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POSTER ABSTRACTS

623.MANTLE CELL, FOLLICULAR, AND OTHER INDOLENT B CELL LYMPHOMAS: CLINICAL AND EPIDEMIOLOGICAL

Ethnic Diversity in Presentation of Waldenström Macroglobulinaemia and IgM Mgcs in the United Kingdom- a Real-World Data Analysis

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Introduction:
Waldenström Macroglobulinaemia (WM) is a low-grade B-cell lymphoma characterised by lymphoplasmacytic marrow infiltration with a circulating IgM protein with an incidence of approximately 0.55 cases per 100,000 in the United Kingdom (UK). WM may be asymptomatic, symptomatic and/or associated with IgM-related entities (monoclonal gammopathies) of clinical significance (MGCS). A central aim of the WMUK Charity and Clinical Forum is to systematically upload demographic, clinical data and treatment outcomes from a significant proportion of the UK's WM population. Such data provide important insights on the epidemiology and clinical features of this distinct uncommon disorder. Clinical correlates with ethnicity are important but sparsely characterised. This analysis focusses on baseline demographics and outcomes across different ethnic groups in the UK.

Methods:
We retrospectively reviewed data from the Rory Morrison WMUK Registry, collating descriptive data of WM, non-IgM lymphoplasmacytic lymphoma and IgM MGCS from 24 centres across the UK, diagnosed between June 1978 and June 2023. Research ethics approval was obtained. Baseline characteristics were compared using χ^2 or Fisher's exact tests (categorical variables) or Wilcoxon Mann-Whitney/Kruskal-Wallis tests (continuous variables). Differences were considered significant at p-values <0.05. Statistical analyses were performed using STATA v17.0 (StataCorp, Texas, USA).

Results:
1073 patients with documented self-reported ethnicity and a diagnosis of WM (n=985), non-IgM LPL (n=32) or IgM MGCS (n=88) were included. Those with asymptomatic IgM MGUS were excluded. Of 982 with a diagnosis of WM, 12% (114/985) had concurrent MGCS. Across the entire cohort, IgM MGCS comprised peripheral neuropathy including anti-MAG neuropathy (n=114), cold agglutinin disease/syndrome (n=43), AL amyloidosis (n=20), mixed autoimmune haemolytic anaemia (n=13), cryoglobulinaemia (n=8), Schnitzler syndrome (n=8) and C1 esterase deficiency (n=2). Non-IgM LPL had similar baseline characteristics to WM although a trend towards a lower presenting M-protein (7g/l vs 18g/l, p=0.07).
Ethnicity was categorised in accordance with the UK National Census (ethnicity-facts-figures.service.gov.uk). The majority was white (90%; 968/1073: English/Welsh/Scottish/Irish) including 35 patients identified as 'other' white. The remaining 105 (10%) were from the following ethnic groups (collectively 'ethnic minorities', EM): 54 Asian (22 Indian, 4 Pakistani, 1 Bangladeshi, 7 Chinese, 20 other), 19 Black (5 African, 11 Caribbean, 3 other), 6 Mixed/multiple, 26 Other ethnic group.
EM presented at a younger age compared to the white cohort (60 vs 65 years, $p<0.001$) with a lower presenting M-protein at WM diagnosis (11g/l vs 18g/l, p=0.028). A similar proportion of patients had IgM MGCS in white vs EM cohorts (11% vs 8%, p=0.69). In those with IgM MGCS alone, presenting M-protein was similar across both ethnic categories (5g/l vs 3g/l, p=0.36). *MYD88 L265P* mutation was assessed in 387 WM patients (36%), of which *MYD88 L265P* was identified in 88% (322/364) and *CXCR4* mutation tested in 91 patients and mutated in 29% (26/91). *MYD88*-mutated WM was observed less frequently in the EM versus white cohorts (79% vs 90%, p=0.05). A similar proportion presented with symptomatic WM across ethnic groups (56% vs 53%, p=0.56). In those with WM diagnosed since 2010 (n=956), median follow up was 8 years (95% CI 7-8), median

overall survival was not reached. International Prognostic Scoring System for WM (IPSSWM) was predictive of overall survival. Overall survival estimates did not differ when comparing ethnic groups.

Conclusions:

Analysis of the national registry for WM shows that ethnic minorities comprise 10% of WM/IgM MGCS, present with WM at a younger age, a lower M-protein and with a higher proportion of *MYD88*-wild type cases which may suggest different disease biology. There was no difference in overall survival in our cohort. Limitations include the retrospective analysis of real-world data and incomplete documentation of baseline data. Further analysis of molecular signatures across ethnicities, treatment and outcome is warranted and ongoing.

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