BRUMIZE: Real-World Zanubrutinib Use and Preliminary Safety in R/R Marginal Zone Lymphoma in Europe

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Background
Zanubrutinib (zanu), a second-generation Bruton tyrosine kinase inhibitor (BTKi), has been available in Europe since 2022 as a treatment option for relapsed/refractory (R/R) marginal zone lymphoma (MZL), following demonstration of efficacy and a favourable safety profile in the phase 2, single arm MAGNOLIA trial (n=68). BRUMIZE was designed to complement MAGNOLIA and describe real-world (RW) use in Europe, capturing prevalent patients (pts) treated in a compassionate use setting and after reimbursement.

Aims
To describe pt and disease characteristics and treatment patterns in pts initiating zanu for R/R MZL in France and Belgium.

Methods
BRUMIZE is an ambispective, longitudinal, non-interventional, multicentre study conducted in 33 sites. Index date is zanu start (D0) regardless of retrospective (R) or prospective (P) enrolment. Pts are followed for 2 years (yrs) after the last prospective pt is enrolled, with visits at M3, M6, and every 6 months (mo) thereafter. This preliminary analysis reports baseline characteristics and early follow-up (FU) data after 9 mo of enrolment.

Results
Among the 90 enrolled pts (73R/17P), 19 (21.1%) had extranodal (E), 49 (54.4%) splenic (S), and 22 (24.4%) nodal (N) MZL. Median age was 74 yrs (IQR: 66.5–80.2; EMZL: 71.8; SMZL: 75.9; NMZL: 70.6), with 25.6% aged ≥80 yrs and 54.4% male. At D0, ECOG-PS was 0–1 for all EMZL/NMZL pts and 77.4% of SMZL pts. Cardiovascular (CV) comorbidities were present in 57.3% of pts (including 50.0% with hypertension).

Median time since diagnosis was 5.1 yrs (IQR: 2.1–9.3; EMZL: 5.3; SMZL: 3.8; NMZL: 6.8). Disease was bulky (>5 cm) in 20.3% (15/74) and bone marrow involvement occurred in 41.7% (25/60). For SMZL, HPLL score at diagnosis was A, B, C in 38.0%, 46.0%, 16.0%; for NMZL, FLIPI was 0–1, 2, 3–5 in 42.9%, 14.3%, 42.9%; for EMZL, MALT IPI score was low, intermediate, high in 36.8%, 31.6%, 31.6%. At D0, 83.0% of pts were stage III or IV (n=53 available) (EMZL: 69.2; SMZL: 83.3; NMZL: 93.8). LDH was elevated in 37.2% (n=51 tested), *TP53* mutated in 47.8% (n=23 tested), and Ki-67 >30% in 26.3% (n=19 tested).

Pts had received 1 (54.4%), 2 (30.0%), or ≥3 (15.6%) prior therapies. SMZL pts most often had 1 prior line (69.4%), while EMZL/NMZL had ≥2 (68.4%/59.1%). All pts were rituximab pretreated; 30.9% were refractory at D0. Latest therapy was rituximab monotherapy (45.6%) or combination (45.6%), lasting a median of 3.7 mo (IQR: 1.4–6.0), achieving CR/PR in 58.6% and progressive

disease in 25.7% at 24 mo. Median time from end of latest therapy to zanu was 10.4 mo (IQR: 2.1–27.4; SMZL: 5.6; EMZL: 15.6; NMZL: 17.2).

Zanu was initiated at labelled dose in 92.0% (40.7% once daily, 59.3% twice daily) and reduced dose in 8.0%. At analysis (median FU: 6.1 mo, IQR: 2.2–16.6), 15.3% had dose reductions and 20.8% temporary interruptions.

Treatment-related adverse events (TRAEs) occurred in 38.9% (28/72 with FU), grade (G) ≥3 in 12.5%, and led to discontinuation in 8.3%. The most frequent were skin and subcutaneous disorders 11.1% (G≥3: 1.4%) and blood disorders 11.1% (G≥3: 5.5%). Three G1/2 vascular TRAEs were reported (2 haematomas, 1 hypertension).

Conclusion

BRUMIZE represents a large European RW cohort enrolling pts with R/R MZL. Although pts were older and had a higher comorbidity burden than pts in MAGNOLIA, early safety profile is consistent with trial data. Ongoing analyses with extended FU will further evaluate RW effectiveness and long-term safety of zanu in this population.