BGB-11417-101

Sonrotoclax Monotherapy
R/R CLL

BGB-11417-101 Trial Design

R/R CLL/SLL

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.

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Baseline Patient Characteristics

Sonrotoclax Monotherapy in R/R CLL/SLL

- As of March 1, 2025, 18 patients with R/R CLL/SLL had received sonrotoclax monotherapy, and 12 (66.7%) remain on treatment
  - Six patients (33.3%) discontinued treatment due to progressive disease (n=3), physician decision (n=2), or patient withdrawal (n=1)
- Across dose cohorts, the median age was 68.0 years, and the median number of prior systemic treatments was 3
  - Among tested patients, 93.3% (14/15) had unmutated IGHV, 28.6% (4/14) had del(17p), and 58.3% (7/12) had del(17p) and/or *TP53* mutation
  - Of the 18 patients, 17 had received prior BTK inhibitor treatment

Characteristic	Sonro 80 mg (n=4)	Sonro 160mg (n=7)	Sonro 320mg (n=7)	All (N=18)
Follow-up, median (range), months	45.2 (44.0-50.5)	23.2 (5.4-42.7)	22.7 (14.6-28.1)	24.7 (5.4-50.5)
Age, median (range), years	65.5 (55-70)	73.0 (61-84)	65.0 (62-79)	68.0 (55-84)
Male, n (%)	4 (100)	3 (42.9)	5 (71.4)	12 (66.7)
ECOG PS				
0	2 (50.0)	3 (42.9)	3 (42.9)	8 (44.4)
1	2 (50.0)	4 (57.1)	4 (57.1)	10 (55.6)
del(17p), n/tested (%)	1/3 (33.3)	1/6 (16.7)	2/5 (40.0)	4/14 (28.6)
del(17p) and/or *TP53* mutation, n/tested (%)	1/2 (50.0)	3/6 (50.0)	3/4 (75.0)	7/12 (58.3)
Unmutated IGHV, n/tested (%)	2/2 (100)	5/6 (83.3)	7/7 (100)	14/15 (93.3)
Prior therapy				
No. of lines of prior systemic therapy, median (range)	2.5 (1-3)	2.0 (1-4)	4.0 (1-5)	3.0 (1-5)
No. of lines of prior systemic therapy, n (%)				
1	1 (25.0)	1 (14.3)	1 (14.3)	3 (16.7)
2	1 (25.0)	3 (42.9)	1 (14.3)	5 (27.8)
≥3	2 (50.0)	3 (42.9)	5 (71.4)	10 (55.6)
Prior BTK inhibitor	3 (75.0)	7 (100)	7 (100)	17 (94.4)
Prior BTK inhibitor duration, median (range), months	47.0 (40.9-53.7)	59.6 (33.8-87.3)	78.5 (24.5-113.0)	61.0 (24.5-113.0)

Data cutoff: March 1, 2025.
BTK=Bruton tyrosine kinase, CLL=chronic lymphocytic leukemia, ECOG PS=Eastern Cooperative Oncology Group performance status, IGHV=IGHV, immunoglobulin heavy chain variable region, R/R=relapsed/refractory, SLL=small lymphocytic lymphoma.
Opat S, et al. Poster Presentation at EHA 2025; PF580.

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TEAE Summary

Sonrotoclax Monotherapy in R/R CLL/SLL

- No patients died due to TEAE or discontinued sonrotoclax due to TEAE
- Toxicity was generally the same among all tested dose levels with no new safety signals identified; the sonrotoclax 320 mg dose level was chosen for expansion

Patients, n (%)	Sonro 80 mg (n=4)	Sonro 160mg (n=7)	Sonro 320mg (n=7)	All (N=18)
Any TEAEs	4 (100)	7 (100)	7 (100)	18 (100)
Grade ≥3	2 (50.0)	6 (85.7)	6 (85.7)	14 (77.8)
Serious	3 (75.0)	3 (42.9)	3 (42.9)	9 (50.0)
Led to Sonro discontinuation	0	0	0	0
Led to Sonro dose interruption	3 (75.0)	5 (71.4)	2 (28.6)	10 (55.6)
Led to Sonro dose reduction	0	2 (28.6)[a]	1 (14.3)[b]	3 (16.7)

Data cutoff: March 1, 2025.
[a]Grade ≤2 diarrhea (n=2). [b]Grade 2 platelet count decreased (n=1).
CLL=chronic lymphocytic leukemia, MTD=maximum tolerable dose, R/R=relapsed/refractory, TEAE=treatment-emergent adverse event, TLS=tumor lysis syndrome.
Opat S, et al. Poster Presentation at EHA 2025; PF580.

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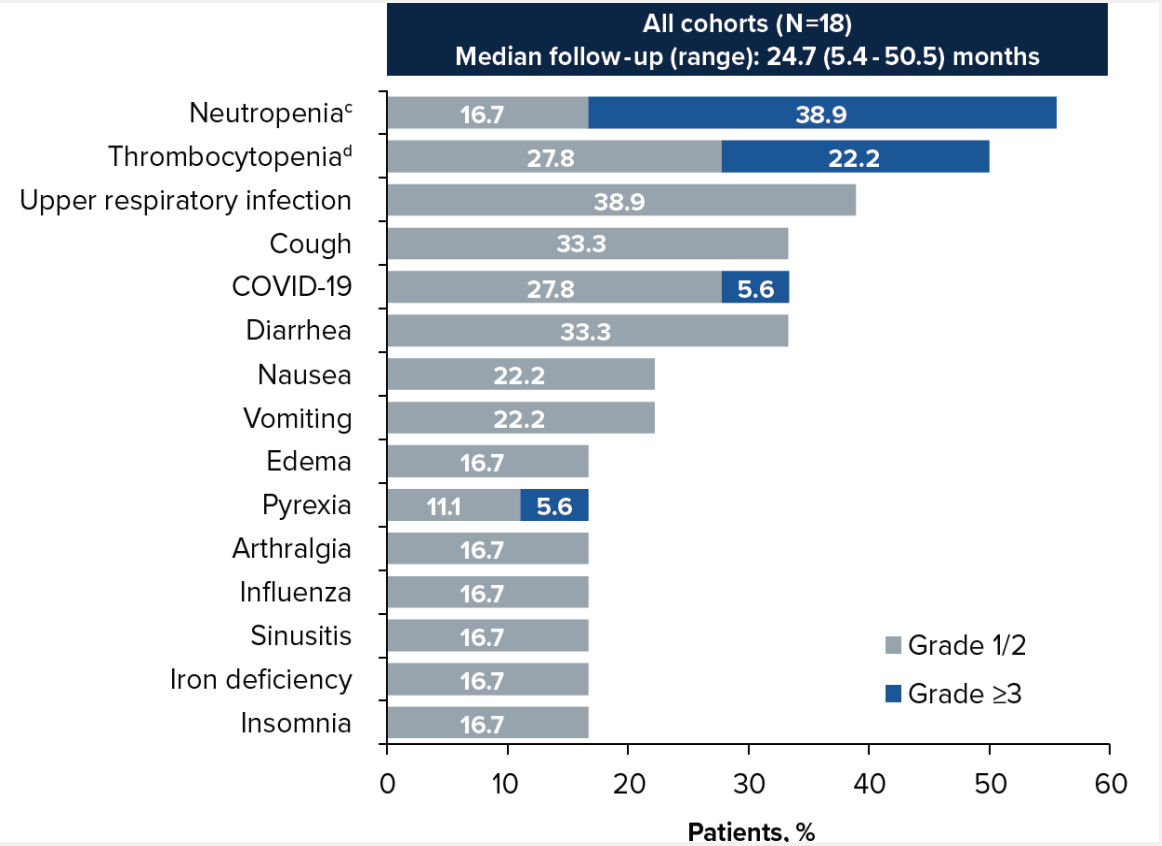
TEAE Summary (Cont'd)

Sonrotoclax Monotherapy in R/R CLL/SLL

- Across all dose cohorts, the most common any-grade TEAEs were neutropenia (55.6%), thrombocytopenia (50.0%), and upper respiratory infection (38.9%); neutropenia was the most common grade ≥3 TEAE
  - Neutropenia was manageable and did not lead to a higher rate of grade ≥3 infections; eight patients used granulocyte-colony stimulating factor
- Two patients (11.1%; n=1 each in 80-mg and 320-mg cohorts) experienced laboratory TLS during sonrotoclax ramp-up; both events resolved within 24 hours without sequelae or dose modification
- While MTD was not reached at 320 mg, the 640-mg dose was not tested in this cohort

TEAEs Occurring in ≥3 Patients[a,b]



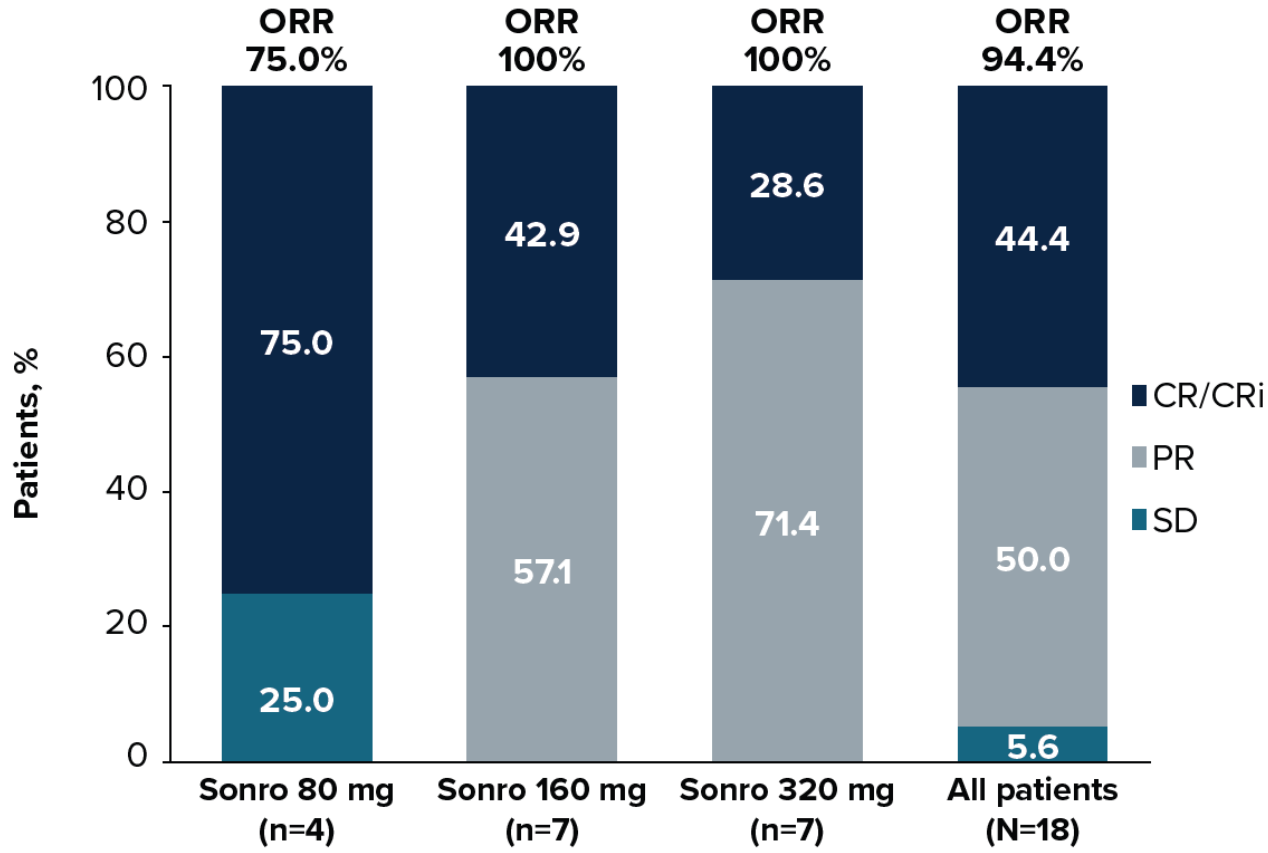
Data cutoff: March 1, 2025.
[a]Grade is listed as worst grade experienced by the patient on any drug. [b]Hematologic TEAEs were graded per iwCLL criteria; nonhematologic TEAEs were graded per CTCAE v5.0 criteria. [c]Neutropenia combines preferred terms *neutrophil count decreased* and *neutropenia*. [d]Thrombocytopenia combines preferred terms *platelet count decreased* and *thrombocytopenia*.
CLL=chronic lymphocytic leukemia, MTD=maximum tolerable dose, R/R=relapsed/refractory, TEAE=treatment-emergent adverse event, TLS=tumor lysis syndrome.
Opat S, et al. Poster Presentation at EHA 2025; PF580.

Efficacy

Sonrotoclax Monotherapy in R/R CLL/SLL

- With a median study follow-up of 24.7 months, the ORR was 94.4% across all dose cohorts
  - CRs were seen in 44.4% of patients, with a median time to CR of 17.8 months (range, 4.4-26.5 months)
  - Median duration of response has not yet been reached
- In the 320-mg cohort, the ORR was 100% with a median 22.7 months of study follow-up
  - CRs were seen in 28.6% of patients, with a median time to CR of 11.6 months (range, 4.4-18.7 months)
- Median PFS was not reached after a median follow-up of 23.7 months (range, 4.0-41.2 months)
  - No PFS events occurred in the 320-mg cohort and all patients remain on treatment

Response Rates

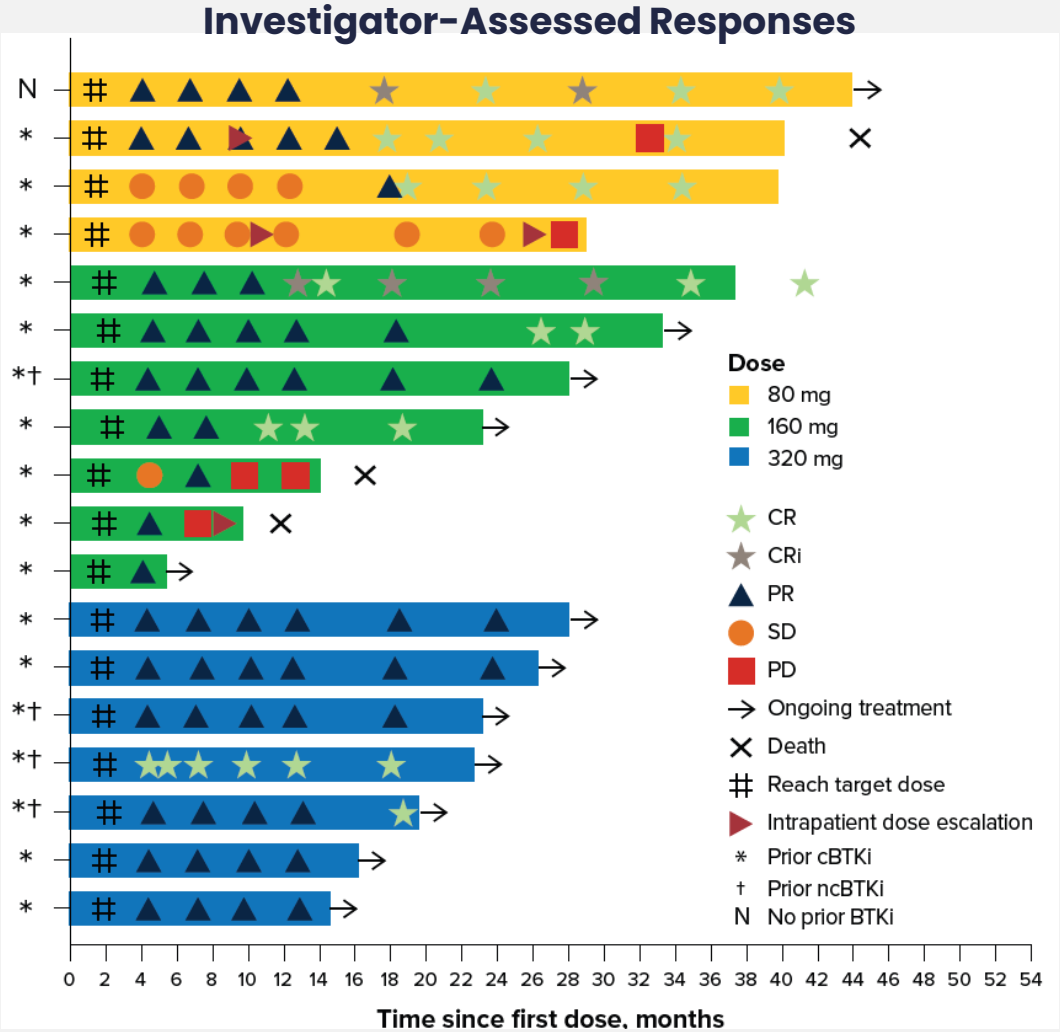


	Sonro 80 mg (n=4)	Sonro 160 mg (n=7)	Sonro 320 mg (n=7)	All patients (N=18)
Follow-up time, median (range), months	45.2 (44.0-50.5)	23.2 (5.4-42.7)	22.7 (14.6-28.1)	24.7 (5.4-50.5)

Data cutoff: March 1, 2025.
CLL=chronic lymphocytic leukemia, CR=complete response, CRI=CRi, complete response with incomplete marrow recovery, ORR=overall response rate, PFS=progression-free survival, PR=partial response, R/R=relapsed/refractory, Sonro=sonrotoclax.
Opat S, et al. Poster Presentation at EHA 2025; PF580.

Efficacy (Cont'd)

Sonrotoclax Monotherapy in R/R CLL/SLL



Data cutoff: March 1, 2025.
BTK=Bruton tyrosine kinase, cBTKi=covalent BTK inhibitor, CLL, chronic lymphocytic leukemia, CR=complete response, CRi=complete response with incomplete marrow recovery, ncBTKi=noncovalent BTKi, PD=progressive disease, PR=partial response, R/R=relapsed/refractory, SD=stable disease.
Opat S, et al. Poster Presentation at EHA 2025; PF580.

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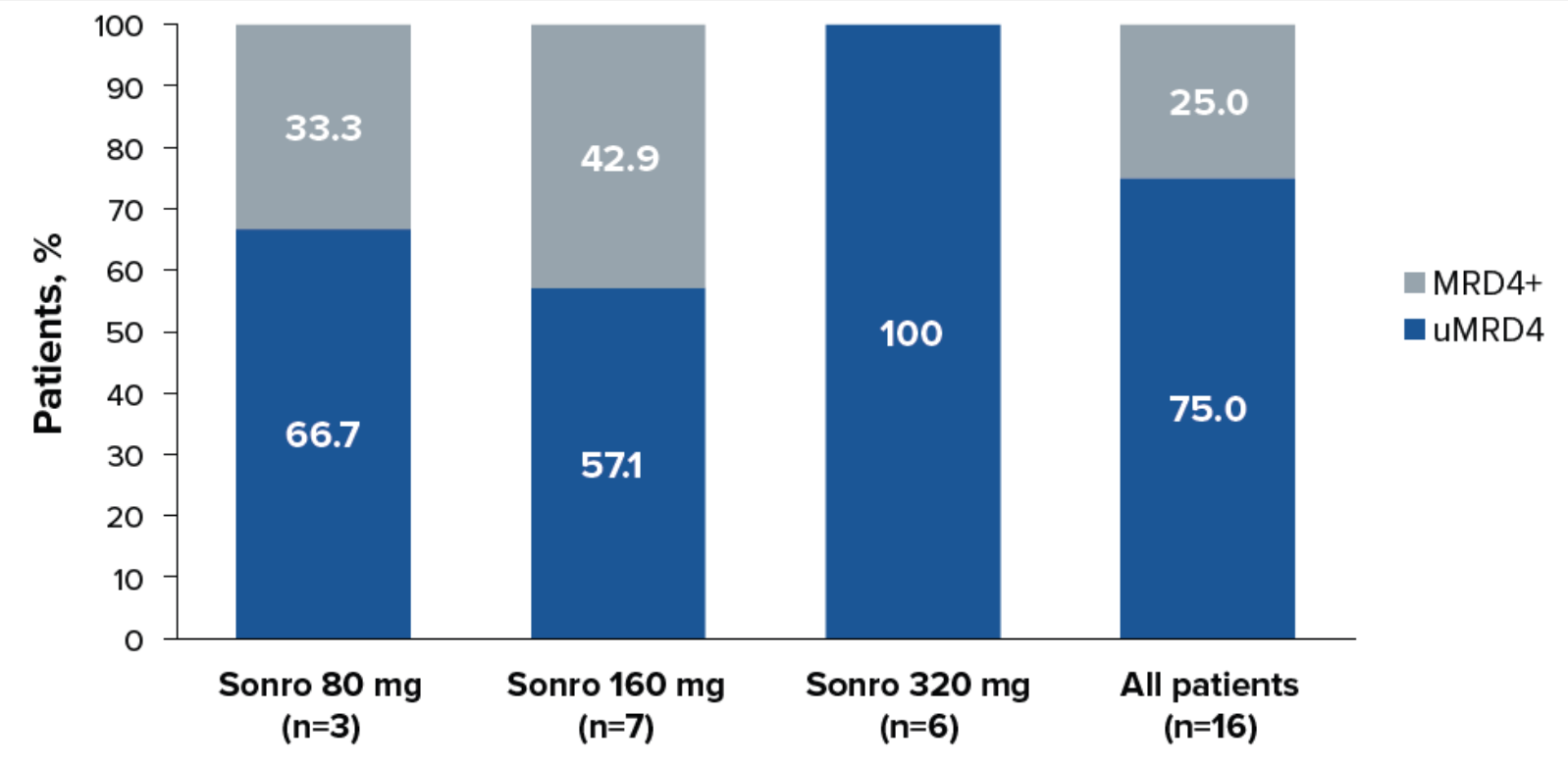
Best Overall MRD in Peripheral Blood by Dose Level[a,b]

Sonrotoclax Monotherapy in R/R CLL/SLL

- The best uMRD rate was 75% across all patients and 100% in the 320-mg cohort



Data cutoff: March 1, 2025.
[a]Measured by ERIC-approved flow cytometry method with 10^{-4} sensitivity. uMRD4 defined as $<10^{-4}$ CLL cells of total WBCs. [b]Two patients were excluded from the MRD evaluable set: 1 patient in the 80-mg cohort had <200,000 total nucleated cells and 1 patient in the 320-mg cohort was missing all MRD samples.
CLL=chronic lymphocytic leukemia, MRD=measurable residual disease, R/R= relapsed/refractory, Sonro=sonrotoclax, uMRD=undetectable MRD, WBC=white blood cell.
Opat S, et al. Poster Presentation at EHA 2025; PF580.