WhiMSICAL (Waldenström's Macroglobulinemia Study Involving CArt-wheeL):

A Global WM Registry for the Patient's Voice

Ibrahim Tohidi-Esfahani, B Med, FRACP[1,2], Andrew Warden[3], Peter DeNardis[4], Elena Malunis[4], Joshua Bomsztyk MBChB MRCP,[5] Shirley D'Sa, MD, FRCP, FRCPath[5], Marie José Kersten, MD, PhD[6], Maria Lia Palomba, MD[7], Ruth Spearing, MBChB , FRACP, FRCPA[8,9], Luke Rowsell BTech MPH PhD,[10] Mario D'Souza MSc PhD,[11] Sheeba K. Thomas, MD[12], Constantine S. Tam, MBBS, MD, FRACP, FRCPA[13-15], Stephen Opat MBBS FRACP FRCPA,[10,16] Clare Scott, MBBS PhD FRACP[17,18], Carl Harrington[4] and Judith Trotman, MBChB, FRACP, FRCPA[1,2]

1. Haematology, Concord Repatriation General Hospital, Sydney, Australia, 2. University of Sydney, Sydney, Australia, 3. WMozzies Australian Patient Support Group for Waldenström's Macroglobulinemia, Sydney, Australia, 4. International Waldenström's Macroglobulinemia Foundation, Sarasota, FL, 5. 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. Lymphoma Service, Memorial Sloan Kettering Cancer Center, New York, NY, 8. Christchurch Hospital, Christchurch, NZ, 9. University of Otago, Otago, NZ, 10. Monash University, VIC, Australia, 11. Clinical Research Centre (Statistics), Sydney Local Health District, NSW, Australia, 12. Lymphoma/Myeloma, MD Anderson Cancer Center, Houston, TX, 13. Haematology, St Vincent's Hospital, VIC, Australia, 14. University of Melbourne, VIC, Australia, 15. Peter MacCallum Cancer Centre, Melbourne, Australia, 16. Monash Health, Clayton, VIC, Australia, 17. Walter and Eliza Hall Institute of Medical Research, Melbourne, Australia, 18. Department of Medical Oncology, Royal Melbourne Hospital, Melbourne, Australia

BACKGROUND

Waldenström's Macroglobulinemia (WM), a rare cancer with easily trackable disease parameters, is difficult to study in large trials. Patient-derived data are an attractive option to increase breadth of knowledge. Patient-reported outcomes (PROs) are becoming increasingly valued, with integration of electronic reporting of symptoms in cancer care shown to improve health outcomes and survival (Basch et al, *JAMA* 2017).

CART-Wheel.org (Centre for Analysis of Rare Tumors) is an ethically-approved, global, online rare cancer database for patient-derived data.

AIM

To develop a continuously expanding patient-derived dataset, providing a foundation for hypothesis generation around WM PROs and improving understanding of this rare disease.

METHOD

- Ethically approved WM-specific extension to www.cart-wheel.org questionnaire developed by clinician and patient investigators (2016)
- Participants complete consent online, enter their symptom, pathology and treatment data
- Recruitment by International Waldenström's Macroglobulinemia Foundation (IWMF) investigators utilized social media platforms
- A pilot validation was performed comparing patient- and data-manager-entered data using Australian and New Zealand Lymphoma and Related Diseases Registry (LaRDR) sites to evaluate data accuracy
- Data analysis conducted utilizing independent samples Mann-Whitney U-test, cross-tabulation and Pearson Chi-squared.

RESULTS

In the six months following international promotion, over 200 patients were recruited. As of June 2018, 303 participants from 14 countries have enrolled in WhiMSICAL.

Participants were predominantly male (61%), from USA (45%) and Australia (23% - Figure 1), with median age 68 years (43-86), diagnosed at median 60 years old (41-83, Figure 2).

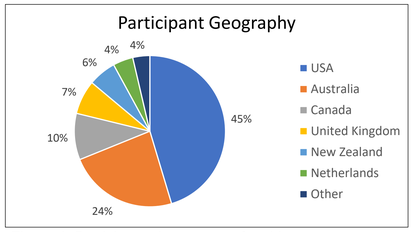


Figure 1. Participants by country of residence

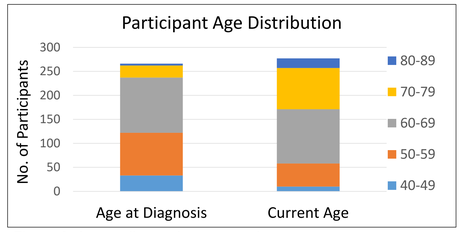


Figure 2. Age at diagnosis compared to current age

Fatigue was the most common symptom at diagnosis (45%, Table 1), correlating with median hemoglobin 10.1g/dL (IQR8.8-12.1g/dL, n=48) compared to 12.3g/dL (IQR 10.9-13.4g/dL, n=55) in those without fatigue (p<0.001).

Symptoms at Diagnosis	No. of patients (% of respondents)
Fatigue	101 (45)
B-symptoms	48 (21)
Peripheral Neuropathy	43 (19)
Dyspnoea	29 (13)
Leg Cramps	23 (10)
Epistaxis	21 (9)
Asymptomatic	64 (29)

Table 1. Most common symptoms at diagnosis (n=224)

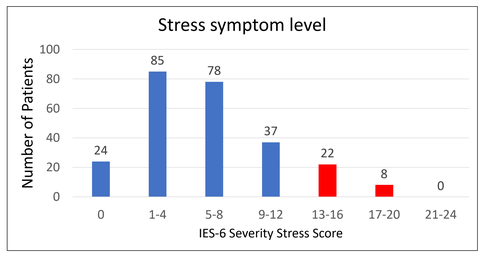


Figure 3. Stress levels measured by Impact of Event-6 Severity Scale

There were fewer government funded and clinical trial therapies in the US (Table 3). However, the median time from diagnosis to first line of therapy for US patients was 48 days (IQR 12-391, n=84) vs. Rest of World (ROW) 114 days (IQR 23.8-671.8, n=100), (p=0.056).

Marked treatment diversity was seen, with 37 unique first-line therapeutic combinations entered by 180 patients (Figure 4).

Using the Impact of Event Scale (no stress=0, maximal=24) for symptoms of post traumatic stress disorder, 11.8% of respondents (30/254) scored ≥13 (PPV 94% for PTSD – red columns, Figure 3).

Median pathology results at diagnosis are listed in Table 2.

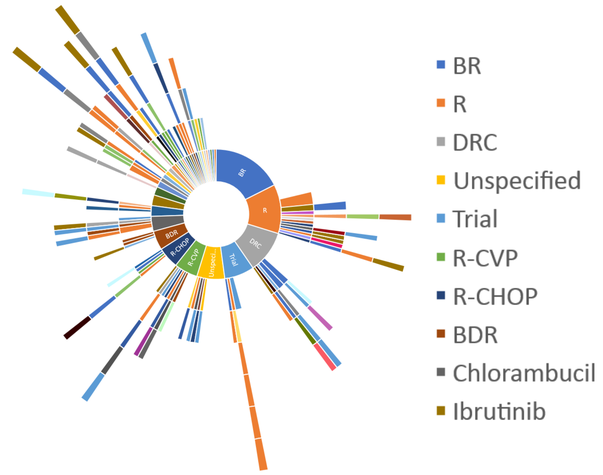
Pathology Test at diagnosis	Median (IQR)	No
IgM (mg/dL)	2750 (1530-3910)	101
Hemoglobin (g/dL)	11.1 (9.4-12.7)	106
Paraprotein (g/dL)	2.1 (1.2-3.3)	64
Bone marrow involvement (%)	47 (27.3-74)	114

Table 2. Median pathology test results at diagnosis

Treatment access	U.S. patients	ROW patients	P value
Government funded	55 (29)	112 (59)	<0.001
Clinical trial	8 (4)	24 (13)	0.003
Total No of Treatments	189	190	NA

Table 3. Treatment access by country of residence

Figure 4. Sunburst chart displaying therapeutic regimens. Each color represents a unique regimen, each ring: a line of therapy (1st line in centre).
BR – Bendamustine Rituximab, R – Rituximab, DRC – Dexamethasone Rituximab Cyclophosphamide, RCVP – Rituximab, Cyclophosphamide, Prednisone, RCHOP – Rituximab Cyclophosphamide Doxorubicin Vincristine, BDR – Bortezomib Dexamethasone Rituximab.



Data for 21 patients were available for validation with LaRDR, with high completion rates and good concordance with diagnosis and treatment data but higher variability with IgM data (Table 4).

	Date of Diagnosis	1st treatment	Date of 1st Treatment	Hb at diagnosis	IgM at diagnosis
LaRDR completion rate (%)	100	100	100	86	67
WhiMSICAL completion rate (%)	100	86	71	62	52
Concordance rate (%)	86	78	80	90	63

Table 4. Comparison of WhiMSICAL patient-derived data with LaRDR data (n=21)

CONCLUSION

WhiMSICAL represents an innovative and robust platform to generate patient-derived data and reported outcomes, with demonstrated good concordance with lymphoma registry data. Further quality of life questions (EORTC QLQ-C30) have recently been added. As an expanding and increasingly reliable body of data, WhiMSICAL has the potential to map real-world PROs, break down clinician-patient barriers and provide a scientific and ethically-approved portal for patients' voices globally.

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

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