European Educational FORUM

Meeting Programme

Meeting programme

Time	Session Title	Speakers
11:15–11:45	Giving Time Back to Patients *Welcome session*	Delora Senft, Christian Buske
11:15–11:45	Understanding Your Treatment Timeline *Current Treatments Panel*	Shirley D'Sa, Jennifer Russell, Christian Buske, Paul Kitchen
11:15–11:45	Closing of the ECWM Meeting	Lisa Kaiser, Shirley d'Sa, Dima El-Sharkawi, Charlampia Kyriakou, Roger Owen, Chris Patterson, Steve Treon, Christian Buske, Efstathios Kastritis
12:45–13:30	Lunch	–
13:30–14:00	Research Poster Walk	Jahanzaib Khwaja, Phillip Nakov, Pierre-Édouard Debureaux, Tina Bagratuni, Anne-Marie Becking, David Moreno, Wouter Verhaar, Pieter Langerhors
14:00–14:20	The Future Arrives in Small Steps *Research Poster Presentations*	Jahanzaib Khwaja, Tina Bagratuni, Anne-Marie Becking
14:20–14:50	When Time Complicates the Picture *Associated Conditions*	Monique Minnema, Efstathios Kastritis
14:50–15:30	Making Time for Each Other *Support Group Session*	Bob Perry, Averil Shulman, Michael Bentley, Gloria McNeill
15:30–16:00	Coffee	–
16:00–16:45	What's Coming Next *Clinical Trials & Future Treatments*	Maria Gavriatopoulou, Steve Treon
16:45–17:30	Your Time to Ask Anything *HCP Q&A Panel*	Steve Treon, Christian Buske, Monique Minnema, Maria Gavriatopoulou
17:30–17:45	Thank you for your time! *Meeting close*	Delora Senft, Paul Kitchen

Wi-Fi information

- Connect to the Wi-Fi - **MGallery** and you will be directed to a portal page
- Select **Complimentary WiFi access** and select **Connect to WiFi**

Submit your questions

You can submit your questions for speakers throughout the day by scanning the QR code or following the link:
https://app.sli.do/event/t3zpMWPEGNV2c4z8j6xMr7
Please include the name of the speaker you would like to address the question to.

Translations

Translations are available in **Greek** and **German**. You will require **headphones** and a device such as a mobile phone in order to access the live translations. (If you do not have headphones, please inform one of the team).
Please see instructions below:

1. Scan and follow the link to listen to the live translations: https://us02web.zoom.us/j/83167485606
2. If using your mobile phone, please ensure that your Zoom application is up to date. You can check via the Apple Store or Google Play Store
3. In your meeting/webinar controls, click Interpretation
4. Click the language that you would like to hear
5. To hear the interpreted language only, click Mute Original Audio

Evaluation

We would love to hear about your experience of the meeting. Your feedback helps us to improve and plan for future meetings making sure that they are better with each year!

Please complete the evaluation form by scanning the QR code.
https://forms.cloud.microsoft/r/DhqYBN6XZ0

Paul Kitchen's journey with WM

Background & Family History

Paul was a schoolteacher from 1975 until 2016. He taught at independent schools that all had Chapel which he attended regularly. The last 29 years of his career were spent as Head of School at a boarding and day school in New Brunswick Canada. Paul's mother (born in 1910) had been diagnosed with WM about 1975 and passed away in1983 at age 73. She received no treatments other than steroids and blood transfusions. Paul's mother had many nose bleeds, and she lost much of her energy and was weary. She was the sole caregiver for her husband who had colon cancer and a colostomy from 1976 until he died in 1982.

Early Signs of WM & Diagnosis

Paul's WM journey began in 2011 with constant respiratory infections from March until June. He was on 4 courses of antibiotics during those months. The infection would almost clear up but then would flare up again and the pattern would repeat. He was sent to a respirologist who concluded the problem was not originating in the lungs and referred him to an immunologist. In September she concluded that it was Paul's immune globulins that were the problem - his IgA was extremely low, and his IgG was 2.5. The immunologist prescribed monthly IVIG infusions. Paul's regular infections were reduced dramatically. He had been typically getting 4-8 infections each year and it immediately decreased to 1-2 respiratory infections per year. The respirologist also diagnosed bronchiectasis from the damage done from constant infections.
Paul was again able to work at a normal level until the fall of 2014. His hemoglobin dropped significantly and he was fatigued most of the time. It got to the point where he could not go up a flight of stairs without resting part way up. Despite all these signs Paul's hematologist/ oncologist was not willing to perform a bone marrow biopsy. (This is probably a significant problem for many WM patients who have a difficult time getting the right diagnosis). After he requested a bone marrow biopsy and pushed, it was performed and WM was diagnosed.

First-Line Treatment

Paul immediately was treated with a16 week regiment of chemo (dexamethasone, rituximab and bortezomib). Within one cycle he started to feel better and the treatment was tolerated very well. At the end of the treatment a two-year maintenance treatment was recommended and Paul agreed. Paul's IgM level continued to drop throughout the maintenance treatment which finished up in April of 2017. Paul reluctantly chose to announce his retirement in June of 2015 for the end of the next school year. In retrospect it was an error but he had no way of knowing if he would feel well enough to be able to perform his duties after another year. In June of 2016, he chose to switch from IVIG to a sub-cutaneous IgG supplement.

Second-Line Treatment

Paul continued to feel well and do well until early 2020. His hemoglobin (Hgb) started to drop and by the fall he was put on Ibrutinib. He again reacted well quickly and his Hgb climbed. Unfortunately, with Ibrutinib the debilitating atrial fib, that had been successfully treated with an ablation in 2011, returned. It once again became intolerable and he was switched to Zanabrutinib in April of 2021. The change did not alter the positive effect the BTK inhibitor had on his WM. The switch was simple - one day he was on Ibrutinib the next he was on Zanabrutinib. The atrial fibrillation again disappeared.

Paul Kitchen's journey with WM

Disease Progression & New Options

This BTK inhibitor continued to work well until early 2024 when for the next year Paul's IgM steadily went up and his Hgb continually went down. He required plasmapheresis in December. By January of 2025 he was getting desperate as his energy was in his boots. After help and guidance from Dana Farber, Paul was able to get on a clinical trial for a BTK degrader. He received his first medication in late March of 2025. Paul did not react nearly as quickly as he had with the Chemo or BTK inhibitor but slowly and after 3-4 months he started to feel much better. Although Paul's energy was slowly returning, so did his severe respiratory infections, much like in 2011. In the first 8 months of 2025 he had at least 6 respiratory infections and or pneumonia. He received advice that he should increase his dose of IgM supplement and go back to IVIG. After doing so, the infections again almost disappeared which has been a huge relief to Paul. He still checks in with his respirologist regularly but has only had one infection so far in the last 6 months.

A Further Reflection from Paul

In 1975, at 65 years of age, my mother was diagnosed with WM. I too was 65 when diagnosed. I have been treated with chemo, Ibrutinib, Zanabrutinib and now, my clinical trial BTK degrader as well as my IVIG. My mother's only treatments were steroids and every-increasingly frequent blood transfusions.

What is even more striking is the quality of life I have had since my diagnosis. I have remained active and have had generally good health. I have hope and optimism about my future. My mother had no treatments, a continuing deterioration of her health. Her fatigue was overwhelming and she had no reason for hope.

Today many WM patients have a very good quality of life, and more importantly, WM patients of today have hope.

Glossary

WM — Waldenstrom's Macroglobulinemia is rare blood cancer in which abnormal B-cells produce excess IgM protein, affecting blood thickness and immune function.

IgA — Immunoglobulin A is an antibody that protects the respiratory and digestive tracts. Low IgA increases vulnerability to infections.

IgG — Immunoglobulin G is the most common antibody in the bloodstream. Low IgG often leads to frequent or severe infections.

IVIG — Intravenous Immunoglobulin is a treatment made from donated antibodies, infused through a vein to strengthen the immune system.

Hgb — Hemoglobin is a protein in red blood cells that carries oxygen throughout the body. Low hemoglobin causes fatigue and shortness of breath.

BTK — Bruton Tyrosine Kinase is a protein involved in B-cell growth. Targeting BTK is a key treatment strategy for WM.

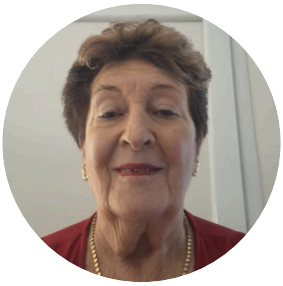
BTK inhibitor — A medication that blocks BTK to slow or stop the growth of abnormal B-cells. Examples: Ibrutinib, Zanubrutinib.

BTK degrader — A newer therapy that removes BTK from the cell entirely, rather than just blocking it.

Meet the Global Patient Advocates

Bob Perry is a 71 yr old retired Soldier and Police Officer who lives in Bournemouth, England. He was diagnosed with WM in 2015 and underwent 8 months of B&R therapy. He is currently on Active monitoring 10 yrs after that treatment. He is a keen cyclist and keeps fit. He runs two WM Support Groups, The Island of Ireland Support Group and the Bournemouth & District Support Group.

Michael Bentley, aged 62, originally hails from the UK and relocated to The Netherlands in 1999 for work in Information Technology. Diagnosed with WM in April 2024, Michael is currently undergoing active monitoring. Married to Kristien, they are proud parents of five children and grandparents to three. Michael volunteers with Hematon, a Dutch organisation supporting individuals affected by blood cancer. In his capacity as Hematon's representative, Michael is committed to strengthening collaboration with the IWMF, aiming to enhance resources and support for WM patients in The Netherlands.



Averil Shulman is a 80 yr old retired English teacher who lives in Herzliya, Israel. She was diagnosed with WM in 2015 and went through 6 months of B&R therapy. She is currently on 3 month monitoring and has been taking the BTK Zanubrutinib for the past 2 years. She is an enthusiastic bridge player and does water aerobics to keep fit. She is a mentor in the Halil HaOr (Flute of the Light) Israel Blood Cancer support group.

Gloria McNeill lives in Toronto, Canada. A retired dentist, she is the proud mother of two sons and one daughter, and a grandmother to six. In June 2015, Gloria was diagnosed with Smoldering WM. Since then, she has remained on a “Watch and Wait” approach, undergoing bloodwork every three months. While she has not required treatment to date, her WM has presented some unique features, including an unexpected transition to Biclonal WM approximately three years ago. Gloria currently serves as an active Board Member of the Waldenström’s Macroglobulinemia Foundation of Canada and as a Support Group Leader for the Metro Toronto WMFC Support Group. These roles provide her with a strong sense of purpose, allowing her to support and connect with others navigating a similar journey.

IWMF Impact Awards 2026

IWMF IMPACT AWARD SUMMARY

The IWMF Impact Awards honor individuals and partners whose contributions embody our mission to educate, empower, and support everyone impacted by WM while advancing research toward a cure. As we look toward 2026, these awards reflect the momentum across our strategic pillars—Patient Support & Education, Research, Investigation & Clinical Practice, and Partnership & Involvement—and the collective commitment driving us toward our vision of a world without WM.

Judith May Volunteer of the Year
Susanne Öhrn

Partnership & Involvement
IWWM - Christopher Patterson

Research Achievement

Prof. Dr. Christian Buske

Steven P. Treon, MD, PhD

Stephen M. Ansell, MD, PhD

The European Educational Forum is organised by the IWMF. The IWMF is a patient-founded and patient-driven, non-profit organisation that is dedicated to a simple but compelling vision and mission.

Our Vision: A World without Waldenstrom macroglobulinemia.

Our Mission: Educate, empower, and support everyone impacted by WM, providing hope through improved patient outcomes and advancing research toward a cure.

www.iwmf.com (+1 941-927-4963) EIN: 54-1784426

The IWMF have been extremely fortunate to be collaborating on this meeting with the European Consortium of Waldenström's Macroglobulinemia (ECWM).

The European Consortium for Waldenström's Macroglobulinemia (ECWM) represents a coordinated effort to combine the expertise of clinicians, pathologists, and researchers across Europe. By combining the strengths of experts from around the globe, the consortium is well-positioned to advance research, diagnosis, prognosis, and treatment strategies for WM, ultimately benefiting patients and improving their quality of life.

www.ecwm.eu

A special thank you to Lisa Kaiser and Professor Christian Buske for the support with the planning for this meeting.

Thank you ECWM doctors, speakers, and poster presenters who took their time to participate in the meeting.

We would like to thank the Lucid Group for their onsite team support.

Thank you to BeOne, for providing independent sponsorship towards the costs of running the meeting.

Young European Consortium for Waldenström's Macroglobulinemia

What is the young ECWM

A European network of young investigators committed to positively impact patients with WM through innovation and research collaboration

Formed in 2025 as part of the wider ECWM

Wouter Verhaar
Amsterdam University Medical Center
Cancer Center Amsterdam, the Netherlands
Work on epcoritamab in WM (HOVON178 study)
Proteomics and IgM characterization in WM

Pieter Langerhorst
Proteomics in B-cell disorders
Sanquin Research, Amsterdam
Decoding Disease Progression and Treatment Response in IgM Gammopathies through Mass Spectrometry Proteomics

Anne-Marie Becking, MD
Amsterdam University Medical Center
Cancer Center Amsterdam, the Netherlands
Work on Patient preferences in WM (WM-VOICE study)
Bing Neel Syndrome & Cold Agglutinin Disease

Jahanzaib Khwaja, MD
University College London Hospitals
National Amyloidosis Centre
Work on sociodemographics and ethnicity in WM

Mouhamad Khouja
University Hospital Schleswig-Holstein, Kiel, Germany
Hematology Laboratory Kiel
Work on Genetics and non-invasive diagnostics in WM

Ryan Low, MD
Haematology Trainee –North London
Work on Patient Reported Outcomes, Clinical Trials

Philipp Nakov, MD
University Hospital Schleswig-Holstein, Kiel, Germany
Hematology Laboratory Kiel
Work on Measurable residual disease in WM

Pierre-Edouard Debureaux, MD PhD
Saint Louis Hospital
Work on Inflammatory Waldenström

Philippe Decruyenaere, MD
Ghent University Hospital, Ghent, Belgium
Work on Cell-free RNA based liquid biopsy in IgM gammopathies
, PhD

Carolyne Croizier
Service de thérapie cellulaire et d'hématologie clinique adulte, CHU Estaing, Clermont-Ferrand, France

Nicolò Danesin, MD
Hematology Unit, University of Padua, Italy
Work on Clinical and translational research focused on rare IgM-related disorders

Cristina Jiménez, MD
University Hospital of Salamanca
Biomedical Research Institute of Salamanca
Work on genomics of WM

David F. Moreno, MD PhD
Hospital Clinic of Barcelona
Work on molecular characterization and prognostic risks of WM

Irene Dogliotti, MD
Hematology Unit, University of Torino, Italy
Work on translational research, prognostic risks of WM and anti-MAG polyneuropathy

Francesco Autore, MD
Gemelli IRCCS, Universita Cattolica del Sacro Cuore
Rome Italy
Work on Italian registry network for clinical research focused on IgM-related disorders

Aims

- Monthly meeting
- Clinical registries
- Clinical review
- e.g. planning facilitate sharing of biobank samples etc.
- Expand & include more young researchers from different countries.
- Collaborating clinical fellowship/research – WM

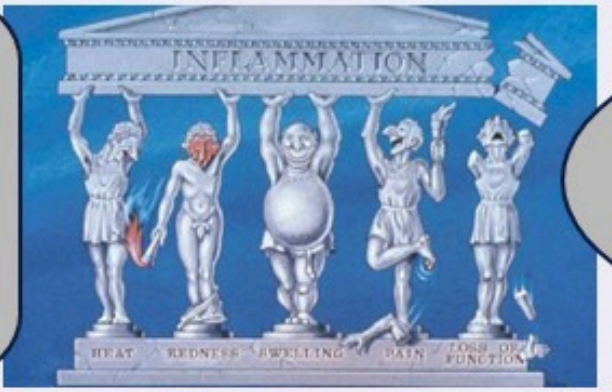
Engage young WM researchers and foster collaboration to ultimately make a positive impact on WM patients!

Inflammatory Waldenstrom's macroglobulinemia (iWM)

Presented by Pierre-Edouard Debureaux (Saint Louis, Paris)

What is inflammatory WM?

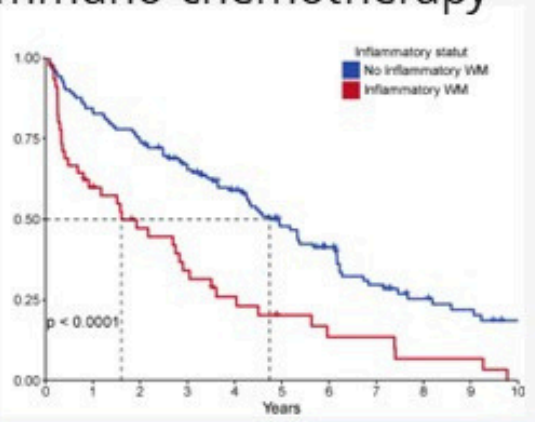
Evaluated by CRP, a blood protein increased during inflammation



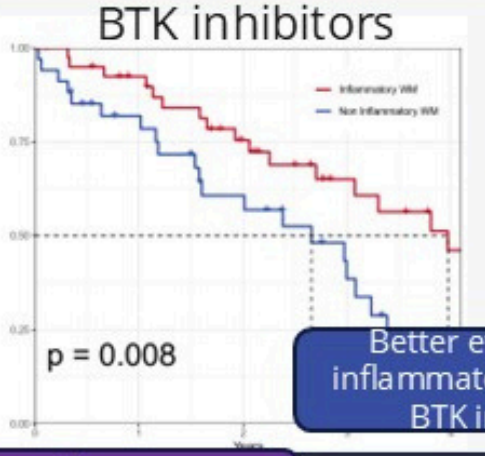
30% of symptomatic patients (who need therapy)

Difference for duration of response (=time before relapse) between non inflammatory (blue) and inflammatory (red)

Immuno-chemotherapy



BTK inhibitors



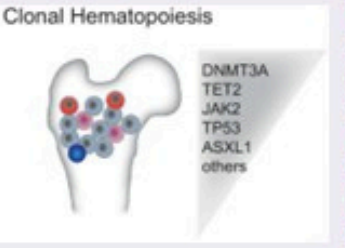
Better evolution for inflammatory patients in BTK inhibitors

Cause ?

Tumoral

Not associated with infiltration of bone marrow tumoral cells or IgM level

Others cells



Increase in inflammatory forms and will produce pro inflammatory proteins

Our results suggest a possible explanation for why BTK inhibitor treatments may work better in some patients. More research is needed to confirm this finding.

iWM: inflammatory WM

March 2026

WM-VOICE study

Patient preferences regarding treatment options for Waldenström macroglobulinemia: An international discrete choice experiment

Why did we do this study ?

- **Treatment options** for Waldenström macroglobulinemia (WM) are **expanding**. However, it remains **incurable** and there is **no consensus** on one preferred approach.
- WM treatments have **different properties** regarding efficacy, side effects, and administration.
- Understanding **patient preferences** is essential for optimizing treatment strategies.

Sample choice set (1 of 16)

Treatment A	Treatment B
Start of treatment → Disease progresses: 4 years	Start of treatment → Disease progresses: 6 years
Oral pills, at home	Infusions in the hospital
Fixed duration (6 months), followed by treatment-free interval	Ongoing treatment, no treatment-free interval
Severe temporary side effects, affecting ability of self-care	No temporary side effects
No persistent side effects	Moderate persistent side effects, affecting daily activities
Increased risk of other cancer (6%)	No increased risk of other cancer (1%)

How did we do this study?

- **1,455 patients** in **5 countries** participated

Australia	Canada	Netherlands	UK	USA
n=209	n=219	n=340	n=214	n=473

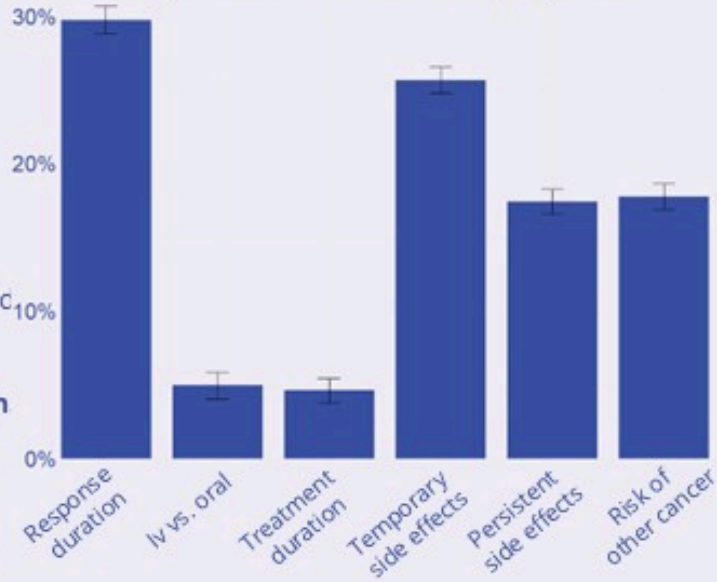
- They completed an **online survey**
- Containing **16 choice sets** with hypothetical treatment options
- Patients had to **choose** repeatedly between **treatment A and B**

What did we find?

- Treatment preferences are very **consistent across the 5 countries.**
- All selected **6 treatment properties influence patient choices**, to different extents.
- Patients mostly preferred **long response duration** and **mild short-term side effects.**
- Results can guide **clinical practice** and **drug selection**

Output
- Presentation at ASH (2025)
- Patient webinars (Q2 2026)
- Publication in scientific journal (±Q3 2026)

Importance of treatment properties



Coördinating study team: Drs. AL Becking, Dr. P. Nieuwkerk, Prof. Dr. MJ Kersten, Dr. JMI Vos (Amsterdam UMC)

International study team: Dr. K Amaador, Dr. S Bemelot Moens, Prof. Dr. M Minnema, Dr. S D'Sa, Dr. D El-Sharkawi, Dr. C. Kyriakou, Dr. I Tohidi-Esfahani, Prof. Dr. J Trotman, Dr. R Low, Dr. C Chen, Dr. D MacDonald, Dr. S Thomas, Dr. L Palomba, Dr. S Sarosiek, Dr. P Kapoor, Dr. S Ansell, Patient representatives from Hematon (NL), IWMF (USA), WM-UK (UK), WMFC (Canada), WMozzies (Australia)

Funding: IWMF

Epidemiology, Real-World Treatment, and Economic Burden of Waldenström Macroglobulinemia in Germany

Christian Buske MD[1], Michael Herold MD[2], Nasim Bahar MPH[3], Keri Yang PhD[4], Boxiong Tang MD[4], Sabrina Müller MSc[5], Georg Hess MD[6]

1 Institut für Experimentelle Tumorforschung, Universitätsklinikum Ulm, Germany
2 GermanyHelios Klinikum Erfurt, Germany
3 BeOne Medicines Ltd, Basel, Switzerland
4 BeOne Medicines Ltd, San Carlos, CA, USA
5 Institut für Pharmakoökonomie und Arzneimittellogistik e.V., Wismar, Germany
6 Department of Hematology and Medical Oncology, University Medical School Mainz, Germany

What was analyzed?

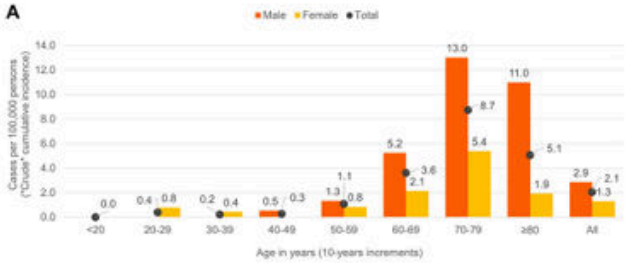
Researchers wanted to learn:

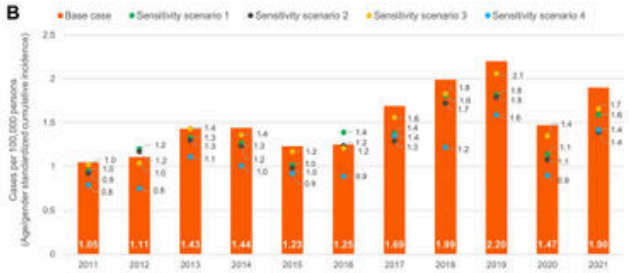
- how often WM was diagnosed in Germany based on health insurance data
- how patients were treated in routine clinical practice
- how long patients lived after diagnosis

Why is this analysis important

- Shows real-life care
- Important for rare diseases
- Helps understand treatment patterns
- **Supports better planning and decision-making**

Incidence and treatment



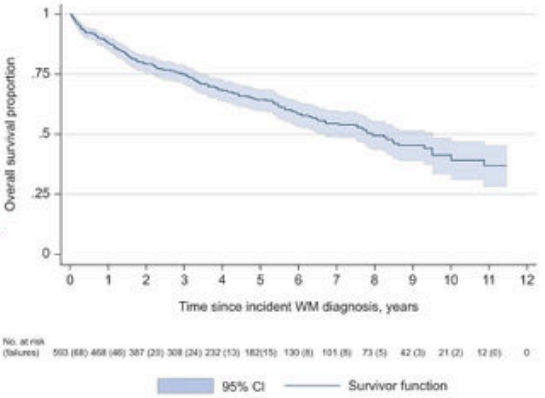


- **593 people in total** with newly identified WM
- Average age: **72.7 years**
- The **disease incidence nearly doubled** between 2011 and 2021
- Many patients did not need treatment right away
- **Nearly 70% of patients were first managed with watch and wait.**
- Most commonly Rituximab/Chemo was used as primary therapy

Survival

- Most patients lived for years after diagnosis
- The study found a **median overall survival of 7.9 years**.
- This means: half of the patients lived longer than 7.9 years, half lived less than 7.9 years.

→It does not predict what will happen to one individual person.



Summary

- **Real-world studies** help us understand how WM is managed in everyday practice.
- **Disease incidence increased** over time
- **Careful monitoring** is often an important part of care.
- **These findings can support better care for patients with WM.**

Contact:
Dr. Philipp Nakov
philipp.nakov@uksh.de
UKSH Campus Kiel
Department of Internal Medicine II
Arnold-Heller-Straße 3, 24105 Kiel

Wissen schafft Gesundheit

UKSH UNIVERSITÄTSKLINIKUM Schleswig-Holstein

Uncovering disease clues in blood

Dr. P. Langerhorst, W. Verhaar, MSc, prof. Dr. M.J. Kersten, prof. Dr. T. Rispens, Dr. M. van den Biggelaar, Dr. J.M.I. Vos

Many thanks to all BCEL Biobank patients and Hematon (NL) for making this research possible!

It is **difficult** to **predict** how **disease progresses** and how well **treatment works** in patients
We need to **better understand** how biological **processes** change during **disease progression** and **treatment**

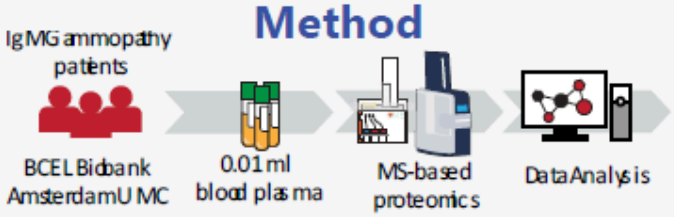
- Proteins in blood hold many clues about active biological processes throughout the body
- Studying these proteins can uncover new disease clues
- This can lead to **improved diagnostic** to predict disease progression and optimal treatment for each patient

Aims of the study

1) Uncover proteins/processes linked to disease progression from MGUS to WM

2) Map what proteins and processes change with treatment

Method



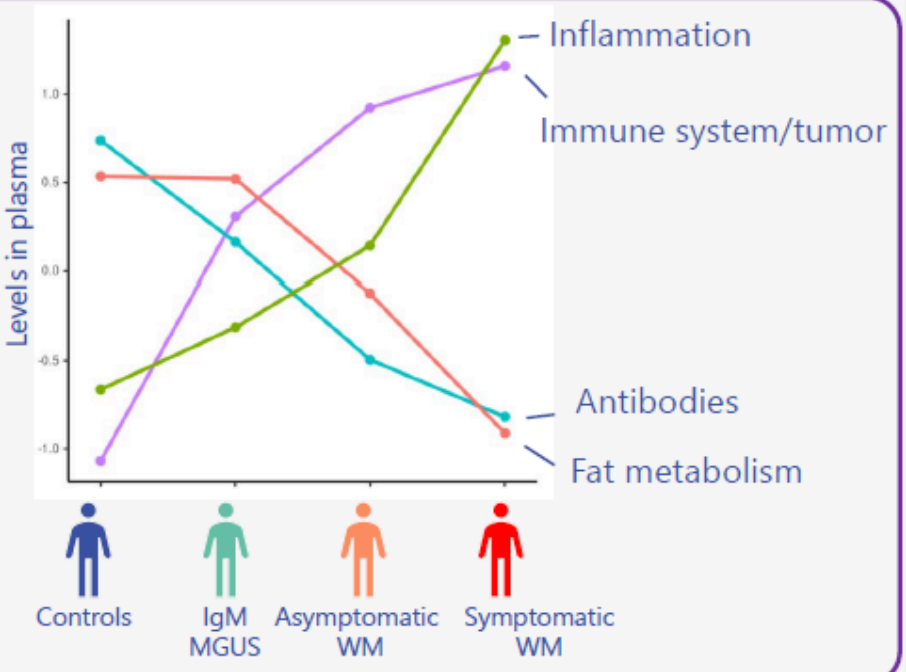
Proteomics measures over 600 proteins in a drop of blood

Disease stages

Protein levels were compared between patients with different disease stages. Next, proteins belonging to the same biological function were grouped.

Inflammation and proteins from the **immune system/tumor** were **increased** with each following disease stage.

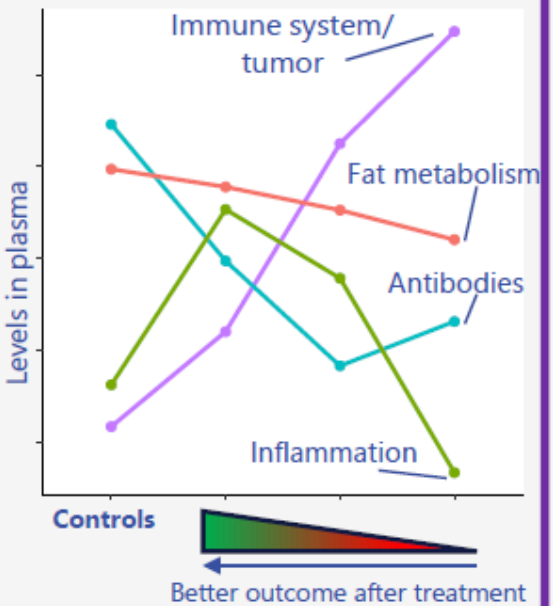
On the other hand, **antibodies** and **fat metabolism** were **decreasing** from MGUS to Symp WM.



Treatment

Next, we investigated how these processes changed during treatment.

Immune system/tumor, fat metabolism, and **antibodies** increasingly **recovered** to Control levels with better response to treatment.
In contrast, **inflammation** levels **did not recover**. This can mean that inflammation is a separate process influencing treatment outcomes.



Conclusions

- We identified proteins and processes linked to disease progression and treatment outcomes
- Inflammation does not recover to control levels with treatment

What is next?

- We are investigating if these proteins can predict progression and treatment outcome towards improved diagnostics
- Understanding inflammation, what the cause is and how it affects disease course

Opening soon (HOVON178): A study with epcoritamab in patients with relapsed and non-responding Waldenström Macroglobulinemia

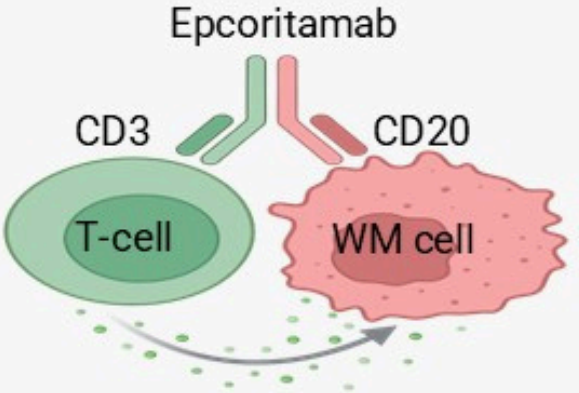
W. Verhaar, prof. dr. M.J. Kersten and dr. J.M.I. Vos

Waldenström Macroglobulinemia (WM) is a rare form of cancer. Although treatment options have increased; WM remains an incurable disease to this day.

WM affects a specific type of white blood cell, called a B-lymphocyte or B-cell for short. B-cells are part of the immune system and have an essential role in the body's defense against infections and diseases.

T-cells are also an important part of the immune system and can be used to fight against cancer.

Epcoritamab is a new treatment, called a "bispecific antibody". It directs T-cells (CD3+) to the WM cells (CD20+).



Epcoritamab is very effective in other B-cell lymphoma and is already approved for use in, for instance, follicular lymphoma.
We believe that it may also be effective in WM. Currently, there is no data on epcoritamab in WM.

Who can participate?

- Adult patients (18 or older)
- Relapsed or non-responding WM
- Need for treatment with at least 1 prior line of therapy

Aim

1. To confirm the **right dose in WM**
2. To test **safety and tolerability**
3. To test the **responses**
4. To test important **biomarkers that might predict response**

Study design (2 parts)

Study design: multicenter, open label, non-randomized *(every patient will receive epcoritamab)*

Part 1: to test aim *1 & 2* with 6 – 12 patients
Part 2: to test aim *3 & 4* with 20 patients
Total: 26-32 patients included in the study

Participating countries and hematologists:

Dr. J.M.I. Vos, professor M. Minnema and dr. H. Kooistra

Dr. L. Deleu and professor A. Janssens

Dr. T. Hammer and dr. I. Kristensen

Epcoritamab regimen during study

Administration will be under the skin with injections

Administration will be done by **step-up** in cycles of 4 weeks (28 days)

Cycle 1-3: weekly dosing (days 1, 8, 15, 22)
Cycle 4-9: twice a month (days 1 and 15)
Cycle 10-24: once a month (day 1)

Total numbers of cycles: 24 (equal to 96 weeks)
Follow-up: until 5 years after entering the study

Correspondence:
w.verhaar@amsterdamumc.nl

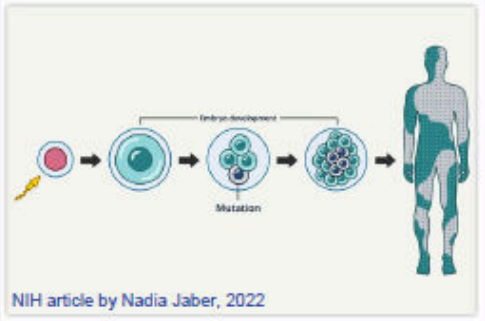
Amsterdam UMC

Additional information HOVON178 study (scan QR code)

Understanding Waldenström macroglobulinemia using novel genetic technologies to improve risk stratification and discover new treatments

David Moreno, MD PhD
Hospital Clínic de Barcelona, IDIBAPS. Spain

The human body is composed of multiple types of cells



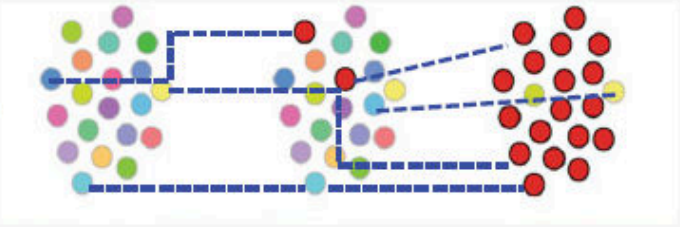
NIH article by Nadia Jaber, 2022

In cancer, tumor cells are unique:
Some cells have an indolent behaviour, and others are more aggresive

Can we track individual Waldenström cells over time?

MGUS: Monoclonal gammopathy of undetermined significance

WM: Waldenström macroglobulinemia



AWM: Asymptomatic WM

SWM: Symptomatic WM

IgM MGUS — Very early stage

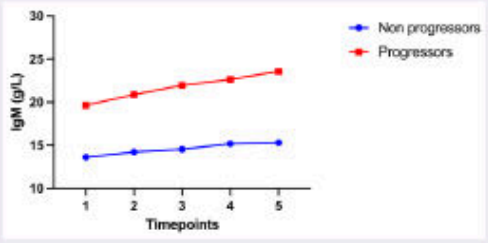
AWM — More advanced stages

SWM

Figure adapted from Langerak, et al. 2016

How?

1. Clinical identification of patients at risk

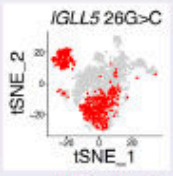


Using a large cohort, patients who progress have a continuous trend of serum IgM increase

Medina, et al. ASH Meeting. 2025

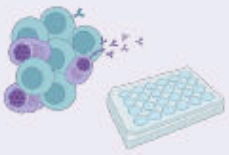
2. Genetic characterization throughout time

Specific tumor cells harboring a mutation in a AWM patient



\+

Each cell's DNA in a plate: whole genome interrogation

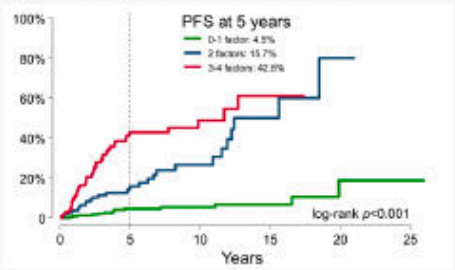


Using longitudinal samples (at diagnosis and years later) to see which alterations appear during follow-up

Moreno, et al. Work submitted. 2026

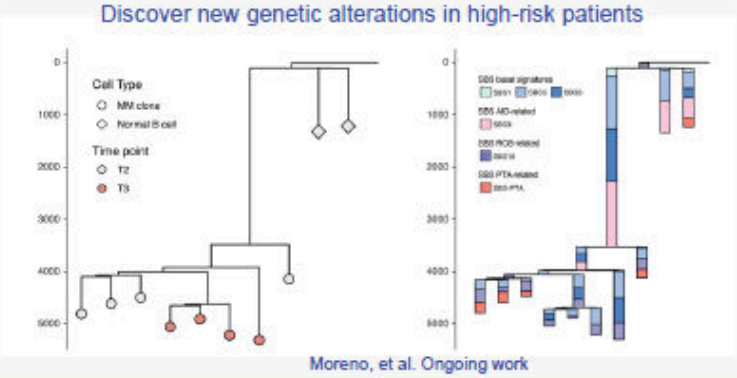
What to expect?

Early identification of high-risk patients: Improve previous risk models



Moreno, et al. 2024

Discover new genetic alterations in high-risk patients



Moreno, et al. Ongoing work

Contact: dfmoreno@clinic.cat

Acknowledgements: IWMF support, ISCIII (Spain), Parse Biosciences

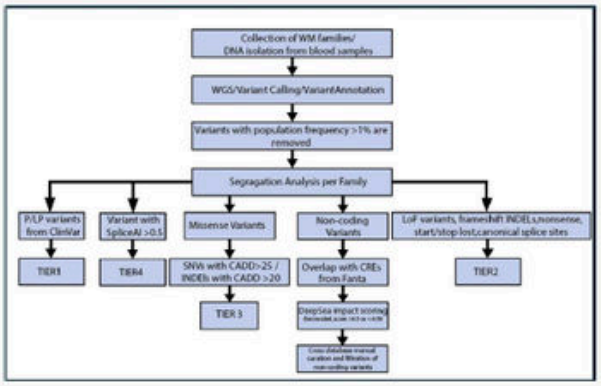
Revising the familial entity and the spontaneous clonal evolution in **W**aldenström macroglobulinemia: **In D**epth analysis from the initial events to the clinical outcome.
ReWInD

Background

Family studies have been central to Waldenström macroglobulinemia (WM) research because having relatives with WM or similar blood cancers greatly raises a person's risk. About one in four people with WM has family members who have had related lymphoid cancers, and close relatives (parents, siblings, children) are more likely to develop WM than people without such a family history. These family-linked cases matter for deciding who should be screened, how closely to watch for disease progression, and how diagnosis and treatment might be managed.

Aim of study

ReWInD will look for inherited genetic changes and early warning signs that put people at risk for WM. The study will deeply analyze DNA and other molecular data from at least 50 families where one person has an abnormal IgM protein in their blood and another has some form of B-cell lymphoma. By combining family genetic searches with monitoring of early disease stages, the project aims to find genes and simple biomarkers that could help identify at-risk people earlier and improve screening.

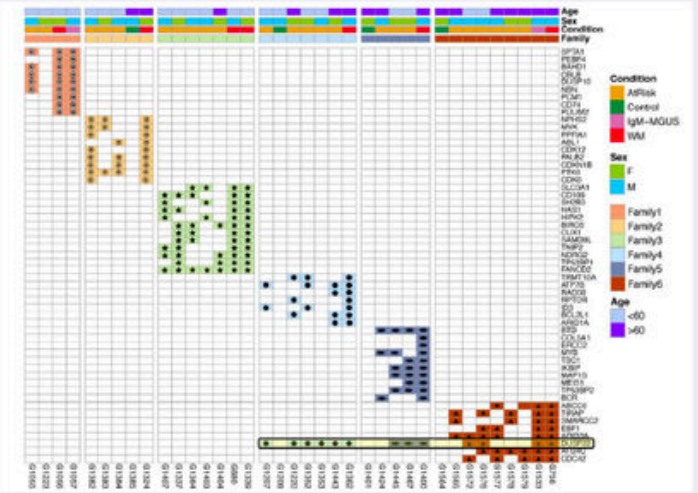


Study design

We aim to collect peripheral blood (PB) samples from at least 50 families with at least one affected patient with IgM monoclonal gammopathies and **a.** with at least one additional individual diagnosed with another type of B-cell lymphoma or **b.** with at least one additional individual diagnosed with non-IgM monoclonal gammopathy or **c.** no other individuals with B-NHL or monoclonal gammopathy but the index case diagnosed at an age <40 years of age in addition to 1st and 2nd degree relatives. PB will also be collected from spouses as a control group (detailed protocol attached). So far, we have stored PBs from 25 families. We will perform WGS using genomic DNA which will be isolated from the PB sample of all patients and family members.

Preliminary data

- Overall, genes that were captured from this analysis were involved in processes such as DNA damage response (*NBN*, *PALB2*, *RAD50*, *CDK12*, *HIPK2*, *CUX1*), apoptosis/ cell survival (*BCL2L1*, *BIRC6*, *ABL1*), PI3K/AKT/mTOR (*RPTOR*, *NDRG2*, *ABL1*) and MAPK/ ERK signaling (*DUSP10*, *PEBP4*, *ABL1*).
- Of particular interest is *DUSP22* gene, variations of which were found 3 out of 6 families. These variations (involving both non-coding and coding regions. None of the controls harbored polymorphisms in this gene.
- Although these variants are not yet classified as pathogenic or likely pathogenic, they show high predicted deleteriousness (median CADD score: 25).



Concluding remarks

- These aims seek to deeply understand why WM runs in families, how the disease changes over time, and how to tell who is most likely to get worse.
- By bringing advanced genetic and laboratory research into patient care, we will build an evidence base to inform future clinical trials and enable more precise, personalized treatments for WM.
- This work will also create a model for using molecular profiles to sort patients by risk and guide clinical decisions.

WGS: Whole genome sequence, *NBN: Nibrin*, *PALB2*: Partner And Localizer of BRCA2, *RAD50*: RAD50 double-strand break repair protein, *CDK12*: Cyclin Dependent Kinase 12, *HIPK2*: Homodomain interacting protein kinase 2, *CUX1*: Cut-like homeobox 1, *BCL2L1*: Bcl-2-like protein 1, *BIRC6*: Baculoviral IAP repeat-containing 6, *ABL1*: Abelson murine leukemia viral oncogene homolog 1; PI3K: phosphatidylinositol 3-kinase; AKT: Protein Kinase B; mTOR : mechanistic Target of Rapamycin, *RPTOR*: Regulatory-associated protein of mTOR, *NDRG2*: N-myc downstream-regulated gene 2, MAPK: mitogen-activated protein kinase; ERK: Extracellular signal-Regulated Kinase, *DUSP10*: dual specificity phosphatase 10, *PEBP4*: Phosphatidylethanolamine-binding protein 4, *DUSP22*: dual specificity phosphatase 22; CADD: Combined Annotation-Dependent Depletion

Quality of Life Questionnaires in Waldenstrom Macroglobulinaemia

Introduction

Patients with Waldenström Macroglobulinaemia may have a diverse range of disabling symptoms which can impact patient quality of life. These include fatigue, lymph node swelling, peripheral neuropathy, cryoglobulinemia and cold agglutinins. A number of Quality of life questionnaires are used in clinical trials to assess symptoms but were developed with patients with Waldenstrom's specifically.

Aims of survey

We conducted an international survey of 120 patients and 34 healthcare professionals to explore how well existing quality of life questionnaires capture what matters most to patients

Results

Out of 415 questions, 257 questions were classified by patients as **relevant**.

Commonly used Quality of Life Questionnaires

Quality-of-Life Questionnaires	Abbreviation
EORTC Core Quality-of-Life-questionnaire	EORTC QLQ-C30
EuroQol 5-Dimension 5-level	EQ-5D-5L
Functional Assessment of Cancer Therapy—General	FACT-G
Functional Assessment of Chronic Illness Therapy—Fatigue	FACIT-F
Functional Assessment of Cancer Therapy—Anaemia	FACT-An
Functional Assessment of Cancer Therapy/Gynaecologic Oncology Group—Neurotoxicity	FACT-GOG/NTx
Functional Assessment of Chronic Illness Therapy—Lymphoma	FACT-Lym
36-Item Short Form Health Survey questionnaire	SF-36
Hospital Anxiety and Depression Scale	HADS
Depression, Anxiety and Stress Scale—21 Items	DASS-21
Quality of Life in Adult Cancer Survivors	QLACS
Impact of Events Scale	IES
Fatigue Severity Scale	FSS
Interpretative Phenomenological Analysis	IPA

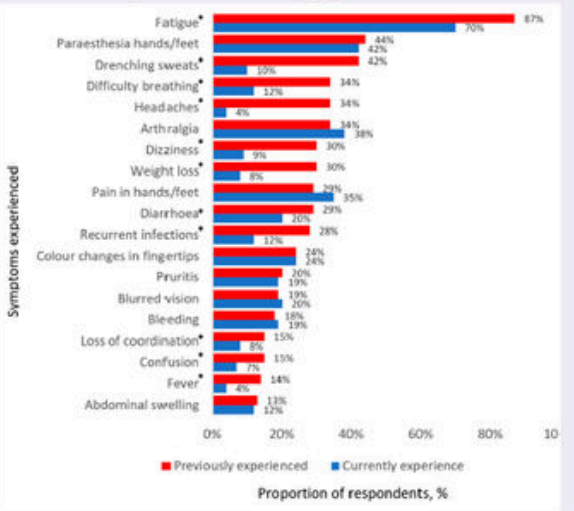
Questions patients considered relevant & not relevant

Relevant:
Fatigue
Mobility
Dyspnoea
Paraesthesia
Pain hands feet
Sleep
Contentment
Social and family support

Not relevant:
Lumps or swellings
Dry mouth
Trouble hearing
Sexual dysfunction
Post traumatic stress
Financial support
Education and training

Word cloud of issues patients considered important

Symptoms commonly experienced by patients



Conclusions

Commonly used questionnaires do not fully reflect patients' real experiences, suggesting the need for Waldenstrom -specific questionnaires.

Full details of research paper: https://www.mdpi.com/2072-6694/17/22/3609

Notes

Notes

Notes