Abstract Title (English): SAFETY AND EFFICACY OF ZANUBRUTINIB IN PATIENTS WITH RELAPSED/REFRACTORY MARGINAL ZONE LYMPHOMA (MAGNOLIA PHASE 2 STUDY)

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Background: Zanubrutinib is a potent, specific next-generation BTK inhibitor with higher selectivity for BTK compared with TEC- and EGFR-family kinases, which may be related to off-target toxicities.

Aim/Objective: The objective of this abstract is to present initial efficacy and safety results of zanubrutinib in patients (pts) with relapsed/refractory marginal zone lymphoma (R/R MZL) enrolled in the MAGNOLIA study (BGB-3111-214; NCT03846427).

Methods: In this single-arm, multicenter study, adults with R/R MZL who had received ≥1 prior therapy including at least one CD20 antibody regimen were treated with 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 (INV) ORR, duration of response (DOR), progression-free survival (PFS), and safety.

Results: As of January 11, 2021, 68 pts were enrolled and treated. Median age was 70 years (range, 37-95), with 28% aged ≥75 years. MZL subtypes included extranodal (38% of

pts), nodal (38%), splenic (18%), and indeterminate (6%). Median number of prior therapies was 2 (range, 1-6), and 32% of pts had disease refractory to last therapy.

Median duration of drug exposure was 59.1 weeks (range, 3.7-84.1). At a median follow-up of 15.5 months (range, 1.6-21.7), INV ORR was 74% with a complete response rate of 24%. Responses were observed in all subtypes, with an ORR of 68%, 84%, 75%, and 50% in extranodal, nodal, splenic, and indeterminate subtypes, respectively. Median DOR and PFS were not reached. IRC review is ongoing.

Twenty-eight (41%) pts discontinued treatment (20 due to disease progression; 4 due to adverse events [AEs]). The most common treatment-emergent AEs reported in ≥10% of pts were diarrhea (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%). AEs leading to treatment discontinuation included fatal COVID-19 pneumonia (n=2), fatal myocardial infarction in one pt with pre-existing coronary artery disease, and pyrexia attributed to disease transformation. No major/serious hemorrhage was reported. No AEs led to dose reductions.

Conclusions: Zanubrutinib demonstrated high response rates and durable disease control with a favorable safety profile in pts with R/R MZL.

Table. Efficacy and Safety Outcomes in 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 (months), median (range)	2.8 (1.7, 8.5)
Safety[c]	**(N=68)[d]**
Any AE, n (%)	65 (96)
Grade ≥3 AE, n (%)	26 (38)
Serious AE, n (%)	25 (37)

[a] Efficacy-evaluable set: pts who received at least one dose of study drug and with centrally-confirmed diagnosis of MZL (two pts were excluded due to MZL transformation to diffuse large B-cell lymphoma).
[b] Three pts with stable disease were continuing on study treatment.
[c] Treatment-emergent AEs.
[d] Safety analysis set: all pts who received at least one dose of study drug.
Abbreviations: AE, adverse event; MZL, marginal zone lymphoma; ORR, overall response rate; pts, patients; R/R, relapsed/refractory.