

Global Real-World Treatment Patterns, Time to Next Treatment, and Quality of Life Outcomes in Waldenström Macroglobulinemia: Insights from the WhiMSICAL Patient-Derived Registry

Ryan Low^{1,2}, Andrew Warden³, Pete DeNardis⁴, Michelle Postek⁴, Shirley D'Sa⁵, Marie Jose Kersten⁶, Adam Olszewski^{7,8}, Ruth Spearing^{9,10}, Judith Trotman^{1,11}, Ibrahim Tohidi-Esfahani^{1,11}

1. Haematology Department, Royal Free Hospital, London, UK.
2. Haematology Department, Concord Repatriation General Hospital, Sydney, Australia.
3. Australian Patient Support Group for WM, WMozzies, Sydney, Australia.
4. Board of Trustees, International Waldenström's Macroglobulinemia Foundation, Sarasota, Florida.
5. UCLH Centre for Waldenström's Macroglobulinemia and Related Conditions, University College London Hospitals NHS Foundation Trust, London, UK.
6. Department of Hematology, Amsterdam UMC, University of Amsterdam and LYMMCARE, Netherlands.
7. Department of Medicine, Warren Alpert Medical School, Brown University, Providence, Rhode Island.
8. Division of Hematology-Oncology, Rhode Island Hospital, Providence, Rhode Island.
9. Otago School of Medicine, University of Otago, New Zealand.
10. Department of Haematology, Christchurch Hospital, New Zealand.
11. Faculty of Medicine and Health, University of Sydney, Sydney, Australia.

Introduction: Fixed-duration chemoimmunotherapy (CIT), e.g. bendamustine-rituximab (BR), Dexamethasone Rituximab and Cyclophosphamide, (DRC), and continuous BTK inhibitors (BTKi) are commonly utilised firstline therapies in WM. However, a randomized trial comparison is unlikely and little data is available to inform sequencing decisions. Real-world data (RWD) is critical to fill this gap. WhiMSICAL (**W**aldenström **M**acroglobulinemia **S**tudy **I**nvestigating **C**linical outcomes **A**nd quality of **L**ife) is the first global, patient-derived WM registry to capture treatment patterns, outcomes and quality of life (QoL) data. We present an updated analysis mapping global practice variation, and the sequencing of CIT and BTKi.

Methods: After online self-consent, WhiMSICAL captures patient-entered demographic, clinical (symptoms, comorbidities, pathology, therapies), and QoL data. Recruitment is primarily by WM consumers through social media. TTNT is defined as duration from therapy initiation to the start of the subsequent line; patients without subsequent therapy are censored at their last data edit. QoL, assessed using the EORTC QLQ-C30 global scale and the Impact of Event Scale-6 (IES-6), were evaluated pre-treatment, within 12 months, and 12–24 months post-treatment initiation. Data cutoff was 1st July 2025.

Results: 714 patients from 23 countries (USA: 51.1%, Australia: 18.2%, UK: 10%) participated, with a median follow-up from diagnosis of 79 months (IQR 42–131). Median age at diagnosis was 62 years (range 24–89). Firstline treatment was received by 512 patients (72%), demonstrating high heterogeneity with 54 unique regimens. USA patients-initiated treatment significantly sooner after diagnosis than the Rest-of-World (median 77 vs. 360 days; $p=0.02$) and received first-line BTKis more frequently (32% vs. 13%).

The four most common first-line therapies were BR (30%), BTKi (14%), rituximab monotherapy (12%), and (DRC, 10%), with BR and BTKi increasing from 16% and 4% prior

to 2016, to 43% and 20%, respectively, post-2016. At a median follow-up of 54 months, median TTNT was similar for firstline BR and BTKi (104 vs 101 months; $p=0.60$) despite comparable self-recorded co-morbidities. Both achieved longer TTNT than DRC (84 months; $p=0.03$) and rituximab monotherapy (36 months; $p<0.001$). In the second-line setting, BTKi ($n=54$) demonstrated longer TTNT than BR ($n=29$) (93 vs 54 months; $p=0.0018$). (Figure 1)

Baseline global QoL was similar between CIT- and BTKi-treated patients. CIT was associated with a transient reduction in global QoL during the first 12 months (mean score 68.6 vs 79.3; $p<0.02$), but by 12–24 months QoL was comparable between groups (78.0 vs 79.4; $p=0.81$). Mean IES-6 scores improved over time (5.7 to 4.5; $p=0.0007$) without significant differences between CIT and BTKi (6.3 vs 5.6; $p=0.51$).

Conclusion: The unique, growing continuous dataset of the global WhiMSICAL registry highlights international variations in WM management. While the adoption of firstline BTKi use is increasing, the data provides further support that initial BR remains a highly effective fixed-duration option with comparable long-term TTNT to BTKi, whereas this comparable efficacy is lost in subsequent lines. While CIT causes an initial short-term QoL deficit relative to BTKi, this resolves after 12 months, highlighting the long-term value of a treatment-free interval to inform shared clinical decision-making.

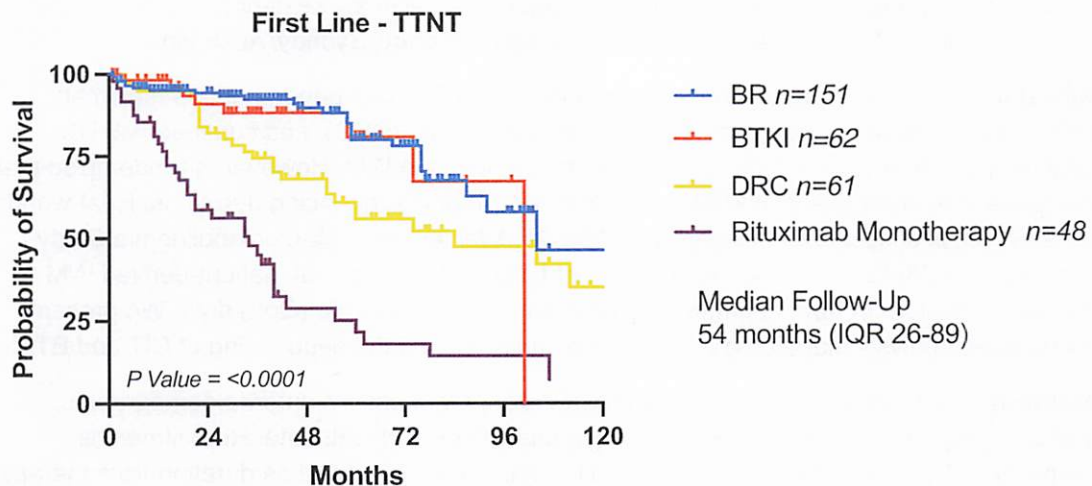


Figure 1 – Kaplan–Meier curves showing time to next treatment (TTNT) according to the four most common first-line treatment regimens. TTNT was defined as the interval from initiation of first-line therapy to commencement of second-line treatment. Patients who did not receive subsequent therapy were censored at the date of their last WhiMSICAL registry update. Differences between treatment groups were assessed using the log-rank test. BR, bendamustine-rituximab; BTKi, Bruton tyrosine kinase inhibitor; DRC, dexamethasone, rituximab, cyclophosphamide.

Form record received

From International Workshop on Waldenstrom's Macroglobulinemia <pattersonkent@outlook.com>

Date Thu 30-Jul-26 6:27 AM

To Patterson, Christopher <Christopher_Patterson@DFCI.HARVARD.EDU>

External Email - Use Caution

Record saved to database with ID: 222

Form ID: 1

Form title: Abstract Submission

Form name: Abstract_Submission

Submitted at: 2026-07-30 06:25:54

Submitter IP: 208.127.193.118

User-ID: 0

Username: -

User full name: -

Submitter provider: Unknown

Submitter browser: Mozilla/5.0 (Windows NT 10.0; Win64; x64) AppleWebKit/537.36 (KHTML, like Gecko)

Chrome/150.0.0.0 Safari/537.36 Edg/150.0.0.0

Submitter operating system: win

First Name: Ryan

Last Name: Low

Email: ryan.low@nhs.net

Registration Type: Delegate in Training

Abstract Title: Global Real-World Treatment Patterns, Time to Next Treatment, and Quality of Life

Outcomes in Waldenström Macroglobulinemia: Insights from the WhiMSICAL Patient-Derived Registry

Special Instructions: Letter of Support for YIA Grant attached

Select abstract file to attach:

/home/dkwolfpk2016/public_html/waldenstromworkshop/media/breezingforms/uploads/iwwm13whimsicalabstract.pdf

Additional file (optional):

/home/dkwolfpk2016/public_html/waldenstromworkshop/media/breezingforms/uploads/letterofsupportprofjudithtroutman.pdf

Please consider me for a YIA grant: YIA Grant Consideration

Conference: IWWM13