

# Zanubrutinib + Obinutuzumab + Sonrotoclax in Patients With Treatment-Naive CLL/SLL: Initial Results From an Ongoing Phase 1/1b Study, BGB-11417-101

Jacob D. Soumerai,<sup>1</sup> Stephen S. Opat,<sup>2</sup> Chan Y. Cheah,<sup>3-5</sup> Mazyar Shadman,<sup>6,7</sup> Emma Verner,<sup>8,9</sup> Monica Tani,<sup>10</sup> Marc S. Hoffmann,<sup>11</sup> Lori A. Leslie,<sup>12</sup> Shuo Ma,<sup>13</sup> Yiqian Fang,<sup>14</sup> Gabriel Man,<sup>15</sup> Binghao Wu,<sup>14</sup> Charity Henrich,<sup>15</sup> Sheel Patel,<sup>15</sup> Remus Veza,<sup>15</sup> Constantine S. Tam<sup>16</sup>

<sup>1</sup>Massachusetts General Hospital Cancer Center and Harvard Medical School, Boston, MA, USA; <sup>2</sup>Lymphoma Research Group, School of Clinical Sciences at Monash Health, Monash University, Clayton, VIC, Australia; <sup>3</sup>Sir Charles Gairdner Hospital, Nedlands, WA, Australia; <sup>4</sup>Medical School, University of Western Australia, Crawley, WA, Australia; <sup>5</sup>Linear Clinical Research, Nedlands, WA, Australia; <sup>6</sup>Fred Hutchinson Cancer Center, Seattle, WA, USA; <sup>7</sup>University of Washington, Seattle, WA, USA; <sup>8</sup>Concord Repatriation General Hospital, Concord, NSW, Australia; <sup>9</sup>University of Sydney, Sydney, NSW, Australia; <sup>10</sup>Santa Maria delle Croci Hospital, Ravenna, Italy; <sup>11</sup>University of Kansas Cancer Center, Kansas City, KS, USA; <sup>12</sup>John Theurer Cancer Center-Hackensack University Medical Center, Hackensack, NJ, USA; <sup>13</sup>Robert H. Lurie Comprehensive Cancer Center, Northwestern University Feinberg School of Medicine, Chicago, IL, USA; <sup>14</sup>BeOne Medicines, Ltd, Shanghai, China; <sup>15</sup>BeOne Medicines, Ltd, San Carlos, CA, USA; <sup>16</sup>Alfred Hospital and Monash University, Melbourne, VIC, Australia

## CONCLUSIONS

- Combination therapy with zanubrutinib + obinutuzumab + sonrotoclax 320 mg was well tolerated by patients with TN CLL/SLL
  - No deaths or discontinuations of any study drug due to TEAEs were observed, and no laboratory or clinical TLS occurred during sonrotoclax ramp-up
- Substantial efficacy was observed, with a 100% ORR
- 100% of patients with an available cycle 15 blood MRD assessment by NGS achieved uMRD5, discontinued treatment per protocol, and remain in remission (median time off treatment, 5.5 months [range, 3.4-8.5 months])
- With a median study follow-up of approximately 18.0 months, no PFS events have occurred, indicating the potential for zanubrutinib + obinutuzumab + sonrotoclax to provide deep and durable remission in TN patients with CLL/SLL
- This combination is being further evaluated in a phase 2 investigator-initiated trial (NCT06849713)

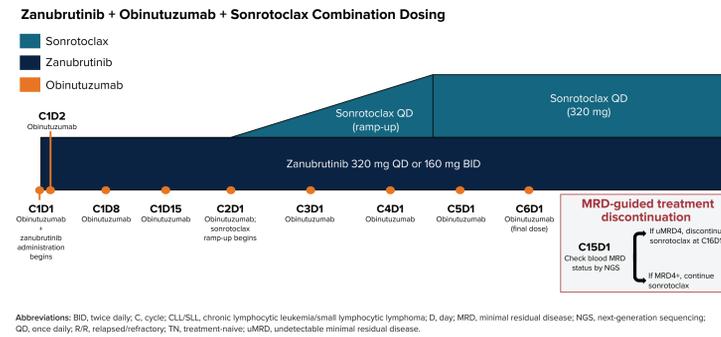
## INTRODUCTION

- Combination therapy with zanubrutinib, obinutuzumab, and venetoclax has demonstrated efficacy in patients with treatment-naive (TN) chronic lymphocytic leukemia/small lymphocytic lymphoma (CLL/SLL), including those with high-risk disease features<sup>1</sup>
- Zanubrutinib is highly effective in patients with TN and relapsed/refractory (R/R) CLL/SLL, regardless of risk factors<sup>2,3</sup>
  - Zanubrutinib has shown superior progression-free survival (PFS) and favorable safety/ tolerability compared with ibrutinib, including fewer cardiac adverse events, in patients with R/R CLL/SLL<sup>4</sup>
- Sonrotoclax (BGB-11417), a next-generation B-cell lymphoma 2 (BCL2) inhibitor, is a more selective and pharmacologically potent inhibitor of BCL2 than venetoclax, with a shorter half-life and no accumulation<sup>5,6</sup>
- BGB-11417-101 is an ongoing, first-in-human, phase 1/1b dose-escalation/expansion study in patients with various B-cell malignancies
- Presented here are initial safety and efficacy data for zanubrutinib + obinutuzumab + sonrotoclax 320 mg combination therapy in patients with TN CLL/SLL in BGB-11417-101

## METHODS

- BGB-11417-101 (NCT04277637) is an ongoing, phase 1/1b, open-label, multicenter, dose-escalation and -expansion study of sonrotoclax as monotherapy or combination therapy in patients with various B-cell malignancies
- On cycle 1 day 1, patients begin treatment with oral zanubrutinib (160 mg twice daily or 320 mg once daily) and intravenous obinutuzumab (cycle 1 to cycle 6); on cycle 2 day 1, oral sonrotoclax is introduced with a ramp-up schedule to reach the recommended phase 2 dose of 320 mg (Figure 1)
- Patients who achieve undetectable minimal residual disease (uMRD4; <1 CLL cell per 10,000 leukocytes) in peripheral blood by next-generation sequencing (NGS) after 15 treatment cycles may discontinue treatment; others may continue to receive treatment until disease progression or unacceptable toxicity
- Study endpoints include safety and tolerability, overall response rate (ORR; defined as a partial response with lymphocytosis or better), and rate of blood uMRD4 as measured by ERIC-approved NGS and/or flow cytometry assay, depending on the time point

Figure 1. BGB-11417-101 Study Design



## RESULTS

- As of August 29, 2025, a total of 15 patients with TN CLL/SLL have been enrolled and have received at least one cycle of zanubrutinib + obinutuzumab + sonrotoclax
- Ten patients (67%) discontinued treatment after reaching uMRD4 per NGS; 5 patients (33%) remain on treatment and have not yet reached cycle 15 as of the data cutoff date
- Across dose cohorts, the median age was 62 years, and 53% were male (Table 1)
  - Ten patients (67%) had unmutated IGHV and 1 patient (7%) had a high tumor burden

Table 1. Baseline Patient Characteristics

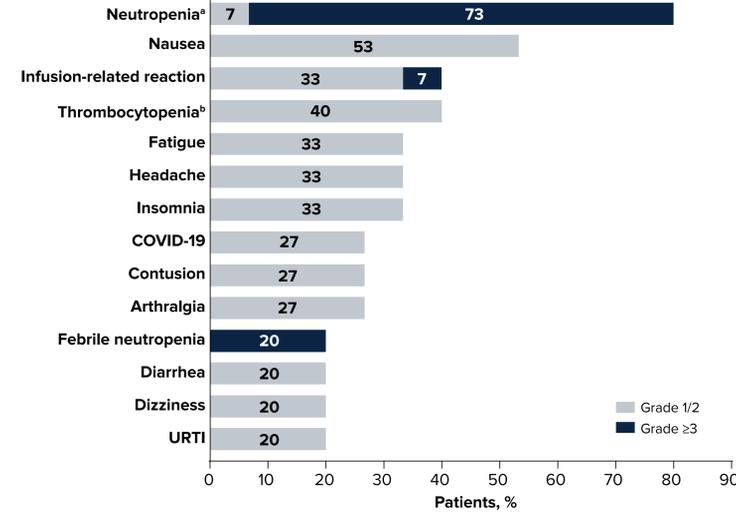
Characteristic	Zanu + O + Sonrotoclax 320 mg (N=15)
Study follow-up time, median (range), months	18.0 (8.4-22.2)
Age, median (range), years	62 (32-76)
Male, n (%)	8 (53)
Risk status, n (%)	
del(17p) and/or TP53 mutation	0
del(13q)	5 (33)
del(11q)	3 (20)
Unmutated IGHV, n (%)	10 (67)
High tumor risk at baseline, n (%) <sup>a</sup>	1 (7)

- An overall summary of treatment emergent adverse events (TEAEs) is shown in Table 2
  - No TEAEs led to death or discontinuation of any study drug
- The most common any-grade TEAEs were neutropenia (80%), nausea (53%), infusion-related reaction (40%), and thrombocytopenia (40%) (Figure 2)
  - The most common grade ≥3 TEAE was neutropenia (73%), which was transient and did not lead to higher rates of grade ≥3 infections
  - The most common serious TEAE was febrile neutropenia (20%)
- Infections occurred in 73% of patients; 13% of patients had grade 3 infections
- No cases of laboratory or clinical tumor lysis syndrome (TLS) occurred during sonrotoclax ramp-up
  - One patient experienced laboratory TLS after obinutuzumab infusion and prior to starting sonrotoclax

Table 2. Safety Summary

Patients, n (%)	Zanu + O + Sonrotoclax 320 mg (N=15)
Any TEAE	15 (100)
Grade ≥3	13 (87)
Serious TEAEs	5 (33)
Led to death	0
Led to zanu discontinuation	0
Led to O discontinuation	0
Led to sonrotoclax discontinuation	0
Relative sonrotoclax dose intensity, median, %	99

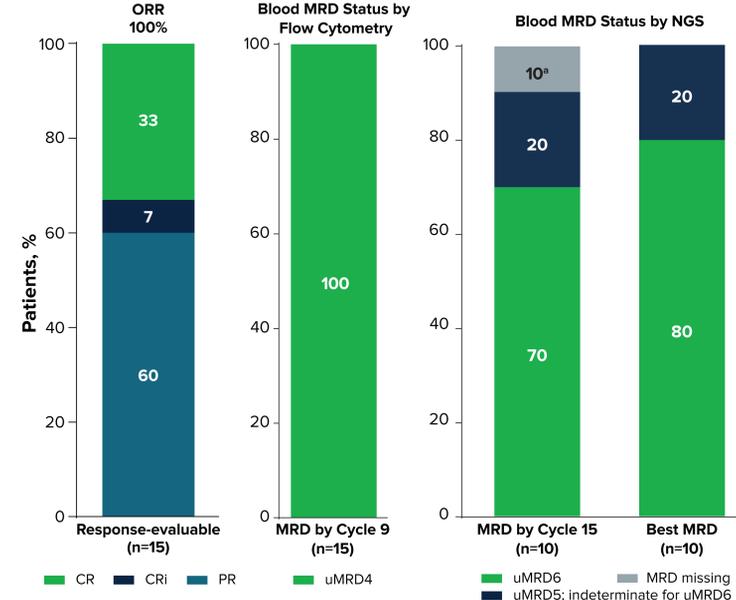
Figure 2. TEAEs in ≥20% of Patients



<sup>a</sup>Neutropenia combines preferred terms "neutrophil count decreased" and "neutropenia." <sup>b</sup>Thrombocytopenia combines preferred terms "platelet count decreased" and "thrombocytopenia." Abbreviations: TEAE, treatment-emergent adverse event; URTI, upper respiratory tract infection.

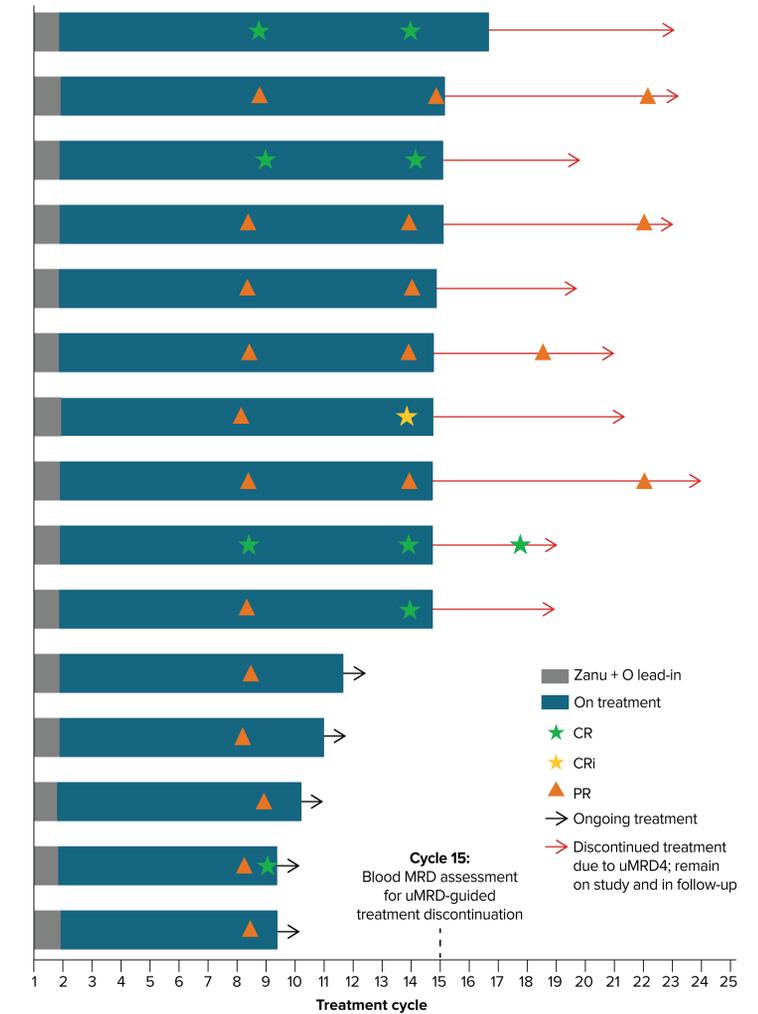
- With a median study follow-up of 18.0 months, the ORR in 15 efficacy-evaluable patients was 100%, which included a complete response/complete response with incomplete marrow recovery (CR/CRi) rate of 40% (Figures 3 and 4)
- As of the data cutoff date, 100% of MRD-evaluable patients achieved uMRD5 per NGS, discontinued treatment as mandated by the protocol, and remain in remission
- The median time off treatment was 5.5 months (range, 3.4-8.5 months)

Figure 3. Response Rates and Blood MRD Status With Sonrotoclax 320 mg Combination Therapy



<sup>a</sup>One patient had a missing MRD evaluation at cycle 15 but it was collected late at cycle 16. Abbreviations: CR, complete response; CRi, complete response with incomplete marrow recovery; MRD, minimal residual disease; NGS, next-generation sequencing; ORR, overall response rate; PR, partial response; uMRD, undetectable minimal residual disease.

Figure 4. Treatment Duration and Investigator-Assessed Responses



Abbreviations: CR, complete response; CRi, complete response with incomplete marrow recovery; MRD, minimal residual disease; O, obinutuzumab; PR, partial response; uMRD, undetectable minimal residual disease; zanu, zanubrutinib.

- With a median study follow-up of 18.0 months (range, 8.4-22.2 months), median PFS was not reached
  - No PFS events were observed, and all patients who achieved uMRD remain in remission

## REFERENCES

- Soumerai JD, et al. *Lancet Haematol*. 2021;8(12):e879-e890.
- Brukins (zanubrutinib). Prescribing information. BeOne Medicines, Ltd; 2024.
- Brukins (zanubrutinib). Summary of product characteristics. BeOne Medicines, Ltd; 2021.
- Brown JR, et al. *N Engl J Med*. 2023;388(4):319-332.
- Guo Y, et al. *J Med Chem*. 2024;67(10):7836-7858.
- Liu J, et al. *Blood*. 2024;143(18):1825-1836.

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