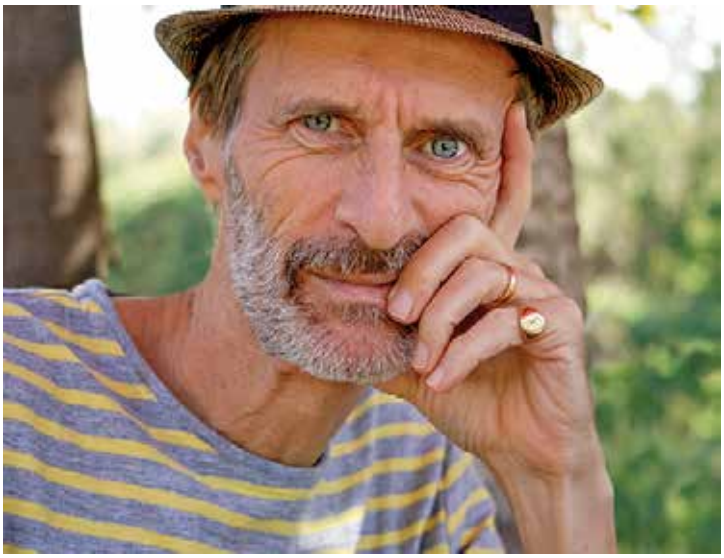
WMozzies
Australian patient support group for Waldenström's Macroglobulinemia

A•NZ BEACON

WM-NZ Support Group
Waldenström's Macroglobulinemia

ISSUE 4 Newsletter for Waldenström Macroglobulinemia community in Australian and New Zealand June 2021

David Young has taken over from Andrew Warden as Leader of WMozzies



In 2003 WMozzies was founded by Gareth Evans with some help from the IWMF. David was lucky enough to meet Gareth in 2012 after being diagnosed with WM. Gareth was a wealth of information and introduced David to WMozzies and the IWMF. They had several meetings until his death in 2013.

In 2014 David started a general cancer support group in Byron Bay and has since set up two more similar groups in Ballina and Lismore. David had joined WMozzies in 2013 and was getting some great advice and help from them. It was about this time he met Andrew Warden who was to become a driving force behind WMozzies with the help of several others on the committee. Andrew who is very persuasive encouraged him to become involved in certain aspects of running WMozzies.

David went on to do a lot more cancer advocacy with different organizations including the Cancer Council, Leukaemia Foundation, NSW Cancer Institute, Cancer Voices and others often with the support of Andrew.
Fast forward to 2020 and Andrew decided he needed to 'retire' from his role as leader of WMozzies and asked David yet again if he would take on the role. After some persuading he agreed and in November 2020 he took on the role as Team Leader of WMozzies. The committee soon realized what a huge job Andrew had done, with the help of Peter Carr, Michael van Ewijk and others and how much work they must have been doing and so they found more people to join them on the committee to 'spread the load'. There are now 10 people on the committee attempting to keep up the good work that Andrew and the previous committee had done over theyears. They sincerely hope they will succeed in this very important task. They are passionate about supporting you, our fellow WM travellers, in the best way they can, so watch this space.

Covax-lymphoma Study

The COVAX-lymphoma study is sponsored by Concord Hospital, Sydney Local Health District and funded by IWMF. It involves top specialists in the fields of WM and immunology and is targeted at patients with WM or Follicular lymphoma only. Up to 40 WMozzies have signed up, had their blood drawn, and their first Pfizer COVID-19 vaccination already.

The first WM patients to get their first Pfzier jab.

Transitional research studies are being co-ordinated by the Kirby Institute, Sydney. Participant's blood samples will be taken prior to vaccination, 21 days after the first Pfizer jab, 28 days and 180 days after the second Pfizer jab.

Antibodies to COVID-19 proteins (including the "spike" protein) will be determined using a novel validated flow cytometric assay devoloped by A/Prof Fabienne Brilot-Turville (Kids Research, Westmead). Testing will also determine the potency of these anti-COVID-19 antibodies by mixing the serum with a solution of live virus.

In addition to B cell antibodies, T cell activation in response to COVID peptides will be measured to see if they have been sensitised by the vaccine to recognise and act against the virus.

The viral neutralisation assays can currently only be performed in a laboratory with the capabilities and containment such as at the Kirby Institute. For those who are interested in more details of the tests I have provided a greatly simplified summary, in layman's terms as much as possible:

- Detection of anti-SARS-CoV-2 (COVID-19) spike, membrane and nucleocapsid antibodies.
- Spike, membrane, and envelope proteins are expressed in human embryonic kidney cells grown in tissue culture – also known as a cell line.
- Diluted patient serum is added to the cell line and any antibodies present will bind to their respective antigens.
- Fluorescent marker (anti-IgM or anti-IgG) is added which will bind to any antibodies which have bound

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to COVID-19 antigens and cause the cells to fluorescence.

- After further treatment the cells are passed through a flow cytometer in single file in front of a laser beam which measures and counts them.
- If the cells show fluorescence above a certain threshold the COVID-19 antibody test is Positive.
- Live virus neutralisation assay.
- Diluted patient serum is mixed with an equal volume of COVID virus solution and incubated at 37 degrees C for one hour.
- The serum/virus mixture is then added to two different human cell lines and left for 72 hours.
- A blue nuclear stain is then added to the cells so they can be examined by a cell analyser for condensed nuclei which is an indicator of cell damage and death caused by contact with the virus.
- If no cells have been damaged, the virus has been fully 'neutralised' by antibodies in the serum. If some cells are damaged, but not others, the count is compared to a fully infected control and a percentage neutralisation calculated.
- If the cells have been fully infected, there is no anti-viral activity in the serum.

Antigen-specific T cell responses

- Patient peripheral blood mononuclear cells (predominantly T cells), previously separated off, are exposed to SARS-CoV-2 peptides at 37 C for 40-48 hours.
- Following incubation the cells are stained with a viability dye and monoclonal antibodies to CD3, CD4, CD8, CD25, and CD134/OX-40.
- After further treatment the cells are passed through a low cytometer to detect their cell surface markers.
- Presence of these cell markers indicates specific activation of CD8+ cytotoxic (killer) T cells and CD4+ helper T cells against SARS-CoV-2.

Tcell testing is particularly important in blood cancer patients as they could provide immunity despite the absence of antibodies. We are fortunate to have access to such sophisticated science, and the results will be fascinating.

Our thanks go to IWMF and to Prof Judith Trotman, Dr Brendan Beaton, Dr Katherine Rankin, Dr Juliette Raedemaeker, Dr Alexander Wong, Andrew Warden (Concord study team), Prof Anthony Kelleher, Dr Sarah Sasson (Kirby Institute), Prof Stephen Larsen (RPA), and Dr Orly Lavee (St Vincent's) for their efforts in making this possible.

Peter Smallwood

The Covax-lymphoma study team members at Concord Hospital

The Latest From New Zealand

Our WM-NZ attendance numbers doubled in size to two with Duncan Kay joining me at 11.30pm., for the second IWMF global Affiliates Zoom meeting. Duncan has agreed to be the Assistant Affiliate Leader for which I am very grateful. We have been working together for some time now and he brings expertise in areas I don't have.

New Zealand has a good percentage of patients enrolled with WhiMSICAL and we look forward to the update from the Zoom presentation. This ongoing study will be invaluable as time goes on as data is examined.

Matthew Eby, support person for Leukaemia & Blood Cancer NZ in the South Island except Southland, organised the first Zoom meeting for our Wallies. We are grateful as with only 39 members we are very few in number. For those of us who were able to join Matt, the meeting was productive. We introduced ourselves and discussion led the way. Great to put faces to people. Almost like meeting in person, except for the lack of travel worries and being safe in our homes we could grab a coffee/tea and sit in our comfortable chairs. Our WM-NZ now has 43 patients and Matt intends to hold another meeting soon. Leukaemia & Blood Cancer NZ have also arranged for Auckland haematologist Dr. Samar Issa to give a webinar on WM later this year.

Lea Hullett - Affiliate Leader WM-NZ

BeiGene Application to the PBAC

In July 2020, the Therapeutic Goods Administration (TGA) accepted the first two Zanubrutinib applications for evaluation. The two applications were for patients with Mantle Cell Lymphoma (MCL) who have received at least one prior therapy and patients with

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WM who have received at least one prior therapy or in first-line treatment for patients unsuitable for chemo-immunotherapy. Consequently, in March 2021, BeiGene requested the inclusion of these two applications in the Pharmaceutical Benefits Scheme (PBS).

As you are aware, both relapsed and refractory MCL and WM are rare and incurable diseases. Given the current treatment situation, a significant unmet clinical need exists for effective and well-tolerated therapies for patients with these two conditions.

COVID Vaccine Studies Shed Light On Our Immune Systems

The Leukemia and Lymphoma Society in the U.S. has commenced a study to track Covid vaccine response of blood cancer patients and is calling on anyone who has been diagnosed with a blood cancer to participate and sign up on the LLS website.

On 22nd March IWMF recommended to WM'ers that they get involved as "citizen scientists". Once they sign up and give consent they are given a lab request form. The blood samples are drawn at the nearest 'Labcorp' collect centre and the number of blood tests depends on whether they have, or are scheduled to, receive the vaccine. After a patient has had two spaced shots of either Pfizer or Moderna vaccine, blood is taken a few weeks later to measure the antibody response.

One of the most attractive features of the study is that patients can access their results online shortly after they are ready. This is because a digital health technology company 'Ciitizen' (spelt with three i's) is a partner in the study and handles the data.

"Ciitizen believes that patients are the rightful owners of their health data in their profiles, and they should decide who gets access," said Ciitizen Chief Regulatory Officer and co-founder Devan McGraw.
Some WM'ers are sharing their antibody results on the discussion forum IWMFConnect .

The test result of particular interest is 'SARS-CoV2 Semi-Quant Total Ab' which measures the antibody level produced by the vaccine against the covid 'spike protein'.

The results that have been shared on the forum are very mixed but can be sorted into three groups:

- No antibodies detected (NEG)
- Low antibody response: 2-4 U/ml (LO)
- High antibody response: more than 250 U/ml (HI)

A summary of 20 WM'ers results so far: NEG (7); LO (4); HI (9)

For those who gave treatment details:
Ibrutinib(7): NEG (3); LO (2); HI (2)
Zanubrutinib(1): HI (1)
Rituxan(2): NEG (2)
Nil treatment(6): NEG (1); LO (1); HI (4)

This gives an interesting snapshot into what WMers can expect post vaccination.

Peter Smallwood

WhiMSICAL Data Published in the American Journal of Hematology

Newly published patient-entered data provides WM-specific data on real-world treatment outcomes. More participants are needed - the more responses there are, the clearer the picture gets for each of the treatments.

The WhiMSICAL registry, built through a patient-clinician investigator partnership, is a global database for WM patients to enter their own data. Results of the WhiMSICAL study have just been published in the prestigious American Journal of Hematology. URL link. Key findings include the longest time to next treatment after 1st line therapy in patients treated with bendamustine rituximab, and a better quality of life in those on Bruton tyrosine kinase inhibitors compared to recent chemotherapy.

Over 450 patients from 19 countries contributed to this first global registry for WM.

Highlights of the study so far include:

- Significant variability in 1st line therapy choice globally, with 46 different types of therapies given!
- USA patients commence their 1st therapy almost 3 times faster than the rest of the world.
- 1st line bendamustine rituximab has outperformed the Bruton tyrosine kinase inhibitors (BTKi, e.g. ibrutinib, zanubrutinib) and rituximab alone in time to next treatment. The findings are preliminary, however, without exact matching of the groups. More participants, and longer follow-up of existing participants are needed to further validate these exciting preliminary results.
- Patients on BTKi report better quality of life scores than those who recently received other treatments.

COVID-19 vaccines are now rolling out globally. WM patients may achieve impaired vaccine responses due to their condition and treatment. To help assess the impact of COVID on patients with WM, the WhiMSICAL registry has included a question (at question 19) on COVID-19 testing, infection and vaccination. Please contribute to this important and urgent research question for WM patients.

From anywhere in the world, you can join the WhiMSICAL registry by registering and completing

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Some data is always better than no data. Your answers can, and are recommended to be, continually updated. Please note that it doesn't all need to be done in one sitting; you can enter as much (or as little) as you are able to provide each time to access the registry. (Naturally, the more data that is collected, the better the outcomes for further research.)

For those already participating in WhiMSICAL, thank you for contributing your patient voice to peer-reviewed research. Please continue to update your data at www.cart-wheel.org, making sure to complete the newly added COVID-19 questions and update any changes to your treatment (question 9) and quality of life (questions 20 and 21). We need your help to provide "big data" to increase the power of this research by increasing the number of participants. Together, we can help answer some important questions in WM research as we search for a cure.
For further information on WhiMSICAL contact whimsical@iwmf.com.

Greg Butterworth's Story

I was diagnosed with WM in 2010. I first noticed that I was unwell when I was attending a Taekwondo training camp in Korea. (I had been on the Australian team and at that stage was the Australian Team coach). Training was twice a day, and three hours each time. It was a unique opportunity, and I didn't want to miss any of the training. However, I noticed after each session my legs were swelling up to the stage that I had "cankles" (no ankles – calf all the way down to my toes!) When I came back to Australia I still had sore legs and fatigue, so I decided to get a check up. My GP found an elevated ESR, which started the search to discover the cause. One of the specialists he sent me to was a rheumatologist, as my GP thought I might have Rheumatoid Arthritis. The Rheumatologist decided that was not the problem, but thought I%should have a test for IgM. This led to my eventual diagnosis.
At first, I was on "wait and watch", but my energy levels were poor, so my oncologist suggested we try a "mild" form of chemo, CHOPR.

After seven months, I went back onto wait and watch, and my energy levels improved marginally,but my IgM improved steadily for several years.
In 2017 my energy levels declined further, and my IgM started to go up again. My oncologist tried to get me onto a study at Box Hill, using Ibrutinib, but I didn't "quite" fit the criteria for that study,so the oncolgists at Box Hil did a ring around to see what else was available.

The next day I got a phone call from the Austin hospital, where they asked me if I would be interested in a new study. I started on the study for HMPLN523 in December 2017. (The drug is so new it doesn't have a name yet). HMPLN523 is in tablet form, taken daily. It blocks a cellular pathway called Spleen tyrosine kinase (Syk). At this stage, it is an experimental drug, and is being used for a variety of blood cancers. After more than 12 months on this drug, I am now the longest"user"on the study. It has improved my IgM, but VERY slowly!
I must say that the Austin, together with the Olivia Newton John Wellness centre, has been a big help in getting me to cope for the past year or so. We are blessed to have this facility in Melbourne, with many ancillary services available to patients.

Since my diagnosis I have retired from full time work as a Physical Education teacher, but still teach Taekwondo. I have been lucky enough to go to two World Championships as coach of the Australian team, but do find that travel is very tiring.

It was several years before I got to meet anyone else with WM, and very much appreciate the help I got from the Leukaemia Foundation. For seven years I was a volunteer driver with the LF, and can recommend this organisation to anyone with queries about blood cancer.

Greg and his wife Bronwyn at Machu Picchu, Peru after Bronwyn won the 2016 World Taekwondo Poomsae Championship.

Greg volunteering for the Leukaemia Foundation.