Zanubrutinib in Patients With Relapsed/Refractory Marginal Zone Lymphoma (MZL): Final Analysis of MAGNOLIA (BGB-3111-214)

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Abstract Content: Advanced-stage MZL, characterized by recurring periods of remission and relapse, is generally considered incurable. Zanubrutinib is a potent, selective next-generation Bruton tyrosine kinase inhibitor recently approved for the treatment of relapsed/refractory MZL. The final analysis of the phase 2 MAGNOLIA (NCT03846427) trial is presented here.

Adults requiring systemic treatment for relapsed/refractory MZL with ≥1 prior CD20-directed regimen received zanubrutinib 160 mg twice daily until disease progression/unacceptable toxicity. Long-term use of antiplatelets/anticoagulants was permitted. Primary endpoint was overall response rate (ORR) by independent review committee (IRC). PET-based Lugano criteria were used for patients with IRC-confirmed fluorodeoxyglucose (FDG)-avid disease at baseline; non-avid patients were assessed by computed tomography (CT)-based criteria. Sensitivity analysis using CT-based criteria was performed. Secondary endpoints included ORR by investigator assessment, duration of response (DOR), progression-free survival (PFS), overall survival, and safety.

As of May 4, 2022, 68 (66 efficacy-evaluable) patients were enrolled and treated. Median age was 70 years (range, 37-95); median number of prior systemic therapies was 2 (range, 1-6); 61 (89.7%) and 7 (10.3%) patients received chemoimmunotherapy or rituximab monotherapy, respectively. MZL subtypes included extranodal (mucosa-associated lymphoid tissue; 38.2%), nodal (38.2%), splenic (17.6%), and unknown (5.9%). Sixty-one (89.7%) patients had IRC-assessed FDG-avid disease.

Median follow-up was 28 months (range, 1.6-32.9); median treatment duration was 24.2 months (range, 0.9-32.9). ORR by IRC was 68.2% (complete response [CR] 25.8%), responses were observed in all MZL subtypes (ORR/CR: 64.0%/40.0% extranodal; 76.0%/20.0% nodal; 66.7%/8.3% splenic; 50.0%/25.0% unknown). At 2 years, >70.0% of patients were alive/progression free. By sensitivity analysis, ORR was 66.7% (CR: 24.2%). Median DOR and PFS were not reached by IRC and CT-based criteria.

At study completion, 31 (45.6%) patients rolled over to a long-term extension study (NCT04170283), 24 (35.3%) discontinued owing to disease progression, 5 (7.4%) discontinued owing to adverse events (AEs), 2 (2.9%) required prohibited medications, and 1 (1.5%) withdrew consent. Most common treatment-emergent AEs were bruising (23.5%), diarrhea (22.1%), constipation (17.6%), arthralgia (14.7%), pyrexia (14.7%), upper respiratory tract infection (13.2%), and abdominal pain and back pain (11.8% each). Most common grade ≥3 AEs were neutropenia (8.8%) and COVID-19 pneumonia (5.9%). Five (7.4%) patients died owing to unrelated AEs. Three (4.4%) patients reported hypertension, 1 (1.5%) atrial fibrillation, and 1 (1.5%) atrial flutter; none led to treatment withdrawal.

The high response rates and durable disease control demonstrate clinically meaningful benefits. Zanubrutinib was generally well tolerated, with no new safety signals at >2 years of follow-up.