Marginal zone lymphoma (MZL) is the third most common lymphoma and represents approximately 10% of all non-Hodgkin lymphomas (NHLs). Patients with MZL are usually older than 60 years, and the disease often presents with constitutional symptoms. MZLs are often indolent, with some patients experiencing relapses or refractory disease despite conventional therapies. In such cases, treatment options are limited, and patients may benefit from novel therapeutic approaches.

Zanubrutinib is a potent, selective, and irreversible BTK inhibitor, designed to maximize BTK targeting and achieve optimal clinical outcomes in patients with B-cell malignancies. This study evaluates the efficacy and safety of zanubrutinib in patients with MZL, including those with relapsed or refractory disease, to assess its potential utility in managing this challenging lymphoma subtype.

**Methods**

Zanubrutinib was administered at 80 mg once daily (QD) or 160 mg bid. The study population included patients with MZL of any disease stage (local, nodal, or splenic), disease duration ≤5 years, and ECOG PS ≤2.

**Endpoints**

- **Clinical Efficacy**: ORR, duration of response (DR), progression-free survival (PFS), and overall survival (OS).
- **Safety**: Incidence of all-grade and grade ≥3 treatment-related adverse events (AEs).

**Results**

At a median follow-up of 27.1 months, the ORR was 80%, with a complete response (CR) rate of 15%. The median PFS was 18 months, and the 24-month OS was 83.2%. No patients experienced grade 5 AEs, and serious AEs were infrequent. Zanubrutinib demonstrated a favorable safety profile, with the most common grade ≥3 AEs including bruising, dyspnea, and sinusitis.

**Conclusions**

Zanubrutinib therapy demonstrated a favorable safety profile in patients with MZL and resulted in durable responses. Responses were observed in all MZL subtypes. At a median follow-up of 27.1 months, ORR was 80%, with a CR rate of 15%. The 24-month OS was 83.2%, and no patients experienced grade 5 AEs. The study included disease-specific cohorts, including relapsed/refractory (R/R) MZL, emphasizing its potential utility in managing this challenging lymphoma subtype.

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**References**