Phase 1/2 Study of Sonrotoclax (BGB-11417) Monotherapy in Bruton Tyrosine Kinase Inhibitor–Pretreated Relapsed/Refractory Mantle Cell Lymphoma: A Chinese Subpopulation Analysis

PF961

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CONCLUSIONS

- Sonrotoclax monotherapy demonstrated clinically meaningful activity in heavily pretreated patients with MCL in China, similar to the overall population, with a 61.8% ORR and median DOR by IRC of 15.8 months
- Treatment with sonrotoclax monotherapy was well tolerated, with no new safety signals identified
  - Consistent with the overall population, the most common grade ≥3 TEAEs were hematologic toxicities and infections, which were manageable
  - TLS rate was low, and events were mostly laboratory abnormalities that were manageable
- Based on the results of BGB-11417-201, sonrotoclax has been approved in the US and China, supporting its use as a treatment option for patients with R/R MCL
- A global phase 3, randomized placebo-controlled trial evaluating sonrotoclax in combination with zanubrutinib in patients with R/R MCL (CELESTIAL-RRMCL; NCT06742996) is ongoing

INTRODUCTION

- Patients with mantle cell lymphoma (MCL) who have disease progression on or after treatment with Bruton tyrosine kinase (BTK) inhibitors, such as zanubrutinib and acalabrutinib, have few effective treatment options[1]
- Venetoclax, the first-generation B-cell lymphoma 2 (BCL2) inhibitor, has shown efficacy in relapsed/refractory (R/R) MCL in the post-BTK inhibitor setting[2], but is not currently approved for MCL
- 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[3,4]
- BGB-11417-201 (NCT05471843) is an ongoing, open label, multicenter, dose-escalation/expansion study of sonrotoclax monotherapy in patients with R/R MCL pretreated with BTK inhibitors[5,6]
  - Sonrotoclax monotherapy demonstrated a significantly improved overall response rate (ORR) versus historic control (52.4% vs 30% [based on post-BTK inhibitor efficacy data][7-9]; $P<.0001$) and was well tolerated
- Presented here are BGB-11417-201 subgroup data for patients in China with R/R MCL who received sonrotoclax monotherapy

METHODS

- In BGB-11417-201, eligible patients were adults with histologically confirmed MCL who were previously treated with ≥1 anti-CD20–based therapy and ≥1 BTK inhibitor (**Figure 1**)
- Sonrotoclax was administered orally at target doses of 160 mg or 320 mg once daily, achieved gradually over a ≈4-week ramp-up period to mitigate tumor lysis syndrome (TLS) risk
- The part 2 primary endpoint was ORR by independent review committee (IRC) per Lugano 2014 criteria; key secondary endpoints include time to response (TTR), duration of response (DOR), progression-free survival (PFS), overall survival (OS), and safety

Figure 1. BGB-11417-201 (NCT05471843) Study Design

- **Sonrotoclax target doses were achieved after a ≈4-week ramp-up that did not require hospitalization or 12- or 24-hour postdose laboratory monitoring**

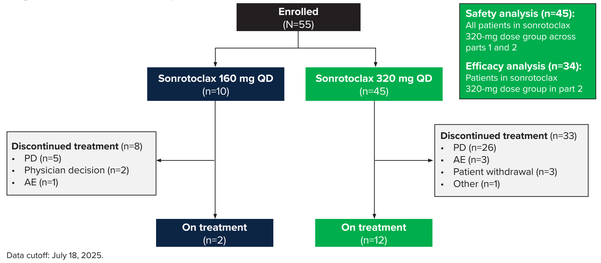
[a]Determined by safety monitoring committee based on part 1 data; will not exceed maximum tolerated dose or maximum administered dose.

Abbreviations: AE, adverse event; BCL2, B-cell lymphoma 2; BTK, Bruton tyrosine kinase; DLT, dose limiting toxicity; DOR, duration of response; ECOG PS, Eastern Cooperative Oncology Group performance status; HR-QOL, health-related quality of life; INV, investigator; IRC, independent review committee; MCL, mantle cell lymphoma; ORR, overall response rate; OS, overall survival; PD, progressive disease; PFS, progression-free survival; QD, once daily; RP2D, recommended phase 2 dose; SAE, serious adverse event; TEAE, treatment-emergent adverse event; TLS, tumor lysis syndrome; TTR, time to response; WHO, World Health Organization.

RESULTS

- As of July 18, 2025, 55 patients in China were enrolled and assigned to receive either target dose of sonrotoclax, 160 mg (n=10) or 320 mg (part 1, n=11; part 2, n=34); of 45 patients assigned to sonrotoclax 320 mg, 26.7% remained on treatment, with most treatment discontinuations attributed to progressive disease (**Figure 2**)

Figure 2. Patient Disposition



Data cutoff: July 18, 2025.

Abbreviations: AE, adverse event; PD, progressive disease; QD, once daily.

- Patients assigned to the sonrotoclax 320-mg target dose (n=45) had the following key characteristics (**Table 1**):
  - Median age was 66 years, and 73.3% were male
  - At study entry, 88.9% of patients had stage III/IV disease, 26.7% had bulky disease (longest diameter ≥5 cm), and 64.4% had high or intermediate simplified MCL International Prognostic Index (s-MIPI) scores
  - *TP53* mutation was observed in 31.4% (11/35) of patients, 46.7% (21/45) had bone marrow involvement, and 46.5% (20/43) had Ki-67 ≥30%
  - Patients had a median of 2 prior lines of therapy (range, 1-8); 20.0% had ≥2 distinct BTK inhibitors, and 80.0% discontinued their last line of prior therapy due to disease progression
- Compared with the global population[5,6], the China subpopulation showed generally similar baseline characteristics, although median age and rates of high s-MIPI score and bulky disease were lower, while rates of ≥30% Ki-67 and discontinuation of last prior therapy due to progressive disease were higher

Table 1. Baseline Patient Characteristics

Parameters	Sonrotoclax 320 mg n=45
Age, median (range), years	66 (50-81)
≥65 years, n (%)	25 (55.6)
Male, n (%)	33 (73.3)
ECOG PS, n (%)	
0	16 (35.6)
1	29 (64.4)
2	0
Disease status at study entry, n (%)	
III	4 (8.9)
IV	36 (80.0)
s-MIPI, n (%)	
High	12 (26.7)
Intermediate	17 (37.8)
Bulky disease status, n (%)	
LDi ≥5 cm	12 (26.7)
LDi ≥10 cm	2 (4.4)
Bone marrow involvement at baseline, n (%)[a]	21 (46.7)
Ki-67 ≥30%, n/N with known status (%)	20/43 (46.5)
***TP53* mutation, n/N with known status (%)**	11/35 (31.4)
Disease response to last prior therapy, n (%)[b]	
Refractory[c]	42 (93.3)
Relapsed[d]	2 (4.4)
No. of prior lines of therapy, median (range)	2 (1-8)
≥3 prior lines, n (%)	21 (46.7)
Prior BTK inhibitor treatment, n (%)	45 (100)
≥2 prior BTK inhibitors, n (%)	9 (20.0)
Reason for discontinuing last line of anticancer therapy, n (%)	
Progressive disease	36 (80.0)
Treatment completed	4 (8.9)
Toxicity	1 (2.2)
Other	4 (8.9)

[a]Four patients had indeterminate bone marrow involvement at baseline. [b]Data for one patient was missing. [c]Nonresponsive to last line or progressive disease within 6 months after the last line end date. [d]Initial treatment response followed by progressive disease >6 months after the last line end date.

Abbreviations: BTK, Bruton tyrosine kinase; ECOG PS, Eastern Cooperative Oncology Group performance status; LDi, longest diameter; s-MIPI, simplified Mantle Cell Lymphoma International Prognostic Index.

- In part 2 (n=34), ORR by IRC was 61.8% and included 26.5% of patients with complete response (**Table 2**); median TTR by IRC was 1.8 months (range, 1.7-3.5 months)
- With a median study follow-up of 15.3 months, the IRC- and investigator-assessed efficacy outcomes were generally comparable with sonrotoclax 320 mg in part 2:
  - Median DOR by IRC was 15.8 months (range, 7.4 months-not estimable) (**Figure 3A**)
  - Median PFS by IRC was 11.9 months (range, 6.3-19.8 months) (**Figure 3B**)
  - Median OS was not reached (range, 7.7 months-not estimable) (**Figure 3C**)

Table 2. Part 2 Efficacy Endpoints

Parameters	Sonrotoclax 320 mg n=34	
	IRC assessed	INV assessed
ORR (PR + CR), n (%)	21 (61.8)	19 (55.9)
95% CI, %	43.6-77.8	37.6-72.8
CR rate, n (%)	9 (26.5)	12 (35.3)
95% CI, %	12.9-44.4	19.7-53.5
TTR, median (range), months	1.8 (1.7-3.5)	1.8 (1.7-3.7)
DOR, median (95% CI), months	15.8 (7.4-NE)	17.2 (7.4-NE)
Follow-up, median (95% CI), months[a]	15.6 (10.2-20.6)	15.6 (10.2-20.6)
PFS, median (95% CI), months	11.9 (6.3-19.8)	9.0 (1.7-19.8)
Follow-up, median (95% CI), months[b]	17.4 (12.0-22.8)	17.4 (12.1-22.8)
OS, median (95% CI), months	NR (7.7-NE)	
Follow-up, median (95% CI), months[c]	18.7 (16.2-21.0)	

For ORR and CR rate, 95% CIs were estimated using the Clopper-Pearson method. For DOR, PFS, and OS, medians were estimated by the Kaplan-Meier method with 95% CIs estimated using the Brookmeyer and Crowley method with log-log transformation. [a]DOR follow-up is defined as the time from first documented response to progression. [b]PFS follow-up is defined as the time from treatment initiation to progression or death. [c]OS follow-up is defined as the time from treatment initiation to death from any cause.

Abbreviations: CR, complete response; DOR, duration of response; INV, investigator; IRC, independent review committee; NE, not estimable; NR, not reached; ORR, overall response rate; OS, overall survival; PFS, progression-free survival; PR, partial response; TTR, time to response.

Figure 3. Efficacy Outcomes With Sonrotoclax 320 mg (Part 2)

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

- For all patients assigned to the target dose of sonrotoclax 320 mg (n=45), neutropenia was the most common any-grade (53.3%) and grade ≥3 (20.0%) treatment-emergent adverse event (TEAE) (**Table 3**)
- Serious TEAEs were observed in 26.7% of patients, with pneumonia and thrombocytopenia observed in 6.7% each
- TEAEs led to treatment discontinuation in four patients (8.9%); all events were considered treatment related, and three were also considered related to underlying disease
- Two patients experienced grade 5 AEs (n=1 each; multiorgan disorder and respiratory failure); both were considered related to underlying disease and to study treatment by the investigator
- TLS occurred in three patients (6.7%; 2 laboratory, 1 clinical); all resolved without sequelae
- Overall, the incidences of grade ≥3 and serious TEAEs and TEAEs leading to treatment discontinuation were generally similar in the China subpopulation and the global population[5,6]

Table 3. TEAE Summary

Patient, n (%)	Sonrotoclax 320 mg n=45	
Any TEAE	44 (97.8)	
Treatment-related	41 (91.1)	
Grade ≥3 TEAEs	21 (46.7)	
Treatment-related	17 (37.8)	
Serious TEAEs	12 (26.7)	
Treatment-related	8 (17.8)	
Grade 5 AEs	2 (4.4)	
TEAEs leading to treatment discontinuation	4 (8.9)	
TEAEs in >5 patients	**Any grade**	**Grade ≥3**
Neutropenia[a]	24 (53.3)	9 (20.0)
White blood cell count decreased	23 (51.1)	3 (6.7)
Hypokalemia	16 (35.6)	0
Hyperuricemia	14 (31.1)	1 (2.2)
Anemia[b]	13 (28.9)	3 (6.7)
AST increased	11 (24.4)	1 (2.2)
Thrombocytopenia[c]	10 (22.2)	4 (8.9)
ALT increased	9 (20.0)	0
Hypocalcemia	8 (17.8)	0
Hypoalbuminemia	7 (15.6)	0
Pneumonia	6 (13.3)	5 (11.1)
Diarrhea	6 (13.3)	2 (4.4)
Blood LDH increased	6 (13.3)	0
Hyponatremia	6 (13.3)	0
Insomnia	6 (13.3)	0
Select TEAEs by category/AE		
Infections (SOC)	16 (35.6)	9 (20.0)
Febrile neutropenia[d]	1 (2.2)	1 (2.2)
TLS[d] (AE)	3 (6.7)	3 (6.7)

[a]Grouped term includes preferred terms *neutrophil count decreased*, *neutropenia*, and *febrile neutropenia*. [b]Grouped term includes preferred terms *anemia* and *hemoglobin decreased*. [c]Grouped term includes preferred terms *thrombocytopenia* and *platelet count decreased*. [d]Per National Cancer Institute Common Terminology Criteria for Adverse Events v5.0, febrile neutropenia and TLS are classified as grade ≥3.

Abbreviations: AE, adverse event; ALT, alanine aminotransferase; AST, aspartate aminotransferase; LDH, lactate dehydrogenase; SOC, system organ class; TEAE, treatment-emergent adverse event; TLS, tumor lysis syndrome.

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DISCLOSURES

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