Global Waldenström's Macroglobulinemia patient-derived data registry, WhiMSICAL, highlights real-world treatment outcomes and COVID-19 data

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INTRODUCTION

Clinical trial data is limited in rare cancers like Waldenström's Macroglobulinemia (WM), which has seen only seven, mostly small sample size, phase III trials published in the last 20 years. Registries can provide real-world complementary data but are often geographically restricted. Capturing patient-derived data, however, makes a global registry feasible. WhiMSICAL (Waldenström's Macroglobulinemia Study Involving CArt-wheeL) is the first global registry capturing patient-derived data in WM (Tohidi-Esfahani et al, Am J Hematol 2021).

AIM

The registry aims to have a continuously expanding patient-derived dataset, generating hypotheses around WM presentations, treatment outcomes and patient-reported outcomes. It was interrogated to identify real-world treatment efficacy, quality of life (QoL) and coronavirus disease 2019 (COVID-19) data.

METHOD

- The registry captures data through www.cart-wheel.org, an online rare cancer database, utilizing a tailored questionnaire developed by clinician and patient investigators.
- WM patients complete consent online, then enter symptom, pathology, treatment, QoL (EORTC QLQ-C30) and COVID-19 data, and can return to update their data on an ongoing basis.
- Recruitment is driven by the International Waldenström's Macroglobulinemia Foundation investigators through social media messaging.
- Time to next treatment (TTNT) was assessed from start of first therapy to start of second therapy. Patients without a documented second therapy were censored at the time of last edit to their account.
- COVID-19 questions included testing, disease severity, vaccination and impact on WM management.

RESULTS

As of July 2021, 558 patients from 20 countries have entered data, most commonly from the USA (50%), Australia (22%) and the UK (9%, Figure 1).

- Median age at diagnosis was 61 years (range 24-83), with male predominance (61%).

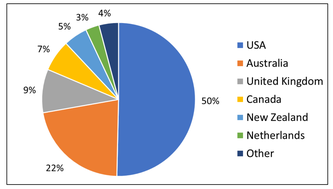

Figure 1. Participants by country of residence

These therapies were selected for outcome analysis. Baseline characteristics of each cohort at 1st treatment are outlined in Table 1. In the treatment naïve setting, BR was superior to DRC and Rit., with trend to superiority to BTKi (Figures 2-3). BTKi, however, was superior in relapsed/refractory patients (Figure 4) and was most common in this setting.

371 patients reported treatment, with a total of 54 unique first-line therapeutic combinations listed. The most common were bendamustine rituximab (BR, n=94), rituximab monotherapy (Rit., n=52), dexamethasone rituximab cyclophosphamide (DRC, n=33) and Bruton tyrosine kinase inhibitors (BTKi, n=32).

	All treated, n=371	BR, n=94	BTKi, n=32	DRC, n=33	R, n=52
Age at treatment – median yrs (range)	62 (57-69)	65 (60-70)	66 (61-69)	61 (52-66)	65 (59-70)
Comorbidities* - any	112 (31)	29 (31)	5 (16)	10 (30)	18 (35)
CVD	38 (10)	10 (10)	2 (6)	3 (9)	6 (12)
Resp	40 (11)	13 (14)	2 (6)	5 (15)	5 (10)
DM	18 (5)	4 (4)	0 (0)	1 (3)	2 (4)
CKD	40 (10)	10 (10)	1 (3)	4 (12)	8 (15)
Multiple	20 (5)	6 (6)	0 (0)	3 (9)	3 (6)
IgM mg/dL – median (IQR)#	3452 (1775-5490), n=155	3500 (1703-5040), n=45	2990 (1524-5755), n=16	3420 (2775-5663), n=15	1907 (962-4066), n=20
Hb g/dL – median (IQR)#	10.3 (8.7-11.5), n=164	10.1 (8.8-11), n=45	10.9 (9.5-12.3), n=17	9.7 (8.7-11.1), n=17	11.4 (8.7-13.8), n=16

Table 1. Baseline characteristics of patients at time of first treatment. CVD – cardiovascular disease, including stroke, Resp – respiratory, DM – diabetes mellitus, CKD – chronic kidney disease.* 5 patients in All treated and 1 patient in BTKi did not enter comorbidity data. # Missing data, cohort size indicated.

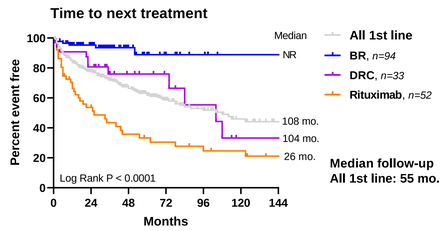

Figure 2. Kaplan-Meier analysis of time to next treatment for all and the three most common 1st-line therapies. Mo. – months, NR – not reached.

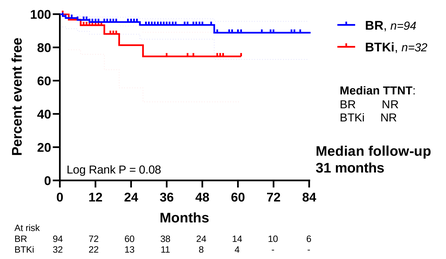

Figure 3. Kaplan-Meier analysis of time to next treatment (TTNT) for BR and BTKi in treatment naïve patients. Mo. – months, NR – not reached.

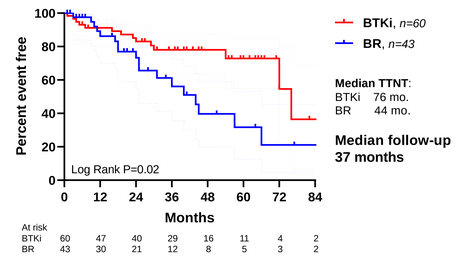

Figure 4. Kaplan-Meier analysis of time to next treatment (TTNT) for BR and BTKi in relapsed/refractory patients. Mo. – months, NR – not reached.

Patients currently on BTKi therapy (n=64) also reported better QoL (EORTC QLQ-C30 global scale) compared to patients treated with chemo/immunotherapy within the last 12 months (n=84), mean scores 82±14 and 73±21, respectively (p=0.005, Figure 5). This was despite more prior lines of treatment (median 2 [IQR 1-4] compared to 1 [IQR 1-1]; p<0.0001).

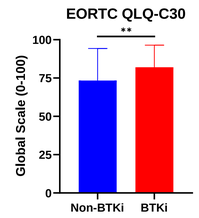

Figure 5. Quality of life, as measured by the EORTC QLQ-C30 global scale, of patients currently on Bruton tyrosine kinase inhibitor (BTKi, n=64) therapy and those not exposed to BTKi and treated within the last 12 months (n=84).
** denotes p<0.01

324 (58%) patients provided COVID-19 data. The majority reported management impact: 53% reported reduced face-to-face consultations and 5% had treatment schedule disruption. 11/144 (8%) tested positive for the virus, none post-vaccine, and 93% were vaccinated (Figure 6).

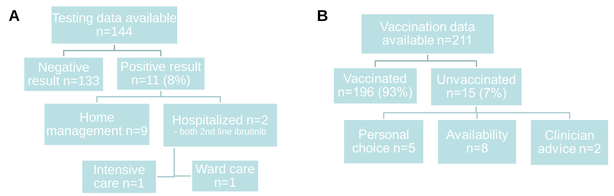

Figure 6. COVID-19 testing (A) and vaccination (B) in the WhiMSICAL registry.

CONCLUSION

The WhiMSICAL registry provides a scientifically robust and ethically approved portal for the patients' voice. The data highlight the real-world efficacy of combination chemoimmunotherapy, particularly first-line BR, while suggesting a better QoL with BTKi than other therapies. As this global data platform grows, the breadth of data allows for new insights into WM with patient reported outcomes advancing knowledge and facilitating treatment decisions for clinicians and patients.

Patients can join WhiMSICAL by registering and consenting at: www.cart-wheel.org

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