publications List from 2013-2014!

On behalf of the Bing Center for WM, the following publications have been published within the past twelve months. ***All publications*** are/will be found on the Bing Center Website at www.bingcenterforwm.org

1. ***Response assessment in Waldenström macroglobulinemia: update from the VIth International Workshop*** (British Journal of Hematology publication, January, 2013)

2. ***MYD88 L265P Waldenström macroglobulinemia, immunoglobulin M monoclonal gammopathy, and other B-cell lymphoproliferative disorders using conventional and quantitative allele-specific polymerase chain reaction*** (Blood publication, March, 2013)

3. ***Patients with Waldenström macroglobulinemia commonly present with iron deficiency and those with severely depressed transferrin saturation levels show response to parenteral iron administration*** *(*Clinical Lymphoma Myeloma Leukemia publication, April, 2013*)*

4. ***Proceedings of the Seventh International Workshop on Waldenström macroglobulinemia*** (Clinical Lymphoma Myeloma Leukemia publication, April, 2013)

5. ***Challenges with serum protein electro-pheresis in assessing progression and clinical response in patients with Waldenström macroglobulinemia*** (Clinical Lymphoma Myeloma Leukemia publication, April, 2013)

6. ***Comparative response assessment by serum immunoglobulin M M-protein and total serum immunoglobulin M after treatment of patients with Waldenström macroglobulinemia*** (Clinical Lymphoma Myeloma Leukemia publication, April, 2013)

7. ***A new era for Waldenström macroglobulinemia: MYD88 L265P*** (Blood publication, May, 2013)

8. ***XIII. Waldenström macroglobulinemia: an indolent B-cell lymphoma with distinct molecular and clinical features*** (Hematology Oncology publication, June, 2013)

9. ***A mutation in MYD88 (L265P) supports the survival if lymphoplasmacytic cells by activation of Bruton tyrosine kinase in Waldenström macroglobulinemia*** (Blood publication August, 2013)

10. ***Proteasome inhibitors in Waldenström macroglobulinemia*** (Blood publication, November, 2013)

11. ***The genomic landscape of Waldenstrom macroglobulinemia is characterized by highly recurring MYD88 and WHIM-like CXCR4 mutations, and small somatic deletions associated with B-cell lymphomagenesis.*** (Blood publication, March 2014)

12. ***MYD88-independent growth and survival effects of Sp1 transactivation in Waldenstrom macroglobulinemia.*** (Blood publication, April, 2014)

13. ***Somatic mutations in MYD88 and CXCR4 are determinants of clinical presentation and overall survival in Waldenstrom macroglobulinemia.*** (Blood publication, May, 2014)

14. ***Survival trends in Waldenström macroglobulinemia: an analysis of the Surveillance, Epidemiology and End Results database.*** (Blood publication, June, 2014)

15. ***The WHIM-like CXCR4 S338X somatic mutation activates AKT and ERK, and promotes resistance to ibrutinib and other agents used in the treatment of Waldenstrom's Macroglobulinemia.*** (Leukemia publication, June, 2014)

16. ***Carfilzomib, rituximab, and dexamethasone (CaRD) treatment offers a neuropathy-sparing approach for treating Waldenström's macroglobulinemia.*** (Blood publication, July, 2014)

17. ***Detection of MYD88 L265P in peripheral blood of patients with Waldenström's Macroglobulinemia and IgM monoclonal gammopathy of undetermined significance.*** (Leukemia publication, August, 2014)

18. ***Treatment recommendations for patients with Waldenström macroglobulinemia (WM) and related disorders: IWWM-7 consensus.*** (Blood publication, August, 2014)

19. ***Transcriptional repression of plasma cell differentiation is orchestrated by aberrant over-expression of the ETS factor SPIB in Waldenström macroglobulinaemia.*** (BR. J. Hematology, publication, September, 2014)

20. ***Waldenström macroglobulinemia.*** *(*Hematol Oncol Clin North Am publication, October 2014*)*

A new national online community provides support for individuals affected by Waldenström's Macroglobulinemia.

I'd like to invite you to join the Waldenström's Macroglobulinemia (WM) national community, brought to you by Dana-Farber Cancer Institute and Cancer Connect. This community connects you with many others from around the world affected by WM for support, guidance, and information about the disease and its related issues. You can share your experiences and knowledge, ask questions, and learn from others who are coping with WM. This community is moderated by Dana-Farber staff with extensive expertise in Waldenström's Macroglobulinemia.

Being the moderator of this online community room for over two years now, it is a very exciting and great way to assist and guide you with your questions, provide you with direction, and take this disease's progress to a new level. Aside from the WM community room, there are other community rooms available at the same site for those who have secondary cancers or who are just inquisitive of other diseases. Looking forward to seeing you in the Community room!

If you would like to join this community, please follow these steps to register:

- Click here: http://cancerconnect.com/danafarber to access the Dana-Farber Welcome page, then click **Join now**.
- Enter your user name, e-mail address, and password, and click **Register**.
- Once you have registered, on the main Dana-Farber Cancer Connect Community page, you can access the Waldenström's community one of two ways, either:
    - Scroll down the right side of the page, under **National group members**, and click **Waldenström's**, or
    - Click this link after you have registered or logged in:

http://cancerconnect.com/group/waldenstrom-macroglobulinemia

Cancer Connect allows individuals to interact in a HIPPA-compliant, confidential, safe, and secure environment. As part of this program, members of the community can also participate in more than sixty disease-specific national communities. Cancer-specific groups are available, as well as groups focused on care giving, health and wellness, clinical trials, insurance, nutrition and survivorship, providing support for anyone affected by a diagnosis of cancer.

WM dedicated Websites:

Please go to any of the websites for current and updated information regarding WM

www.BingCenterforWM.org

We regularly update our Bing Center website in order to keep the content up to date.

- **Focus on Patients, Physicians/Researchers, and Caregivers**: Information that can be used "bench to bedside".
- **About the Bing Center**: Description of the Bing Center, clinic and staff.
- **News & Events**: Announcements for recent and upcoming conferences and support group meetings.
- **Clinical Trials**: Updates to current and pending clinical trials, and participating institutions.
- **Basic Research**: Updated with our most recent research projects and studies.
- **Publications**: Updated with our most recent abstracts and published papers (i.e. "How I Treat Waldenstrom's Macroglobulinemia" by Dr. Steven Treon).
- **Bing Center Spotlight:** Focus on topic of special interest to patients, physicians or caregivers.
- **Media Gallery:** Videos and photos from our conferences and special events.

www.stevenptreon.com

The official website of Dr. Steven Treon, its main focus is on Dr. Treon's research of WM.

- **Media**: Galleries of photos in several categories (Bing Center, Conferences, Support Groups).
- **Papers & Publications**: Papers which Dr. Treon has authored or co-authored, sorted by year of publication. Also includes "featured impact articles".
- **WM Info**: The complete description of Waldenstrom's Macroglobulinemia. Dr. Treon co-authored this paper with Dr. G. Merlini. A biography of Dr. Jan Gosta Waldenstrom is also included.
- **Patient Resources**: Links to our partner groups and organizations.

www.wmworkshop.org

This website includes all the abstracts, agenda, photos, and other information from all the International Physician Workshops for WM held from 2000 to the present. The last Physician conference was held on August 14-17, 2014 in the city of London, UK. For additional updated information on the next Workshop in 2016 in Amsterdam, Netherlands, please go to www.wmworkshop.org

To research archival information from our previous eight workshops (London, 2014, Newport 2012, Venice 2010, Stockholm 2008, Kos 2007, Paris 2004, Athens 2002, and Washington DC 2000), please visit the website.

www.wmctg.org

ADDITIONAL LOCATIONS ARE BEING ADDED!
This website is devoted to the Waldenström's Macroglobulinemia Clinical Trials Group. It is a resource for patients interested in the status of WM-related clinical trials, as well as links to general information about WM to a physician located close to home.

- **Physicians (USA)**: The list of USA-based physician members of the WMCTG and their locations are currently being updated.
- **Physicians (Int'l)**: The list of international-based physician members of the WMCTG and their locations are currently being updated.
- **Physician Pages**: Photos and biographies of each physician, as well as links to their corresponding institution websites (where available) and contact info. Each physician also has a link to the NIH website (ClinicalTrials.gov) showing their WM-related clinical trials (where applicable).
- **Contact Us**: An online form where comments or questions may be submitted for review by a WMCTG member.
- **Additional Resources**: Links to related websites.

http://wmfc.ca/

(NEWLY ADDED!) The purpose of WMFC is to provide support and information to the Canadian WM community. If you are a Canadian and have WM, or are a caregiver, friend, or relative of a WMer, or are an interested member of the Canadian medical community we would welcome you as a member of WMFC. Members of WMFC automatically become members as well of the International Waldenstrom's Macroglobulinemia Foundation (IWMF).

WMFC was incorporated under Canadian legislation in early 2002.

For further information about meetings, lectures, etc., please contact the WMFC president, Arlene Hinchcliffe at ahinchcliffe@wmfc.ca or by telephone at 905-337-2450

www.ewmnetwork.eu &
www.waldenstrom.info

The (EWM network) are members of the European Cancer Patient Coalition, (ECPC) and European Organization for Rare Diseases (EURORDIS). Their aim is to collectively represent all WM patients' interests at a European level. This way, WM patients are given a voice at European health institutions and in European health politics. Hence their motto "Patients for Patients". EWM network is an umbrella organization for European WM patient support groups or patient support organizations.

EWM network was initiated in 2008 by the Dutch MM&WM Patient Association (CMWP), The Netherlands and is registered as a not-for-profit organization under Dutch Law. EWM network aims to represent the interests of WM patients on a European level. It is an organization run by patients and their relatives for patients ("Patients for Patients").

http://portail.waldenstromfrance.org/

The Waldenstrom's France associate was officially established in 2009. Their website has just been released in hopes to benefit all French-speaking patients, caregivers, physicians, and medical specialists and to guide them properly in the knowledge of WM on a clinical, research, and patient-support direction.

Currently, the association has a very active Talk list for all Francophone members (more than 153) from Canada, Belgium, Brazil, Switzerland, North Africa and France. Please visit their website for more information http://portail.waldenstromfrance.org, become a community member or contact the president of the association of WM France, Michel Houche at houchemichel@wanadoo.fr with any questions.

www.wmsupportgroup.org.uk
& http://www.wmuk.org.uk/

The Waldenstrom's Macroglobulinemia (WM) United Kingdom (UK) Support Group was officially established in 2000. They are a non-profit organization created to support those suffering from WM as well as their family and friends in UK and Eire. A specific UK support group chat line is available. For more information, contact ***Roger Brown*** at info@wmuk.org.uk or telephone 0117 3735 733.

The next WMUK Patient forum is being held on April 11th, 2015 at the iconic Birmingham library. For more details, please visit their website.

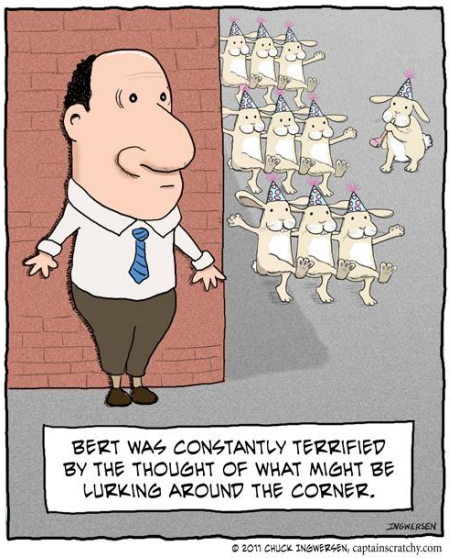
www.iwmf.com

The IWMF, International Waldenstrom's macroglobulinemia Foundation, is a dedicated non-profit, all-volunteer organization, developed and financed solely by patients and their friends and families. It mission is to provide a means for those with Waldenstrom's macroglobulinemia , their family members, doctors, and others with an interest in the disease to find mutual support and encouragement, to provide information and educational programs that address patients' concerns, and to promote and support research leading to a cure.

For additional information, please contact

Sara McKinnie, IWMF Business Office, 6144 Clark Center Avenue, Sarasota FL 34238
Tel: (941)927-4963, Email: info@iwmf.com

What's Around the Corner??



In a Clinical Aspect at the Bing Center for WM, there are a few new trials that will begin shortly under the guise of Drs Castillo and Treon, and NP Sandra Kanan.

(1) ***A Randomized, Double-Blind, Placebo-Controlled, Phase 3 Study of Ibrutinib or Placebo in Combination With Rituximab in Subjects with Previously Treated Waldenstrom's Macroglobulinemia***
Open and accruing for previously treated

(2) Phase II Trial of ixazomib, dexamethasone and rituximab in patients with untreated Waldenstrom's Macroglobulinemia Untreated. Estimated opening March 2015. **Ixazomib** is in the same class of drugs as Velcade® (bortezomib) and is made by the same company, Millennium: The Takeda Oncology Company. Ixazomib is considered to be a second-generation proteasome inhibitor because it has improved characteristics and activity over Velcade. In addition, ixazomib is available as a pill whereas Velcade is only available as an injection (subcutaneous or intravenous).

(3) Phase II Study of Phosphatidylinositol-3-kinase (PI3K) Inhibitor Idelalisib (GS-1101) in Waldenström Macroglobulinemia previously treated. Estimated opening Spring 2015. US Brand name of Idelalisib is Zydelig. Idelalisib is an investigational, targeted, highly selective oral inhibitor of phosphoinositide 3-kinase (PI3K) delta, a molecular target that is critical for the activation, proliferation and survival of B lymphocytes. PI3K delta signaling is hyperactive in many B-cell leukemias and lymphomas and drives proliferation, survival and trafficking to lymphoid tissue. - See more at: http://www.gilead.com/news/press-releases/2013/6/gilead-announces-interim-phase-2-data-for-idelalisib-showing-response-in-refractory-indolent-nonhodgkins-lymphoma#sthash.uIn7Wy8a.dpuf

For more information about the clinical trials at the Bing Center for WM, please contact our Clinical research coordinator, Kirsten Meid at kirsten_meid@dfci.harvard.edu or 617.632.5598

Ibrutinib…

Yesterday…Today…Tomorrow….

Yesterday

Ibrutinib is a newly discovered drug that is being developed as an anti-cancer agent. Ibrutinib is a Bruton's tyrosine kinase (Btk) inhibitor drug which interrupts B cell receptor (BCR) signaling in lymphomas by selectively and irreversibly binding to the Btk protein, which then results in malignant cell death. This drug has been used in laboratory experiments and other research studies in B-cell malignancies and information from those other research studies suggests that ibrutinib is a very good treatment strategy for B-cell malignancies, including Waldenstrom's Macroglobulinemia.

Today

For WM patients, Ibrutinib is generally well tolerated. The dose for WM is 420 mg (3 pills) daily and should be taken approximately the same time each day. It should be taken with 8 ounces of water and can be taken with or without food, according to the package insert. Avoid grapefruit, star fruit, Seville oranges and the juices from these fruits as this can affect the metabolism of ibrutinib. There can be some gastrointestinal symptoms from ibrutinib, which include diarrhea, nausea, heart burn or acid reflux. You may take Imodium which is an over the counter medication if needed to help with the diarrhea or obtain a prescription for anti-nausea medication if needed. Switching to night time administration may help if you continue to have diarrhea. Ibrutinib can affect platelet aggregation (platelets are the blood component that helps stop bleeding).

Labs should be monitored closely to make sure platelet counts are within an acceptable range. Let your doctor know if you are having any bleeding such as nosebleeds. You should avoid or minimize medications that can thin the blood such as aspirin, NSAIDs (ibuprofen, Aleve, etc) and fish oil supplements while on ibrutinib. Ibrutinib will need to be held for a few days if you are going to have an invasive procedure (usually 3 days before, the day of and 3 days after the procedure). There are drug interactions with ibrutinib and medications that are strong CYP3A4/5 inhibitors, inducers or substrates. Taking one of these medications can either increase the ibrutinib levels in your blood or decrease the levels. This can either cause more side effects/make you feel sick or cause ibrutinib drug concentration levels to be too low to be effective.

Check with your doctor prior to starting any new medications, including antibiotics and over the counter medications. Other possible side effects include minor skin rash, mouth sores or sensitivity, scalp tenderness, joint pains, bruising more easily and minor cuts that take longer to heal. There have been some reports of atrial fibrillation especially in patients with a prior history of this condition. If this occurs, it should be managed between a cardiologist and your oncologist especially if new medications are

recommended to make sure they are safe to take while on ibrutinib. Utilize your resources if you have any questions or concerns about taking ibrutinib.

Overall, it is a great drug that has been a tremendous impact and helped a lot of WM patients. The response rate is approximately 80% and the onset of response is around four weeks. The duration to be on ibrutinib is long term, as long as it is working and you are tolerating it well.

Tomorrow

October 20, 2014: Pharmacyclics Files Supplemental New Drug Application for IMBRUVICA® for Waldenstrom's Macroglobulinemia; Filing completed just three months after receipt of third FDA approval.

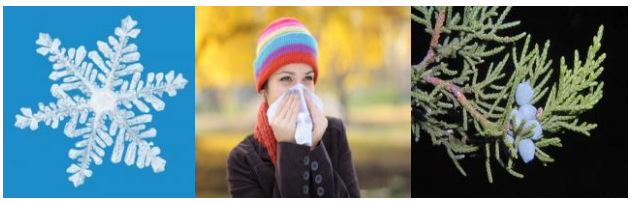
IMBRUVICA is currently approved by the FDA for three indications: for the treatment of patients with mantle cell lymphoma (MCL) or chronic lymphocytic leukemia (CLL) who have received at least one prior therapy, and for CLL patients with a deletion of the short arm of chromosome 17 (del 17p), including
treatment-naive and previously treated del 17p CLL patients. Accelerated approval was granted for the MCL indication based on overall response rate (ORR).
Improvements in survival or disease-related symptoms have not been established. Continued approval for the MCL indication may be contingent upon verification of clinical benefit in confirmatory trials IMBRUVICA is being studied alone and in combination with other treatments in several blood cancers including CLL, MCL, Waldenstrom's macroglobulinemia (WM), diffuse large B-cell lymphoma (DLBCL), follicular lymphoma (FL) and multiple myeloma (MM).
Approximately 3,500 patients have received IMBRUVICA in clinical trials conducted in 35 countries, by more than 800 investigators around the world. As of June 30, 2014, 12 Phase III trials have been initiated with IMBRUVICA and approximately 50 trials are registered on www.clinicaltrials.gov. The overall clinical development program in CLL currently includes seven Phase III trials and covers all lines of therapy and various combinations of treatments.

For a comprehensive list of affordability programs, please visit
www.youandiacess.com

For specialty pharmacy provider network, please contact Chris Patterson at
cpatterson1@partners.org and he will supply you with the summary sheet.

Additional information on IMBRUVICA, go to www.imbruvica.com or call
1.877.877.3536.

Winter Health Tips



Winter Allergies

Think that allergies aren't a problem during the winter? Think again. Some areas of the country experience their worst allergy season during the wintertime, when mountain cedar pollinates. And even when the plants outside aren't pollinating, other triggers still exist to make your nose congested and runny. From outdoor mold to irritants such as cold and windy weather, there are a number of non-pollen sources of wintertime nasal symptoms. In addition, cold temperatures can lead to hives, which is called cold urticaria.

Winter Pollen Allergies Mountain cedar is a type of juniper tree found mainly in South and Central Texas that pollinates in the winter, from December through March. In the areas where it grows, it is usually the only major pollen present during the wintertime. Mountain cedar is a major cause of hay fever, and people who suffer from this form of pollen allergy typically refer to it as "cedar fever." Learn more about mountain cedar allergy.

Runny Noses in Cold Weather As the weather starts to turn cold and crisp around the country, people are packing their pockets with tissues to combat their runny noses. But this usually isn't due to allergies -- rather, it's caused by vasomotor rhinitis. This non-allergic form of rhinitis may result in a runny nose, post-nasal drip and/or nasal congestion. It is caused by a number of triggers, including temperature changes, windy weather, and changes in humidity, as well as strong odors, perfumes and smoke. Learn more about the causes and treatment of a runny nose in cold weather.

Mold Allergies in the Winter Airborne molds are well-known causes of allergic rhinitis and asthma symptoms, and can be present outdoors and indoors. In colder climates, molds can be found in the outdoor air starting in the late winter to early spring, especially during the rainy season. While indoor molds can occur year round and are dependent on moisture levels in the home, indoor mold levels are higher when outdoor mold levels are higher. Therefore, a common source of indoor mold is from the outside environment, although can also be from indoor mold contamination. Learn more about mold allergy.

Hives in the Cold Cold urticaria is a form of physical urticaria that is characterized by the development of hives and swelling with cold exposure. A variety of cold triggers can cause symptoms in people with this syndrome, including cold weather, cold food and drinks, and swimming in cold water. Learn more about the causes and types of cold urticaria, as well as the treatments available.

See you in January!