Long-Term Efficacy and Safety of Zanubrutinib in Patients With Relapsed/Refractory (R/R) Marginal Zone Lymphoma (MZL): Final Analysis of the MAGNOLIA (BGB-3111-214) Trial

Authors: Stephen Opat[1], Alessandra Tedeschi[2], Bei Hu[3], Kim M. Linton[4], Pamela McKay[5], Henry Chan[6], Jie Jin[7], Mingyuan Sun[8], Magdalena Sobieraj-Teague[9], Pier Luigi Zinzani[10], Peter Browett[11], Xiaoyan Ke[12], Craig A. Portell[13], Catherine Thieblemont[14], Kirit Ardeshna[15], Fontanet Bijou[16], Patricia Walker[17], Eliza A. Hawkes[18], Shir-Jing Ho[19], Keshu Zhou[20], Zhiyu Liang[21], Jianfeng Xu[21], Chris Tankersley[21], Richard Delarue[21], Melannie Co[21], and Judith Trotman[22]

Affiliations: [1]Monash Health and Monash University, Clayton, VIC, Australia; [2]ASST Grande Ospedale Metropolitano Niguarda, Milan, Italy; [3]Levine Cancer Institute/Atrium Health, Charlotte, NC, USA; [4]Manchester Cancer Research Centre, Division of Cancer Sciences, Manchester, UK; [5]Beatson West of Scotland Cancer Centre, Glasgow, UK; [6]North Shore Hospital, Auckland, New Zealand; [7]The First Affiliated Hospital, Zhejiang University, Hangzhou, Zhejiang, China; [8]Institute of Hematology & Blood Diseases Hospital, Chinese Academy of Medical Sciences and Peking Union Medical College, Tianjin, China; [9]Flinders Medical Centre, Bedford Park, SA, Australia; [10]Institute of Hematology “Seràgnoli” University of Bologna, Bologna, Italy; [11]Auckland City Hospital, Grafton, New Zealand; [12]Peking University Third Hospital, Beijing, China; [13]University of Virginia, Comprehensive Cancer Center, Charlottesville, VA, USA; [14]APHP, Hôpital Saint-Louis, Hemato-oncology, Paris University Diderot, Paris, France; [15]University College London Hospitals, London, UK; [16]Institut Bergonié, Bordeaux, France; [17]Peninsula Private Hospital, Frankston, VIC, Australia; [18]Box Hill Hospital, Box Hill, VIC, Australia; [19]St. George Hospital, Kogarah, NSW, Australia; [20]Henan Cancer Hospital, Zhengzhou, Henan, China; [21]BeiGene (Beijing) Co., Ltd., Beijing, China, BeiGene Switzerland GmbH and BeiGene USA, Inc., San Mateo, CA, USA; and [22]Concord Repatriation General Hospital, University of Sydney, Concord, NSW, Australia

ABSTRACT

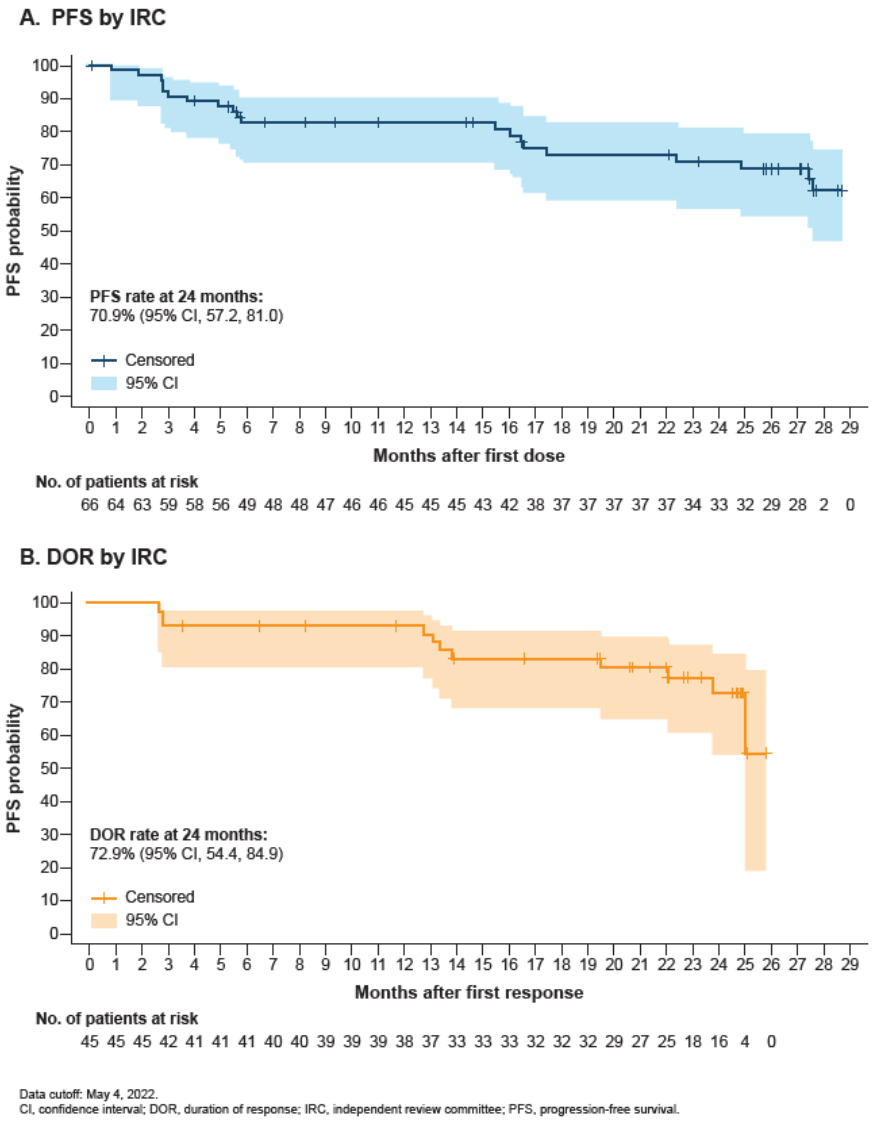
Introduction: Advanced MZL is generally incurable, with periods of remission and relapse. Zanubrutinib (BGB-3111), a potent and highly specific next-generation Bruton tyrosine kinase (BTK) inhibitor, was approved in the US and Canada for R/R MZL based on the MAGNOLIA primary analysis (BGB-3111-214; NCT03846427); here, the final MAGNOLIA analysis is presented.

Methods: This was a phase 2, multicenter, single-arm study of adult patients (pts) with R/R MZL (≥1 prior CD20-directed therapy). Zanubrutinib (160 mg twice daily) was given until disease progression or unacceptable toxicity. The primary endpoint was overall response rate (ORR) by independent review committee (IRC) per Lugano classification. Secondary endpoints were investigator-assessed ORR, duration of response (DOR), progression-free survival (PFS), overall survival (OS), and safety. Efficacy was assessed by positron emission tomography (PET)-based Lugano criteria for IRC-confirmed fluorodeoxyglucose (FDG)-avid disease at baseline; non-avid disease was assessed by computed tomography (CT)-based criteria.

Results: As of May 4, 2022, 68 pts were treated (median age=70 y [range 37-95]; ≥75 y=27.9%). MZL subtypes included extranodal (38.2%), nodal (38.2%), splenic (17.6%), and unknown (5.9%). The median number of prior therapies was 2 (range 1-6); 32.4% of pts had disease refractory to last therapy, most (89.7%) had prior chemoimmunotherapy, and 7 (10.3%) had rituximab monotherapy as their only prior treatment. Sixty-one pts (89.7%) had FDG-avid disease. After a median follow-up of 28.0 mos (range 1.6-32.9) and a median treatment duration of 24.2 mos (range 0.9-32.9), 66 pts were efficacy-evaluable. IRC-assessed ORR (complete response [CR]+partial response [PR]) was 68.2% (CR=25.8%). By subtype, ORR/CR rates were 64.0%/40.0% (extranodal), 76.0%/20.0% (nodal), 66.7%/8.3% (splenic), and 50.0%/25.0% (unknown). Median DOR, PFS, and OS were not reached. Over 70.0% of pts were alive or progression-free after 2 years (**Figure**). Sensitivity analysis using only CT-based criteria (n=66) showed an ORR of 66.7% and CR of 24.2%. The most common treatment-emergent AEs were bruising (23.5%), diarrhea (22.1%), and constipation (17.6%). Neutropenia (8.8%) and COVID-19 pneumonia (5.9%) were the

most common Grade ≥3 AEs. Five pts (7.4%) died due to unrelated AEs: COVID-19 pneumonia=2, acute myeloid leukemia=1, myocardial infarction=1, septic encephalopathy=1. Hypertension occurred in 3 pts (4.4%), atrial fibrillation and atrial flutter in 1 pt (1.5%) each; none led to treatment withdrawal. One pt (1.5%) had a Grade 3 gastrointestinal hemorrhage while receiving rivaroxaban. None of the pts required dose reduction.

Conclusions: In this final analysis with over 2 years of median follow-up, zanubrutinib continues to demonstrate durable disease control and was generally well tolerated, with no new safety signals observed.



Data cutoff: May 4, 2022.
CI, confidence interval; DOR, duration of response; IRC, independent review committee; PFS, progression-free survival.