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Treatment decisions in Waldenstrom's Macroglobulinaemia; outcomes from the South East Scotland Cancer Network

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SCAN
South East Scotland Cancer Network

INTRODUCTION

Waldenstrom's macroglobulinaemia (WM), also known as lymphoplasmacytic lymphoma, is a rare type of **indolent non-Hodgkin's lymphoma** typically characterised by an **IgM paraprotein** produced by clonal lymphoplasmacytic cells that harbour an ***MYD88* mutation.**

Although clinical presentation can be varied, the diagnosis of WM often results from an incidental finding in asymptomatic patients. Cohort studies report around 50% of patients do not require treatment 3 years following diagnosis. At present there is **no standard of care** for first line treatment of WM; treatment tends to combine Rituximab with a range of chemotherapy.

The recent **approval by NICE of ibrutinib**, for patients who have received at least one other line of treatment, has significantly changed treatment options for patients with WM. Mutated MYD88 activates BTK, the target of ibrutinib, which results in a downstream pro-survival cell signalling via NF-kB. **Ibrutinib is highly active in WM**, provides durable responses, and is generally well tolerated.

AIMS

We studied patients diagnosed with WM between 2014-2019 to:

1. Describe treatment indications and choice of first line management.
2. Review use of Ibrutinib to highlight a potential unmet need.

METHODS

70 patients were retrospectively identified as having a new diagnosis of WM between 2014 and 2019 from South East of Scotland Cancer Network (SCAN) Multidisciplinary Meeting records.

All patients had a **minimum of 12 months follow up**. The data collected from electronic records included: demographics, symptoms, haematology and biochemistry laboratory parameters, pathology, molecular diagnostics, treatment and outcomes.

Careful attention was given to the reason for treatment initiation, haematological parameters and paraprotein levels at diagnosis and at treatment initiation. Side effects were also recorded where available.

RESULTS

Median age at diagnosis was 74.5 (35-90 years) in our predominantly male cohort (n=55). Most patients were **asymptomatic** at diagnosis (67%, n=47). 20 patients had symptoms necessitating immediate treatment. A further 8 went on to require treatment during the study period. The indications for treatment are summarised in Figure 1.

Of those with symptomatic disease, **9 patients required more than 1 line of therapy**, 2 patients required 3 or more lines. Median duration of response to first-line therapy was 33 months.

INDICATIONS FOR TREATMENT

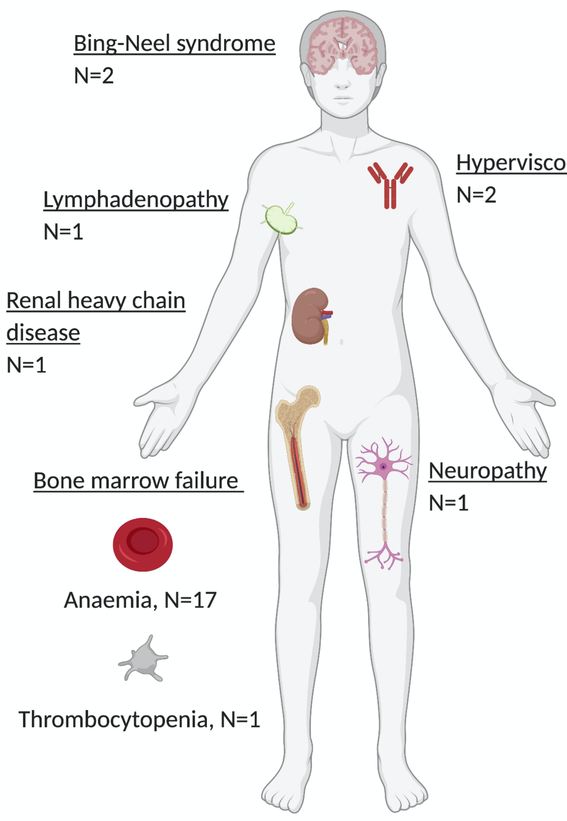
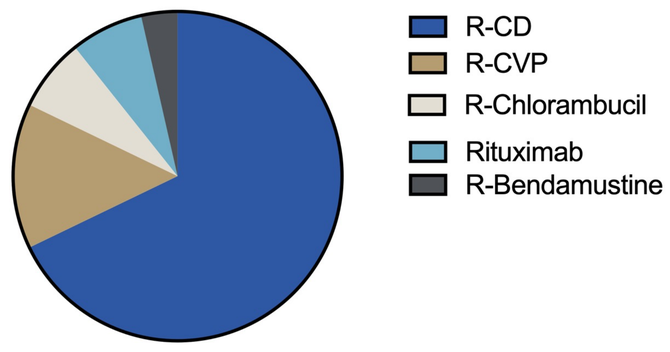
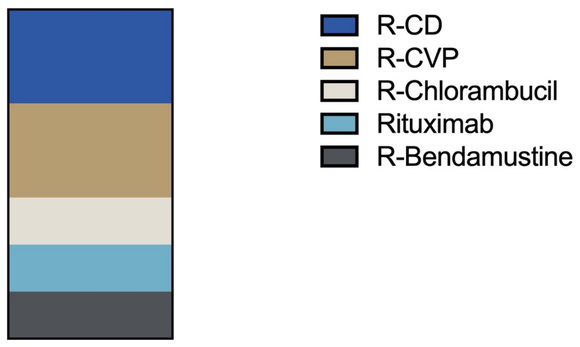


Figure 1: Triggers to treat. *40% of patients required treatment: most common indication was anaemia (n=17).* Overall the mean haemoglobin concentration at the start of treatment was 97g/L (range 58-147g/L).



Total=28

Figure 2a: First line treatment. *Most patients requiring treatment received R-CD as first line therapy. None of our cohort received Ibrutinib as first line therapy.*



Total=7

Figure 2b: Failure of front line therapy. *Proportions of patients requiring a second line of therapy within 1 year of starting initial treatment due to progressive disease or early relapse, categorised by the first line treatment given.*

Three patients in our cohort received Ibrutinib after treatment failure; mean duration 10 months. Ibrutinib has been well tolerated with Grade 3 atrial fibrillation in one patient the only significant toxicity.

12 patients died during the follow up period. 4 of these patients died to due progressive disease prior to the routine availability of ibrutinib. Of these patients one patient declined treatment and two were felt to be unfit for chemoimmunotherapy.

CONCLUSIONS

In many cases, WM behaves in an **indolent** manner, with many patients not requiring treatment. However, our cohort highlights **significant heterogeneity** in a subgroup of patients who went on to require multiple lines of treatment.

Prior to the introduction of ibrutinib, we found that patients unfit for R-CD were experiencing high rates of treatment failure. Indeed, some unfit patients declined chemoimmunotherapy or were offered symptomatic management only. It is clear that many of these patients may have benefited from Ibrutinib and there will no doubt be an increase in ibrutinib use going forward in this patient group.

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