Zanubrutinib in Older Patients With Relapsed/Refractory Marginal Zone Lymphoma (MZL): Subgroup Analysis of the Magnolia Study

Abstract P1162

Stephen Opat,[1] Bei Hu,[2] Alessandra Tedeschi,[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] Morton Coleman,[11] Peter Browett,[12] Xiaoyan Ke,[13] Craig A. Portell,[14] Catherine Thieblemont,[15] Kirit Ardeshna,[16] Fontanet Bijou,[17] Patricia Walker,[18] Eliza A. Hawkes,[19] Shir-Jing Ho,[20] Ke-Shu Zhou,[21] Melannie Co,[22] Jianfeng Xu,[22] Zhiyu Liang,[22] Joanna Anderson,[22] Chris B. Tankersley,[22] Jane Huang,[22] and Judith Trotman[23]

[1]Monash Health and Monash University, Clayton, Victoria, Australia; [2]Levine Cancer Institute/Atrium Health, Charlotte, NC, USA; [3]ASST Grande Ospedale Metropolitano Niguarda, Milan, Italy; [4]The Christie Hospital NHS Foundation Trust, 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, South Australia, Australia; [10]Institute of Hematology "Seràgnoli" University of Bologna, Bologna, Italy; [11]Clinical Research Alliance/Weill Cornell Medicine, Lake Success, NY, USA; [12]Auckland City Hospital, Grafton, New Zealand; [13]Peking University Third Hospital, Beijing, China; [14]University of Virginia Health System, Charlottesville, VA, USA; [15]APHP, Hôpital Saint-Louis, Hemato-oncology, Paris University Diderot, Paris, France; [16]University College London Hospitals, London, UK; [17]Institut Bergonié, Bordeaux, France; [18]Peninsula Private Hospital, Frankston, Victoria, Australia; [19]Box Hill Hospital, Box Hill, Victoria, Australia; [20]St. George Hospital, Kogarah, New South Wales, Australia; [21]Henan Cancer Hospital, Zhengzhou, Henan, China; [22]BeiGene (Beijing) Co., Ltd., Beijing, China and BeiGene USA, Inc., San Mateo, CA, USA; and [23]Concord Repatriation General Hospital, University of Sydney, Concord, New South Wales, Australia

INTRODUCTION

- Marginal zone lymphoma (MZL) is the second most common lymphoma in older patients
  - Choosing an optimal treatment can be challenging because of patient- or disease-related risk factors and treatment-related toxicities[1]
- Zanubrutinib (BGB-3111) is a next-generation Bruton tyrosine kinase (BTK) inhibitor designed to maximize BTK occupancy and minimize off-target inhibition of TEC- and epidermal growth factor receptor (EGFR)–family kinases
- Zanubrutinib received accelerated approval from the United States Food and Drug Administration for the treatment of patients with relapsed/refractory (R/R) MZL based on the results of the MAGNOLIA (BGB-3111-214) study[2,3]
  - Enrollment in this study is complete; a total of 68 patients received at least 1 dose of zanubrutinib[3]
- Here, we present efficacy and safety of zanubrutinib in a subgroup of patients with R/R MZL aged ≥65 years

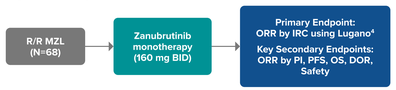
OBJECTIVE

- The primary endpoint was overall response rate (ORR) as determined by an independent review committee (IRC) based on the Lugano 2014 classification[4]

METHODS

- The MAGNOLIA (BGB-3111-214) is a phase 2, single-arm, multicenter study of zanubrutinib in patients with R/R MZL who had received ≥1 CD20-based regimen (**Figure 1**)

Figure 1. Study Schema



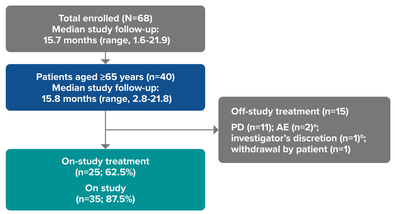
BID, twice a day; DOR, duration of response; IRC, independent review committee; MZL, marginal zone lymphoma; ORR, overall response rate; OS, overall survival; PFS, progression-free survival; PI, principal investigator; R/R, relapsed/refractory.

Key Eligibility Criteria

- Age ≥18 years
- Histologically confirmed MZL including splenic, nodal, and extranodal subtypes
- Previously received ≥1 CD20-directed regimen, with documented failure to achieve at least partial response or documented progressive disease after the most recent systemic treatment
- Measurable disease by computerized tomography or magnetic resonance imaging
- Adequate organ function
- No prior BTK inhibitor exposure

RESULTS

Figure 2. Patient Disposition



Data cutoff: 18 January 2021.
[a]Two patients discontinued due to fatal AEs: myocardial infarction in a patient with pre-existing cardiovascular disease and COVID-19 pneumonia.
[b]One patient discontinued per the investigator's discretion (required prohibited medications).
AE, adverse event; PD, progressive disease.

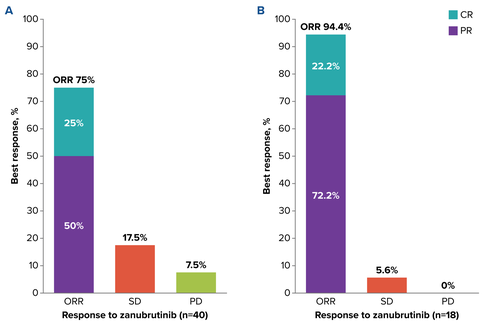
RESULTS (cont.)

Table 1. Patient and Disease Characteristics in Patients Aged ≥65 Years

Characteristic	Total (n=40)
Age, median (range), years	**73 (65-85)**
Age category, n (%), years	
≥65 and <75	22 (55.0)
≥75	18 (45.0)
Male, n (%)	23 (57.5)
ECOG performance status, n (%)	
0-1	35 (87.5)
2	5 (12.5)
Disease status, n (%)	
Relapsed	29 (72.5)
Refractory	10 (25.0)
MZL subtypes, n (%)	
Extranodal	17 (42.5)
Nodal	14 (35.0)
Splenic	8 (20.0)
Unknown[a]	1 (2.5)
Lymphoma involvement in bone marrow, n (%)	18 (45.0)
Prior lines of systemic therapy, median (range)	2 (1-6)

[a]One patient presented with both nodal and extranodal lesions; investigator was unable to classify the MZL subtype.
ECOG, Eastern Cooperative Oncology Group; MZL, marginal zone lymphoma.

Figure 3. Best Overall Response by Independent Review in Patients Aged (A) ≥65 Years or (B) ≥75 Years



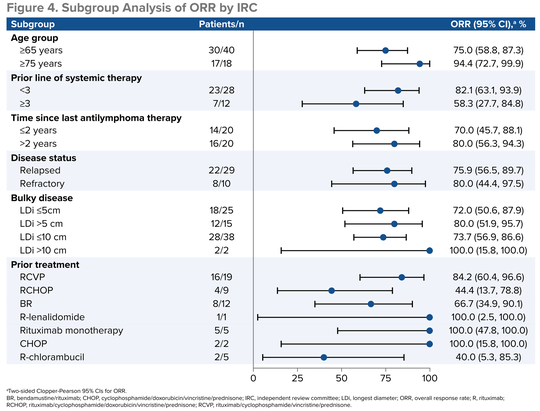
CR, complete response; ORR, overall response rate; PD, progressive disease; PR, partial response; SD, stable disease.

Table 2. Best Overall Response by Independent Review and MZL Subtypes in Patients Aged ≥65 Years

Best response, n (%)	Extranodal (n=17)	Nodal (n=14)	Splenic (n=8)	Unknown (n=1)	Total (n=40)
ORR (CR or PR)	12 (70.6)	12 (85.7)	6 (75.0)	0	30 (75.0)
95% CI[a]	44.0, 89.7	57.2, 98.2	34.9, 96.8	0.0, 97.5	58.8, 87.3
Complete response	7 (41.2)	3 (21.4)	0	0	10 (25.0)
Partial response	5 (29.4)	9 (64.3)	6 (75.0)	0	20 (50.0)
Stable disease	4 (23.5)	2 (14.3)	1 (12.5)	0	7 (17.5)
Progressive disease	1 (5.9)	0	1 (12.5)	1 (100.0)	3 (7.5)

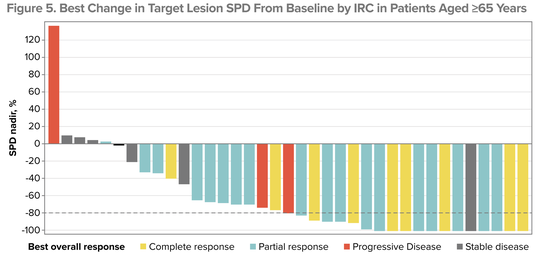
[a]Two-sided Clopper-Pearson 95% CI.
CR, complete response; MZL, marginal zone lymphoma; ORR, overall response rate; PR, partial response.

Figure 4. Subgroup Analysis of ORR by IRC



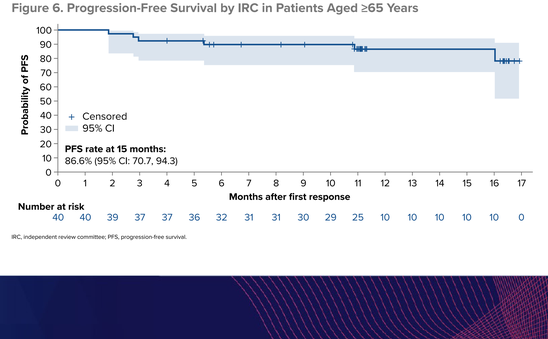
[a]Two-sided Clopper-Pearson 95% CIs for ORR.
BR, bendamustine/rituximab; CHOP, cyclophosphamide/doxorubicin/vincristine/prednisone; IRC, independent review committee; LDi, longest diameter; ORR, overall response rate; R, rituximab; RCHOP, rituximab/cyclophosphamide/doxorubicin/vincristine/prednisone; RCVP, rituximab/cyclophosphamide/vincristine/prednisone.

Figure 5. Best Change in Target Lesion SPD From Baseline by IRC in Patients Aged ≥65 Years



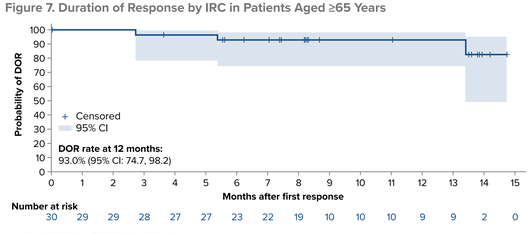
Data cutoff: 18 January 2021
Note: only patients with nonmissing best overall response and SPD percent changes were included (n=37). Dashed lines = median reduction in SPD (-80%).
IRC, independent review committee; SPD, sum of products of perpendicular diameters.

Figure 6. Progression-Free Survival by IRC in Patients Aged ≥65 Years



IRC, independent review committee; PFS, progression-free survival.

Figure 7. Duration of Response by IRC in Patients Aged ≥65 Years



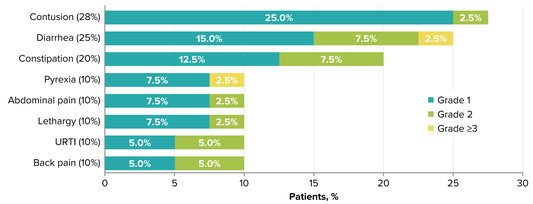
DOR, duration of response; IRC, independent review committee.

Table 3. Safety Summary in Patients Aged ≥65 Years

TEAEs, n (%)	N=40
Patients with ≥1 TEAE	37 (92.5)
Grade ≥3	18 (45.0)
Serious TEAE	16 (40.0)
Leading to dose interruption	13 (32.5)
Leading to study drug discontinuation	2 (5.0)[a]
Leading to death	2 (5.0)[a]
Leading to dose reduction	0

[a]Two fatal unrelated Adverse events: myocardial infarction and COVID-19 pneumonia.
TEAE, treatment-emergent adverse event.

Figure 8. TEAEs Occurring in ≥10% of Patients Regardless of Causality in Patients Aged ≥65 Years



TEAE, treatment-emergent adverse event; URTI, upper respiratory tract infection.

Table 4. TEAE of Interest in Patients Aged ≥65 Years

TEAE of interest	All grade (N=40)	Grade ≥3 (N=40)
Patients with ≥1 TEAE of interest	30 (75.0)	10 (25.0)
Hemorrhage	19 (47.5)	0
Infection[a]	18 (45.0)	5 (12.5)
Diarrhea	10 (25.0)	1 (2.5)
Thrombocytopenia[b]	5 (12.5)	1 (2.5)
Neutropenia[c]	5 (15.2)	3 (7.5)
Second primary malignancy[d]	3 (7.5)	1 (2.5)
Atrial fibrillation/flutter[e]	2 (5.0)	1 (2.5)
Hypertension[f]	2 (5.0)	1 (2.5)
Anemia	1 (2.5)	0
Major hemorrhage	0	0

[a]Includes 2 patients with COVID-19 infection and 2 patients with COVID-19 pneumonia. [b]Combined terms thrombocytopenia and platelet count decreased. [c]Combined terms neutropenia and neutrophil count decreased. [d]Includes basal cell and squamous cell carcinoma (in 2 patients with history of skin cancer); grade 3 recurrent bladder cancer (in 1 patient with history of bladder cancer). [e]Includes atrial flutter (n=1) which occurred 238 days after treatment start and atrial fibrillation (n=1) in a patient with pre-existing atrial fibrillation (21 days after end of treatment due to disease progression). [f]Combined terms hypertension and prehypertension.
TEAE, treatment-emergent adverse event.

CONCLUSIONS

- Zanubrutinib was well tolerated and highly effective in patients aged ≥65 years with R/R MZL
- After a median study follow-up of 15.8 months:
  - High ORR of 75% and complete response rate of 25% by IRC
    - Responses were observed in all MZL subtypes
  - Median PFS and median DOR not reached
    - 93% of responders were progression free/alive 12 months after initial response
    - PFS rate was 86.6% at 15 months
  - Treatment discontinuation due to unrelated fatal adverse events in 2 patients (myocardial infarction and COVID-19 pneumonia)
  - No treatment-emergent adverse event led to dose reduction
  - Atrial flutter/fibrillation (n=2) and hypertension (n=2); did not lead to treatment withdrawal
  - No major hemorrhage was reported
- These results were consistent with previously published results[3]
- Final analysis with longer study follow-up is planned

REFERENCES

1. Bron et al. *Curr Opin Oncol* 2019;31(5):386-393
2. Cheah et al. *Haematologica* 2022;107(1):35-43
3. Opat et al. *Clin Cancer Res* 2021;27(23):6323-6332
4. Cheson et al. *J Clin Oncol* 2014;32(27):3059-3067

DISCLOSURES

SO: honoraria from AbbVie, BeiGene, AstraZeneca, BMS, CSL Behring, Gilead. Janssen, Merck, Roche, Takeda; consulting with AbbVie, BeiGene, AstraZeneca, BMS, CSL Behring, Gilead, Janssen, Merck, Roche, Takeda; research funding from AbbVie, AstraZeneca, BeiGene, CSL Behring, Gilead, Janssen, Merck, Pharmacyclics, Roche, Takeda
BH: serves on the advisory board with BeiGene, Kite, Morphosys, ADC Therapeutics, Cellectar
AT: consulting with AbbVie, Janssen Spa, BeiGene, AstraZeneca; speakers bureau with AbbVie, Janssen Spa, BeiGene, AstraZeneca
KML: funding from BeiGene; serves on the advisory board with BeiGene, Celgene, Gilead, Karyopharm, Roche, Takeda
PM: honoraria from Roche, Gilead, Kite, Takeda; speakers bureau with Janssen, BeiGene, BMS/Celgene/Incyte; travel expenses from Gilead, Takeda, Janssen; serves on the advisory board with Roche, Kite, Takeda, BeiGene, BMS/Celgene; advocacy roles with Lymphoma Action and Blood Cancer UK
HC: serves on the advisory board with Janssen, AbbVie, EUSA Pharma, GSK
PLZ: consultancy with MSD, EUSA Pharma, Novartis; speakers bureau with Celltrion, Gilead, Janssen-Cilag, BMS, Servier, MSD, TG Therapeutics, Takeda, Roche, EUSA Pharma, Kyowa Kirin, Novartis, Incyte, BeiGene; serves on the advisory board with Secura Bio, Celltrion, Gilead, Janssen-Cilag, BMS, Servier, Sandoz, MSD, TG Therapeutics, Takeda, Roche, EUSA Pharma, Kyowa Kirin, Novartis, ADC Therapeutics, Incyte, BeiGene
MCol: stock with Immunomedics; research funding from AbbVie, BMS, Celgene, Genentech, Gilead, BeiGene, InnoCare, Merck, Pfizer, Roche
PB: advisory board with ALLG SDMC; holds leadership with LBC (NZ)
CAP: consulting with BeiGene, TG Therapeutics, Epizyme
CT: consulting with Novartis, Gilead, Roche; honoraria from Roche, Kite/Gilead, Novartis, Janssen, Amgen, Takeda, Incyte, BMS/Celgene; travel with Roche, Gilead, Novartis, Amgen, Takeda, BMS/Celgene; serves on the advisory board for Novartis
KA: honoraria from Celgene, Gilead, Takeda, Roche, BeiGene; consulting with ADC Therapeutics
PW: consulting with BeiGene and Acerta Pharma
EAH: research funding from Roche, BMS Merck KGaA, AstraZeneca; serves on the advisory board with Roche, BMS, AstraZeneca, Merck Sharp & Dohme, Gilead, Janssen, Antigen, Novartis, BeiGene, Specialized Therapeutics; travel expenses from Roche, Janssen; speakers bureau with Roche, AstraZeneca, Janssen, Regeneron
JX, ZL: employment and stock with BeiGene
CBT: employment, travel, and stock with BeiGene
JH: employment and patents with BeiGene; leadership with BeiGene and Protarx; research funding with BeiGene; stock with BeiGene and Roche
JT: research funding from BeiGene, BMS, Roche, Cellectar, Janssen; serves on the advisory board with Roche, BeiGene
JJ, MS, MST, XK, FB, SJH, KSZ, MC, JA: nothing to disclose

CORRESPONDENCE

Stephen Opat, MBBS (Hons), FRACP, FRCPA
Monash Health and Monash University
Clayton, Victoria
Australia
opat@monashhealth.org

ACKNOWLEDGMENTS

We would like to thank the investigators, site support staff, and especially the patients for participating in this study.
This study was sponsored by BeiGene. Editorial support was provided by Bio Connections LLC and funded by BeiGene.

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