BGB-11417-101

Sonrotoclax Plus Zanubrutinib

R/R MCL

BGB-11417-101 Trial Design

R/R MCL

Phase 1

Study Identifier:
BGB-11417-101, NCT04277637

Primary Endpoints: Safety (TEAEs, SAEs, AEs leading to discontinuation, TLS), MTD, RP2D,
Secondary Endpoints: PK/PD, ORR by investigator

Eligibility criteria

Confirmed diagnosis of:

- R/R MZL: ≥2L, extranodal, splenic, or nodal
- R/R FL: ≥2L, grade 1-3a
- R/R DLBCL: ≥3L
- Transformed indolent B-cell NHL
- CLL/SLL: TN or R/R
- **R/R MCL: ≥2L**
- R/R WM
- ECOG PS 0-2
- No prior therapy ≥2 months with, or progression on, a BCL2 inhibitor

Monotherapy Cohorts

Part 1: Dose Escalation (Sonrotoclax Monotherapy)

Cohort	Population	Disease	N
1A	R/R	NHL (*FL, DLBCL, MZL, or transformed NHL*)	15-30
1B	R/R (*low TLS risk*)	CLL/SLL	15-30
1C	R/R (*high TLS risk*[a])	CLL/SLL	3-6
1D	R/R	MCL	3-6
1E	R/R	WM	3-6

RP2D

RP2D per disease type will be decided based on SMC review of available safety and activity data

Part 2: Expansion (Sonrotoclax Monotherapy)

Cohort	Population	Disease	N
2A	R/R (*Food effect*)	Indolent NHL (*FL, MZL*)	10
2B	R/R (*food effect*)	Aggressive NHL (DLBCL, transformed NHL)	10
2C	R/R (*low TLS risk*)	CLL/SLL	20
2D	R/R (*high TLS risk*[a])	CLL/SLL	10
2E	R/R (*prior ven*)	CLL/SLL	10
2F	R/R	MCL	20
2G	R/R	WM	20

Combination Cohorts

Part 3: Dose Finding (Sonrotoclax + Zanubrutinib Combination)

Cohort	Population	Disease	Planned N
3A	R/R	CLL/SLL	15-30
3B	R/R	MCL	3-6

RP2D

RP2D per disease type will be decided based on SMC review of available safety and activity data

Part 4: Dose Expansion (Sonrotoclax + Zanubrutinib Combination)

Cohort	Population	Disease	Planned N
4A	R/R	CLL/SLL	30
4B	TN	CLL/SLL	20
4C	R/R	MCL	20

[a]High TLS risk defined as the presence of any lymph node ≥10 cm or the presence of any lymph node ≥5 cm with concurrent absolute lymphocyte count ≥25×109/L.
AE=adverse event, BCL2=B-cell lymphoma-2, CLL=chronic lymphocytic leukemia, CTCAE=Common Terminology Criteria for Adverse Events, DLBCL=diffuse large B-cell lymphoma, ECOG PS=Eastern Cooperative Oncology Group performance status, FL=follicular lymphoma, iwCLL=International Workshop on Chronic Lymphocytic Leukemia, MCL=mantle cell lymphoma, MTD=maximum tolerated dose, MZL=marginal zone lymphoma, NHL=Non-Hodgkin lymphoma, ORR=objective response rate, PD=pharmacodynamic, PK=pharmacokinetics, QD=once daily, RP2D=recommended phase 2 dose, R/R=relapsed/refractory, SAE=serious adverse event, SLL=small lymphocytic lymphoma, SMC=safety monitoring committee, TEAE=treatment-emergent adverse event, TLS=tumor lysis syndrome, TN=treatment naïve, WM=Waldenström macroglobulinemia.
1. Cheah C et al. Oral presentation presented at ASH 2022. Abstract 962 2. Opat et al. EHA Presentation. 2022. Abstract number: P687.

BGB-11417-101

Baseline Characteristics and Demographics

R/R MCL

Characteristic	Sonro 80 mg + Zanu (n=6)	Sonro 160 mg + Zanu (n=13)	Sonro 320 mg + Zanu (n=27)	Sonro 640 mg + Zanu (n=5)	All (N=51)
Study follow-up, median (range), months	40.4 (3.9-42.4)	16.4 (1.0-38.5)	13.2 (0.7-31.6)	15.8 (3.4-21.5)	16.4 (0.7-42.4)
Age, median (range), years	60.0 (46-84)	69.0 (45-81)	67.0 (45-85)	71.0 (68-80)	68.0 (45-85)
Male, n (%)	5 (83.3)	11 (84.6)	17 (63.0)	3 (60.0)	36 (70.6)
ECOG PS, n (%)					
0	4 (66.7)	8 (61.5)	6 (22.2)	3 (60.0)	21 (41.2)
1	2 (33.3)	5 (38.5)	20 (74.1)	2 (40.0)	29 (56.9)
Tumor bulk, n (%)[a]					
High	1 (16.7)	2 (15.4)	4 (14.8)	0	7 (13.7)
Ki67 proliferation index, n (%)					
<30%	3 (50.0)	3 (23.1)	8 (29.6)	1 (20.0)	15 (29.4)
≥30%	2 (33.3)	2 (15.4)	4 (14.8)	2 (40.0)	10 (19.6)
Missing	1 (16.7)	8 (61.5)	15 (55.6)	2 (40.0)	26 (51.0)
***TP53* mutation status, n (%)**					
Mutated	2 (33.3)	1 (7.7)	1 (3.7)	2 (40.0)	6 (11.8)
Unmutated	0	3 (23.1)	3 (11.1)	1 (20.0)	7 (13.7)
Missing	4 (66.7)	9 (69.2)	23 (85.2)	2 (40.0)	38 (74.5)
Prior therapy					
No. of lines of prior therapy, median (range)	1 (1-1)	1 (1-4)	1 (1-3)	1 (1-1)	1 (1-4)
Prior BTK inhibitor, n (%)[b]	0	0	4 (14.8)	0	4 (7.8)
Prior BTK inhibitor duration, median (range), months	NA	NA	8.4 (0.3-24.1)	NA	8.4 (0.3-24.1)

Data cutoff: March 1, 2025.
[a]High tumor bulk: any lymph node ≥10 cm or lymph node ≥5cm and ALC ≥25×10^9/L. bAll patients discontinued prior BTK inhibitor due to toxicity.
ALC=absolute lymphocyte count, BTK=Bruton tyrosine kinase, ECOG PS=Eastern Cooperative Oncology Group performance status, MCL=mantle cell lymphoma, NA=not applicable, sonro=sonrotoclax, TLS=tumor lysis syndrome, zanu=zanubrutinib.
Tam CS, et al. Oral Presentation at EHA 2025; S234.

BGB-11417-101

Safety Summary

R/R MCL

- Safety profile was generally similar across all doses tested and sonrotoclax 160-mg and 320-mg doses were chosen for expansion
- No DLTs occurred and MTD was not reached up to sonrotoclax 640 mg; 320 mg was chosen as RP2D

Patients, n (%)	Sonro 80 mg + Zanu (n=6)	Sonro 160 mg + Zanu (n=13)	Sonro 320 mg + Zanu (n=27)	Sonro 640 mg + Zanu (n=5)	All (N=51)
Any TEAEs	4 (66.7)	13 (100)	26 (96.3)	5 (100)	48 (94.1)
Grade ≥3	4 (66.7)	7 (53.8)	14 (51.9)	3 (60.0)	28 (54.9)
Serious TEAEs	3 (50.0)	4 (30.8)	7 (25.9)	1 (20.0)	15 (29.4)
Leading to death	1 (16.7)	1 (7.7)	1 (3.7)	0	3 (5.9)[a]
Leading to zanu discontinuation	1 (16.7)	3 (23.1)	4 (14.8)	0	8 (15.7)[b]
Leading to zanu dose reduction	1 (16.7)	1 (7.7)	0	0	2 (3.9)
Treated with sonro	6 (100)	11 (84.6)	24 (88.9)	5 (100)	46 (90.2)
Leading to death	0	1 (7.7)	0	0	1 (2.0)[c]
Leading to sonro discontinuation	0	3 (23.1)	2 (7.4)	0	5 (9.8)[d]
Leading to sonro dose reduction	0	0	0	0	0

Data cutoff: March 1, 2025.
[a]Pleural effusion (80 mg; due to PD), abdominal sepsis (320 mg), pneumonia (160 mg). [b]Lymph node pain (160 mg, due to PD), diarrhea (320 mg), MDS (160 mg), abdominal sepsis (320 mg), pneumonia (160 mg), diarrhea (80 mg), cryptococcal meningoencephalitis (320 mg), abdominal pain (320 mg). [c]Pneumonia (160 mg). [d]Diarrhea (320 mg), MDS (160 mg), abdominal sepsis (320 mg), pneumonia (160 mg), lymph node pain (160 mg, due to PD).
DLT=dose-limiting toxicity, MCL=mantle cell lymphoma, MDS=myelodysplastic syndrome, MTD=maximum tolerated dose, PD=progressive disease, RP2D=recommended phase 2 dose, sonro=sonrotoclax, TEAE=treatment-emergent adverse event, zanu=zanubrutinib.
Tam CS, et al. Oral Presentation at EHA 2025; S234.

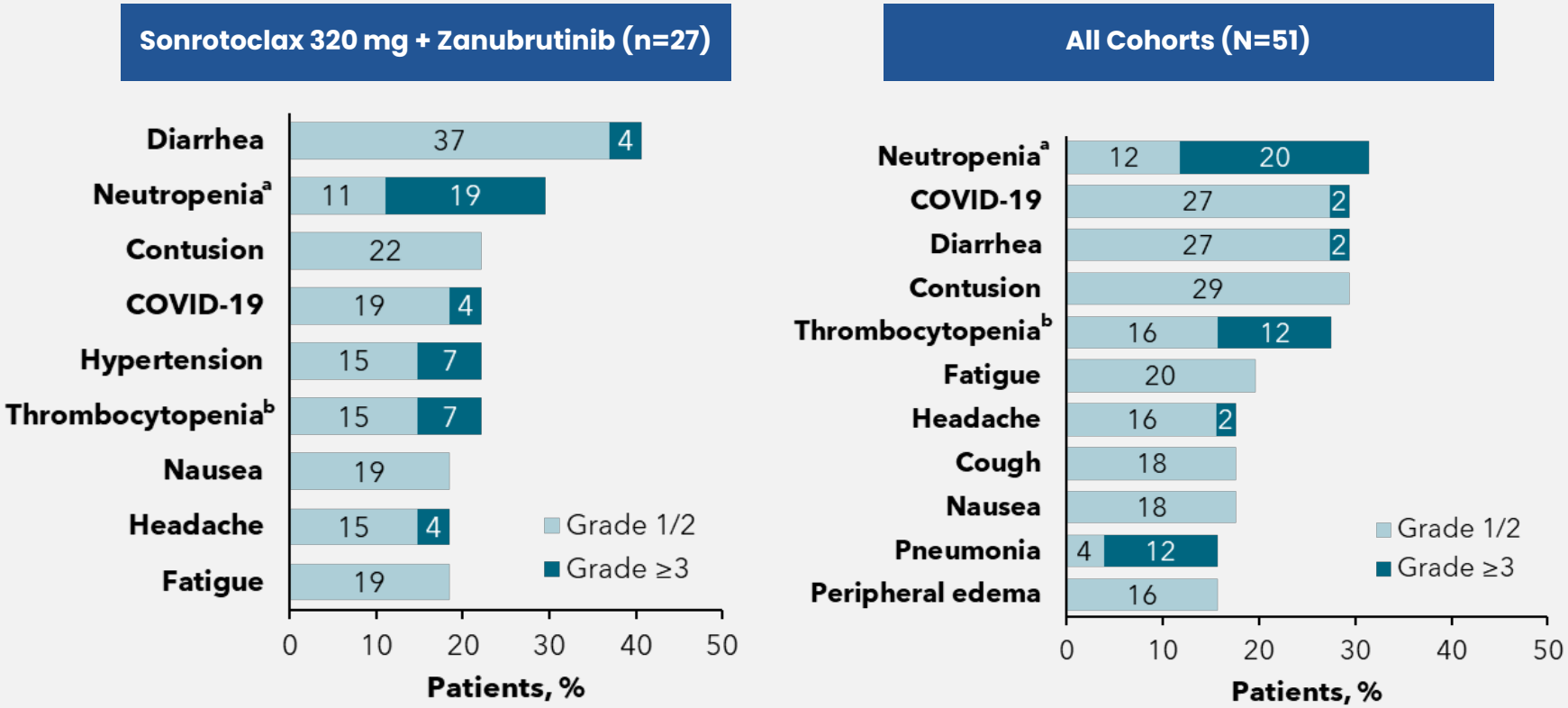
BGB-11417-101

Most Common TEAEs

R/R MCL

- No laboratory or clinical TLS
- No atrial fibrillation/flutter
- Safety profile was similar across all dose levels

TEAEs in ≥15% of patients at the sonrotoclax RP2D (320 mg) and in all patients



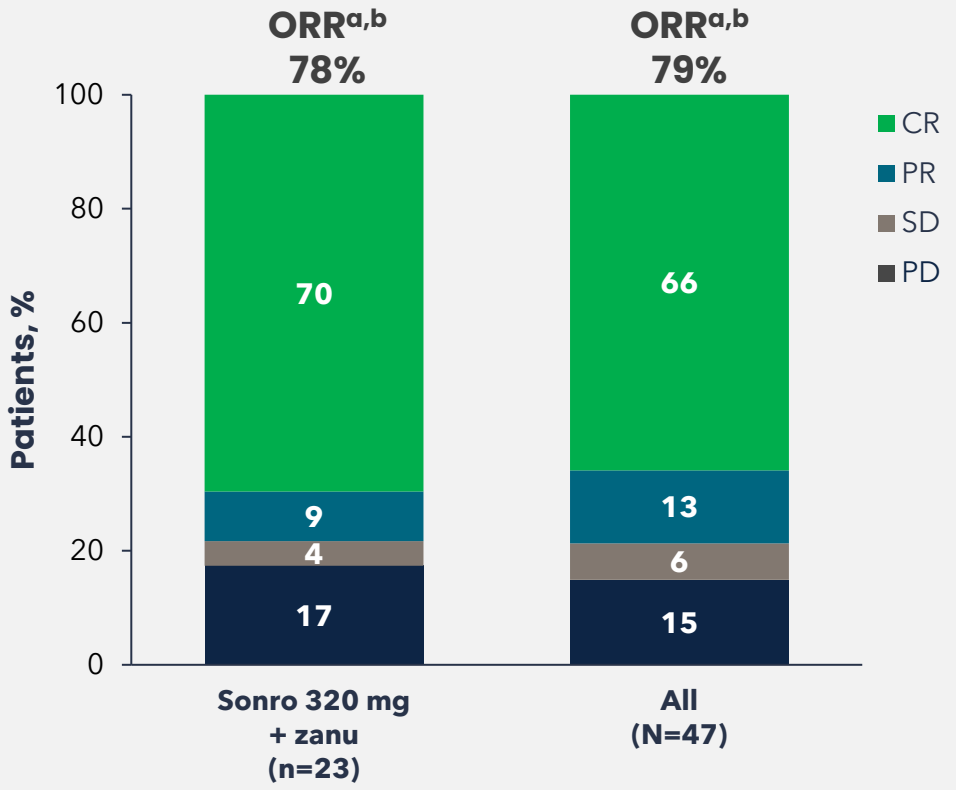
Data cutoff: March 1, 2025.
[a]Neutropenia combines preferred terms neutrophil count decreased and neutropenia. [b]Thrombocytopenia combines preferred terms platelet count decreased and thrombocytopenia.
MCL=mantle cell lymphoma, RP2D=recommended phase 2 dose, TEAE=treatment-emergent adverse event, TLS=tumor lysis syndrome.
Tam CS, et al. Oral Presentation at EHA 2025; S234.

BGB-11417-101

Overall Response Rate

R/R MCL

- With a median study follow-up of 16.4 months, ORR[a,b] was 79% with a CR rate of 66% across all doses in efficacy-evaluable patients
  - ORR was 78% in the 320-mg dose group, with a CR rate of 70%
  - All patients who had a BOR of PD progressed during zanubrutinib lead-in (4 patients in the 320-mg cohort)
- The median time to CR was 6.7 months (range, 1.5-28.2 months)
- Three patients (80 mg, n=1; 160 mg, n=2) electively discontinued treatment after ≥96 weeks of therapy; as of the data cutoff date, all patients were in remission and had a median time of 2.5 months off treatment (range, 0.8-2.9 months)



	Sonro 320 mg + zanu (n=23)	All (N=47)
Study follow-up, median (range), months[c]	13.2 (0.7-31.6)	16.4 (0.7-42.4)

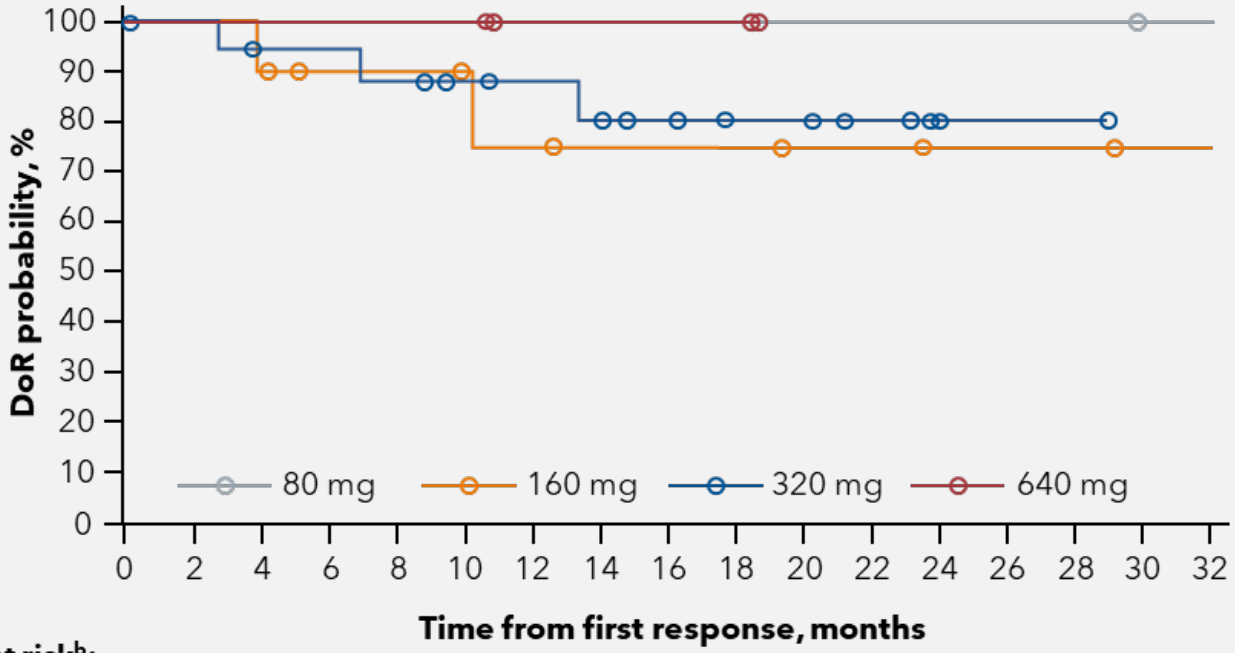
Data cutoff: March 1, 2025.
[a]Responses were assessed per Lugano 2014 criteria and are shown as the percentages of responding patients who had ≥1 post-baseline tumor assessment after dosing with sonrotoclax unless treatment was discontinued due to clinical progression or death prior to tumor assessment. [b]ORR was defined as PR or better. [c]For all patients as treated (N=51).
BOR=best overall response, BTK=Bruton tyrosine kinase, CR=complete response, MCL=mantle cell lymphoma, ORR=overall response rate, PD=progressive disease, PR=partial response, SD=stable disease.
Tam CS, et al. Oral Presentation at EHA 2025; S234.

BGB-11417-101

Duration of Response[a]

R/R MCL

- Median DoR in all patients was not reached (95% CI, 34.8-NE)
  - DoR rate at 24 months was 84.0% (95% CI, 65.3%-93.1%; mFU, 17.7 months)
- Median DoR in the 320-mg dose group was not reached (95% CI, 3.3-NE)
  - DoR rate at 24 months was 80.1% (95% CI, 49.4%-93.3%; mFU, 14.8 months)
- Of 18 patients in the 320-mg dose group who achieved CR, 16 remain in CR (mFU, 13 months)
  - DoCR rate at 18 months was 84.4% (95% CI, 50.4%-95.9%; mFU, 10.2 months)



No. at risk[b]:

80 mg	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	4	4	4				
160 mg	10	10	10	10	9	8	7	7	7	7	6	5	5	4	4	4	4	4	4	4	3	3	3	3	2	2	2	2	2	2	1	1	1			
320 mg	22	18	18	17	15	15	15	14	14	13	12	11	11	11	10	8	8	7	6	6	6	5	4	4	1	1	1	1	1	0	0	0	0			
640 mg	4	4	4	4	4	4	4	4	4	4	4	2	2	2	2	2	2	2	2	0	0	0	0	0	0	0	0	0	0	0	0	0	0			

Data cutoff: March 1, 2025.

[a]Includes four patients in zanubrutinib lead-in. [b]For all patients as treated (N=51).

CI=confidence interval, CR=complete response, DoCR=duration of complete response, DoR=duration of response, MCL=mantle cell lymphoma, mFU=median follow-up, NE=not evaluable.

Tam CS, et al. Oral Presentation at EHA 2025; S234.