

Real-world effectiveness and safety of zanubrutinib in waldenström macroglobulinemia: results from the Belgian WIZARD study

Authors: Willem Daneels,¹⁻³ Jeroen Claes,⁴ Tom Feys,⁵ Caroline Pieters,⁶ Sandrine Dupont,⁷ Anke Verheyen⁸

Affiliations: ¹Ghent University Hospital, Ghent, Belgium; ²Department of Internal Medicine and Pediatrics, Ghent University, Ghent, Belgium; ³Cancer Research Institute Ghent, Ghent, Belgium; ⁴Cropland, Antwerp, Belgium; ⁵Tom Feys Medical Writing, Izegem, Belgium; ⁶BeOne Medicines, Ltd, Antwerp, Belgium; ⁷BeOne Medicines, Ltd, Brussels, Belgium; ⁸Novellas Healthcare, Brussels, Belgium

Objectives: Zanubrutinib is a potent, highly selective, irreversible, second-generation Bruton tyrosine kinase (BTK) inhibitor. In the pivotal phase III ASPEN trial, zanubrutinib demonstrated high efficacy and favorable tolerability in patients with Waldenström macroglobulinemia (WM), establishing it as a standard BTK inhibitor in this setting. In November 2021, the European Medicines Agency approved zanubrutinib for adult patients with WM who had received at least one prior therapy or as first-line therapy for those unsuitable for immunochemotherapy. The objective of the multicenter, observational WIZARD study was to collect Belgian real-world data (retrospective and prospective) on the efficacy and safety of zanubrutinib in adult patients with WM.

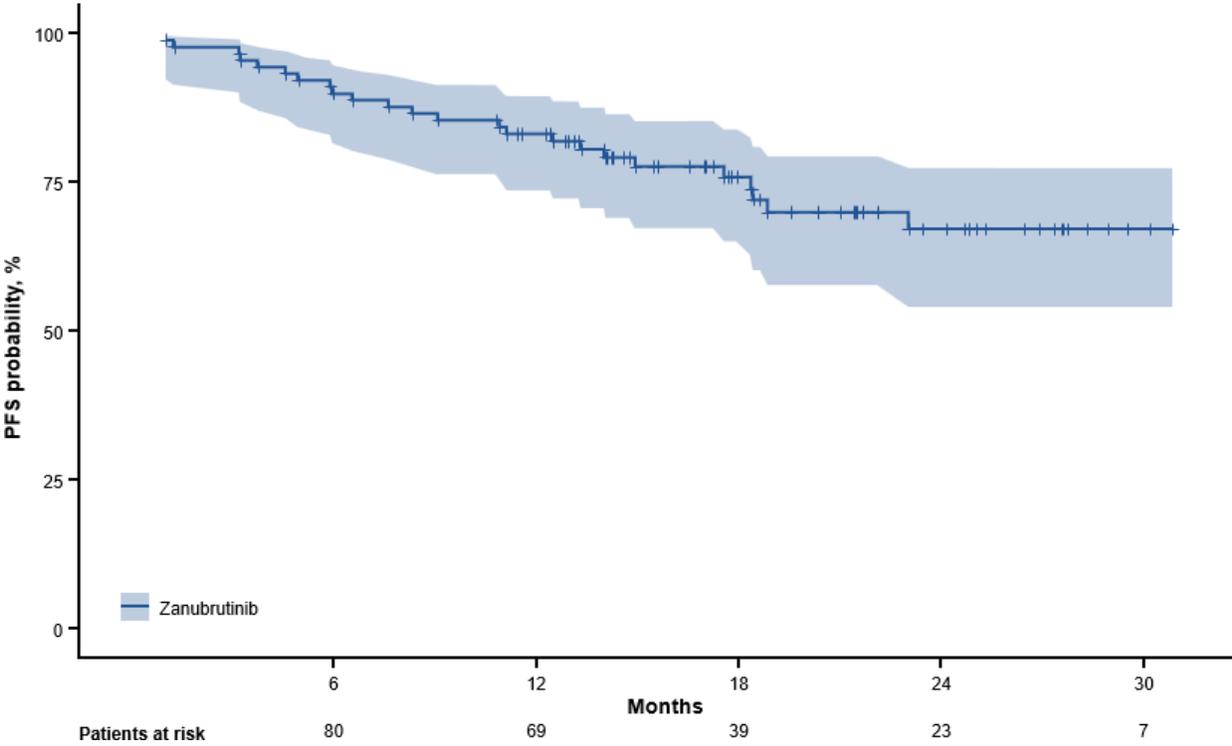
Methods: WIZARD was a retrospective and prospective, multicenter, observational study conducted in Belgium. Eligible participants were adult patients with symptomatic WM who had received zanubrutinib in accordance with Belgian reimbursement criteria, with treatment initiated between October 1, 2022, and September 1, 2024. The primary objective was to evaluate the real-world effectiveness of zanubrutinib, assessed by major response rate (MRR), overall response rate (ORR), best individual response, and

progression-free survival (PFS). Responses were evaluated using the International Workshop on Waldenström's Macroglobulinemia criteria. Secondary objectives included time to (patient best) response, (best) response duration, overall survival (OS), and time to next treatment. Baseline clinical and demographic characteristics and treatment modalities of zanubrutinib use were also described.

Results: Eighty-nine patients were included, with a median age of 76 years and a median of two prior treatment lines. In total, 37 patients (41.6%) had not received prior treatment and received zanubrutinib in first line; of the 52 pre-treated patients, 20 (22.5%) had previously received an ibrutinib-containing regimen. Of the 89 patients treated with zanubrutinib, the MRR and ORR were 64.0% (95% CI, 53.2–73.9) and 77.5% (95% CI, 67.4–85.7), respectively, with 23 patients (25.8%) achieving at least a very good partial response. Subgroup analyses of MRR and ORR according to baseline patient or disease characteristics revealed no significant associations. The ORR was 81.1% in treatment-naive patients and 75.0% in the relapsed/refractory cohort. At 1 and 2 years, PFS rates were 83.1% and 67.1% (Figure 1), respectively, with corresponding OS rates of 89.8% and 81.4%. Responses were durable, with 1- and 2-year duration of response rates of 77.3% and 70.3%. The treatment was generally well tolerated, with grade ≥ 3 adverse events (AEs) in 8.9% of patients. The most common (all-grade) AEs were hematoma (5.6%), muscle cramps/pain (4.5%), diarrhea, (3.4%), fatigue (3.4%) and hypertension (3.4%). The only grade ≥ 3 AE occurring in more than one patient was neutropenia (2.2%). AEs led to treatment interruption in 5.6% and discontinuation in 4.5% of patients.

Conclusions: The WIZARD study corroborates the efficacy and safety of zanubrutinib in patients with WM in a real-world Belgian setting, aligning with the outcomes observed in the pivotal ASPEN trial.

Figure 1. Progression-free survival in the WIZARD trial



PFS, progression-free survival.