Primary Analysis of a Multicenter, Open-Label, Phase 2 Study of Sonrotoclax (BGB-11417) Monotherapy in Patients with Relapsed/Refractory Chronic Lymphocytic Leukemia or Small Lymphocytic Lymphoma

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CONCLUSIONS

- In the primary analysis of BGB-11417-202, sonrotoclax monotherapy showed meaningful clinical activity in heavily pretreated patients with R/R CLL/SLL
  - Patients treated with sonrotoclax achieved a high IRC-assessed ORR of 77.0%
  - Sonrotoclax treatment demonstrated deep responses, with an IRC-assessed CR rate of 25.0% and a best blood uMRD4 rate of 77.9% (53/68) in the MRD-evaluable population
  - The median time to first response was 3.7 months and median time to first blood uMRD4 was 6.4 months
  - Responses were seen across high-risk categories, including patients with *BTK* mutation, unmutated IGHV, and del(17p) and/or *TP53* mutation
- Sonrotoclax monotherapy was well tolerated with a manageable safety profile, low rates of treatment discontinuation due to TEAEs, and no treatment-related deaths
- These results support sonrotoclax monotherapy as a potential treatment in patients with R/R CLL/SLL

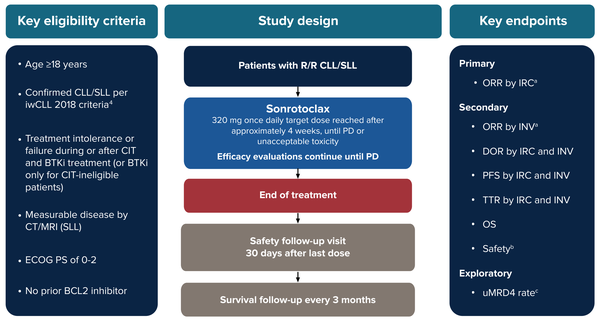
INTRODUCTION

- B-cell lymphoma 2 (BCL2) inhibition is an established treatment strategy in chronic lymphocytic leukemia/small lymphocytic lymphoma (CLL/SLL) with the potential to induce deep and durable responses[1]
- The treatment approach for patients with CLL/SLL in China is similar to that in Western countries; however, the availability of novel treatment options is limited in China
- Sonrotoclax (BGB-11417), a next-generation BCL2 inhibitor, is a more selective and pharmacologically potent inhibitor of BCL2 than venetoclax, with a shorter half-life and no drug accumulation[2]
- In the phase 1 BGB-11417-102 (NCT04883957) study, sonrotoclax monotherapy was well tolerated and induced deep responses in patients with relapsed/refractory (R/R) CLL/SLL[3]
- Presented here are primary efficacy and safety data of the phase 2 BGB-11417-202 (NCT0547994) study of sonrotoclax monotherapy in patients with R/R CLL/SLL

METHODS

- BGB-11417-202 is an ongoing, single-arm, open-label, multicenter, phase 2 study conducted in China (**Figure 1**)
- Patients received once-daily, oral sonrotoclax at target dose of 320 mg, which was gradually achieved over approximately 4 weeks, until disease progression, unacceptable toxicity, withdrawal of consent, or death

Figure 1. BGB-11417-202 Study Design



[a]ORR was defined as partial response (PR) or better per iwCLL 2018[4] criteria for CLL or Lugano 2014 classification[5] for SLL. [b]Includes incidence and severity of treatment-related adverse events and serious adverse events graded per National Cancer Institute Common Terminology Criteria for Adverse Events v5.0 and the Grading Scale for Hematologic Toxicity in CLL Studies. Tumor lysis syndrome was assessed by Howard criteria.[6] [c]Undetectable measurable residual disease 4 (uMRD4) was defined as <1 CLL cell in 10,000 total nucleated cells (<10^{-4}).
Abbreviations: BTKi, Bruton tyrosine kinase inhibitor; CIT, chemoimmunotherapy; CLL, chronic lymphocytic leukemia; CT, computed tomography; DOR, duration of response; ECOG PS, Eastern Cooperative Oncology Group performance status; INV, investigator; IRC, independent review committee; MRI, magnetic resonance imaging; ORR, overall response rate; OS, overall survival; PD, progressive disease; PFS, progression-free survival; R/R, relapsed/refractory; SLL, small lymphocytic lymphoma; TTR, time to response.

RESULTS

- As of August 7, 2025, 100 patients were enrolled, had received at least one dose of sonrotoclax, and were included in both the Efficacy and Safety Analysis populations
  - 54 patients (54.0%) remain on treatment; the most common reason for treatment discontinuation was progressive disease (30.0%)
- Median study follow-up was 20.4 months (range, 0.2-33.4 months)
- Patients had a median age of 64.5 years and had received a median of two prior lines of therapy (**Table 1**)
  - Of patients with biomarker evaluable results, 38.1% had a del(17p) and/or *TP53* mutation, 62.8% had unmutated immunoglobin heavy chain variable region (IGHV), and 25.5% had Bruton tyrosine kinase (*BTK*) mutation(s)

Table 1. Baseline Patient Characteristics

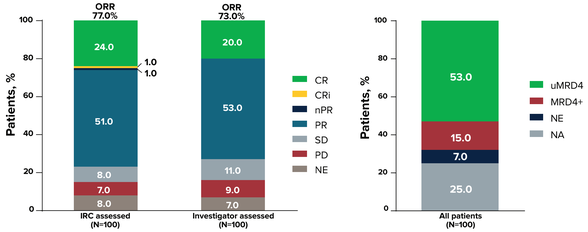
Characteristic	All patients (N=100)
Age, median (range), years	64.5 (37-82)
Male, n (%)	61 (61.0)
ECOG performance status, n (%)	
0	28 (28.0)
1	52 (52.0)
2	20 (20.0)
Bulky disease, n (%)	
LDi ≥5 to <10 cm	19 (19.0)
LDi ≥10 cm	3 (3.0)
Binet stage C, n (%)[a]	35/90 (38.9)
del(17p), n/N (%)	32/97 (33.0)
***TP53* mutation, n/N (%)**	26/98 (26.5)
del(17p) and/or *TP53* mutation, n/N (%)	37/97 (38.1)
del(13q), n/N (%)	29/97 (29.9)
del(11q), n/N (%)	12/97 (12.4)
Unmutated IGHV, n/N (%)	54/86 (62.8)
***BTK* mutation, n/N (%)**	25/98 (25.5)
No. of prior lines of therapy, median (range)	2 (1-6)
≥3 prior therapies, n (%)	27 (27.0)
Prior therapies, n (%)	
BTK inhibitor	100 (100)
Anti-CD20	46 (46.0)

n/N represents the number of patients with evaluable results (ie, patients with missing or unknown status are excluded).
[a]Percentage based on the number of patients with chronic lymphocytic leukemia (n=90).
Abbreviations: BTK, Bruton tyrosine kinase; ECOG, Eastern Cooperative Oncology Group; IGHV, immunoglobulin heavy chain variable region ; LDi, longest diameter.

Efficacy

- Independent review committee (IRC)- and investigator-assessed overall response rates (ORRs) were 77.0% and 73.0%, respectively, with complete response (CR)/CR with incomplete bone marrow recovery rates of 25.0% and 20.0%, respectively (**Figure 2**)
  - Median time to response was 3.7 months (range, 1.3-11.1 months) per IRC and 3.7 months (range, 2.7-11.0 months) per investigator
  - High IRC-assessed response rates were achieved regardless of poor prognostic markers. In patients with and without poor prognostic markers detected, respectively, ORR was as follows: *BTK* mutation, 72.0% (18/25) and 78.1% (57/73); unmutated IGHV, 75.9% (41/54) and 84.4% (27/32); and del(17p) and/or *TP53* mutation, 70.3% (26/37) and 81.7% (49/60)
- The best rate of undetectable measurable residual disease (uMRD4) in peripheral blood was 53.0% (53/100) in the Efficacy Analysis population (**Figure 2**) and 77.9% (53/68) in the MRD-evaluable population
- The median time to uMRD4 was 6.4 months (range, 3-16 months)

Figure 2. IRC- and Investigator-Assessed Response Rates and Best Blood MRD[a] Rates in the Intent-To-Treat Population

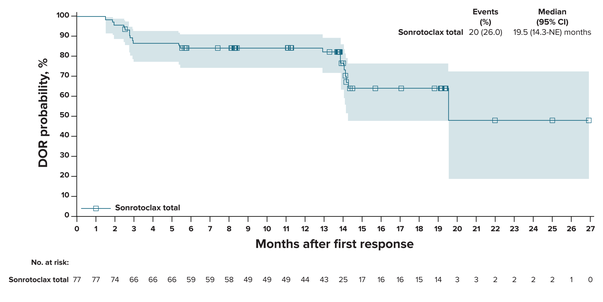


[a]MRD was measured using flow cytometry.
Abbreviations: CR, complete response; CRi, complete response with incomplete bone marrow recovery; IRC, independent review committee; MRD, measurable residual disease; NA, not available; NE, not estimable; nPR, nodular partial response; ORR, overall response rate; PD, progressive disease; PR, partial response; SD, stable disease uMRD, undetectable measurable residual disease.

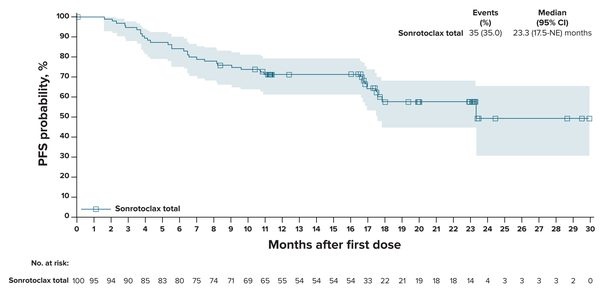
- Median IRC-assessed duration of response (DOR) was 19.5 months (95% CI, 14.3 months-not estimable [NE]) (**Figure 3A**)
  - The estimated 12-month DOR event-free rate was 84.3% (95% CI, 74.0%-90.8%)
- Median IRC-assessed progression-free survival (PFS) was 23.3 months (95% CI, 17.5 months-NE) (**Figure 3B**)
  - The estimated 12- and 15-month PFS rate were both 71.5%
- At the data cutoff, 12 patients had died from the disease under study
- Median overall survival (OS) was not reached (**Figure 3C**)
  - The estimated 12- and 18-month OS rates were 85.5% and 84.3%, respectively

Figure 3. Kaplan-Meier Curves of DOR, PFS, and OS

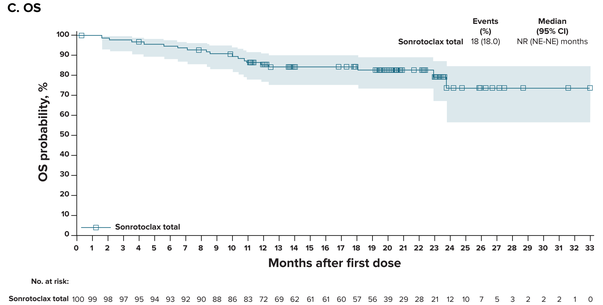
A. IRC-Assessed DOR



B. IRC-Assessed PFS



C. OS



Abbreviations: DOR, duration of response; IRC, independent review committee; NE, not estimable; NR, not reached; OS, overall survival; PFS, progression-free survival.

Safety

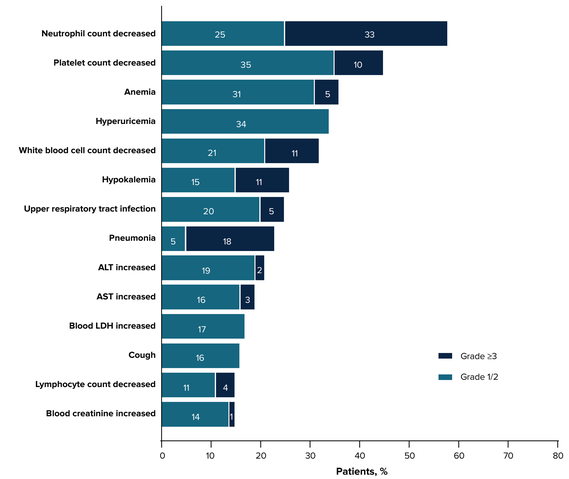
- An overall summary of treatment-emergent adverse events (TEAEs) is shown in **Table 2**
  - 66.0% of patients experienced a grade ≥3 TEAE
- Neutrophil count decreased was the most common TEAE of any grade and grade ≥3, and was observed in 58.0% and 33.0% of patients, respectively (**Figure 4**)
- No clinical tumor lysis syndrome (TLS) nor fatal TLS occurred
  - Laboratory TLS was reported in 4.0% of patients; all events of laboratory TLS were grade 3, manageable, and resolved without sequelae within a median of 3.5 days (range, 2-8 days)
- TEAEs led to death in 5 patients, none of which were related to treatment (**Table 2**)

Table 2. Overall Safety Summary

	All patients (N=100)
Any TEAE	98 (98.0)
Any treatment-related TEAE	91 (91.0)
Grade ≥3 TEAE	66 (66.0)
Treatment-related grade ≥3	53 (53.0)
Serious adverse event	41 (41.0)
Treatment-related serious adverse event	21 (21.0)
AEs leading to death[a]	5 (5.0)
Treatment-related AE leading to death	0
AEs leading to treatment discontinuation	7 (7.0)
Treatment-related AE leading to treatment discontinuation	3 (3.0)
AEs leading to dose interruption	43 (43.0)
Treatment-related AE leading to dose interruption	29 (29.0)
AEs leading to dose reduction	5 (5.0)
Treatment-related AE leading to dose reduction	5 (5.0)

[a]TEAEs leading to death included death of unknown cause (n=2), pneumonia (n=2), and acute cardiac failure (n=1).
Abbreviations: AE, adverse event; TEAE, treatment-emergent adverse event.

Figure 4. Any-Grade TEAEs in ≥15% of Patients



Abbreviations: ALT, alanine aminotransferase; AST, aspartate aminotransferase; LDH, lactate dehydrogenase; TEAE, treatment-emergent adverse event.

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