The all-oral investigational combination of sonrotoclax and zanubrutinib reports on safety and efficacy

Updated data from the ongoing Phase 1/1b study BGB-11417-101 across TN and R/R patients with CLL/SLL or R/R MCL with high-risk features.[1-3]

Design highlights

TN CLL/SLL (n=137)
- 13.1% with del(17p) or *TP53* mut
- 59.9% unmutated IGHV

R/R CLL/SLL (n=47)
- 37.2% with del(17p) or *TP53* mut
- 73.9% unmutated IGHV

R/R MCL (n=51)
- 41.2% *TP53* mut
- 19.6% Ki-67 ≥30%

Zanubrutinib → lead-in for 8-12 weeks

Zanubrutinib + sonrotoclax until disease progression, intolerance or elective discontinuation after 96 weeks

Selected primary endpoints

RP2D, safety and tolerability

Selected secondary/exploratory endpoints

ORR, MRD

Preliminary safety and efficacy outcomes — TN CLL/SLL

With a median follow-up of 33.6 months (range: 3.1-48.8)

Safety profile of sonrotoclax + zanubrutinib in TN CLL/SLL

TEAEs (n=137)

Any TEAE	99.3%
Grade ≥3	63.5%
Serious TEAEs	34.3%
Leading to death	0%
Leading to discontinuation of sonrotoclax	3.6%

The most common any-grade TEAEs in over 30% of patients were neutropenia, COVID-19, contusion/bruising, diarrhea, and upper respiratory tract infection

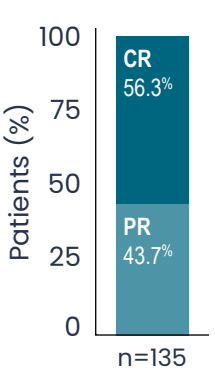
- No clinical or laboratory TLS occurred
- No TEAE led to death

See the presentation for TEAEs for each dosing.

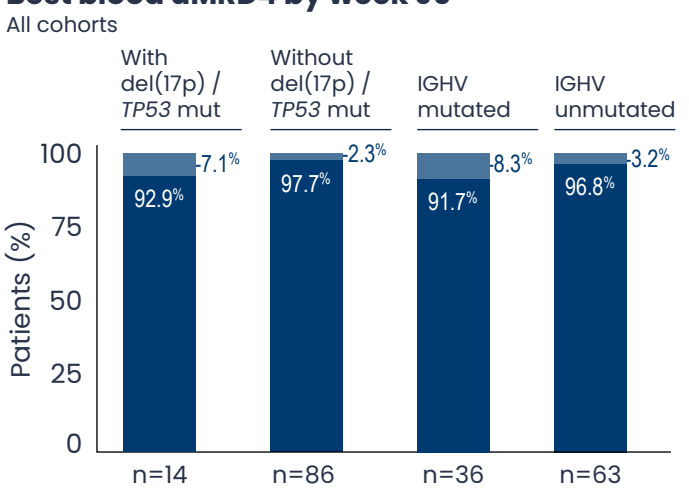
Sonrotoclax + zanubrutinib reported high response rates and uMRD4 rates regardless of risk factors

ORR
Efficacy-evaluable

100%



Best blood uMRD4 by week 96
All cohorts



See the presentation for other dosing.

Read the BGB-11417-101 study presentation on **TN CLL/SLL** from Cheah *et al.*[1] →

Preliminary safety and efficacy outcomes — R/R CLL/SLL

With a median follow-up of 40.6 months (range: 10.2-60.6)

Safety profile of sonrotoclax + zanubrutinib in R/R CLL/SLL

TEAEs (n=47)

Any TEAE	97.9%
Grade ≥3	72.3%
Serious TEAEs	48.9%
Leading to death	2.1%
Leading to discontinuation of sonrotoclax	10.6%

The most common any-grade TEAEs were COVID-19 (42.6%), upper respiratory tract infection (38.3%), and diarrhea (38.3%)

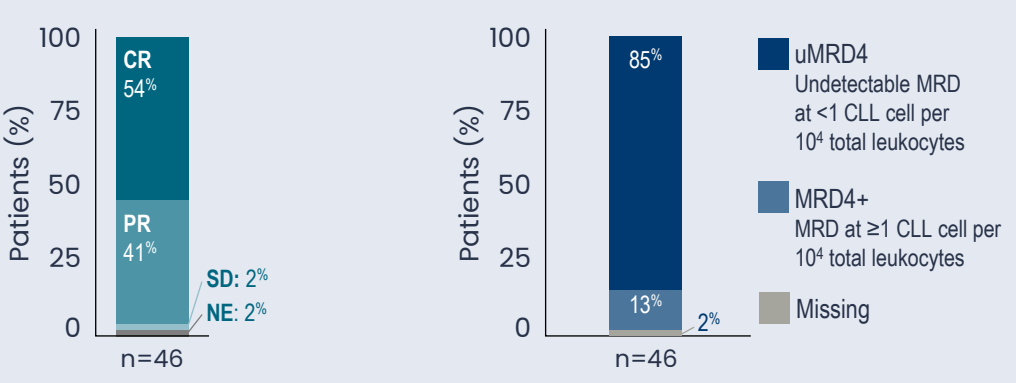
- The most common grade ≥3 TEAE was neutropenia (29.8%)
- One patient had an AE leading to death (histiocytic sarcoma; not related to study treatment) >30 days from last dose
- No laboratory or clinical TLS occurred

Sonrotoclax + zanubrutinib reported high response rates and high rates of uMRD4

ORR*
Efficacy-evaluable

95.7%

Overall best MRD
MRD-evaluable patients



See the poster for other dosages.
*Defined as PR with lymphocytosis or better per International Workshop on CLL 2018 guidelines.

Read the BGB-11417-101 study poster on **R/R CLL/SLL** from Opat *et al.*[2] →

Preliminary safety and efficacy outcomes — R/R MCL

With a median follow-up of 28.3 months (range: 0.7-54.4)

Safety profile of sonrotoclax + zanubrutinib in R/R MCL

TEAEs (n=51)

Any TEAE	96.1%
Grade ≥3	64.7%
Serious TEAEs	41.2%
Leading to death	7.8%
Leading to discontinuation of sonrotoclax	9.8%

The most common any-grade treatment-emergent AEs were diarrhea (39.2%), neutropenia (33.3%), and COVID-19 (33.3%)

- The most common grade ≥3 TEAE was neutropenia (21.6%)
- Four patients had AEs leading to death: one related to sonrotoclax and zanubrutinib and three unrelated to study drug
- No laboratory or clinical TLS occurred

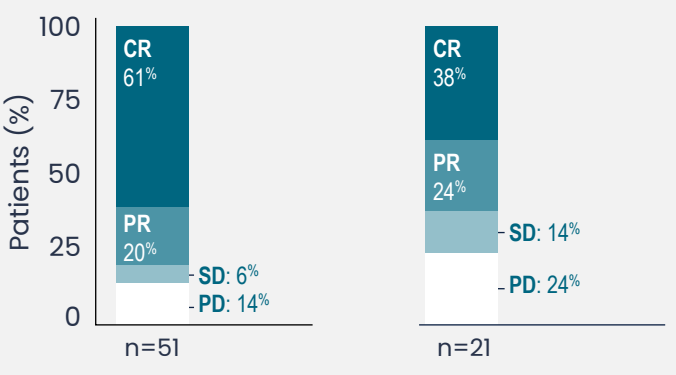
Sonrotoclax + zanubrutinib reported high response rates

ORR*
Efficacy-evaluable

80%

ORR*
With *TP53* mut

62%



See the poster for other dosages.
*Defined as PR or better per Lugano 2014 criteria.

Read the BGB-11417-101 study poster on **R/R MCL** from Soumerai *et al.*[3] →

AE: adverse event; **CLL**: chronic lymphocytic leukemia; **CI**: confidence interval; **CR**: complete response; **dMRD**: detectable minimal residual disease; **IGHV**: immunoglobulin heavy chain; **MCL**: mantle cell lymphoma; **MRD**: minimal residual disease; **MRD4+**: MRD at ≥1 CLL cell per 10^4 total leukocytes; **NE**: non-evaluable; **ORR**: overall response rate; **PD**: progressive disease; **PR**: partial response; **R/R**: relapsed/refractory; **RP2D**: recommended Phase 2 dose; **SD**: stable disease; **TEAEs**: treatment-emergent adverse events; **TLS**: tumor lysis syndrome; **TN**: treatment-naive; **uMRD**: undetectable minimal residual disease; **uMRD4**: uMRD at <1 CLL cell per 10^4 total leukocytes.

The investigational BTK degrader tacabrutideg demonstrated promising safety and effectiveness across B-cell malignancies

Updated safety and efficacy data from the ongoing Phase 1/2 CaDAnCe-101 study in heavily pre-treated patients, including those with high-risk features.[4–6]

Design highlights

R/R CLL/SLL

67 patients with R/R CLL/SLL

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

76.8% unmutated IGHV

65.7% with del(17p) and/or *TP53* mut

53.5% complex karyotype (≥3 abnormalities)

R/R WM

43 patients with R/R WM

2–11 (median: 3) prior lines of therapy

78.6% *MYD88* mut

45.2% *CXCR4* mut

54.8% *TP53* mut

31.0% *BTK* mut

7.1% *PLCG2* mut

BTKi-naive B-cell malignancies

54 patients with: CLL/SLL (29), MCL (8), MZL (10), WM (5), RT (2)

1–9 (median: 2) prior lines of therapy

CLL/SLL risk features

Unmutated IGHV (n/N=6/6)

del(17p) and/or *TP53* mut (n/N=8/25)

Complex karyotype (≥3 abnormalities; n/N=1/4)

Tacabrutideg once daily (BGB-16673)

25.4 months median study follow-up (range 0.3–40.1)

16.6 months median study follow-up (range 0.8–39.7)

8.3 months median study follow-up (range 0.4–12.8)

Selected primary objectives

Safety and tolerability, RP2D

Selected secondary objectives

Preliminary efficacy

Preliminary safety | **R/R CLL/SLL**

Safety profile for tacabrutideg in heavily pre-treated R/R CLL/SLL

TEAEs, all doses (n=67)

Any TEAE	97.0%
Any TRAEs	77.6%
Grade ≥3 TRAEs	34.3%
Serious TRAEs	13.4%
TRAEs leading to dose reduction	7.5%
TRAEs leading to discontinuation	6.0%
TRAEs leading to death	0%

The most common any-grade TEAEs were fatigue (37%), contusion (bruising; 33%), diarrhea (31%), neutropenia (30%), and anemia (22%)

- The most common grade ≥3 TEAE was neutropenia (25%)
- 3 cases of atrial fibrillation, all transient

Preliminary efficacy | **R/R CLL/SLL**

Tacabrutideg demonstrated high and durable responses

All patients across all doses

ORR

85.1%

n=67

PFS (median)

24.4 months

Range: 0-35.9+

PFS (24 months)

53.8%

95% CI: 38.8%-66.6%

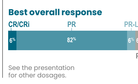
200 mg (RP2D)

ORR

94.1%

n=17

Best overall response



See the presentation for other dosages.

High ORRs* observed in high-risk subgroups

	ORR*	n/N
All patients	**85.1%**	**57/67**
Prior cBTKi + BCL2i (no ncBTKi)	93.0%	40/43
Prior cBTKi + ncBTKi + BCL2i	75.0%	9/12
Refractory to last cBTKi + last BCL2i	83.8%	31/37
≥5 prior lines of therapy	86.2%	25/29
del(17p) and/or *TP53* mut	79.5%	35/44
Unmutated IGHV	88.4%	38/43
Complex karyotype (≥3 abnormalities)	73.9%	17/23
BTK mutation	76.0%	19/25
PLCG2 mutation	90.0%	9/10

*Defined as PR-L or better.

Read the CaDAnCe-101 study presentation in **R/R CLL/SLL** from Stilgenbauer *et al.*[4] →

Preliminary safety | **R/R WM**

Safety profile for tacabrutideg in R/R WM

TEAEs, all doses (n=43)

Any TEAE	97.7%
Any TRAEs	81.4%
Grade ≥3 TRAEs	41.9%
Serious TRAEs	16.3%
TRAEs leading to dose reduction	7.0%
TRAEs leading to discontinuation	9.3%
TRAEs leading to death	4.7%

The most common any-grade TEAEs were neutropenia (37%), diarrhea (30%), contusion (bruising; 28%), thrombocytopenia (21%), and COVID-19 (21%)

- The most common grade ≥3 TEAE was neutropenia (35%)
- No atrial fibrillation occurred

Preliminary efficacy | **R/R WM**

Tacabrutideg demonstrated high responses in heavily pre-treated patients and those with high-risk features

All patients across all doses

ORR

83.7%

N=43

PFS (18 months)

68.6%

95% CI: 51.2%-80.9%

High ORRs* observed in high-risk subgroups

	ORR*	n/N
All patients	**83.7%**	**36/43**
≥4 prior lines of therapy	80.0%	16/20
≥2 prior BTKi	88.9%	16/18
Refractory to last BTKi	80.0%	24/30
MYD88 mutated	87.9%	29/33
CXCR4 mutated	100%	19/19
TP53 mutated	91.3%	21/23
BTK mutated	100%	13/13
PLCG2 mutated	100%	3/3

*Defined as having a best overall response of SD or less or PD within 7 days of the end of treatment.

Read the CaDAnCe-101 study poster in **R/R WM** from Trotman *et al.*[5] →

Preliminary safety | **BTKi-naive B-cell malignancies**

Safety profile for tacabrutideg across B-cell malignancies

TEAEs, all doses (n=54)

Any TEAE	83.3%
Any TRAEs	64.8%
Grade ≥3 TRAEs	24.1%
Serious TRAEs	3.7%
TRAEs leading to dose reduction	0%
TRAEs leading to discontinuation	0%
TRAEs leading to death	0%

The most common any-grade TEAEs were contusion (bruising; 28%), neutropenia (21%), petechiae (19%), and anemia (13%)

- The most common grade ≥3 TEAE was neutropenia/neutrophil count decreased (14.8%)
- One patient with MCL developed grade 3 paroxysmal atrial fibrillation, which resolved to sinus rhythm

Preliminary efficacy | **BTKi-naive CLL/SLL**

Efficacy is only reported for BTKi-naive patients with CLL/SLL due to small sample sizes in other B-cell malignancies.

Tacabrutideg demonstrated high responses in CLL/SLL patients with high-risk features

Evaluable patients

ORR*

86.4%

n=22

Best overall response

*Proportion of patients who achieved a best overall response of PR-L or better.

Response rates to tacabrutideg were consistent in patients with high-risk disease features

66.7% of evaluable patients **with del(17p) and/or *TP53* mut** responded (n/N=4/6)

100% of evaluable patients **with unmutated IGHV** responded (n/N=4/4)

Read the CaDAnCe-101 study poster in **BTKi-naive B-cell malignancies** from Mocanu *et al.*[6] →

BCL2i: B-cell lymphoma 2 inhibitor; **BTK**: Bruton tyrosine kinase; **BTKi**: Bruton tyrosine kinase inhibitor; **cBTKi**: covalent BTKi; **CI**: confidence interval; **CLL**: chronic lymphocytic leukemia; **CR/CRi**: complete response/complete response with incomplete marrow recovery; **IGHV**: immunoglobulin heavy chain; **MCL**: mantle cell lymphoma; **MZL**: marginal zone lymphoma; **ncBTKi**: non-covalent BTKi; **ORR**: overall response rate; **PD**: progressive disease; **PFS**: progression-free survival; **PR**: partial response; **PR-L**: partial response with lymphocytosis; **R/R**: relapsed/refractory; **RP2D**: recommended Phase 2 dose; **RT**: Richter transformation; **SD**: stable disease; **TEAEs**: treatment-emergent adverse events; **TRAEs**: treatment-related adverse events; **WM**: Waldenström macroglobulinemia.

What's the efficacy of frontline zanubrutinib in advanced age patients?

A subgroup analysis of zanubrutinib TN CLL/SLL patients aged ≥80 years from the Phase 3 SEQUOIA trial.[7]

Design highlights

352 patients with TN CLL/SLL

Subgroup analysis

38 patients aged over 80
81 years median age (range 80-87)

without del(17p) (n=28)	with del(17p) (n=10)
79.15 months median follow-up (95% CI: 0.3-96.0)	82.73 months median follow-up (95% CI: 5.0-92.9)

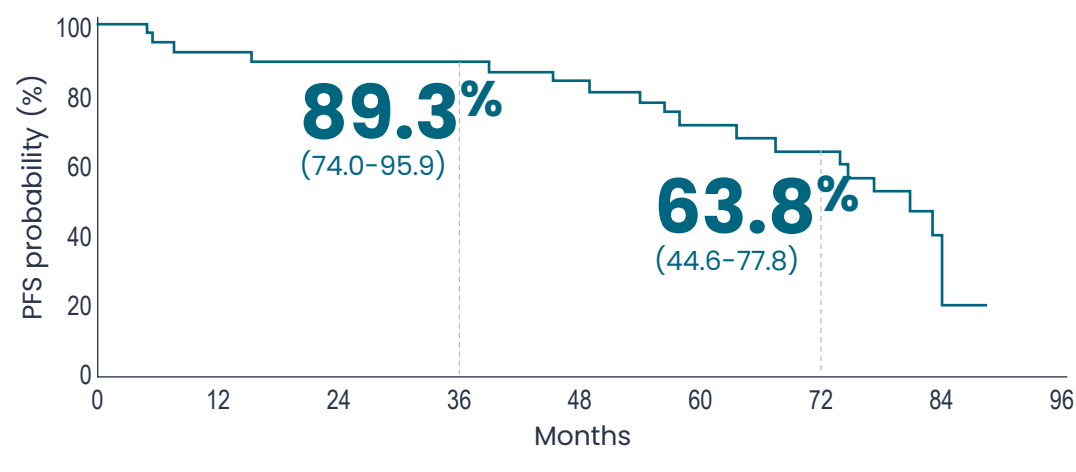
→ **Zanubrutinib 160 mg BID** until PD, unacceptable toxicity, or end of study

Selected endpoints

PFS, ORR, OS, safety

Long-term follow-up results | **≥80 years subgroup**

Zanubrutinib reported high investigator-assessed PFS rates in patients aged ≥80 years



ORR
100%
n=38

Estimated OS
(36 months)
86.8% 95% CI: 71.2%-94.3%

(72 months)
75.8% 95% CI: 58.6%-86.6%

Key safety and tolerability profile | **≥80 years subgroup**

The tolerability profile observed was consistent with expectations for a very elderly population and aligned with the established safety profile of zanubrutinib

TEAEs of any grade (n=38)

Atrial fibrillation/flutter	15.8%
Major hemorrhage	21.1%
Hypertension	28.9%
Grade ≥3 infections	36.8%
Second primary malignancy (excluding non-melanoma skin cancer)	15.8%

- Atrial fibrillation/flutter events occurred infrequently and were consistent with the general population for age adjusted atrial fibrillation risk.
- TEAEs leading to treatment discontinuation occurred in 7.9% of patients in the first 3 years of follow-up

Read the **SEQUOIA subgroup** analysis poster from Tedeschi *et al.*[7] →

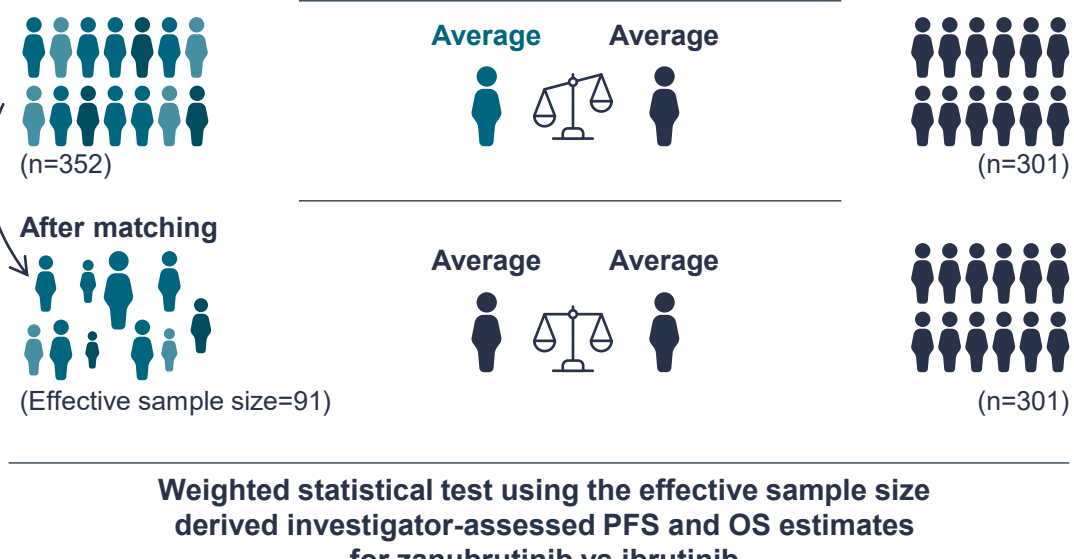
BID: twice a day; **CI**: confidence interval; **CLL**: chronic lymphocytic leukemia; **ORR**: overall response rate; **OS**: overall survival; **PD**: progressive disease; **PFS**: progression-free survival; **TEAEs**: treatment-emergent adverse events; **TN**: treatment-naive.

How does zanubrutinib compare to ibrutinib in TN CLL?

In the absence of head-to-head trials, a MAIC was used to indirectly evaluate these two treatments[8]

Analysis design highlights

SEQUOIA individual patient data were re-weighted to match key characteristics of the CLL17 study

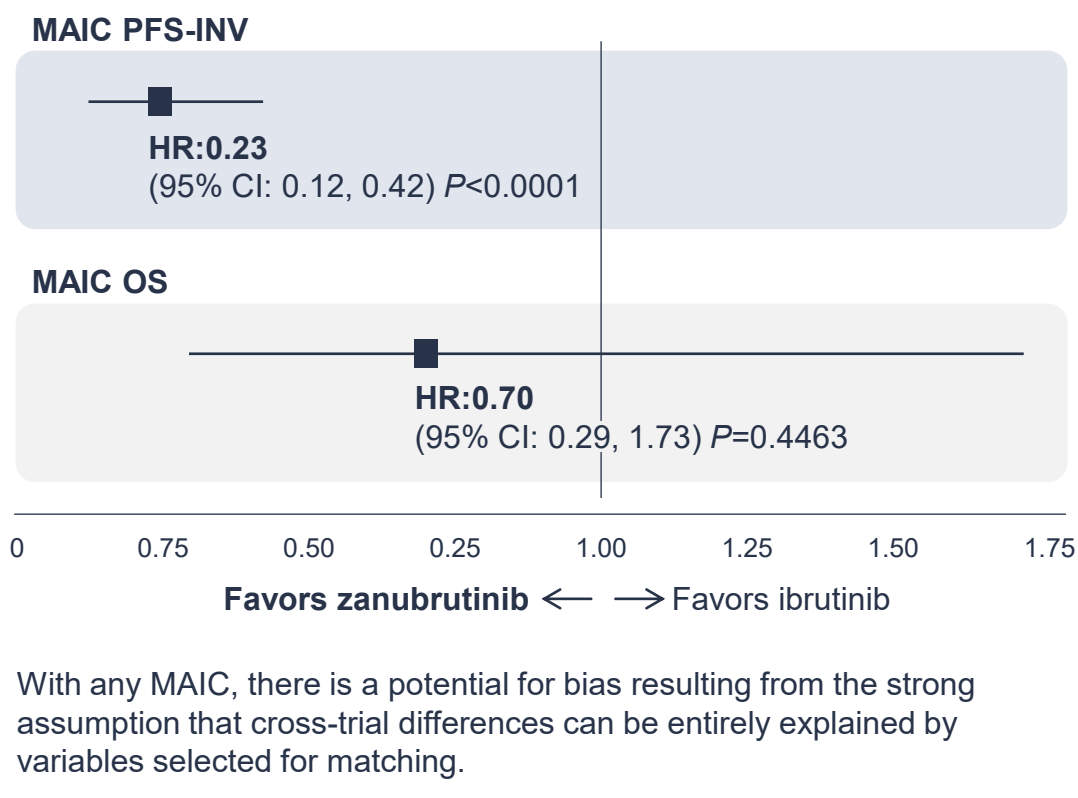


Weighted statistical test using the effective sample size derived investigator-assessed PFS and OS estimates for zanubrutinib vs ibrutinib

MAICs do not establish the superiority of one product over another. Interpret MAIC findings as hypothesis-generating, not definitive.

Key MAIC outcomes

The MAIC analyses from the effective sample size suggested an improved COVID-adjusted PFS-INV for zanubrutinib over ibrutinib, but not OS



With any MAIC, there is a potential for bias resulting from the strong assumption that cross-trial differences can be entirely explained by variables selected for matching.

Read the **MAIC analysis** poster from Munir *et al.*[8] →

CI: confidence interval; **CLL**: chronic lymphocytic leukemia; **HR**: hazard ratio; **MAIC**: matching-adjusted indirect comparison; **OS**: overall survival; **PFS**: progression-free survival; **PFS-INV**: investigator-assessed PFS; **TN**: treatment-naive.

References

1. Cheah, C.Y. *et al.* First-Line Treatment of CLL/SLL With the All-Oral Combination of Sonrotoclax and Zanubrutinib Achieves Undetectable Minimal Residual Disease Rates of >90%, Including in Patients With del(17p)/*TP53*. Presented at the EHA2026 Congress; 11-14 June 2026; Stockholm, Sweden.

2. Opat, S.S. *et al.* Updated Safety and Efficacy of All-Oral Sonrotoclax + Zanubrutinib in Relapsed/Refractory Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma, Including Patients With del(17p)/TP53. Poster Presentation PS1697 at the EHA2026 Congress; 11-14 June 2026; Stockholm, Sweden.

3. Soumerai, J.D. *et al.* Combination Treatment With Novel B-Cell Lymphoma 2 Inhibitor Sonrotoclax (BGB-11417) and Zanubrutinib in Patients With Relapsed/Refractory Mantle Cell Lymphoma: Results From a Phase 1/1b Study. Poster Presentation PF933 at the EHA2026 Congress; 11-14 June 2026; Stockholm, Sweden.

4. Stilgenbauer, S. *et al.* Tacabrutideg (BGB-16673), A Bruton Tyrosine Kinase Degrader, in Patients With Relapsed/Refractory Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma: A Phase 1 CaDAnCe-101 Study Update. Presented at the EHA2026 Congress; 11-14 June 2026; Stockholm, Sweden.

5. Trotman, J. *et al.* BGB-16673, a Bruton Tyrosine Kinase Degrader, in Patients With Relapsed/Refractory Waldenström Macroglobulinemia: a Phase 1 CaDAnCe-101 Study Update. Poster Presentation PS2033 at the EHA2026 Congress; 11-14 June 2026; Stockholm, Sweden.

6. Macanu, I. *et al.* Bruton Tyrosine Kinase Degrader BGB-16673 in BTK Inhibitor–Naïve Patients With CLL/SLL and Other B-Cell Malignancies: Results From the Phase 1 CaDAnCe-101 Study. Poster Presentation PS1693 at the EHA2026 Congress; 11-14 June 2026; Stockholm, Sweden.

7. Tedeschi, A. *et al.* Long-Term Follow-Up for Safety and Efficacy of Zanubrutinib in Elderly (≥80 Years) Treatment-Naïve CLL/SLL Patients, Including Those With del(17p): Subgroup Analysis From the SEQUOIA Trial. Poster Presentation PS1703 at the EHA2026 Congress; 11-14 June 2026; Stockholm, Sweden.

8. Munir, T. *et al.* Zanubrutinib vs Ibrutinib in Treatment-Naive Chronic Lymphocytic Leukemia: Implications for Interpreting Fixed-Duration Outcomes From CLL17. Poster Presentation PS1718 at the EHA2026 Congress; 11-14 June 2026; Stockholm, Sweden.

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