Title:

Effectiveness and safety of first-line zanubrutinib in chronic lymphocytic leukemia: The Spanish ReaLLCZa study

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Abstract (maximum 4500 characters (incl. spaces); current: 4413):

Introduction: Zanubrutinib is a next-generation Bruton tyrosine kinase inhibitor that has been available for the treatment of chronic lymphocytic leukemia (CLL) in Spain since July 2023. However, Spanish real-world (RW) evidence on zanubrutinib remains limited, particularly in patients with comorbidities and concomitant medications who are underrepresented in clinical trials The ReaLLCZa study evaluated zanubrutinib effectiveness, safety, and treatment patterns in a Spanish RW CLL/small lymphocytic lymphoma (SLL) cohort. This analysis reports outcomes in patients treated with zanubrutinib in the first-line setting.

Methods: ReaLLCZa was an observational, retrospective, multicenter, national study including adult patients with CLL or SLL treated with zanubrutinib in routine clinical practice in Spain. Patients initiating treatment with zanubrutinib from its first availability (July 2023) to the data cut-off (November 25, 2024) were included. Data collected were pseudonymized and restricted to the information recorded in medical records. Clinical characteristics, treatment patterns, effectiveness, and safety data were analyzed. Effectiveness outcomes included overall response rate (ORR; including complete response, partial response, and partial response with lymphocytosis), duration of response (DOR), progression-free survival (PFS), and overall survival (OS). DOR was assessed from response onset to disease progression or death from any cause, whichever occurred first. PFS was measured from zanubrutinib initiation to progression or death, and OS from zanubrutinib initiation to death. Patients without an event were censored at last follow-up.

Results: A total of 158 patients from 28 centers were identified, 92 (58.2%) of whom received zanubrutinib in the first-line setting and were included for analysis. Median age at diagnosis was 72.5 years (interquartile range [IQR]: 66.5-79.0) and 65.2% of patients were male. Of the 53 patients with available cytogenetic/molecular data, 12 (22.6%) had del(17p) and 18 (34.0%) mutated *TP53*. Among those with known IGHV status (n=69), 48 (69.5%) patients had unmutated IGHV. Karyotypic abnormalities were present in 25 (27.2%) patients; all cases had fewer than 5 abnormalities. At zanubrutinib treatment initiation, most patients with available CLL International Prognostic Index (CLL-IPI) data had high or very high risk of poor 5-year survival (n=42/50; 84.0%). Among 36 patients with documented Cumulative illness Rating Scale (CIRS) data, 16 (44.4%) had a high comorbidity burden (CIRS ≥6). The most common comorbidities included hypertension (58.7%), dyslipidemia (42.4%), and diabetes (28.3%). Notable concomitant medications included antihypertensives (46.7%), antiplatelet agents (14.1%), and direct oral anticoagulants (7.6%). Most patients (n=87; 94.6%) received a daily zanubrutinib dose of 320 mg (n=26 once daily, n=61 twice daily).

In the overall cohort (regardless of line of therapy for zanubrutinib), adverse events (AEs) occurred in 73 (46.2%) patients, serious AEs occurred in 17 (10.8%) patients, and AEs of special interest (AESIs) occurred in 26 (16.5%) patients. No cases of atrial fibrillation (AF) were observed. Among patients receiving first-line zanubrutinib, 16 (17.4%) experienced at least one AESI, most commonly cytopenia (n=9; 9.8%) and bleeding (n=5; 5.4%). Eighteen (19.6%) patients discontinued first-line zanubrutinib during the study period, with toxicity reported as the main reason for discontinuation (n=12; 13.0% of first-line cohort, 66.7% of discontinuations). A comparable proportion of patients discontinued zanubrutinib in the overall cohort (n=31; 19.6%).

Median zanubrutinib exposure in the first-line setting was 14.0 months (IQR: 9.7-18.5). Among 82 patients with evaluable data for zanubrutinib treatment response, the ORR was 90.2% (n=74). Median DOR, PFS, and OS were not reached. At 18 months, PFS and OS rates were 82.7% (95% CI: 69.8%-90.4%) and 87.6% (95% CI: 75.5%-90.4%), respectively.

Conclusions: First-line treatment with zanubrutinib was safe and effective in this Spanish RW cohort of patients with CLL, including those with high-risk disease and a high comorbidity burden encountered in routine clinical practice. No AF was observed. These RW findings with first-line zanubrutinib treatment are consistent with those reported in the SEQUOIA trial and in RW studies from other regions.

Additional information:

Category:

906. Outcomes Research: Lymphoid Malignancies Excluding Plasma Cell Disorders

Type of preferred presentation:

- Poster