Safety and efficacy of zanubrutinib in patients with relapsed/refractory marginal zone lymphoma (MAGNOLIA Phase 2 Study)

Aim: Zanubrutinib is a potent, next-generation BTK inhibitor with higher selectivity for BTK versus the TEC- and EGFR-family kinases. The initial efficacy and safety results of zanubrutinib in patients with relapsed/refractory marginal zone lymphoma (R/R MZL) enrolled in the MAGNOLIA study (BGB-3111-214; NCT03846427) are presented.

Methods: In this single-arm, multicenter study, adults with R/R MZL who previously received ≥1 prior therapy including ≥1 CD20 antibody regimen received zanubrutinib 160 mg twice daily until disease progression or unacceptable toxicity. The primary endpoint was overall response rate (ORR) by independent review committee (IRC). Secondary endpoints included investigator-assessed ORR (ORR_{INV}), duration of response (DOR), progression-free survival (PFS), and safety.

Results: As of January 11, 2021, 68 patients were enrolled and treated. Median age was 70 years (range, 37-95), with 28% aged ≥75 years. In these patients, MZL subtypes included extranodal (38%), nodal (38%), splenic (18%), and indeterminate (6%). Median number of prior therapies was 2 (range, 1-6), and 32% of patients had disease refractory to last therapy.

Median duration of exposure was 59.1 weeks (range, 3.7-84.1). After a median follow-up of 15.5 months (range, 1.6-21.7), ORR_{INV} was 74% with a complete response rate of 24% (**Table**); responses were observed in all subtypes. Median DOR and PFS were not reached. IRC review is ongoing.

Twenty-eight (41%) patients discontinued treatment (n=20, disease progression; n=4, adverse events [AEs]). The most common treatment-emergent AEs reported in ≥10% of patients were diarrhoea (22%), bruising (21%), and constipation (15%); neutropenia was the most common grade ≥3 AE (10%). All-grade AEs of interest included neutropenia (13%), thrombocytopenia (13%), atrial fibrillation/flutter (3%), and hypertension (3%). No major/serious haemorrhage was reported. No AEs led to dose reductions.

Conclusion: Zanubrutinib demonstrated high response rates and durable disease control with a favourable safety profile in patients with R/R MZL.

Efficacy (investigator assessment)	**(N=66)[a]**
ORR, n (%) [95% CI]	49 (74%) [62, 84]
Complete response	16 (24%)
Partial response	33 (50%)
Stable disease[b]	11 (17%)
Progressive disease	5 (8%)
Discontinued study before first assessment	1 (2%)
Time to response in months, median (range)	2.8 (1.7, 8.5)
Safety	**(N=68)[c]**
Any AE, n (%)	65 (96%)
Grade ≥3 AE, n (%)	26 (38%)
Serious AE, n (%)	25 (37%)
AE leading to dose interruption, n (%)	19 (28%)

[a]Efficacy-evaluable set: patients who received at least one dose of study drug and with centrally-confirmed diagnosis of MZL (two patients were excluded due to MZL transformation to diffuse large B-cell lymphoma).
[b]Three patients with stable disease were continuing on study treatment.
[c]Safety analysis set: all patients who received at least one dose of study drug.