An Analysis from the Rory Morrison Registry for Waldenström's: Patient Demographics, Disease Characteristics and Evolving Treatment Choices

Olive Tomkins, Joshua Bomsztyk, Helen McCarthy, Jaimal Kothari, Dima EL Sharkawi, Guy Pratt, Charalampos Kyrakiou, Ali Rismani and Shirley D'Sa

1University College London Hospitals 2Royal Bournemouth Hospitals 3Oxford University Hospitals 4The Royal Marsden Hospital 5University Hospitals Birmingham 6London North West Healthcare

Background

Waldenström macroglobulinaemia (WM) is a rare non-Hodgkin B cell lymphoma. Information about patient demographics and disease characteristics are limited. Treatment is indicated for symptomatic patients. Treatment regimens have evolved significantly in recent years and now include novel, targeted therapies. The Rory Morrison Registry (RMR) has granular clinical data on close to 1000 UK patients with IgM-related conditions. Through detailed analysis, we seek to draw conclusions about UK patient demographics and disease characteristics, as well as to evaluate how treatment practices have evolved.

Methods

The RMR was launched in 2017. It is a secure web-based registry, serially updated with comprehensive diagnostic, treatment and response data from centres across England and Wales under Section 251 of the Health Research Authority of the National Health Service. The RMR was interrogated for demographics, pathological characteristics, treatment information and survival status. Kaplan Meier and log rank analyses were performed.

Results

671 patients fulfilled fulfils diagnostic criteria for WM. The median age at diagnosis was 64 years (range 27-92, Figure 1). Year of diagnosis spanned 1978-2019. Male to female ratio was 1.62:1. Ethnicity: 90.4% Caucasian, 5.9% Asian, 1.3% Afro-Caribbean, 0.7% mixed, and 1.6% of other categories.

Diagnostic Workup

- Median Hb 112g/L (33-170), platelets 242 x 10^9/L (3-806), B2M 3 mg/L (0.2-56.3) and M-protein 17g/L (0-110.5).
- MYD88 L265P was detected in 84.2% (160/190); CXCR4 mutations were detected in 26.3% (20/76).
- IPSSWM scores [1] at diagnosis was available for 352 patients: 122 were low risk (34.7%), 109 intermediate risk (29.3%) and 123 high risk (45%).
- Notable associations: peripheral neuropathy (n=74), cryoglobulinaemia (26), amyloidosis (12), Schnitzler’s syndrome (7).

Treatment Information

440 patients (65.6%) had received treatment:

- Median time from diagnosis to treatment was two months (0-312)
- Treatment indications: hyperviscosity 24.8%, fatigue 21.6% and peripheral neuropathy 9.8%, Hb <100g/L 47%
- CNS involvement was a feature in 1.5% and high-grade transformation (HGT) 1.5%.
- Number of treatment lines received: 43.6% one line, 24.1% two lines, 4.8% three lines, 6.6% four lines and 10.9% five lines.

Treatment Regimens

In the past decade, 27.8% had received DRC, 16.4%, R-Bendamustine, 8.9% rituximab monotherapy, 7.7% R-CHOP and the rest varying combinations. 2.2% had received Bortezomib-containing therapy. Prior to 2010, chlorambucil (21.8%), R-CHOP (10.9%) and FC (9.3%) were the most frequently used first line treatments. BTK-inhibitors have become more used second line therapy, with 88 patients having received this at some point in their disease course, representing 23% of regimens after 2010 (Figure 3).

Survival Analysis

- 118 patients are deceased. Only 30 patients have a recorded cause of death: 7 progressive disease, 6 from pneumonia, 5 from sepsis (2 were neutropenic), 3 from HGT, 2 from haemorrhage, 2 from thrombotic events, and 1 from WM CNS relapse.
- 5-year and 10-year overall survival (OS) rates from diagnosis were 90.5% and 79.4%, with a significant difference in OS rates according to IPSSWM risk at diagnosis (p<0.001, figure 2).
- There was a trend towards difference in OS rates (P 0.065) according to MYD88 status, with somewhat poorer OS rate amongst MYD88 wild-type patients. CXCR4-status did not impact the OS rate in this cohort (p 0.93).

Conclusions

The median age at diagnosis was 64 years, with a third of patients diagnosed under the age of 60. The lower than average MYD88 L265P incidence likely reflects earlier methodology for detection which was less sensitive; CXCR4 is not routinely commissioned in the UK until it influences treatment choices. Although diverse, the most frequent indications for treatment in this cohort are hyperviscosity, fatigue and peripheral neuropathy. OS rates are high and correlate with IPSSWM risk, but a majority of patients had received multiple lines of therapy reflecting the chronically relapsing nature of WM. Treatment practices are clearly evolving, with increasing first line use of DRC and R-Bendamustine, as well as BTK inhibitors for relapsed disease.