ASH 2025 highlights
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American Society of Hematology

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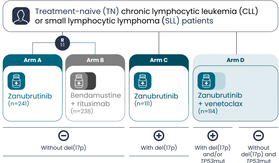
Zanubrutinib as frontline option regardless of del(17p) and/or *TP53*mut status

Updates on zanubrutinib monotherapy in high-risk, treatment-naive (TN) CLL/SLL from the SEQUOIA study.[1,2]

Design highlights

Treatment-naive (TN) chronic lymphocytic leukemia (CLL) or small lymphocytic lymphoma (SLL) patients



*Patients are considered del(17p) positive if >7% of peripheral blood cells (i.e., >14 of 200 nuclei) show the deletion, as confirmed by a central laboratory using the FDA-approved Abbott Vysis assay.

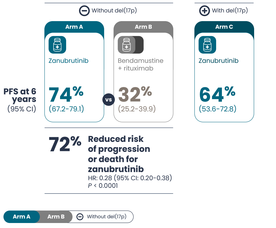
Read the **ARM D** poster from Shadman *et al.*[2]

Key endpoints

PFS ORR OS Safety

Key 6-year follow-up results

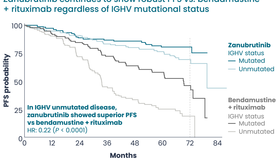
Zanubrutinib continues to demonstrate robust progression-free survival (PFS) regardless of del(17p) and/or *TP53*mut status



72% **Reduced risk of progression or death for zanubrutinib**
HR: 0.28 (95% CI: 0.20-0.38)
P < 0.0001

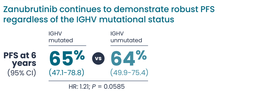
Arm A **Arm B** Without del(17p)

Zanubrutinib continues to show robust PFS vs. bendamustine + rituximab regardless of IGHV mutational status



Arm C With del(17p)

Zanubrutinib continues to demonstrate robust PFS regardless of the IGHV mutational status



HR: 1.21; *P* = 0.0585

Key safety and tolerability profile

The safety profile of zanubrutinib remains consistent with prior reports and no new safety signals were observed

	Arm A	Arm B	Arm C
	Zanubrutinib	Bendamustine + rituximab	Zanubrutinib
Grade ≥3 treatment-emergent adverse events (TEAEs)	72%	74%	74%
Treatment-emergent and post-treatment AESIs	93%	93%	93%

AESIs of any grade in ≥15% of patients included:
Anemia, neutropenia, contusion, hypertension, COVID-19, upper respiratory tract infection, pneumonia, urinary tract infection and basal cell carcinoma

These long-term results continue to support zanubrutinib as an effective, tolerable frontline option for CLL/SLL, including in those with high-risk features.[1]

Read the **SEQUOIA ARM A, B, and C** poster from Tam *et al.*

The new Bruton tyrosine kinase (BTK) degrader BGB-16673 demonstrated to be safe and effective in heavily pre-treated CLL/SLL

Updated safety and efficacy data from the ongoing phase 1/2 CaDAnCe-101 study in high-risk patients resistant to BTK and BCL2 inhibitors.[3]

Design highlights

68 patients with relapsed/refractory (R/R) CLL/SLL

2-10 prior lines of therapy (median: 4)

19.8 months median study follow-up (range 0.3-34.0)

BGB-16673 at 50, 100, 200, 350 and 500 mg

78% unmutated IGHV

68% with del(17p) and/or *TP53*mut

50% complex karyotype (≥3 abnormalities)

39% *BTK* mutation

15% *PLCG2* mutation

Primary endpoints

Safety and tolerability
MTD, RDFE

Secondary endpoints

PK, PD,
preliminary antitumor activity

Key safety and tolerability profile

BGB-16673 was well tolerated and the most common TAEAs included:

≥20%: fatigue, contusion (bruising), diarrhea, neutropenia, anemia

≥10% - <20%: cough, pyrexia, arthralgia, COVID-19, dyspnea, lipase increased, peripheral edema, pneumonia, thrombocytopenia, sinusitis, amylase increased, nausea, upper respiratory tract infection

0 treatment-related deaths

3 patients discontinued treatment due to a treatment-related TEAE

No new toxicities identified with median treatment duration of 13.6 months

Preliminary results

BGB-16673 demonstrated significant antitumor activity and high overall response rate (ORR)

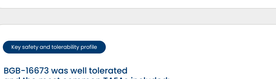
200 mg **ORR** **94%** n=18

All patients across all doses **ORR** **85%** n=68

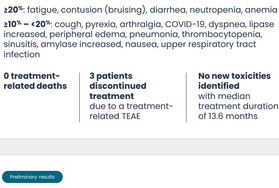
PFS (12 months) **74%** 95% CI: 59.3%-83.3%

PFS (18 months) **65%** 95% CI: 50.6%-77.4%

Best overall response



High ORRs observed in high-risk subgroups



The CaDAnCe-101 study demonstrated antitumor activity, including in patients with BTKi-resistance mutations and those previously exposed to cBTK, ncBTK, and BCL2 inhibitors.[3]

Read the **CaDAnCe-101 study** presentation from Ahn *et al.*

BGB-16673 is currently under investigation in the phase 3 CaDAnCe-304 trial

A head-to-head phase 3 study comparing the efficacy and safety of BGB-16673 vs pirtobrutinib in patients with R/R CLL/SLL.[4-6]

Design highlights

≈500 patients with R/R CLL/SLL

≥1 line of therapy including a cBTKi

No prior BTK protein degraders or ncBTKi

R 1:1

BGB-16673
200 mg oral QD
(n≈250)

Pirtobrutinib
200 mg oral QD
(n≈250)

Treatment continued until progressive disease or unacceptable toxicity

Primary endpoint

PFS

Key Secondary endpoints

OS, ORR, DOR, TTNT, safety and tolerability, PROs

Submission is ongoing, and recruitment will begin soon. Contact us for information about open study centres in Switzerland.[4]

Read the **CaDAnCe-304** study design from Thompson *et al.*[4]

Sonrotoclax combinations continued to demonstrate safety and efficacy in TN CLL/SLL

Updated data from the ongoing phase 1/1b study BGB-11417-101, regardless of risk factors.[7,8]

Design highlights

137 patients with treatment-naive (TN) CLL/SLL patients
- 14% with del(17p) or *TP53*mut
- 61% unmutated IGHV

Zanubrutinib lead-in for 8-12 weeks

Zanubrutinib **+ sonrotoclax** (160 or 320 mg) until disease progression, intolerance or elective discontinuation

30.7 months median follow-up (range: 3.1-45.5)

Key endpoints

Safety and tolerability, RP2D, ORR, MRD

55 patients with treatment-naive CLL/SLL patients
- 9% with del(17p) or *TP53*mut
- 58% unmutated IGHV

Obinutuzumab lead-in for 8-12 weeks

Obinutuzumab **+ sonrotoclax** (160 or 320 mg) until disease progression, intolerance or elective discontinuation

12.3 months median follow-up (range: 0.4-28.8)

Key endpoints

Safety and tolerability, ORR, MRD

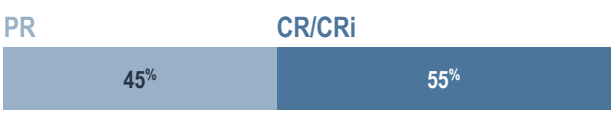
Preliminary safety and efficacy outcomes | combination with **zanubrutinib**

Sonrotoclax + zanubrutinib demonstrated high response rates

ORR

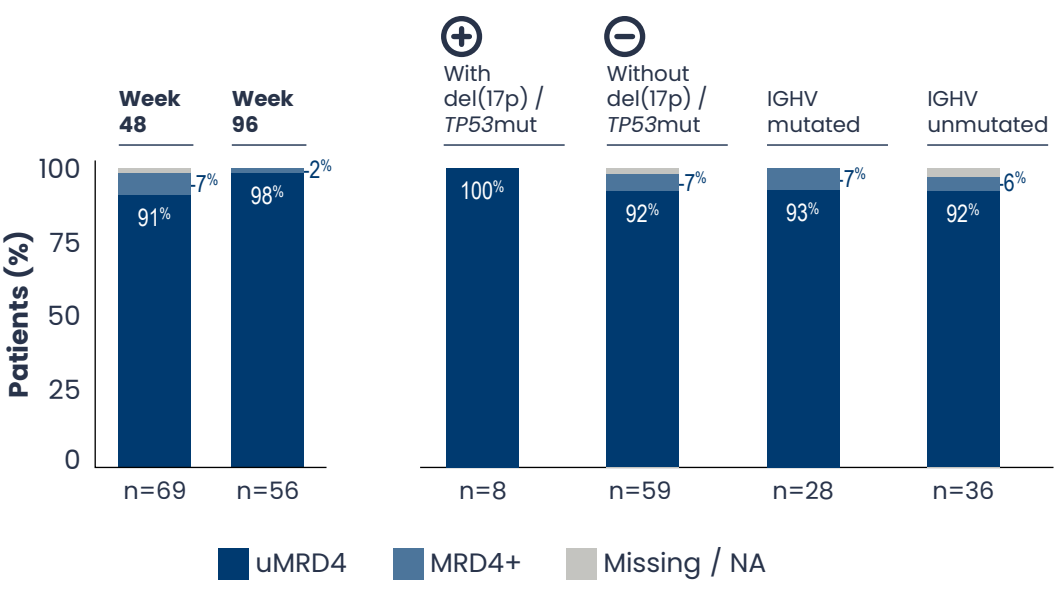
All doses **100%** n=135

320 mg **100%** n=84



MRD

High rates of uMRD4 were achieved regardless of risk factors in patients who received sonrotoclax 320 mg + zanubrutinib



Sonrotoclax + zanubrutinib demonstrated encouraging safety profile and was well tolerated

The majority of TEAEs occurred at grades 1 and 2

No TEAEs led to death

5 patients discontinued sonrotoclax treatment due to TEAEs

The most common grade ≥3 TEAE was neutropenia (27%), which was transient and did not lead to higher rates of grade ≥3 infections

No clinical or laboratory tumour lysis syndrome occurred

These preliminary data highlight the potential for the all-oral therapy sonrotoclax + zanubrutinib combination. The currently enrolling phase 3 CELESTIAL-TNCLL trial will provide further evidence in patients with TN CLL.[7]

Read the **BGB-11417-101 study** poster from Tam *et al.*[7]

Preliminary safety and efficacy outcomes | combination with **obinutuzumab**

Sonrotoclax + obinutuzumab demonstrated high response rates

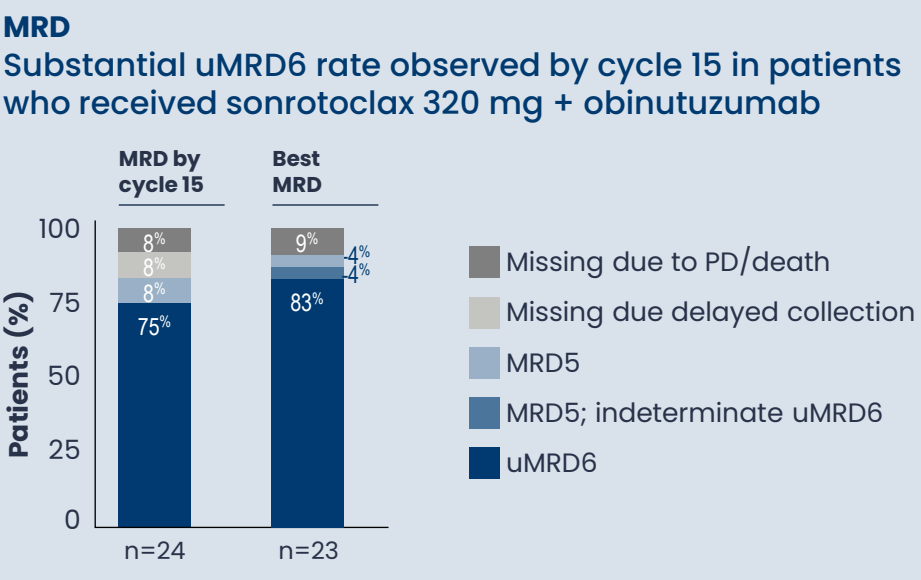
ORR

All doses **94%** n=53

320 mg **94%** n=35

MRD

Substantial uMRD6 rate observed by cycle 15 in patients who received sonrotoclax 320 mg + obinutuzumab



Sonrotoclax + obinutuzumab was well tolerated

The majority of TEAEs occurred at grades 1 and 2

No AEs led to death

No treatment discontinuation were attributable to sonrotoclax

The most common grade ≥3 TEAE were neutropenia (25%) and thrombocytopenia (25%)

- Neutropenia did not translate to serious or life-threatening infections
- Thrombocytopenia did not translate to major bleeding

No tumour lysis syndrome during sonrotoclax ramp-up

The currently recruiting phase 3 CELESTIAL-RRCLL trial will further assess the sonrotoclax + obinutuzumab combo in patients with R/R CLL.[8]

Read the **BGB-11417-101 study** presentation from Hoffmann *et al.*[8]

Sonrotoclax monotherapy showed promising efficacy in heavily pretreated R/R MCL

Results from the ongoing phase 1/1b study BGB-11417-101, in patients with R/R mantle cell lymphoma (MCL).[9]

Design highlights

125 patients with R/R MCL and ≥1 line of anti-CD20-based therapy and ≥1 BTK inhibitor

- 35% with *TP53*mut
- 1-8 prior lines of therapy (median: 3)
- 59% with ≥3 prior lines
- 19% with ≥2 prior BTK inhibitors

R 1:1

- Sonrotoclax 160mg QD (n=10)
- Sonrotoclax 320 mg QD (n=115)

Key endpoints

ORR, DOR, PFS, safety

14.2 months median follow-up (range: 0.3-24.9)

Key safety and tolerability profile

Sonrotoclax was well tolerated and the most common any grade TEAEs included:

≥20%: neutropenia, thrombocytopenia, anemia, white blood cell count decreased

≥10% – <20%: hyperuricemia, hypokalemia, pneumonia, diarrhea, AST increased, ALT increased, constipation, Lymphopenia

16 patients discontinued treatment due to a treatment-related TEAE

15 TEAEs led to death

- 11 considered related to disease under study
- 1 due to pneumonia, 1 due to pneumothorax, and 2 unknown

8 TLS events were reported (2 clinical, 6 laboratory)

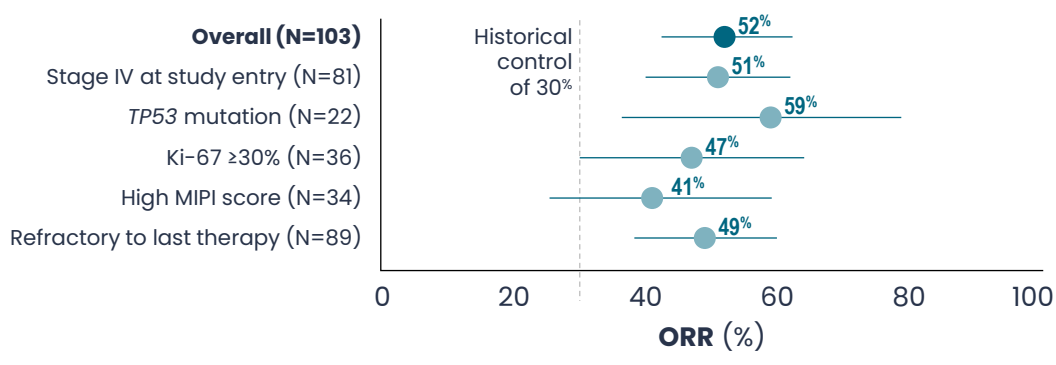
- All events resolved without sequelae
- No events resulted in death or treatment discontinuation

Preliminary results

Sonrotoclax revealed a promising efficacy in heavily pretreated patients

320 mg n=103	ORR	CR rate	median PFS	DOR
	52%	**16%**	**6.5 months**	**15.8 months**
	95% CI: 42.4-62.4		95% CI: 4.0-10.4	95% CI: 7.4-not estimable

ORR benefit was consistent across patients with high-risk subgroups



Sonrotoclax monotherapy was well tolerated and demonstrated clinically meaningful benefits in heavily pretreated patients with advanced MCL.[9]

Read the **BGB-11417-101 study** presentation from Wang *et al.*[9]

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Acronyms

AE: adverse events; **AESI**: adverse events of special interest; **ALT**: alanine aminotransferase; **AST**: aspartate aminotransferase; **BCL2i**: B-cell lymphoma 2 inhibitor; **cBTKi**: covalent Bruton tyrosine kinase inhibitor; **CI**: confidence interval; **CLL**: chronic lymphocytic leukemia; **CR**: complete response; **CRi**: complete response with incomplete marrow recovery; **DoR**: duration of response; **HR**: hazard ratio; **IGHV**: immunoglobulin heavy chain; **MCL**: mantle cell lymphoma; **MRD**: minimal residual disease; **MRD4+**: $<10^{-4}$ CLL cells of total WBCs; **MRD5**: $<10^{-5}$ CLL cells of total WBCs; **MTD**: maximum tolerated dose; **ncBTKi**: noncovalent Bruton tyrosine kinase inhibitor; **ORR**: objective response rate; **OS**: overall survival; **PD**: progressive disease; **PK**: harmacokinetic; **PR**: partial response; **PROs**: patient-reported outcomes; **QD**: once daily; **PFS**: progression-free survival; **R/R**: relapsed/refractory; **RDFE**: recommended dose for expansion; **RP2D**: recommended phase 2 dose; **SD**: stable disease; **SLL**: small lymphocytic lymphoma; **TEAEs**: treatment-emergent adverse events; **TLS:** tumor lysis syndrome; **TN**: treatment naive; **TTNT**: time to next treatment; **uMDR**: undetectable measurable residual disease; **uMRD6**: $<10^{-6}$ CLL cells of total WBCs; **WBCs**: white blood cells.

References

1. Tam, C.S., *et al*. Sustained Efficacy of Zanubrutinib vs Bendamustine + Rituximab in Treatment-Naive Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma and Continued Favorable Survival in Non-randomized Patients With del(17p): 6-Year Follow-Up in the Phase 3 SEQUOIA Study. Poster Presentation 2129 at the ASH Annual Meeting and Exposition; 6-9 December 2025; Orlando, USA.

2. Shadman, M., *et al*. Zanubrutinib + Venetoclax for Treatment-Naive Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma (CLL/SLL), Including Patients With del(17p) and/or *TP53* Mutation and Unmutated Immunoglobulin Heavy-Chain Variable Status: 3-Year Results From SEQUOIA Arm D. Poster Presentation 5669 at the ASH Annual Meeting and Exposition; 6-9 December 2025; Orlando, USA.

3. Ahn, I.E., *et al*. Updated Efficacy and Safety Results of the Bruton Tyrosine Kinase Degrader BGB-16673 in Patients With Relapsed/Refractory Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma From the Ongoing Phase 1 CaDAnCe-101 Study. Presentation at the ASH Annual Meeting and Exposition; 6-9 December 2025; Orlando, USA.

4. Thompson, M.C., *et al*. CaDAnCe-304, a Phase 3, Open-Label, Randomized Study to Evaluate the Safety and Efficacy of Bruton Tyrosine Kinase Degrader BGB-16673 Compared With Pirtobrutinib in Patients With Relapsed/Refractory Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma. Poster Presentation 5691 at the ASH Annual Meeting and Exposition; 6-9 December 2025; Orlando, USA.

5. ClinicalTrials.gov. https://clinicaltrials.gov/study/NCT06973187. Accessed December 2025.

6. BeOne. Investor R&D Day presentation, June 26, 2025.

7. Tam, C.S., *et al*. Frontline Treatment of Sonrotoclax (BGB-11417) + Zanubrutinib for CLL/SLL Demonstrates High uMRD Rates With Favorable Tolerability: Updated Data From BGB-11417-101, An Ongoing Phase 1/1b Study. Poster Presentation 3891 at the ASH Annual Meeting and Exposition; 6-9 December 2025; Orlando, USA.

8. Hoffmann, M.S., *et al*. 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. Presentation at the ASH Annual Meeting and Exposition; 6-9 December 2025; Orlando, USA.

9. Wang, M., *et al*. Sonrotoclax (BGB-11417) Monotherapy in Patients With R/R MCL Previously Treated With a BTK Inhibitor: Results From a Phase 1/2 Study. Presentation at the ASH Annual Meeting and Exposition; 6-9 December 2025; Orlando, USA.

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