OBSERVATIONAL RETROSPECTIVE STUDY OF THE TREATMENT OF WALDENSTRÖM'S MACROGLOBULINEMIA WITH IBRUTINIB IN ROUTINE CLINICAL PRACTICE IN SPAIN

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Background

Ibrutinib is an oral Bruton tyrosine kinase inhibitor (BTKi) that triggers apoptosis in Waldenström Macroglobulinemia (WM) cells and has reported long-term robust outcomes in clinical trials. Real world evidence (RWE) studies in WM are scarce but helpful to confirm efficacy and safety observed in clinical trials in unselected patient populations.

Methods

The MACRO study is a multicenter, retrospective, observational chart review study that included adult patients with WM treated with ibrutinib in routine clinical practice in Spain to understand the characteristics of this real-world patient population and describe the effectiveness, tolerability, and management of Ibrutinib.

Results

Fifty-two patients from 17 Spanish sites were included from February to June 2023. At Ibrutinib treatment, 30.8% of patients were refractory, and 28.8% had experienced an early progression to the previous line of therapy. *MYD88* L265P mutation was detected in 93.1% of the patients and a mutation of *CXCR4* was only detected in 1 out of 11 with mutational status available. At the time of ibrutinib initiation, most patients (66%) had an iPSSWM score of ≥2; 89.7% had an ECOG 0-1 and a significant proportion of the patients (84.6%) had relevant comorbidities, being the most common previous cardiovascular disease (32.7%), endocrine related diseases (26.9%), previous neoplasia (25%) and respiratory diseases (21.2%). Accordingly, most patients (96.2%) were receiving concomitant medications, with the most common being proton pump inhibitors (56%) and antihypertensives (44%). Additionally, 17.3% and 15.4% of the patients were on anticoagulants and/or antiplatelet agents, respectively. Forty-seven

patients received ibrutinib as monotherapy and 5 in combination with rituximab. The most common clinical manifestations prompting therapy initiation were anemia (32.7%) and fatigue (30.8%). Ibrutinib was predominantly used as a second-line treatment (42.3%) and median treatment duration was 18 months (95% CI: 11.7-30.7). Overall response rate was 92.2%, with a major response rate of 80.5% (56.9% partial response, 21.6% very good partial response, and 2% complete response). Median time to best response was 4 months (95% CI 4.7-10.3). Levels of Hb and IgM improved significantly ($p<0.001$) during treatment. The median progression-free survival (PFS) was 57.2 months (95% CI: 42.3-72), and the median overall survival (OS) and duration of response (DoR) were not reached (Fig. 1). We did not find significant differences in PFS based on the line of treatment, regimen used or initial dose. The most common adverse events (AEs) of any grade were bleeding (30.8%; 87.5% G1-2), diarrhea (23.1%; 100% G1-2), infections (15.4%; 85.7% G1-2), and atrial fibrillation (13.5%; 6/7 G1-2). The most common G≥3 AEs were infections (7.7%, n=3), bleeding (3.8%, n=2) and neutropenia (3.8%, n=2). Mainly due to AEs and surgical procedures, 10 and 28 patients experienced dose reductions and treatment interruptions, respectively. Six patients have been treated after Ibrutinib, predominantly with chemotherapy-based regimens.

Conclusions

This study shows that Ibrutinib in Spain is most used for first relapse treatment in elderly patients with comorbidities, who are often not eligible for clinical trials. Nevertheless, Ibrutinib showed good efficacy and a manageable safety profile.

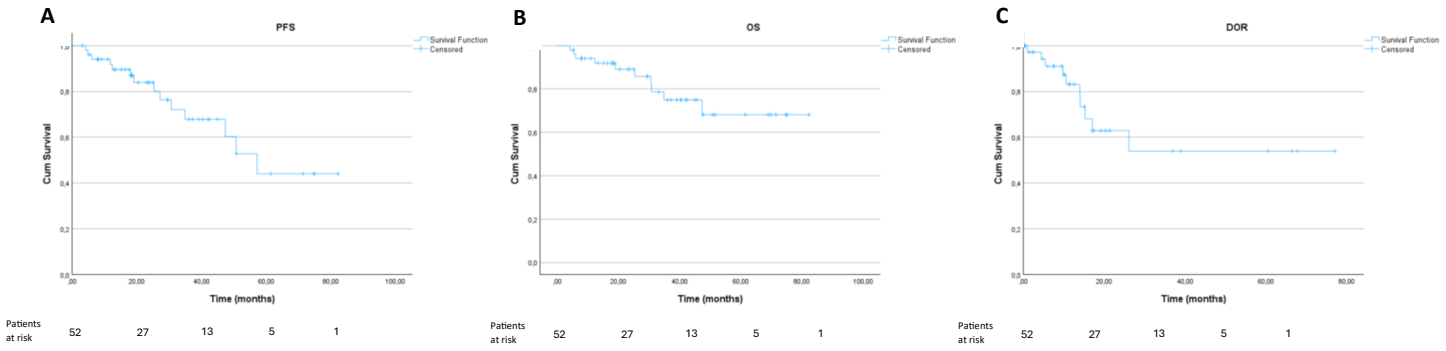

Figure 1. Progression free survival (A), Overall Survival (B) and Duration of Response (C) of Waldenstrom Macroglobulinemia patients treated with Ibrutinib in Spain in routine clinical practice included in our study.