WMozzies
Australian patient support group for Waldenström's Macroglobulinemia

A•NZ BEACON

WM-NZ Support Group
Waldenström's Macroglobulinemia

ISSUE 3 Newsletter for Waldenström Macroglobulinemia community in Australian and New Zealand JANUARY 2021

Andrew Warden Steps down as Leader of WMozzies

After 7 years as leader and 14 years membership of the WMozzies Andrew decided he needed to hand over the responsibility of Leader. With that aim a ZOOM meeting was held on November 24, 2020 with Andrew, Kathy Fulham, Peter Carr, David Young, David Rabie, Neil Motyer, Michael van Ewijk, Paul Lenon, Peter Freese, Jacqui Merchant and Lea Hullett (NZ WM)

It became apparent very quickly how much work Andrew has been doing by himself for so long. It took a good hour for the group to go through all the different roles Andrew has done single-handedly. As each role was discussed the meeting member who had some expertise in that area volunteered to take it over. The WMozzies Interim Management Committee is now as follows:

- Kathy Fulham - Administrator
- David Young - Team Leader, PBAC. LF FB WM chat group, LF WM Webinar
- Peter Carr - Website and Leukaemia Foundation liaison
- Michael van Ewijk - Website & Beacon newsletter
- Neil Motyer - Meetings chairman
- Peter Freese - IWMF relations. New IWMF chair 2021 Paul Kitchen taking over from Elena Malunis
- David Rabie – Vice Team Leader, PBAC, Leukaemia Foundation liaison and Clinical Practice Guidelines
- Jacqui Merchant – PBAC and Liaise with LF on National Action Plan for Blood Cancer
- Paul Lenon – Liaise with LF on National Action Plan for Blood Cancer
- At the behest of Prof. Judith Trotman Andrew retains his role with CART-Wheel/WhiMSICAL

It was decided that the Committee make up will be reviewed sometime in 2021.

WM in New Zealand

The situation for Waldenström Macroglobulinemia patients has improved over the past few years in New Zealand with the funding of Bendamustine after studies found the combination of Bendamustine with Rituximab improved the impact of Rituximab. The newer treatments, BTK inhibitors etc., are not funded, though a few people have been able to go on trials or been in a position to pay for it themselves. For most people the cost is prohibitive.

Generally though New Zealand lags well behind other countries in funding for health.

A report by PharmaDispatch dated June, 2020 commissioned by Medicine New Zealand ranked us last in the list of 20 countries for publicly funded access to new medicines. Australia performed better but still ranked at only 17.

"The report from market intelligence firm IQVIA is the second of its kind comparing funded access to new medicines in New Zealand to 20 other developed countries."

The article stated that New Zealanders have access to only 24 of the 403 medicines registered and launched in 20 OECD countries between 2011 and 2018. Added to that the average time to fund a new medicine increased from 512 to 659 days.

"When other countries are looking at the same clinical evidence and saying yes to publicly funding medicines, why is New Zealand deciding our patients and health systems aren't worth it? How is that fair?" asked Dr Lee Mathias, chairman of Medicines New Zealand.
"Not only does New Zealand compare very poorly to other countries in terms of access to these modern medicines, but the timeliness of funding is dire. If New Zealanders can't get access to these modern medicines now, what's going to happen when the more personalised and game-changing medicines come down the pipeline?"

On the bright side for Waldenströms patients, a huge amount of reliable information is now available through organisations such as the IWMF and Leukaemia and Blood Cancer NZ. I am convinced that the more we know, the better we will cope with living with Waldenströms.

We can make better decisions on the treatments offered. We are living longer and better lives.

At the moment we have 39 patients (24 males and 14 females) listed on the IWMF list I look after. How to reach out to more patients is something I think about and whether our haematologists tell patients about the IWMF NZ affiliate and the growing support available. The wonderful WhiMSICAL study seems to be well supported by NZers so I think that some haematologists do encourage people to join.

The formerAustralian Affiliate Leader, Andrew Warden, has been a huge help to me and I want to thank him here for all that he has done. Without his support we would not be drawing closer to the larger community of Australian WMozzies.

Lea Hullett (NZ WM)

WMozzies Australian patient support group for Waldenström's Macroglobulinemia

A•NZ BEACON

WM-NZ Support Group Waldenström's Macroglobulinemia

ISSUE 3 Newsletter for Waldenström Macroglobulinemia community in Australian and New Zealand JANUARY 2021

Zanubrutinib After Only 2 Weeks

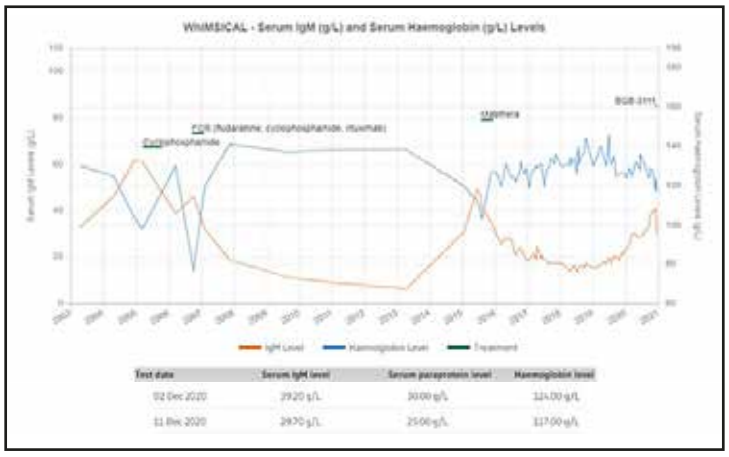
After only two weeks treatment with Zanubrutinib Andrew Warden's IgM has been reduced by 25% from 39.3g/l to 29.7g/l.

The WhiMSICAL Registry chart below gives a picture of his Waldenström's macroglobulinemia disease progression over 17 years from his diagnosis in 2003 to 2020.

It shows the benefit of the four treatments Andrew has received (2005 Cyclophosphamide, 2006 Fludarabine, Cyclophosphamide and Rituximab, 2015 Rituximab, Zanubrutinib (BGB-3111).

The need for treatment is generally indicated two years in advance by adverse movements in the key markers IgM and Haemoglobin.

For those interested in having your own personal WM graph, details are provided at IWMF WhiMSICAL Registry - WMozzies on how you do this in the WhiMSICAL Registry:
https://wmozzies.com.au/index.php/whimsical/



Ibrutinib After 6 Years

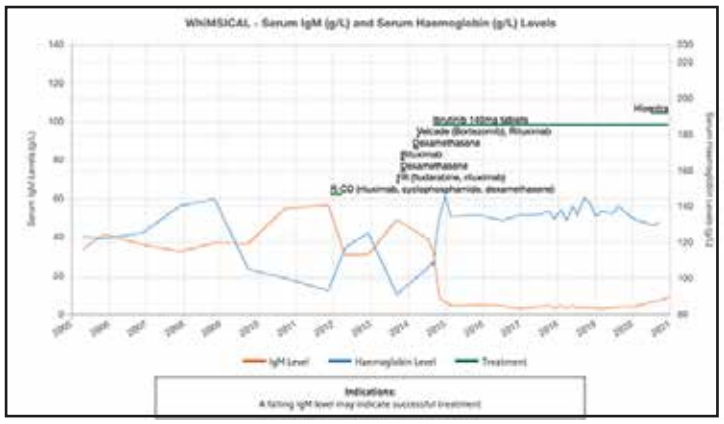
Michael van Ewijk was the first Australian WM patient to receive Ibrutinb on the iNNOVATE Trial at Concord Hospital under Prof. Judith Trotman. He began the trial in September 2014. His Igm came down quickly from 33g/L to 4.4g/L in just 4 months. His Hb rose correspondingly. However after 6 years his Igm is slowly creeping up. This also seems to be the experience in the US where Ibrutinib has been used with WM for longer.

There are not too many other options for him available in Australia other than chemotherapy.

LOXO-305 is a BTK inhibitor that has been designed to prevent acquired resistance and intolerance to currently available BTK inhibitors. There is a trial in WA for patients with previously treated CLL/SLL or NHL but not WM.

Venetoclax (ABT-199) is another promising drug that targets a different protein, BCL-2, that plays a major role in cellular apoptosis.

It was developed in Melbourne at the Walter and Elisa Hall institue. It already has FDA approval in the US and TGA approval in Australia for treatment of CLL (chronic lymphocytic leukaemia). There are currently trials in Australia for other forms of blood cancer but not WM. The chart below shows the gradual rise of Michael's Igm.



a BLOODY great night out!

A Bloody Great Night Out! is a fundraising initiative supporting world-leading blood cancer clinical trials at the Concord Hospital, Sydney Australia.

The event is organised by The Bloody Great Committee through Foundation for a Bloody Great Cause Limited-made up of local community volunteers and representatives from the Haematology Department.

It's an event held every two years when the community gathers to help raise funds for these clinical drug trials. Typically, the funds raised are utilised for the employment of additional clinical research nurses.

"This means that more patients with life-threatening blood cancers can participate in our clinical trials and access millions of dollars' worth of innovative medicines, long before they are publicly funded" said Professor Judith Trotman who heads the Haematology Department at the hospital. It is home to the largest clinical research unit for blood cancer in New South Wales.

The Bloody Great Night Out! has raised over $600,000

Cont.

WMozzies Australian patient support group for Waldenström's Macroglobulinemia

A•NZ BEACON

WM-NZ Support Group Waldenström's Macroglobulinemia

ISSUE 3 Newsletter for Waldenström Macroglobulinemia community in Australian and New Zealand JANUARY 2021

for clinical trial nurses at Concord Cancer Centre. Over two dozen WMozzies have directly benefited from The Bloody Great Night Out! fund raising initiative. The funds raised have enabled them to participate in the clinical trials providing them with access to the latest BTK treatments such as Ibrutinib and Zanubrutinib. Without these clinical trials at Concord Hospital, access to the new BTK treatments is not likely to have been within their financial reach. The BTK drugs are not funded by PBS and would have cost each patient around AUD $140,000 per annum.

As the name implies, A Bloody Great Night Out! is a magical night of music, dancing, entertainment, fun and fundraising. There are corporate sponsors, individual sponsors and companies donating gifts and/or services. Sales are made by lottery tickets and an auction. I have witnessed some rather enthusiastic bidding driving prices upwards by an experienced auctioneer.

David Rabie

BTK Inhibitors and WM

The following are extracts from 'Onclive' published September 30, 2020 by Erica DiNapoli.

BTK inhibitors have transformed the treatment of patients with Waldenström macroglobulinemia, according to Steven P. Treon, MD, PhD.

"In the Waldenström macroglobulinemia treatment armamentarium, we have never seen agents as active and safe as BTK inhibitors. We're very blessed because, if we choose to stop administering 1 BTK inhibitor due to a toxicity concern, patients can be switched to a different BTK inhibitor," said Dr Treon.

The 3 key agents in the United States are ibrutinib (Imbruvica), zanubrutinib (Brukinsa), and acalabrutinib (Calquence). In Japan, another agent has been under active investigation: tirabrutinib hydrochloride (Velexbru). In August 2020, the BTK inhibitor received a supplemental approval for the BTK inhibitor in Japan for use in patients with Waldenström macroglobulinemia and lymphoplasmacytic lymphoma.

"When I first started in the field, a young patient presented with a bad case of this disease. The patient died shortly after his first cycle of therapy due to severe complications from chemotherapy," Treon added. "As I reflect back on other past cases, I wish we discovered BTK inhibitors in this space much sooner because they have completely changed the playing field for the disease."

"It's been a very exciting time for Waldenström macroglobulinemia and BTK inhibitors lie at the center of the progress that has been made for this disease. The reason why we became interested in BTK inhibitors has to do with the discovery of the MYD88 mutation; this is found in about 95% to 97% of all patients with the disease. What's important about this mutation is that it activates Bruton's tyrosine kinase through a protein called HCK. Both HCK and BTK are targeted by ibrutinib, zanubrutinib, and acalabrutinib. All 3 agents have shown great clinical activity." said Dr Treon.

"Along with tirabrutinib hydrochloride (Velexbru) from Japan we now have 4 BTK inhibitors in the space that are all are showing response rates greater than 90% and, across the board, major response rates around 80% in this population."

"Notably, when you look at the activity in previously treated patients, whether they're relapsed or refractory; have had 1, 2, 3, or more lines of prior therapy; or they are treatment-naïve; the[se] drugs [are] active, and almost at the same level. This shows that we have a real targeted therapy, which is right on point with what we would have expected based on the whole genomic analysis that allowed us to discover MYD88 mutations in this disease."

"It's really a new era; we're no longer just pulling agents off the shelf that our colleagues in myeloma and lymphoma have generated. We would borrow agents used in other diseases; that used to be the main approach for treatment in Waldenström, a hand-me-down approach. Whole genome sequencing really has given us a playbook that has allowed us to rationally develop drugs."

The full article can be read at:
https://www.onclive.com/view/btk-inhibitors-transform-waldenstr-m-macroglobulinemia-management

Parliamentary Inquiry Into Approval Processes For New Drugs and Novel Medical Technologies in Australia

WMozzies welcomes the Parliamentary Inquiry into approval processes for new drugs and novel medical

Cont.

WMozzies Australian patient support group for Waldenström's Macroglobulinemia

A•NZ BEACON

WM-NZ Support Group Waldenström's Macroglobulinemia

ISSUE 3 Newsletter for Waldenström Macroglobulinemia community in Australian and New Zealand JANUARY 2021

technologies in Australia. We are pleased to have the opportunity to contribute to this inquiry on behalf of the Australian Waldenström's macroglobulinemia (WM) community.

We also thank the Minister for Health the Hon Greg Hunt MP for establishing this inquiry under the guidance of the Standing Committee on Health, Aged Care and Sport. Our submission provides input exemplifying how the current process negatively impacts WM patients. The challenges faced by patients are hindering a fair and transparent process for all Australians.

We are fully supportive of the current system that is evidence based and can demonstrate cost effectiveness. However, the current processes utilise models that are designed primarily for more common diseases. This presents challenges for reimbursement decisions for WM patients. Smaller patient numbers impact cost effectiveness. The cost of a PBAC application is also a significant disincentive for companies making an application for the rare disease WM. Our submission regarding Terms of Reference #4 includes a recommendation to ensure rare cancers such as WM have special consideration to ensure equity with other Australians for access to treatments.

WMozzies in collaboration with WM clinicians and researchers established the IWMF WhiMSICAL Registry. *https://wmozzies.com.au/index.php/whimsical/*

The Registry is designed to address some of the barriers facing effective research into our rare cancer. The aim is to gain a better, understanding of WM symptoms and correlation to pathology results, family history and genetics. The research also covers triggers to commence therapy, different treatments, their efficacy and tolerance, as well as disparities in treatment access within countries and internationally. In April 2020 WhiMSICAL was enhanced to include specific questions on the impact on WM patients of COVID-19 irrespective of actual COVID-19 infection or not.

Prof. Judith Trotman and WMozzies Committee member Michael van Ewijk meeting the Hon. Greg Hunt Minister For Health in Canberra.

Without compromising the assessment of safety, quality, efficacy, or cost-effectiveness, whether the approval process for new drugs and novel medical technologies, could be made more efficient, including through greater use of international approval processes, greater alignment of registration and reimbursement processes or post market assessment.

For rare diseases such as WM the current approval processes are not providing equitable outcomes compared to more common blood cancers.

PBS funds ibrutinib treatments for refractory/relapsed chronic lymphocytic leukaemia or small lymphocytic lymphoma (CLL/SLL) and mantle cell lymphoma (MCL), but not WM. This is not equitable!

The benefits of ibrutinib for a WM patient are equally well established as for the other approved blood cancers by:

- The iNNOVATE randomised clinical trial which confirmed that the progression-free survival rate was 82% with ibrutinib–rituximab versus 28% with placebo–rituximab.
- Approval by the US Food and Drug Administration in 2015 and European Commission also in 2015
- As well as the US FDA approval there has been patients in England, Scotland, Ireland, and some states in Canada.

Despite the strong evidence as above to support an application for funding of ibrutinib, no application has been made. It seems that the high cost of PBAC of applications is making it not commercially viable for a company to seek reimbursement for a rare disease such as WM. Whatever the reason the outcome for WM patients is not equitable. Other blood cancer patients receive funded access to ibrutinib but WM patients do not. The approval process needs to evolve and have appropriate flexibility to handle current inequities being experienced by rare cancers.

It is recommended that "Equity" be added as an extra principle to the existing underpinning Austalian HTA Processes:

- Sustainability
- Transparent, accountable and independent
- Consultativeand reflective of Australian community values
- Administratively efficient
- Flexible and fit for purpose
- Informed by robust and relevant evidence

It is recommended to achieve equity fir rare cancers including WM that less costlystreamlined approachbe used, which takes fully into account the evidence and approvals from other overseas authorities.

It is difficult, if not impossible, for a non-pharmaceutical sponsor such as WMozzies to apply to the PBAC. Without government

Cont.

WMozzies Australian patient support group for Waldenström's Macroglobulinemia

A•NZ BEACON

WM-NZ Support Group Waldenström's Macroglobulinemia

ISSUE 3 Newsletter for Waldenström Macroglobulinemia community in Australian and New Zealand JANUARY 2021

reimbursement, new medicines are unaffordable for people living with a rare disease such as WM.

The current cost of approval processes are adversely impacting WM patients' access to new drugs and emerging technologies. This is inequitable for WM patients. Indirectly, the processes may also be impacting the pharmaceutical industry's appetite to bring new drugs and emerging technologies to the Australian market and to conduct clinical trials in Australia. Australia is seen as a challenging market for rare disease medicines such as WM. The costly rigid evidentiary criteria, and complex and uncertain HTA approval processes appear to make applications for WM non-commercial. Approval processes seem long and cumbersome and lack transparency. Rare disease products are not typically approved the first time around and multiple resubmissions are required. This perception alone is damaging as it deters companies from applying and results in Australia failing to be identified as a priority market. When there is limited Australian data for WM, our HTA system does not seem to value or encourage other forms of evidence when appropriate, such as overseas trials and approvals.

Australia's current HTA system is over-reliant on pharmaceutical company sponsor-led applications. If companies are not commercially interested in applying, there is currently no viable way for WMozzies to assess a health technology, regardless of levels of unmet need. This means that people with WM have challenges accessing a re-purposed medicine such as Ibrutinib that is prescribed by their doctor but only funded for use with a more common condition such as CLL/SLL and MCL. There needs to be a way that clinicians and rare disease organisations can work with the HTA Consumer Evidence and Engagement Unit to apply for public reimbursement of a technology eligible for assessment by the Office of Health Technology Assessment (OHTA). The TGA and OHTA need to work together to develop clear processes and pathways for sponsors considering submitting applications for the re-purposing of medicines already approved for use in treatment of other conditions such as Ibrutinib for CLL

It is particularly important for those with WM and rare disease to participate in HTA processes. With limited data and uncertainties, WM patients can provide much needed narrative and context to the data presented in HTA. It is critical that HTA processes formally embed, capture, and promote the voice of people living with WM as a rare disease and their families and carers. The HTA Consumer Evidence and Engagement Unit is a great initiative that will assist in the provision of education and support to people living with WM and their families and carers, as well as WMozzies to support them.

Andrew Warden

Andrew Warden receives IWMF Volunteer of the Year Award

Andrew received the 2019 IWMF Judith May Volunteer of the Year at the IWMF Educational Forum in Philadelphia.

Michael's 700km Cancer Ride

A rare form of blood cancer called Waldenstrom Macroglobulinemia was not enough to prevent Michael van Ewijk from completing a solo 700km bike ride through the Riverina to raise funds for the Leukaemia Foundation's WMozzies IWMF (International Waldenstrom's Macroglobulinemia Foundation)/LLS Strategic Roadmap campaign.

He began the ride on September 24, 2020 in Balranald and completed 702 kilometres at Wagga on October 2. He decided on 700kms because he turned 70 in April 2020.

While the Riverina is relatively flat the winds were not so favourable. However he still managed to average over 25 kph for the 702 kilometres.

Michael raised over $11000. Completing a 700km bike ride is a testament to the fact that it is possible to have a healthy life with WM.