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Treatment and Survival Outcomes of Symptomatic Waldenström's Macroglobulinemia in the Czech Republic Over the Last 10 Years: A Retrospective Analysis from the Registry of Monoclonal Gammopathies

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Introduction

Waldenström's macroglobulinemia (WM) is a rare lymphoplasmacytic lymphoma with unique biological and clinical features. The treatment landscape of WM has changed significantly in the last ten years with the approval of Bruton tyrosine kinase (BTK) inhibitors as an alternative option to anti-CD20 monoclonal antibody-based chemoimmunotherapy. However, there is no universal consensus on the choice of therapy, and real-world treatment patterns may differ. We explore the treatment choices and survival outcomes of symptomatic WM in the Czech Republic over the last ten years.

Methods

A retrospective analysis was performed in a cohort of symptomatic WM patients with clinical and biological data who began treatment between January 2014 and January 2024. Data were analysed retrospectively from the Registry of Monoclonal Gammopathies of the Czech Myeloma Group. All patients signed the written consent before entrance to the registry. The primary endpoints were treatment indication, preferred regimens, response rates, progression-free survival (PFS), time to next treatment (TTNT), and overall survival (OS). The new simplified 11th International Workshop on WM criteria was used for response assessment. Statistical analyses were performed using R software (version 4.4.0).

Results

In total, 109 patients (median age 68.9 years, minimum-maximum 38-90 years, 4.6% ≤50 and 6.4% >80 years old, 58% male) were selected for analysis. The International Prognostic Scoring System for WM (IPSSWM) was known for 78 (72%) patients: low risk 15%, intermediate risk 27%, and high risk 58%. Molecular genetic testing data was available for 71 (65%) patients, with 90% and 30% tested for MYD88 and CXCR4 mutations, respectively. Among the patients evaluated for mutations, 90% tested positive for the $MYD88^{L265P}$ variant, and concurrently, 28.6% tested positive for mutations in the CXCR4 gene. Cytopenia, IgM-associated complications, and B symptoms were the most frequent indications for treatment initiation. In the front-line setting, 84% of patients received chemoimmunotherapy (54% cyclophosphamide, 22% bendamustine, and 8% bortezomib-based combinations), 8% received other combinations, and 3%

received monotherapy. Dexamethasone, rituximab, cyclophosphamide (DRC), and bendamustine, rituximab (BR) were the most commonly used regimens. Only 3 (3%) patients received rituximab maintenance, and one patient had an autologous transplant as consolidation. With a median follow-up of 52 months, the overall response rate was 86% (complete response 1,1%, very good partial response 30,1%, partial response 51,6%), median PFS was 52.8 months (42-74.4 months, 95% CI), and median TTNT was not reached after first-line treatment. Second-line and third-line therapies were administered to 29 and 5 patients, respectively (71% received combination regimens and 21% received ibrutinib). The 3-year and 5-year OS rates from beginning of first line treatment were 89.2% (83.0–95.8%, 95% CI) and 79.3% (70.4–89.3%, 95% CI), respectively. High-risk patients according to the IPSSWM had worse overall survival compared to low-risk patients, 3-year OS rate 87,7% (78.1–98.5, 95% CI) versus 100% (100.0–100.0, 95% CI).

Conclusion

In the last decade, immunochemotherapy was the main WM treatment option in the Czech Republic. Broader use of BTK inhibitors is limited by reimbursement needs. More mutation testing is needed to optimize BTK inhibitor use and further enhance patient outcomes.