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

Empowering patients internationally to contribute patient-derived data for observational research

Ibrahim Tohidi-Esfahani, B Med, FRACP[1,2], Andrew Warden[3], Peter DeNardis[4], Elena Malunis[4], Shirley D'Sa, MD, FRCP, FRCPath[5], Marie Jose Kersten, MD, PhD[6], Maria Lia Palomba, MD[7], Ruth Spearing, MD, FRACP, FRCPA[8,9], Loic Ysebaert, MD, PhD[10], Sheeba K. Thomas, MD[11], Constantine S. Tam, MBBS, MD, FRACP, FRCPA[12,13,14], Clare Scott, MBBS PhD FRACP[15,16], Carl Harrington[4] and Judith Trotman, MBChB, FRACP, FRCPA[17]

1. Haematology, Concord Repatriation General Hospital, Concord, 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. University College Hospital, London, GBR, 6. Department of Hematology, Academic Medical Center, Amsterdam, Netherlands, 7. Lymphoma Service, Memorial Sloan Kettering Cancer Center, New York, NY, 8. Christchurch Hospital, Christchurch, NZL, 9. University of Otago, Otago, NZL, 10. Departement d'Hematologie, IUCT-Oncopole, Toulouse, France, 11. Lymphoma/Myeloma, UT MD Anderson Cancer Center, Houston, TX, 12. Haematology, St Vincent's Hospital, Kew, VIC, Australia, 13. University of Melbourne, Melbourne, Australia, 14. Peter MacCallum Cancer Centre, Melbourne, Australia, 15. Walter and Eliza Hall Institute of Medical Research, Melbourne, Australia, 16. Department of Medical Oncology, Royal Melbourne Hospital, Melbourne, Australia, 17. Concord Repatriation General Hospital, Sydney, 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

- An ethically approved WM-specific extension to the www.cart-wheel.org questionnaire, developed by clinician and patient investigators, went online June 2016
- Participants complete an online consent form and provide data on their symptoms, pathology results, and treatments including tolerance, response parameters and how treatments were accessed.
- International promotion by the International Waldenström's Macroglobulinemia Foundation was undertaken through utilization of multiple social media platforms
- Data analysis is conducted utilizing independent samples Mann-Whitney U-test, cross-tabulation and Pearson Chi-squared.

RESULTS

The local recruitment drive (69 patients) and user testing demonstrated initial project feasibility. Following international promotion May 2017, 210 additional patients were recruited in 6 months.

The 279 patients were predominantly from USA (45%), and Australia (23%), (Figure 1), with median age at participation 67 years (43-85), median age at diagnosis 60 years (41-83, Figure 2), and a male predominance (61%).

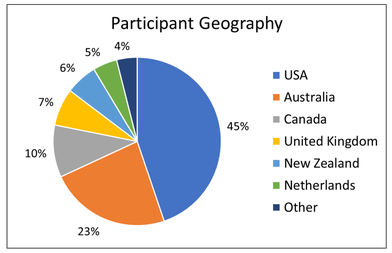

Figure 1. Country of residence (n=279)

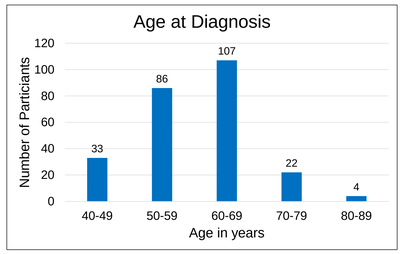

Figure 2. Age at diagnosis (n=252)

Fatigue was the most common symptom at diagnosis (44%, Table 1), correlating with median hemoglobin 10.2g/dL (5.2-15.4g/dL, n=48) compared to 12.5g/dL (5.4-15.7g/dL, n=53) in those without fatigue (p<0.0001), and trend to higher IgM (median IgM 3125mg/dL, non-fatigued 2125mg/dL, p=0.097).

Symptoms at Diagnosis	Number of patients (% of question respondents)
Fatigue	92 (44)
B-symptoms	61 (29)
Peripheral Neuropathy	45 (21)
Dyspnoea	26 (12)
Leg Cramps	23 (11)
Epistaxis	21 (10)
Asymptomatic	58 (28)

Table 1. Most common symptoms at diagnosis (n=210)

Pathology Test	Median at Diagnosis (range)	No	Median at first treatment (Range)	No	p-value
IgM (mg/dL)	2750 (78-9779)	101	3510 (1-12045)	78	0.027
Hemoglobin (g/dL)	11.3 (4.4-15.7)	107	10.6 (4.4-15.4)	88	0.015
Paraprotein (g/dL)	2.1 (0.1-8.9)	65	2.9 (0.3-9.7)	49	0.144
Neutrophils (x 10^9/L)	3.6 (0.6-75)	80	3.4 (0.3-75)	64	0.532
Platelets (x 10^9/L)	240.5 (44-531)	104	219.5 (44-531)	82	0.741
% bone marrow involvement	45 (3-98)	104	68.5 (5-95)	24	0.013

Table 2. Median pathology test results at diagnosis compared to first treatment

Median IgM at diagnosis was 2750mg/dL & hemoglobin 11.3g/dL. At first treatment, medians were 3510mg/dL (p=0.027) & 10.6g/dL (p=0.015), respectively (Table 2).

From diagnosis, median time to first treatment was 82 days (0-8803, n=170). Median for USA patients was 48 days (0-8803, n=79) and Rest of World (ROW) 122 days (0-5765, n=91), (p=0.086).

Forty different first-line therapeutic combinations were entered by 173 patients (Table 3).

1st line Treatment (n= 173)	Number of participants (% of respondents)
Rituximab, Bendamustine	29 (17%)
Rituximab	23 (13%)
Dexamethasone, Cyclophosphamide, Rituximab	18 (10%)
R-CHOP	11 (6%)
R-CVP	10 (6%)
Bortezomib, Dexamethasone, Rituximab	9 (5%)

Table 3. Most common first line therapeutic combinations (n=173)

Most patients were either untreated (24%) or had only one line of therapy (47% - Figure 3).

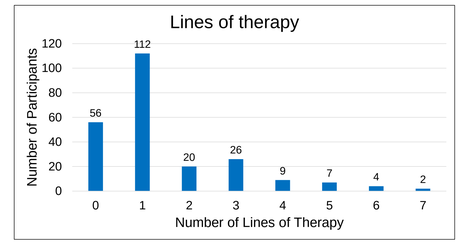

Figure 3. Number of lines of therapy listed by respondents (n=236)

Treatment access data was available for 180/194 (93%) therapies entered by USA patients: 55/180 (31%) therapies were government funded and 7/180 (4%) accessed through clinical trial participation. In ROW patients, access data was available for 177/201 (88%) therapies: 108/177 (61%) were government funded and 20/177 (11%) through clinical trial participation.

CONCLUSION

The WhiMSICAL study demonstrates a robust data-collection platform via www.cart-wheel.org and the feasibility of its global use for WM patient-derived data. Future database additions will include validated PROs (EuroQol EQ-5D-5L). Results appear comparable to registry data and formal validation is planned. With further recruitment and ongoing data entry by each participant, an expanding body of "big data" will increase knowledge of the presentations and treatment experiences of WM patients. WhiMSICAL has the potential to map real-world therapy compliance and efficacy, along with global patterns of treatment access.

ACKNOWLEDGMENTS

The Concord Repatriation General Hospital Research Committee kindly provided funding support for travel to the presenting author.

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

Disclosures: Tohidi-Esfahani: *Janssen Cilag:* Other: Funding facilitating research paid to third party (BioGrid Australia). **Warden:** *Janssen Cilag:* Other: Funding facilitating research paid to third party (BioGrid Australia). **D'Sa:***Janssen Cilag:* Consultancy, Honoraria, Other: Education grant, Research Funding; *Amgen:* Consultancy, Honoraria, Research Funding. **Kersten:** *Kite Pharma:* Honoraria; *Novartis Pharmaceuticals Corporation:* Honoraria; *MSD:* Honoraria; *BMS:* Honoraria; *Gilead Sciences:* Honoraria; *Mundipharma:* Honoraria; *Milennium/Takeda:*Honoraria, Research Funding; *Celgene:* Honoraria, Research Funding; *Roche:* Honoraria, Research Funding; *Amgen:* Honoraria. **Ysebaert:** *Janssen:* Consultancy, Research Funding, Speakers Bureau. **Thomas:** *Celgene:*Research Funding; *Bristol Myers Squibb:* Research Funding. **Tam:** *Janssen Cilag:* Honoraria, Research Funding; *Abbvie:* Honoraria, Research Funding; *Roche:* Honoraria, Research Funding. **Harrington:** *Abbvie:* Equity Ownership; *Gilead:* Equity Ownership. **Trotman:** *Celgene:* Membership on an entity's Board of Directors or advisory committees, Other: Funding facilitating research paid to third parties. All positions non-remunerated; *Roche:* Membership on an entity's Board of Directors or advisory committees, Other: All positions non-remunerated, Speakers Bureau; *Takeda:* Membership on an entity's Board of Directors or advisory committees, Other: Position non-remunerated; *Janssen Cilag:* Membership on an entity's Board of Directors or advisory committees, Other: Funding facilitating research paid to third parties. All positions non-remunerated, Speakers Bureau.