ZANUBRUTINIB (ZANU) IN OLDER PATIENTS (PTS) WITH RELAPSED/REFRACTORY (R/R) MARGINAL ZONE LYMPHOMA (MZL): SUBGROUP ANALYSIS OF THE MAGNOLIA STUDY

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ABSTRACT

MZL, the second most common lymphoma in older pts, can be challenging to treat due to pt- or disease-related risk factors and treatment toxicity. The next-generation Bruton tyrosine kinase (BTK) inhibitor zanu, which was designed to minimize off-target effects, has received accelerated approval in the United States for R/R MZL. MAGNOLIA (BGB-3111-214; NCT03846427) is a phase 2, multicenter, single-arm study of adults with R/R MZL; here, we present a subgroup analysis of pts ≥65 y. Eligible pts had ≥1 prior therapy (ie, ≥1 anti-CD20 regimen); long-term antiplatelet/anticoagulant use was permitted. Zanu dosing was 160 mg twice daily. Primary endpoint was overall response rate (ORR) by independent review committee (IRC) per Lugano classification. Secondary endpoints were investigator-assessed (INV) ORR, duration of response (DOR), progression-free survival (PFS), and safety. As of 18Jan2021, 68 pts were enrolled (≥65 y: n=40; ≥75 y: n=18); median age was 73 y (range, 65-85). Median number of prior lines was 2 (range, 1-6); 10 pts (25%) were refractory to their last therapy. Most pts had prior rituximab/cyclophosphamide/vincristine/prednisone (48%) or bendamustine/rituximab (30%); 5 pts (13%) had prior rituximab monotherapy. MZL subtypes included extranodal (n=17; 43%), nodal (n=14; 35%), and splenic (n=8; 20%). Median treatment duration was 14.4 mo (range, 0.9-19.6). At a median follow-up of 15.8 mo (range, 2.8-21.8), ORR by IRC was 75% (table). ORRs were 71%, 86%, and 75% for extranodal, nodal, and splenic subtypes, respectively (complete response 41%, 21%, and 0%, respectively). Median DOR and PFS were not reached; 15-mo PFS was 87% and 12-mo DOR was 93%. 63% of pts remain on zanu. Discontinuation (d/c) due to disease progression was 28% by INV. Treatment-emergent adverse events (AEs) in ≥20% of pts were contusion (28%), diarrhea (25%), and constipation (20%). Grade ≥3 neutropenia occurred in 5% of pts. The most common infection was upper respiratory tract infection (10%). 2 pts (5%) had unrelated fatal AEs (COVID-19 pneumonia and myocardial infarction in a pt with preexisting coronary artery disease). Atrial fibrillation/flutter and hypertension occurred in 2 pts (5%) each and did not lead to zanu d/c. No pts required dose reductions, or had major or serious hemorrhage. In summary, zanu was well tolerated in older pts with R/R MZL and had a safety profile consistent

with previous findings. High response rates and durable disease control were also observed.

Table: Baseline Characteristics, Efficacy, and Safety Outcomes

	Patients ≥65 Years (n = 40)	**Patients ≥75 Years (n = 18)**
Baseline Characteristics		
Male sex, n (%)	23 (58)	11 (61)
ECOG PS 0-1, n (%)	35 (88)	15 (83)
Bone marrow involvement, n (%)	18 (45)	9 (50)
Prior lines of therapy, median (range)	2 (1-6)	1 (1-4)
Efficacy (IRC assessment)		
ORR (CR+PR), n (%) [95% CI]	30 (75) [58.8, 87.3]	17 (94) [72.7, 99.9]
CR	10 (25)	4 (22)
PR	20 (50)	13 (72)
SD	7 (18)	1 (6)
PD	3 (8)	0 (0)
Time to response (months), median (range)	2.81 (1.7, 11.1)	2.83 (1.7, 5.6)
Safety		
Any TEAE, n (%)	37 (93)	16 (89)
Grade ≥3 TEAE, n (%)	18 (45)	9 (50)
Serious TEAE, n (%)	16 (40)	8 (44)

CI, confidence interval; CR, complete response; ECOG PS, Eastern Cooperative Oncology Group performance status; IRC, independent review committee; ORR, overall response rate; PD, progressive disease; PR, partial response; SD, stable disease; TEAE, treatment-emergent adverse event