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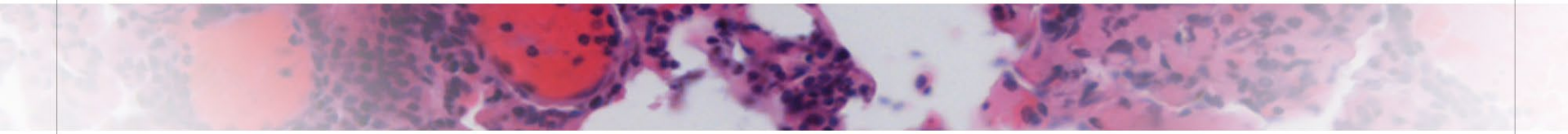

MRD-Guided Therapy of Sonrotoclax (BGB-11417) + Obinutuzumab in Patients With Treatment-Naive CLL: Initial Results From an Ongoing Phase 1/1b Study, BGB-11417-101

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Introduction

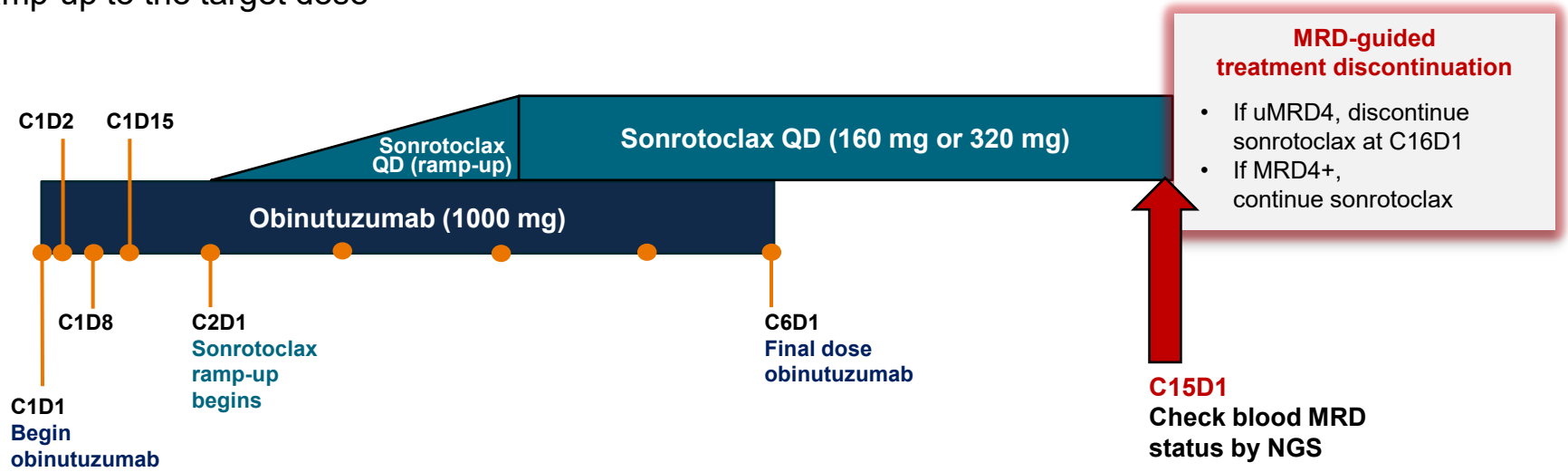
- BCL2 inhibitor + anti-CD20 combination therapy is a viable treatment option for patients with TN CLL, demonstrating deep and durable responses[1]
- First-generation BCL2 inhibitor use may be limited warranting a new combination treatment designed to have improved efficacy and safety
- Sonrotoclax (BGB-11417), 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[2,3]
- Here, we present the first results for MRD-guided combination therapy with sonrotoclax and obinutuzumab in patients with TN CLL/SLL in the BGB-11417-101 clinical trial

BCL2, B-cell lymphoma 2; CLL, chronic lymphocytic leukemia/small lymphocytic lymphoma; MRD, minimal residual disease; SLL, small lymphocytic lymphoma; TN, treatment-naïve.

1. Fischer K, et al. *NEJM*. 2019;380(23):2225-2236; 2. Guo Y, et al. *J Med Chem*. 2024;67(10):7836-7858; 3. Liu J, et al. *Blood*. 2024;143(18):1825-1836.

BGB-11417-101 (NCT04277637) Study Design

- BGB-11417-101 is a global phase 1/1b study evaluating sonrotoclax as monotherapy or in combination with zanubrutinib and/or obinutuzumab in patients with B-cell malignancies
- Study endpoints included safety/tolerability, ORR (iwCLL 2018), MRD status by modified ERIC flow cytometry assay or NGS
- Obinutuzumab (IV) monotherapy starts on C1D1 for 6 cycles, then sonrotoclax (oral) is added on C2D1 with ramp-up to the target dose



C, cycle; D, day; IV, intravenous; MRD, minimal residual disease; NGS, next-generation sequencing; ORR, overall response rate; PD, progressive disease; QD, once daily; uMRD, undetectable minimal residual disease.

Baseline Demographics and Disease Characteristics

Characteristics	Sonrotoclax 160 mg + Obinutuzumab (n=20)	Sonrotoclax 320 mg + Obinutuzumab (n=35)	All Patients (N=55)
Study follow-up, median (range), months	9.8 (0.4-12.5)	19.5 (2.9-28.8)	12.3 (0.4-28.8)
Age, median (range), years	61 (46-81)	63 (42-78)	62 (42-81)
≥65 years, n (%)	7 (35)	16 (46)	23 (42)
Male, n (%)	15 (75)	21 (60)	36 (65)
Risk status, n/known status (%)			
del(17p) or *TP53* mutation[a]	2/17 (12)	2/28 (7)	4/45 (9)
del(11q)	2/17 (12)	1/31 (3)	3/48 (6)
Unmutated IGHV, n/tested (%)	10/20 (50)	21/33 (63)	31/53 (58)
High tumor bulk[b] at baseline, n/tested (%)	4/19 (21)	4/34 (12)	8/53 (15)

Data cutoff: August 29, 2025.
[a]*TP53* mutations were defined as ≥10% VAF. [b]Any LN ≥10 cm or LN ≥5 cm and ALC ≥25×10^9/L.
ALC, absolute lymphocyte count; IGHV, immunoglobulin heavy chain variable region; LN, lymph node; VAF, variant allele frequency.

Sonrotoclax + Obinutuzumab Was Well Tolerated Across Dose Levels

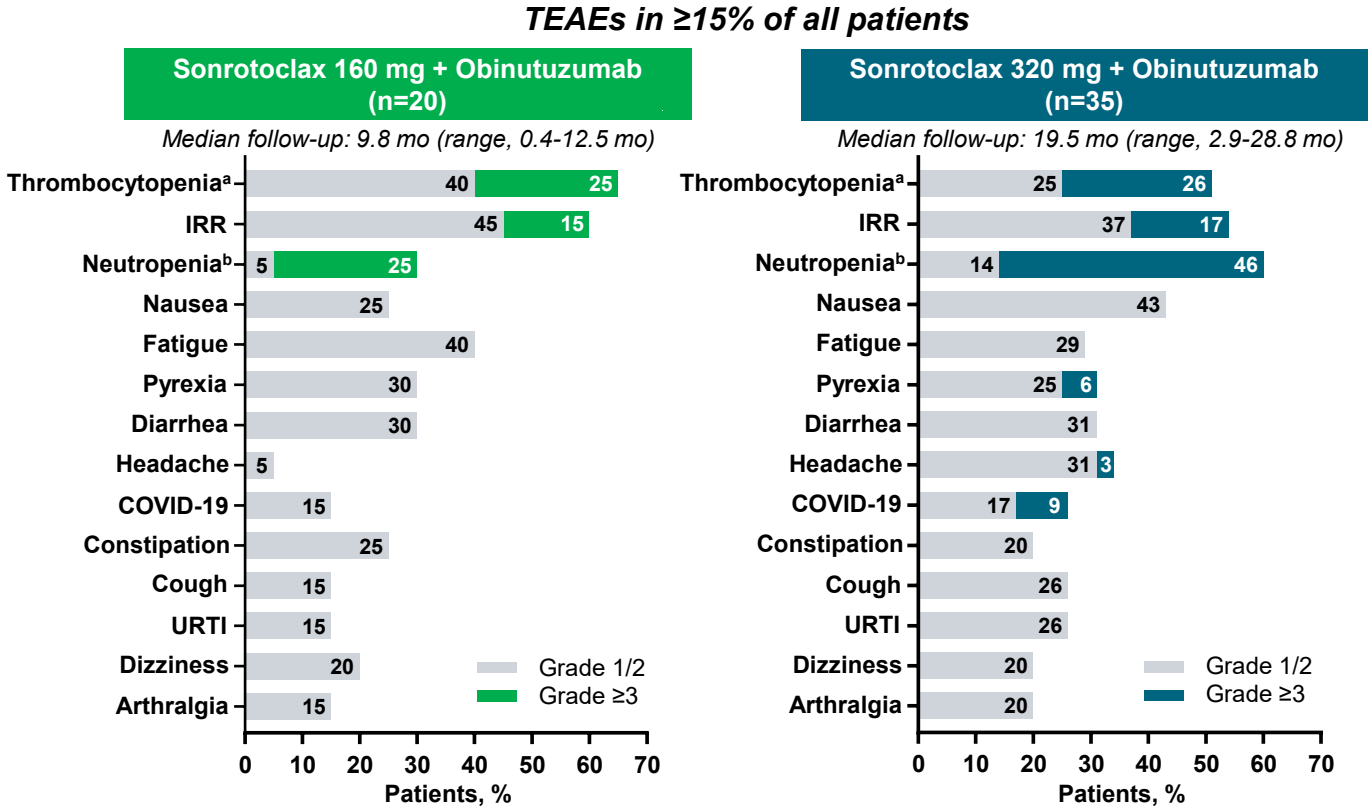
Patients, n (%)	Sonrotoclax 160 mg + Obinutuzumab (n=20)	Sonrotoclax 320 mg + Obinutuzumab (n=35)	All Patients (N=55)
Duration of exposure, median (range), months	9.8 (0-12.5)	13.7 (1.5-17.8)	11.8 (0-17.8)
Any TEAEs	20 (100)	35 (100)	55 (100)
Grade ≥3	11 (55)	27 (77)	38 (69)
Serious TEAEs	10 (50)	16 (46)	26 (47)
Leading to death	0	0	0
Leading to discontinuation of obinutuzumab[a]	1 (5)	2 (6)	3 (5)
Leading to discontinuation of sonrotoclax	0	0	0
Relative dose intensity of sonrotoclax, median, %	99.7	99.7	99.7

No treatment discontinuations were attributable to sonrotoclax
No deaths due to adverse events occurred on the study

[a]Reasons for discontinuation of obinutuzumab treatment were prostate cancer (160 mg; n=1), platelet count decreased (320 mg; n=1), and thrombocytopenia (320 mg; n=1).
TEAE, treatment-emergent adverse event.

TEAEs Observed With Combination Treatment Were Mostly Low Grade

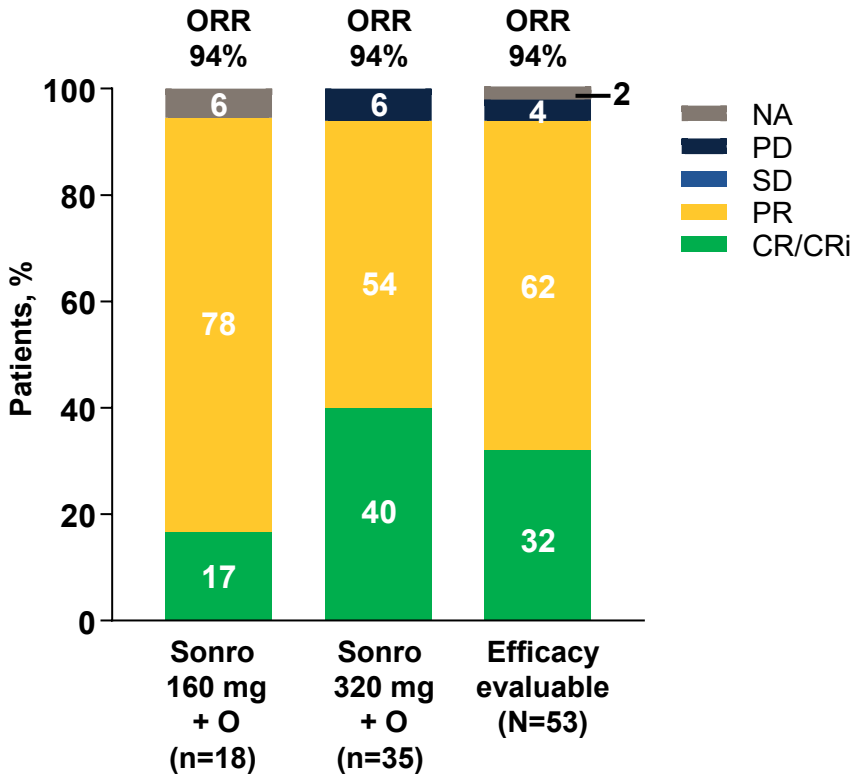
- No DLTs
- No TLS was observed during sonrotoclax ramp-up
- Grade 3+ neutropenia did not translate to serious or life-threatening infections
- Thrombocytopenia did not translate to major bleeding



[a]Includes the combined preferred terms *platelet count decreased* and *thrombocytopenia*. [b]Includes the combined preferred terms *neutrophil count decreased* and *neutropenia*.
DLT, dose-limiting toxicity; IRR, infusion-related reaction; TEAE, treatment-emergent adverse event; TLS, tumor lysis syndrome; URTI, upper respiratory tract infection.

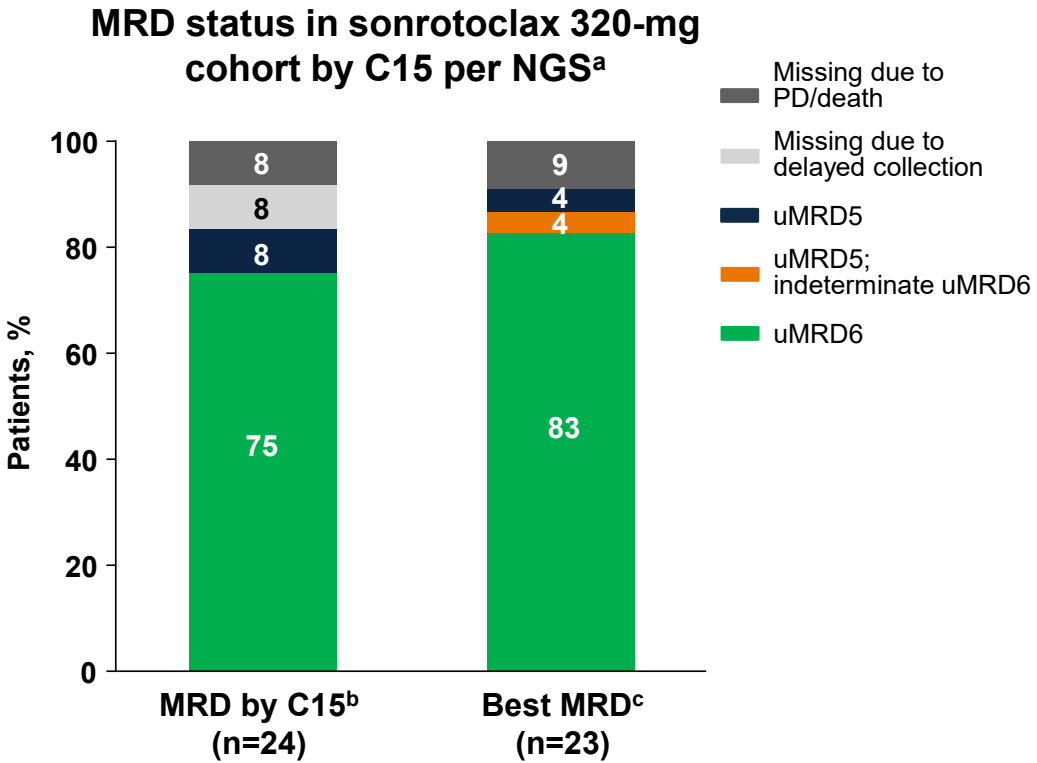
High Response Rates Were Observed With Sonrotoclax + Obinutuzumab

- An ORR of 94% was achieved across both dose levels and a CR/CRi rate of 40% was observed in the 320-mg cohort
- With a median study follow-up of 12.3 months, 3 patients (6%) had PFS events:
  - Sonrotoclax 160-mg cohort: 1 death (passed away 4 months after EOT due to indeterminate cause)
  - Sonrotoclax 320-mg cohort: 2 patients had RT (1 each at C2 and C6)
- Estimated 18-month PFS rate: 94.3% (95% CI, 83.5%-98.1%)



C, cycle; CR, complete response; CRi, complete response with incomplete hematopoietic recovery; D, day; EOT, end of treatment; NA, not assessable; O, obinutuzumab; ORR, overall response rate; PD, progressive disease; PFS, progression-free survival; PR, partial response; RT, Richter transformation; SD, stable disease; sonro, sonrotoclax; uMRD, undetectable minimal residual disease.

Substantial Peripheral Blood uMRD6 Rates Were Observed by Cycle 15



- All patients who reached C15 with a NGS sample analyzed (n=21) achieved at least uMRD5 and discontinued therapy as defined per protocol (ie, achieved at least uMRD4)
  - 19/21 (91%) achieved uMRD6
  - All patients remain in remission with a median time off treatment of 7.2 months (range, 1.7-14.4 month)

[a]No patients in the 160-mg cohort have reached C15, with a median follow-up of 9.8 months (range, 0.4-12.5 months). [b]MRD by C15 included any patient who should have reached C15 based on first dose date.
[c]Best MRD included any patient with ≥1 post-baseline MRD sample assessed by NGS, or who had disease progression or death prior to MRD assessment.
C, cycle; MRD, minimal residual disease; NGS, next generation sequencing; uMRD, undetectable minimal residual disease.

Conclusions

- Sonrotoclax + obinutuzumab was well tolerated in patients with TN CLL/SLL, with no TEAEs leading to death
- No laboratory or clinical TLS events occurred during sonrotoclax ramp-up
- Potent activity and high rates of uMRD were observed at the sonrotoclax 320-mg dose level
  - 94% of patients achieved ORR with 40% CR/CRi rate in the 320-mg cohort
  - **Among patients who reached C15 with a NGS sample analyzed, 100% achieved uMRD5 and 91% achieved uMRD6**
  - **All discontinued therapy per protocol and remain in remission, with a median of 7.2 months off treatment (range, 1.7-14.4 months)**
- A registrational phase 3 study (CELESTIAL-RRCLL, BGB-11417-303) assessing this combination with sonrotoclax 320 mg is currently recruiting patients with R/R CLL

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