

# BGB-11417-103

R/R AML



# Sonrotoclax in Patients With Acute Myeloid Leukemia

## BGB-11417-103 – R/R AML

### Phase 1/2

**Study Identifier:**  
BGB-11417-103, NCT04771130

**Primary Endpoint:** Part 1 & 2: safety (DLTs, TEAEs); part 3: CR + CRh rate, PK/PD parameters  
**Key Secondary Endpoints:** Part 1 & 2: CR + CRh rate, PK/PD; part 3: safety (TEAEs)

### Key eligibility criteria

- ≥18 years old
- AML (non-APL)
- TN unfit for intensive chemotherapy
- R/R with no prior BCL2 inhibitor or azacitadine exposure
- ECOG PS 0-2
- Not receiving warfarin, moderate or strong CYP3A4 inhibitor or inducer within 5 half-lives

### Treatment

**Sonrotoclax (BGB-11417)**  
(10 d or 28 d with 4-d ramp-up in cycle 1) + **Azacitadine**  
(75mg/m<sup>2</sup> for 7 days SC or IV)



Sonrotoclax dose		
40 mg x 10d	160 mg x 10d	320 mg x 21d
80 mg x 10d	160 mg x 28d	320 mg x 28d
Intermediate doses		
80 mg x 14d	160 mg x 14d 160 mg x 14d (R/R)	320 mg x 14d

**Part 3**  
~20 patients

AML=acute myeloid leukemia, APL=acute promyelocytic leukemia, BCL2=B-cell lymphoma 2, CR=complete response, CRh=complete response with partial hematologic recovery, CYP3A4=cytochrome P450 3A4, d=day, DLT=dose-limiting toxicity, ECOG PS=Eastern Cooperative Oncology Group performance status, IV=intravenous, PD=pharmacodynamic, PK=pharmacokinetics, PS=performance status, R/R=relapsed/refractory, RP2D=recommended phase 2 dose, SC=subcutaneous, TEAE=treatment-emergent adverse event, TN=treatment naïve.  
1. Döhner et al. *Blood*. 2017;129(4):424-447; 2. Bloomfield et al. *Blood Rev*. 2018;32(5):416-425; 3. Shortt et al. EHA Presentation. 2022. Abstract number: P590; 4. Montesinos P et al. Poster Presentation at EHA 2024;P562.

# Baseline Patient Characteristics and Treatment Exposure in R/R AML

## R/R AML

- The median age was 60 years and the median number of prior lines of therapy was 1.0
- The median number of study treatment cycles was 2; median average cycle length was 35.0 days
- The median relative dose intensity of sonrotoclax was >80%, except in the 80-mg × 10-day cohort (74.9%)

	Sonro dose + aza									Total (N=68)
	Sonro 40 mg × 10 d (n=7)	Sonro 80 mg × 10 d (n=6)	Sonro 80 mg × 14 d (n=8)	Sonro 160 mg × 10 d (n=8)	Sonro 160 mg × 14 d (n=9)	Sonro 160 mg × 21 d (n=6)	Sonro 160 mg × 28 (n=9)	Sonro 320 mg × 14 d (n=13)	Sonro 320 mg × 21 d (n=2)	
<b>Follow-up, median (range), months</b>	15.4 (9.2-39.5)	20.8 (1.5- 37.8)	5.0 (2.2-10.2)	6.8 (0.2-24.5)	5.5 (1.5-11.1)	6.8 (4.6-16.5)	4.9 (1.2-31.2)	5.9 (0.9-17.0)	12.1 (2.6-21.6)	6.2 (0.2-39.5)
<b>Age, median (range), years</b>	64.0 (36-80)	70.0 (54-78)	57.5 (48-83)	52.5 (36-71)	53.0 (27-72)	53.0 (42-66)	57.0 (29-69)	64.0 (43-81)	70.0 (67-73)	60.0 (27-83)
<b>Male, n (%)</b>	3 (42.9)	3 (50.0)	5 (62.5)	5 (62.5)	5 (55.6)	4 (66.7)	6 (66.7)	9 (69.2)	1 (50.0)	41 (60.3)
<b>AML type, n (%)</b>										
De novo	7 (100)	4 (66.7)	7 (87.5)	7 (87.5)	5 (55.6)	6 (100)	8 (88.9)	12 (92.3)	1 (50.0)	57 (83.8)
Secondary	0	2 (33.3)	1 (12.5)	1 (12.5)	4 (44.4)	0	1 (11.1)	1 (7.7)	1 (50.0)	11 (16.2)
<b>HMA failure, n (%)<sup>a</sup></b>	0	0	1 (12.5)	0	1 (11.1)	1 (16.7)	1 (11.1)	2 (15.4)	1 (50.0)	7 (10.3)
<b>ELN 2017 AML risk stratification, n (%)</b>										
Favorable	2 (28.6)	1 (16.7)	0	2 (25.0)	2 (22.2)	0	3 (33.3)	5 (38.5)	0	15 (22.1)
Intermediate	1 (14.3)	1 (16.7)	4 (50.0)	2 (25.0)	3 (33.3)	2 (33.3)	1 (11.1)	1 (7.7)	0	15 (22.1)
Adverse	4 (57.1)	4 (66.7)	4 (50.0)	4 (50.0)	4 (44.4)	4 (66.7)	5 (55.6)	7 (53.8)	2 (100)	38 (55.9)
<b>Positive genetic abnormality, n (%)<sup>b</sup></b>										
IDH1/IDH2	2 (28.6)	3 (50.0)	1 (12.5)	3 (37.5)	1 (11.1)	1 (16.7)	3 (33.3)	1 (7.7)	0	15 (22.1)
FLT3	0	1 (16.7)	1 (12.5)	1 (12.5)	0	1 (16.7)	2 (22.2)	2 (15.4)	1 (50.0)	9 (13.2)
NPM1	2 (28.6)	1 (16.7)	0	2 (25.0)	1 (11.1)	0	3 (33.3)	1 (7.7)	0	10 (14.7)
TP53 aneuploidy or -17/abn(17p)	1 (14.3)	1 (16.7)	1 (12.5)	0	0	1 (16.7)	0	1 (7.7)	1 (50.0)	6 (8.8)
<b>Prior therapy</b>										
Prior aza exposure, n (%)	0	1 (16.7)	3 (37.5)	0	2 (22.2)	1 (16.7)	1 (11.1)	3 (23.1)	1 (50.0)	12 (17.6)
No. of lines of prior systemic therapy, median (range)	1.0 (1-2)	1.0 (1-2)	1.5 (1-5)	2.0 (1-2)	2.0 (1-4)	2.0 (1-6)	1.0 (1-3)	1.0 (1-3)	1.5 (1-2)	1.0 (1-6)
<b>Treatment exposure</b>										
No of cycles, median (range)	2.0 (2.0-15.0)	10.5 (1.0-36.0)	2.0 (1.0-8.0)	2.5 (1.0-20.0)	2.0 (1.0-5.0)	2.0 (1.0-7.0)	2.0 (1.0-4.0)	3.0 (1.0-12.0)	3.5 (1.0-6.0)	2.0 (1.0-36.0)
Average cycle duration, median (range), days	35.0 (29.5-41.5)	33.3 (21.0-40.9)	34.8 (28.0-44.0)	35.0 (5.0-48.7)	33.2 (22.0-44.0)	36.8 (22.0-44.0)	36.8 (25.0-53.0)	35.0 (25.3-55.0)	42.3 (35.7- 49.0)	35.0 (5.0-55.0)
Relative sonro dose intensity, median (range), %	100.0 (76.5-100.0)	74.9 (57.0-112.7)	91.1 (47.9-100.0)	100.0 (33.9-100.0)	100.0 (79.4-103.9)	89.8 (54.9-100.0)	90.0 (54.9-100.0)	96.3 (50.7-116.8)	82.1 (64.3-100.0)	97.6 (22.0-156.0)
Relative aza dose intensity, median (range), %	100.0 (52.3-100.3)	85.5 (45.8-101.0)	99.9 (69.5-101.5)	99.8 (73.0-101.1)	99.5 (79.2-100.8)	99.5 (64.9-103.4)	100.0 (69.9-100.9)	99.7 (52.5-109.1)	92.7 (84.3-101.1)	99.7 (45.8-109.1)

Data cutoff: January 10, 2025.

<sup>a</sup>HMA failure received ≥1 cycle of HMA and had PD or no PR or better hematologic improvement after four cycles of >75% of planned dose. <sup>b</sup>As reported by investigator.

aza, azacitidine, AML=acute myeloid leukemia, ELN=European LeukemiaNet, HMA=hypomethylating agent, PD=progressive disease, PR=partial response, R/R=relapsed refractory, sonro=sonrotoclax.

1. Döhner H, et al. Blood. 2017;129(4):424-447.

Montesinos P, et al. Poster Presentation at EHA 2025; PF491.

# TEAE Summary



## R/R AML

- TEAEs were similar in frequency and severity across doses
- No cases of laboratory or clinical TLS were reported
- One DLT, grade 4 thrombocytopenia, occurred with 320 mg × 14 day

	Sonro dose + aza									
	Sonro 40 mg × 10 d (n=7)	Sonro 80 mg × 10 d (n=6)	Sonro 80 mg × 14 d (n=8)	Sonro 160 mg × 10 d (n=8)	Sonro 160 mg × 14 d (n=9)	Sonro 160 mg × 21 d (n=6)	Sonro 160 mg × 28 (n=9)	Sonro 320 mg × 14 d (n=13)	Sonro 320 mg × 21 d (n=2)	Total (N=68)
<b>Any TEAEs</b>	7 (100)	6 (100)	8 (100)	8 (100)	9 (100)	6 (100)	9 (100)	13 (100)	2 (100)	68 (100)
Grade ≥3	7 (100)	5 (83.3)	7 (87.5)	7 (87.5)	8 (88.9)	5 (83.3)	9 (100)	13 (100)	2 (100)	63 (92.6)
Neutropenia <sup>a</sup>	5 (71.4)	5 (83.3)	7 (87.5)	6 (75.0)	8 (88.9)	5 (83.3)	9 (100)	11 (84.6)	1 (50.0)	57 (83.8)
Thrombocytopenia <sup>b</sup>	2 (28.6)	2 (33.3)	4 (50.0)	7 (87.5)	4 (44.4)	1 (16.7)	7 (77.8)	9 (69.2)	0	36 (52.9)
Infections and infestations	4 (57.1)	4 (66.7)	0	5 (62.5)	6 (66.7)	1 (16.7)	2 (22.2)	4 (30.8)	2 (100)	28 (41.2)
<b>Serious TEAEs</b>	5 (71.4)	4 (66.7)	4 (50.0)	7 (87.5)	8 (88.9)	4 (66.7)	7 (77.8)	8 (61.5)	2 (100)	49 (72.1)
<b>DLT, n/N (%)</b>	0	0	0	0	0	0	0	1/12 (8.3) <sup>c</sup>	0	1/62 (1.6)

Data cutoff: January 10, 2025.

<sup>a</sup>Neutropenia includes the terms *neutropenia*, *febrile neutropenia*, *neutrophil count decreased*, and *neutropenic sepsis*. <sup>b</sup>Thrombocytopenia includes the terms *thrombocytopenia* and *platelet count decreased*. <sup>c</sup>Achieved best response of CRi/CRh and continued treatment with a dose (duration) reduction after count recovery.

aza=azacitidine, AML=acute myeloid leukemia, CR=complete response, CRh=CR with partial hematologic recovery, CRi=CR with incomplete hematologic recovery, DLT=dose-limiting toxicity, PD=progressive disease, R/R=relapsed refractory, sonro=sonrotoclax, TEAE=treatment-emergent adverse event, TLS=tumor lysis syndrome.

Montesinos P, et al. Poster Presentation at EHA 2025; PF491.

# TEAE Summary (Cont'd)



## R/R AML

- Six patients (8.8%) had a TEAE leading to death; 2 cases were treatment related (160 mg × 28 day, neutropenic sepsis; 320 mg × 14 day, pneumonia); the 30-d mortality rate was 1.5%
- Treatment discontinuation due to TEAEs occurred in 7 patients (10.3%)
  - The most common TEAE classes leading to discontinuation of sonrotoclax (n=4, 5.9%) or azacitidine (n=4, 5.9%) were infection and infestations
- TEAEs leading to dose reduction occurred in 8 patients (11.8%) and 2 patients (2.9%) with sonrotoclax and azacitidine, respectively
  - The most common TEAE class leading to dose reduction of sonrotoclax was neutropenia (n=7, 10.3%) and of azacitidine was neutropenia and thrombocytopenia (n=1 each, 1.5%)

	Sonro dose + aza									
	Sonro 40 mg × 10 d (n=7)	Sonro 80 mg × 10 d (n=6)	Sonro 80 mg × 14 d (n=8)	Sonro 160 mg × 10 d (n=8)	Sonro 160 mg × 14 d (n=9)	Sonro 160 mg × 21 d (n=6)	Sonro 160 mg × 28 (n=9)	Sonro 320 mg × 14 d (n=13)	Sonro 320 mg × 21 d (n=2)	Total (N=68)
<b>Led to death<sup>a</sup></b>	0	0	0	1 (12.5)	1 (11.1)	0	3 (33.3)	1 (7.7)	0	6 (8.8)
<b>Led to discontinuation</b>										
Aza	1 (14.3)	0	0	2 (25.0)	1 (11.1)	1 (16.7)	1 (11.1)	2 (15.4)	0	8 (11.8)
Sonro	1 (14.3)	0	0	2 (25.0)	1 (11.1)	1 (16.7)	1 (11.1)	2 (15.4)	0	8 (11.8)
<b>Led to reduction</b>										
Aza	0	1 (16.7)	0	0	0	0	0	1 (7.7)	0	2 (2.9)
Sonro	0	2 (33.3)	1 (12.5)	1 (12.5)	0	1 (16.7)	1 (11.1)	1 (7.7)	1 (50.0)	8 (11.8)
<b>Led to interruption</b>										
Aza	0	2 (33.3)	0	2 (25.0)	3 (33.3)	1 (16.7)	0	0	0	8 (11.8)
Sonro	0	1 (16.7)	0	2 (25.0)	2 (22.2)	2 (33.3)	2 (22.2)	0	0	9 (13.2)

Data cutoff: January 10, 2025.

<sup>a</sup>Aorto-bronchial fistula (160 mg × 28 d), bone marrow failure (160 mg × 28 d; related to PD), Klebsiella sepsis (160 mg × 10 d), neutropenic sepsis (160 mg × 28 d; related to aza, sonro, and disease), pneumonia (320 mg × 14 d; related to aza, sonro, and disease), and pulmonary mucormycosis (160 mg × 14 d; related to PD).

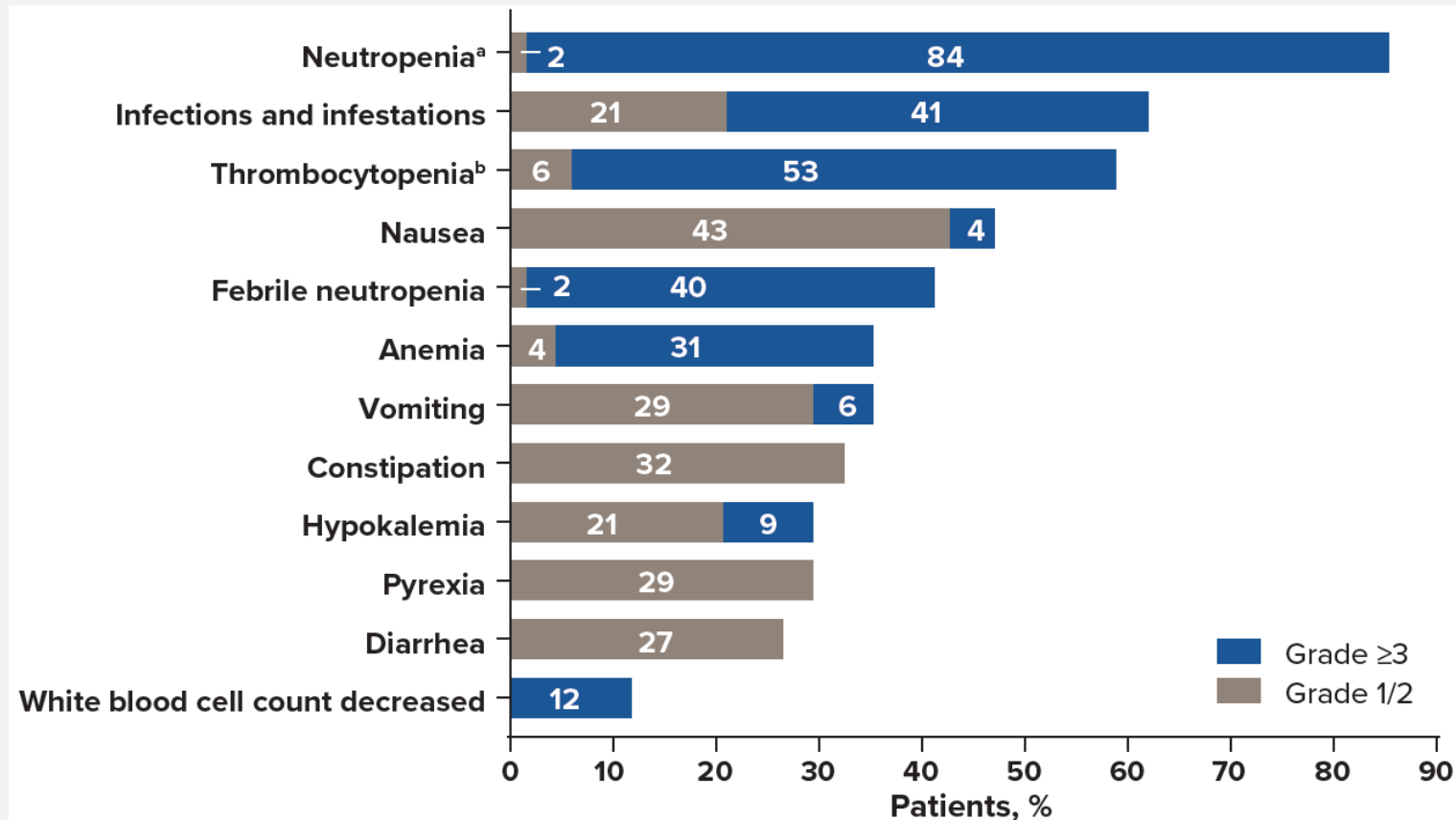
aza=azacitidine, AML=acute myeloid leukemia, CR=complete response, CRh=CR with partial hematologic recovery, CRI=CR with incomplete hematologic recovery, DLT=dose-limiting toxicity, PD=progressive disease, R/R=relapsed refractory, sonro=sonrotoclax, TEAE=treatment-emergent adverse event.

Montesinos P, et al. Poster Presentation at EHA 2025; PF491.

# TEAEs in $\geq 20\%$ (All Grades) or $\geq 10\%$ (Grade $\geq 3$ ) of Patients With R/R AML

## R/R AML

- The most common any-grade and grade  $\geq 3$  TEAEs were neutropenia, infections and infestations, and thrombocytopenia



Data cutoff: January 10, 2025.

<sup>a</sup>Neutropenia includes the terms *neutropenia*, *febrile neutropenia*, *neutrophil count decreased*, and *neutropenic sepsis*. <sup>b</sup>Thrombocytopenia includes the terms *thrombocytopenia* and *platelet count decreased*.

AML=acute myeloid leukemia, R/R=relapsed refractory, TEAE=treatment-emergent adverse event.

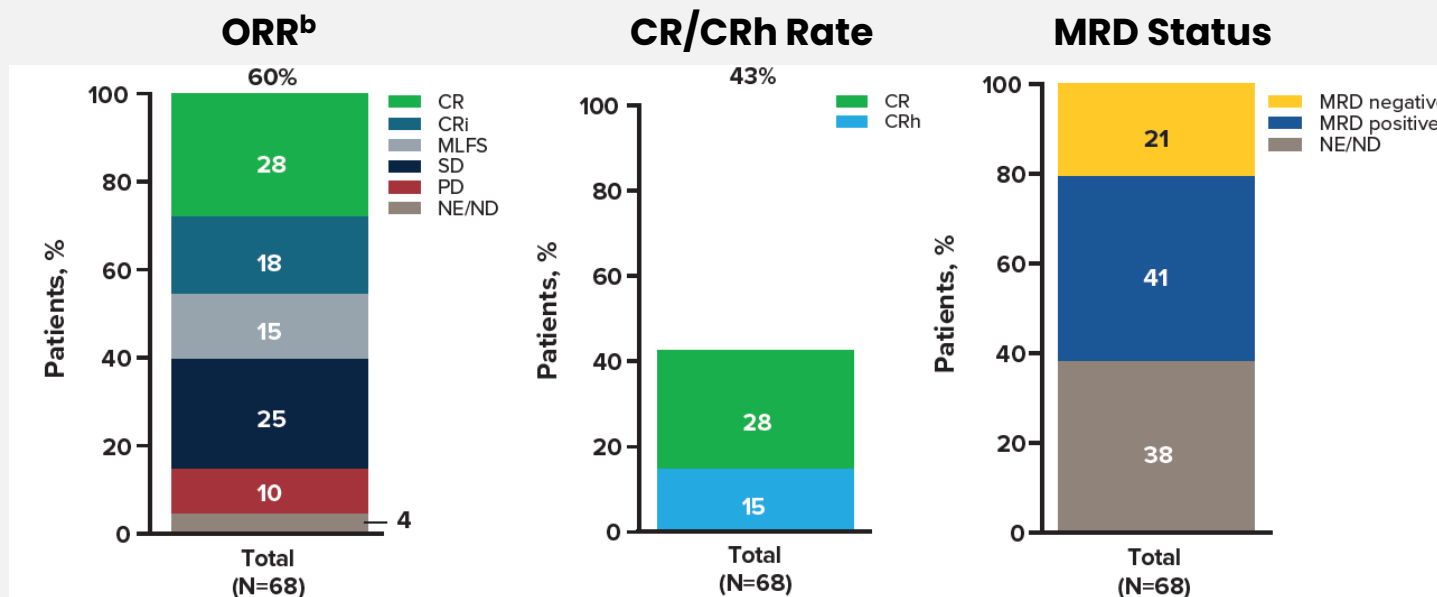
Montesinos P, et al. Poster Presentation at EHA 2025; PF491.

# Summary of Disease Responses<sup>a</sup>



## R/R AML

- With a median follow-up of 6.2 months, the ORR in all patients was 60.3%
  - CR/CRh was achieved in 42.6% (95% CI, 30.7%-55.2%) of patients by a median time of 1.7 months; CR was achieved in 27.9% (95% CI, 17.7%-40.1%) of patients by a median of 1.9 months
  - In the cohorts with the longest follow-up (40, 80, and 160 mg × 10 days), 50%, 75% and 100% of patients who achieved CR/CRh, respectively, remained alive and progression free at 12 months since the first determination of response
- Overall, 23.5% of patients proceeded to transplant
- MRD-negative status was achieved by 20.6% of patients



Data cutoff: January 10, 2025.

<sup>a</sup>Responses were determined using the ELN 2017 criteria and partial hematology recovery criteria for AML. <sup>b</sup>ORR included CR, CRi, MLFS, and PR.

AML=acute myeloid leukemia, CR=complete response, CRh=CR with partial hematologic recovery, CRi=CR with incomplete hematologic recovery, MLFS, morphologic leukemia-free state, MRD=minimal residual disease, ND=not done, NE=not evaluable, ORR=overall response rate, PD=progressive disease, PR=partial response, R/R=relapsed refractory.

Montesinos P, et al. Poster Presentation at EHA 2025; PF491.

# Summary of Disease Responses (Cont'd)<sup>a</sup>

## R/R AML

	Sonro dose + aza									
	Sonro 40 mg × 10 d (n=7)	Sonro 80 mg × 10 d (n=6)	Sonro 80 mg × 14 d (n=8)	Sonro 160 mg × 10 d (n=8)	Sonro 160 mg × 14 d (n=9)	Sonro 160 mg × 21 d (n=6)	Sonro 160 mg × 28 (n=9)	Sonro 320 mg × 14 d (n=13)	Sonro 320 mg × 21 d (n=2)	Total (N=68)
<b>CR, n (%)</b>	2 (28.6)	3 (50.0)	2 (25.0)	2 (25.0)	1 (11.1)	2 (33.3)	2 (22.2)	5 (38.5)	0	19 (27.9)
Time to CR, median (range), months	3.2 (1.5-4.9)	4.1 (3.7-4.6)	1.9 (1.7-2.1)	3.2 (1.9-4.4)	2.3 (2.3-2.3)	1.4 (0.9-1.9)	1.3 (1.1-1.4)	1.2 (0.8-5.1)	–	1.9 (0.8-5.1)
By end of cycle 2, n (%)	1 (14.3)	0	2 (25.0)	1 (12.5)	1 (11.1)	2 (33.3)	2 (22.2)	4 (30.8)	0	13 (19.1)
<b>CR/CRh, n (%)</b>	5 (71.4)	4 (66.7)	2 (25.0)	3 (37.5)	1 (11.1)	2 (33.3)	3 (33.3)	8 (61.5)	1 (50.0)	29 (42.6)
Time to CR/CRh, median (range), months	2.4 (1.2-3.5)	3.9 (1.1-4.6)	1.9 (1.7-2.1)	1.9 (1.0-1.9)	1.4 (1.4-1.4)	1.4 (0.9-1.9)	1.1 (0.8-1.4)	1.3 (0.8-5.1)	7.7 (7.7-7.7)	1.7 (0.8-7.7)
<b>CR/CRi, n (%)</b>	4 (57.1)	4 (66.7)	4 (50.0)	3 (37.5)	1 (11.1)	2 (33.3)	3 (33.3)	9 (69.2)	1 (50.0)	31 (45.6)
Time to CR/CRi, median (range), months	2.0 (1.2-3.2)	3.0 (1.1-4.1)	1.9 (0.8-2.4)	1.0 (0.8-1.9)	1.4 (1.4-1.4)	1.4 (0.9-1.9)	1.1 (0.8-1.4)	1.2 (0.8-5.1)	7.7 (7.7-7.7)	1.4 (0.8-7.7)
<b>Proceeded to transplant, n (%)</b>	3 (42.9)	1 (16.7)	2 (25.0)	2 (25.0)	3 (33.3)	2 (33.3)	2 (22.2)	1 (7.7)	0	16 (23.5)
<b>MRD negative, n (%)</b>	2 (28.6)	1 (16.7)	0	1 (12.5)	1 (11.1)	2 (33.3)	1 (11.1)	5 (38.5)	1 (50.0)	14 (20.6)
<b>MRD NE/ND, n (%)</b>	2 (28.6)	1 (16.7)	3 (37.5)	2 (25.0)	5 (55.6)	2 (33.3)	7 (77.8)	3 (23.1)	1 (50.0)	26 (38.2)

Data cutoff: January 10, 2025.

<sup>a</sup>Responses were determined using the ELN 2017 criteria and partial hematology recovery criteria for AML.

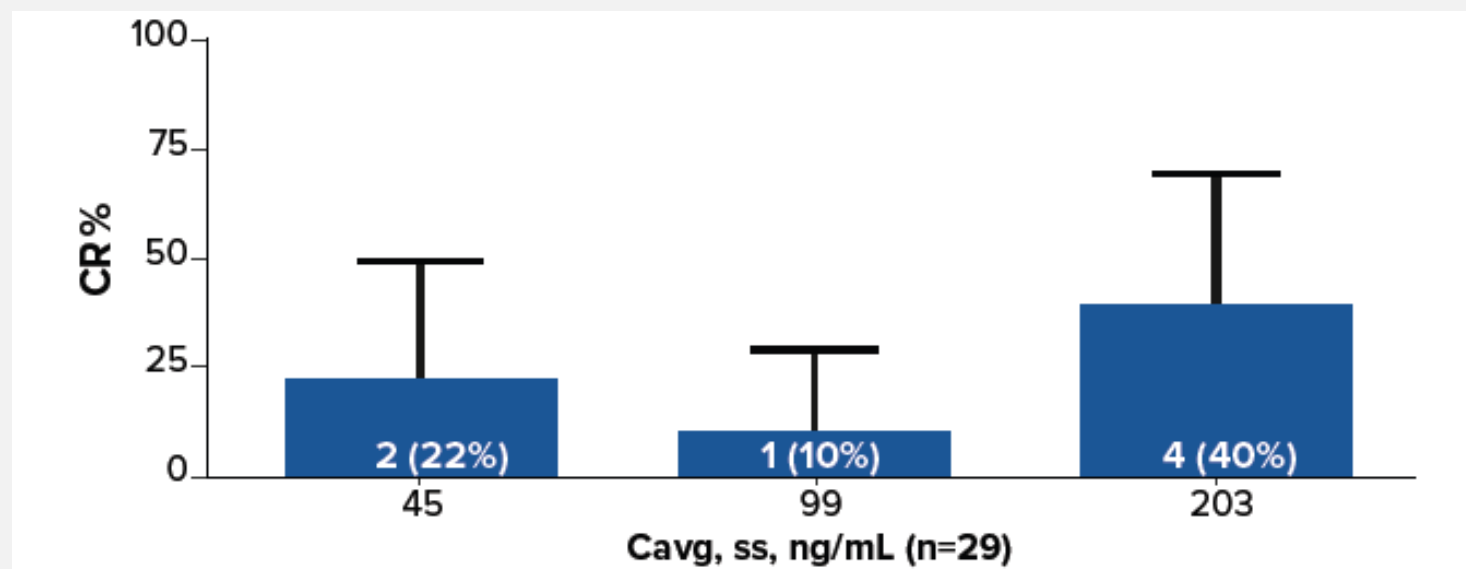
AML=acute myeloid leukemia, aza=azacitidine, CR=complete response, CRh=CR with partial hematologic recovery, CRi=CR with incomplete hematologic recovery, MRD=minimal residual disease, ND=not done, NE=not evaluable, R/R=relapsed refractory, Sonro=sonrotoclax.

Montesinos P, et al. Poster Presentation at EHA 2025; PF491.

# CR Rate by End of Cycle 2 by Sonrotoclax Exposure in 14-Day Cohorts

## R/R AML

- In the 14-day cohorts with comparable follow-up, exploratory exposure-response analysis showed that CR rates by the end of cycle 2 for the third (highest) tertile of sonrotoclax exposure were higher than those in lower tertiles<sup>a</sup>



Data cutoff: January 10, 2025.

<sup>a</sup>Median Cavg, ss for the 80-mg, 160-mg, and 320-mg dose levels was 60 ng/mL, 86 ng/mL, and 176 ng/mL, respectively.

AML=acute myeloid leukemia, Cavg, ss=average sonrotoclax concentration at steady state, CR=complete response, R/R=relapsed refractory.

Montesinos P, et al. Poster Presentation at EHA 2025; PF491.