Real-world treatment outcomes in the global Waldenström's Macroglobulinemia patient-derived data registry, WhiMSICAL

Authors:

Ibrahim Tohidi-Esfahani,[1,2] Andrew Warden,[3] Peter L. DeNardis,[4] Elena Malunis,[4] Michelle Postek,[4] Shirley D'Sa,[5] Marie José Kersten,[6] Sheeba Thomas,[7] M. Lia Palomba,[8,9] Adam J. Olszewski,[10,11] Newton Guerin,[4] Clare L. Scott,[12,13] Judith Trotman[1,2]

Affiliations

[1]Haematology Department, Concord Repatriation General Hospital, Sydney Australia; [2]University of Sydney, Sydney, Australia; [3]WMozzies, Australian Patient Support Group for WM; [4]International Waldenstrom's Macroglobulinemia Foundation, Sarasota, Florida, USA; [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 Lymphoma/Myeloma, The University of Texas MD Anderson Cancer Center, Houston, TX; [8]Lymphoma Service, Department of Medicine, Memorial Sloan Kettering Cancer Center, NY, USA; [9]Department of Medicine, Weill Cornell Medical College, New York, USA; [10]Department of Medicine, Warren Alpert Medical School, Brown University, Providence, RI, USA; [11]Division of Hematology-Oncology, Rhode Island Hospital, Providence, RI, USA; [12]Walter and Eliza Hall Institute of Medical Research, Melbourne, Australia; [13]Department of Medical Oncology, Royal Melbourne Hospital, Melbourne, Australia

Introduction: WhiMSICAL (Waldenström's Macroglobulinemia Study Involving CArt-wheeL) is the first global Waldenström's Macroglobulinemia (WM) registry capturing patient-derived data to complement clinical trials data in this rare cancer (Tohidi-Esfahani et al, Am J Hematol 2021). The registry was interrogated for treatment outcomes of chemoimmunotherapy (CIT) compared to Bruton tyrosine kinase inhibitors (BTKi).

Methods: WhiMSICAL 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, quality-of-life (QoL, EORTC QLQ-C30) and COVID-19 data, and can return to update their data on an ongoing basis. Recruitment is driven by social media messaging by the International Waldenström's Macroglobulinemia Foundation investigators. Time to next treatment (TTNT) was assessed from start of therapy to start of next therapy. Patients without a documented next therapy were censored at the time of last edit to their account. TTNT was compared between first-line CIT and BTKi-containing regimens. From within these cohorts, BTKi monotherapy (mBTKi) was compared with the three most common CIT regimens. mBTKi was also compared to the most common CIT in the relapsed/refractory setting, with QoL scores compared after both first-line and relapse/refractory use.

Results: As of data cut-off 26th July 2022, 642 patients from 21 countries have participated in the registry, predominantly from USA (53%), Australia (20%) and the UK (9%). Median age at diagnosis was 62 years (range 24-89) with male predominance (61%). 439 patients documented first-line therapies; the most common therapies were bendamustine rituximab (BR, n=110), rituximab monotherapy (n=63), dexamethasone rituximab cyclophosphamide (DRC, n=37) and ibrutinib (n=31). The CIT cohort (n=370) was marginally younger, median age 62 (range 35-85) years, BTKi-containing cohort (n=53) 66 (43-93) years (p=0.02), but with a trend to more comorbidities; 33% and 25%, respectively (p=0.29). The DRC cohort was significantly younger than mBTKi (n=42), median 61 years vs 68, respectively (p<0.01), but otherwise, there was no significant difference between any of the cohorts with respect to age, comorbidities, baseline IgM or haemoglobin. With median follow-up of 56 months, TTNT after first-line CIT and BTKi was not significantly different: 78 months vs not reached,

respectively (p=0.25, figure 1A). mBTKi was equivalent to BR and DRC, but superior to rituximab (figure 1B-D). In the relapsed/refractory setting, mBTKi (n=86) had a significantly longer TTNT than BR (n=43): 86 vs 45 months, respectively (p=0.003, figure 1E). This was coupled with better reported EORTC QLQ-C30 global scale scores. Across all lines of therapy, the first available QoL scores within 12 months of BR treatment (n=51) or while still on mBTKi (n=91) were compared. Patients on mBTKi had mean score 78 ± (SD) 17, while BR-treated patients reported mean score 65±21 (p=0.0001). This was despite heavier treatment burden in the mBTKi cohort (mBTKi treatment lines: median 2 [IQR 1-3], BR: 1 [IQR 1-2]; p<0.001, figure 1F).

Conclusion: WhiMSICAL, a large global patient-derived data registry, is accumulating valuable data on a key endpoint of relevance for WM patients, TTNT, together with QoL data. With a comparable TTNT of CIT and BTKi in 1st line, but superiority of BTKi in relapse, these real-world data suggest BTK inhibitors are best reserved for use in the relapse setting.

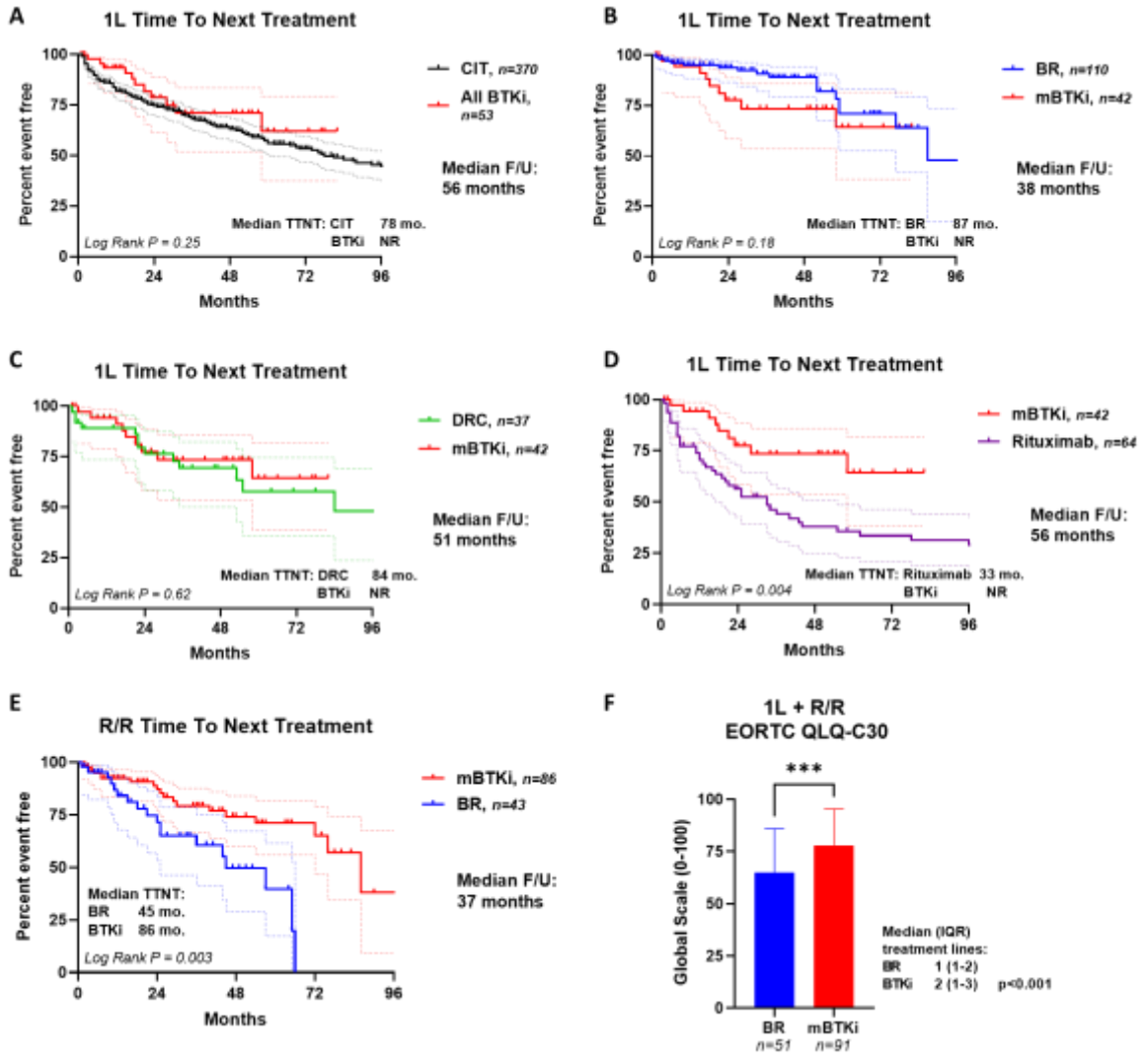

Figure 1. Time to next treatment (TTNT) and quality of life (QoL) outcomes for chemoimmunotherapy (CIT) and Bruton tyrosine kinase inhibitors (BTKi). Kaplan-Meier survival analysis of time from start of first-line CIT and BTKi-containing regimens (All BTKi) to start of next treatment (A). Within these cohorts, Kaplan-Meier analysis was used to compare TTNT between BTKi

monotherapy (mBTKi) and the most common CIT regimens (B-D). In the relapsed/refractory (R/R) setting, TTNT after mBTKi was compared to bendamustine rituximab (BR) (E). Across all lines, the first available EORTC QLQ-C30 global scale QoL scores within 12 months of BR treatment or while still on mBTKi were compared (F). Mean and standard deviation are shown. 1L – first-line, F/U – follow-up, mo. – months, NR – not reached, DRC – dexamethasone rituximab cyclophosphamide, IQR – interquartile range. ***p<0.001