W27: Waldenstrom Macroglobulinaemia: Patient characteristics and outcomes according to *MYD88* status in a UK population

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There is a lack of prospective randomised controlled trials to investigate optimal management in Waldenstrom Macroblobulinaemia (WM) due to the rarity and indolent nature of the disease leading to variation in treatment approaches. To capture a UK-wide perspective of patient characteristics, management and outcomes a national registry has been set-up through doctor-patient collaboration, the Rory Morrison Registry for Waldenstrom Macroglobulinaemia.

As of 12th June 2018, 16 centres had entered 427 patients (61% male) with a confirmed diagnosis of WM. The median age was 63 years (range 16-89) at diagnosis (12 patients did not have a known date of diagnosis). Amyloid was diagnosed in 7 of the patients; autoimmune haemolytic anaemia was seen in 16; high grade transformation was diagnosed in 12 patients with a median time of 3 years (range 0-10) from diagnosis of WM to transformed disease. Of the 117 with known *MYD88* status, 95 had the L265P mutation(*MYD88*^{mut}) (81%).

Analysing patients according to *MYD88* status did not reveal any differences between age, haemoglobin, β2M or M protein level between patients with and without the L265P mutation (Table 1). With a median follow-up of 6 years (95%CI 5.3-6.6) by the reverse Kaplan-Meier method, the median overall survival was 29 years (95%CI 15-43) from both diagnosis and

first treatment. In the 117 patients with known *MYD88* status, median survival had not been reached but the mean survival was 20 years from diagnosis for *MYD88*^{mut} patients compared to 13 years for the *MYD88*^{WT} cohort.

283 (66%) patients had received at least one line of treatment. Median time from diagnosis to treatment was 4 months (range 0-312). Median number of lines of treatment was 2 (range 1-10). 27 patients underwent an autologous stem cell transplant and 4 an allogeneic stem cell transplant after a median of 2 lines of chemotherapy. The median time to next treatment was 17 months and 10 months for patients with *MYD88*^{mut} and *MYD88*^{WT} respectively (Figure 1).

Conclusion: There are limitations to this data set including incomplete data entry, the potential for human error in retrospective data entry and that this is likely to be a skewed population as currently centres involved in the registry are tertiary referral centres. Nonetheless, this is a large retrospective series of patients with WM that reflects the variability in characteristics and outcomes of patients with WM. Although the numbers are small and thus lack significance, as has been previously reported there is a suggestion that the outcomes of patients wild-type for *MYD88* is worse than those with the L265P mutation, particularly the shorter time to next treatment. Ibrutinib has only recently been approved for use in relapsed or refractory WM by the National Institute for Health and Care Excellence (NICE) in the UK and this registry will provide invaluable information on the long-term outcomes over the next few years.

TABLE 1

	Overall	*MYD88* L265P	*MYD88* WT	*P* value for mutant vs wild-type
Numbers	427	95	22	
% male	61	62	41	0.06
Median age at diagnosis, years (Range)	63 (16-89)	60(34-84)	58(36-76)	0.35
Median Hemoglobin (g/L) (Range)	112 (33-167)	112 (69-149)	110 (93-144)	0.71
Median M protein (g/L) (Range)	19 (0-110)	25 (0-58)	28 (3-45)	0.93
Median B2M (mg/L) (Range)	3.1 (1-27)	3.65 (2-27)	3.65 (2.4-5.7)	0.49
Median time from diagnosis to treatment 1 (months) (95% CI)	4 (2-6)	5 (2-8)	3 (0-6)	0.2
Median Time from treatment 1 to treatment 2 (months) (95% CI)	13 (8-18)	17 (7-27)	10 (2-18)	0.08
Median number of lines of chemotherapy (Range)	2 (1-10)	2 (1-7)	2(1-8)	0.5
Mean OS from diagnosis (years) (95% CI)	23 (19-27)	20 (17-23)	13 (10-16)	0.7

FIGURE 1 Time from treatment 1 to treatment 2 according to MYD88 status