

BGB-11417-103

TN AML



Sonrotoclax in Patients With Acute Myeloid Leukemia

BGB-11417-103 – TN 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/m² for 7 days SC or IV)

Part 1
Dose escalation

Part 2
Dose expansion

RP2D

Part 3
Efficacy expansion

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
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Part 3

~20 patients

Baseline Patient Characteristics and Treatment Exposure

TN AML

- The median study follow-up was 7.7 months (range, 0.3–34.0 months); median age was 74 years
- The median number of study treatment cycles was four, and the median average cycle length was 34.0 days
- The median relative dose intensity of sonrotoclax was >80%, except in the 160-mg × 28-day and 320-mg × 21-day cohorts

	Sonro dose + aza								Total (N=79)
	Sonro 40 mg × 10 d (n=9)	Sonro 80 mg × 10 d (n=11)	Sonro 80 mg × 14 d (n=13)	Sonro 160 mg × 10 d (n=8)	Sonro 160 mg × 14 d (n=11)	Sonro 160 mg × 28 d (n=9)	Sonro 320 mg × 14 d (n=14)	Sonro 320 mg × 21 d (n=4)	
Follow-up, median (range), months	9.5 (0.5–38.8)	20.6 (0.3–43.4)	5.5 (0.6–10.4)	14.1 (1.4–35.1)	6.4 (1.1–8.6)	13.6 (5.1–26.9)	5.3 (3.5–15.1)	16.4 (8.8–22.0)	7.7 (0.3–43.4)
Age, median (range), years	72.0 (64–91)	77.0 (67–85)	74.0 (68–83)	78.0 (70–87)	71.0 (65–79)	70.0 (65–80)	73.0 (66–89)	76.0 (72–81)	74.0 (64–91)
Male, n (%)	6 (66.7)	5 (45.5)	7 (53.8)	6 (75.0)	6 (54.5)	7 (77.8)	12 (85.7)	3 (75.0)	52 (65.8)
AML type, n (%)									
De novo	5 (55.6)	11 (100)	12 (92.3)	6 (75.0)	8 (72.7)	6 (66.7)	11 (78.6)	3 (75.0)	62 (78.5)
Secondary	4 (44.4)	0	1 (7.7)	2 (25.0)	3 (27.3)	3 (33.3)	3 (21.4)	1 (25.0)	17 (21.5)
ELN 2017 AML risk stratification, n (%)									
Favorable	0	2 (18.2)	4 (30.8)	1 (12.5)	2 (18.2)	1 (11.1)	1 (7.1)	1 (25.0)	12 (15.2)
Intermediate	4 (44.4)	4 (36.4)	6 (46.2)	2 (25.0)	3 (27.3)	3 (33.3)	6 (42.9)	3 (75.0)	31 (39.2)
Adverse	5 (55.6)	5 (45.5)	3 (23.1)	4 (50.0)	6 (54.5)	4 (44.4)	7 (50.0)	0	34 (43.0)
Positive genetic abnormality, n (%)									
IDH1/IDH2	1 (11.1)	1 (9.1)	2 (15.4)	1 (12.5)	2 (18.2)	0	1 (7.1)	0	8 (10.1)
FLT3	1 (11.1)	2 (18.2)	2 (15.4)	1 (12.5)	1 (9.1)	0	2 (14.3)	1 (25.0)	10 (12.7)
NPM1	0	3 (27.3)	3 (23.1)	1 (12.5)	0	0	1 (7.1)	1 (25.0)	9 (11.4)
TP53 aneuploidy or -17/abn(17p)	1 (11.1)	2 (18.2)	1 (7.7)	2 (25.0)	1 (9.1)	1 (11.1)	1 (7.1)	0	9 (11.4)
Treatment exposure									
No of cycles, median (range)	4.0 (1.0–27.0)	15.0 (1.0–44.0)	4.0 (1.0–9.0)	8.5 (1.0–33.0)	3.0 (1.0–8.0)	5.0 (1.0–16.0)	3.0 (1.0–13.0)	13.0 (7.0–21.0)	4.0 (1.0–44.0)
Average cycle duration, median (range), days	32.0 (13.0–44.5)	30.0 (8.0–46.9)	29.3 (17.0–39.0)	34.4 (22.0–45.3)	39.5 (26.0–48.2)	35.1 (2.0–73.0)	36.0 (31.8–65.5)	32.4 (25.4–34.8)	34.0 (2.0–73.0)
Relative sonro dose intensity, median (range), %	100.0 (41.8–161.0)	91.5 (38.8–100.0)	100.0 (71.3–410.2)	92.6 (48.3–109.4)	90.2 (47.0–100.0)	63.3 (29.5–100.0)	83.1 (48.0–100.0)	64.4 (27.4–94.0)	90.0 (27.4–410.2)
Relative aza dose intensity, median (range), %	72.9 (35.2–101.2)	69.6 (37.2–100.4)	96.0 (83.0–100.8)	85.1 (52.3–100.2)	94.6 (61.8–102.1)	94.1 (44.3–100.2)	87.9 (43.3–99.8)	72.7 (47.5–87.4)	90.0 (35.2–102.1)

Data cutoff: January 10, 2025.

^aAs reported by investigator.

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

AML=acute myeloid leukemia, aza=azacitidine, ELN, European LeukemiaNet, sonro=sonrotoclax, TN=treatment naïve.

Shortt J, et al. Poster Presentation at EHA 2025; PF477.

TEAE Summary



TN AML

- TEAE frequency and severity were similar across doses
- TLS occurred in four patients (laboratory, n=2; clinical, n=2); all resolved in ≤4 days without sequelae
- DLTs occurred in four patients; all were hematologic

	Sonro dose + aza								
	Sonro 40 mg × 10 d (n=9)	Sonro 80 mg × 10 d (n=11)	Sonro 80 mg × 14 d (n=13)	Sonro 160 mg × 10 d (n=8)	Sonro 160 mg × 14 d (n=11)	Sonro 160 mg × 28 d (n=9)	Sonro 320 mg × 14 d (n=14)	Sonro 320 mg × 21 d (n=4)	Total (N=79)
Any TEAEs	9 (100)	11 (100)	13 (100)	8 (100)	11 (100)	9 (100)	14 (100)	4 (100)	79 (100)
Grade ≥3	9 (100)	10 (90.9)	13 (100)	8 (100)	11 (100)	9 (100)	13 (92.9)	4 (100)	77 (97.5)
Neutropenia ^a	9 (100)	9 (81.8)	12 (92.3)	8 (100)	9 (81.8)	8 (88.9)	12 (85.7)	4 (100)	71 (89.9)
Thrombocytopenia ^b	7 (77.8)	9 (81.8)	9 (69.2)	4 (50.0)	7 (63.6)	7 (77.8)	9 (64.3)	1 (25.0)	53 (67.1)
Infections and infestations	5 (55.6)	7 (63.6)	6 (46.2)	4 (50.0)	4 (36.4)	6 (66.7)	7 (50.0)	1 (25.0)	40 (50.6)
Serious TEAEs	8 (88.9)	10 (90.9)	10 (76.9)	7 (87.5)	7 (63.6)	8 (88.9)	9 (64.3)	2 (50.0)	61 (77.2)
Laboratory TLS	0	0	0	1 (12.5)	0	0	1 (7.1)	0	2 (2.5)
Clinical TLS	0	0	0	0	1 (9.1)	0	1 (7.1)	0	2 (2.5)
DLT, n/N (%)	0	2/10 (20.0) ^c	0	0	1/11 (9.1) ^d	0	1/13 (7.7) ^d	0	4/69 (5.8)

Data cutoff: January 10, 2025.

^aNeutropenia includes the terms *neutropenia*, *febrile neutropenia*, *neutrophil count decreased*, and *neutropenic sepsis*. ^bThrombocytopenia includes the terms *thrombocytopenia* and *platelet count decreased*. ^cGrade 4 neutropenia, n=1; grade 4 thrombocytopenia, n=2. ^dGrade 4 thrombocytopenia. ^eHospital-acquired pneumonia (80 mg × 10 d), neutropenic sepsis (160 mg × 10 d; related to disease), bronchopulmonary aspergillosis (80 mg × 10 d; related to disease), pulmonary sepsis without preceding confirmed pneumonia (40 mg × 10 d), metastatic squamous cell carcinoma (80 mg × 10 d), anemia (80 mg × 14 d; related to sonro, aza, and disease), coronary artery thrombosis (160 mg × 14 d), general physical health deterioration (80 mg × 14 d; related to disease), death from unknown cause (80 mg × 14 d; related to disease), neutropenic sepsis (160 mg × 14 d; related to sonro and aza), pneumonia (80 mg × 14 d; related to disease), and respiratory failure (80 mg × 14 d; related to disease). AML=acute myeloid leukemia, aza=azacitidine, DLT=dose-limiting toxicity, RDI=relative dose intensity, Sonro=sonrotoclax, TEAE=treatment-emergent adverse event, TLS=tumor lysis syndrome, TN=treatment naïve.

Shortt J, et al. Poster Presentation at EHA 2025; PF477.

TEAE Summary (Cont'd)



TN AML

- Twelve patients (15.2%) had a TEAE leading to death; two were treatment related (80 mg × 14 days, anemia; 160 mg × 14 days, neutropenic sepsis); the 30-day mortality rate was 3.8%
- Treatment discontinuation due to TEAEs occurred in 11 patients (13.9%)
 - The most common TEAE class leading to discontinuation of sonrotoclax (n=7, 8.9%) or azacitidine (n=7, 8.9%) was infections and infestations
- TEAEs leading to dose reduction occurred in 22 patients (27.8%) and 14 patients (17.7%) with sonrotoclax and azacitidine, respectively
 - The most common TEAE class leading to sonrotoclax (n=18, 22.8%) and azacitidine (n=12, 15.2%) dose reduction was neutropenia
- Shorter treatment schedules (<21 day) were better tolerated with RDIs of >80%, and <30% of patients required sonrotoclax dose reduction

	Sonro dose + aza								
	Sonro 40 mg × 10 d (n=9)	Sonro 80 mg × 10 d (n=11)	Sonro 80 mg × 14 d (n=13)	Sonro 160 mg × 10 d (n=8)	Sonro 160 mg × 14 d (n=11)	Sonro 160 mg × 28 d (n=9)	Sonro 320 mg × 14 d (n=14)	Sonro 320 mg × 21 d (n=4)	Total (N=79)
Led to death^a	1 (11.1)	3 (27.3)	5 (38.5)	1 (12.5)	2 (18.2)	0	0	0	12 (15.2)
Led to discontinuation									
Aza	1 (11.1)	3 (27.3)	0	3 (37.5)	4 (36.4)	1 (11.1)	0	0	12 (15.2)
Sonro	2 (22.2)	3 (27.3)	0	2 (25.0)	4 (36.4)	1 (11.1)	0	0	12 (15.2)
Led to reduction									
Aza	3 (33.3)	6 (54.5)	0	1 (12.5)	0	2 (22.2)	1 (7.1)	1 (25.0)	14 (17.7)
Sonro	2 (22.2)	3 (27.3)	3 (23.1)	0	3 (27.3)	4 (44.4)	4 (28.6)	3 (75.0)	22 (27.8)
Led to interruption									
Aza	2 (22.2)	5 (45.5)	2 (15.4)	1 (12.5)	2 (18.2)	1 (11.1)	2 (14.3)	0	15 (19.0)
Sonro	1 (11.1)	5 (45.5)	6 (46.2)	2 (25.0)	2 (18.2)	6 (66.7)	4 (28.6)	0	26 (32.9)

Data cutoff: January 10, 2025.

^aHospital-acquired pneumonia (80 mg × 10 d), neutropenic sepsis (160 mg × 10 d; related to disease), bronchopulmonary aspergillosis (80 mg × 10 d; related to disease), pulmonary sepsis without preceding confirmed pneumonia (40 mg × 10 d), metastatic squamous cell carcinoma (80 mg × 10 d), anemia (80 mg × 14 d; related to sonro, aza, and disease), coronary artery thrombosis (160 mg × 14 d), general physical health deterioration (80 mg × 14 d; related to disease), death from unknown cause (80 mg × 14 d; related to disease), neutropenic sepsis (160 mg × 14 d; related to sonro and aza), pneumonia (80 mg × 14 d; related to disease), and respiratory failure (80 mg × 14 d; related to disease).

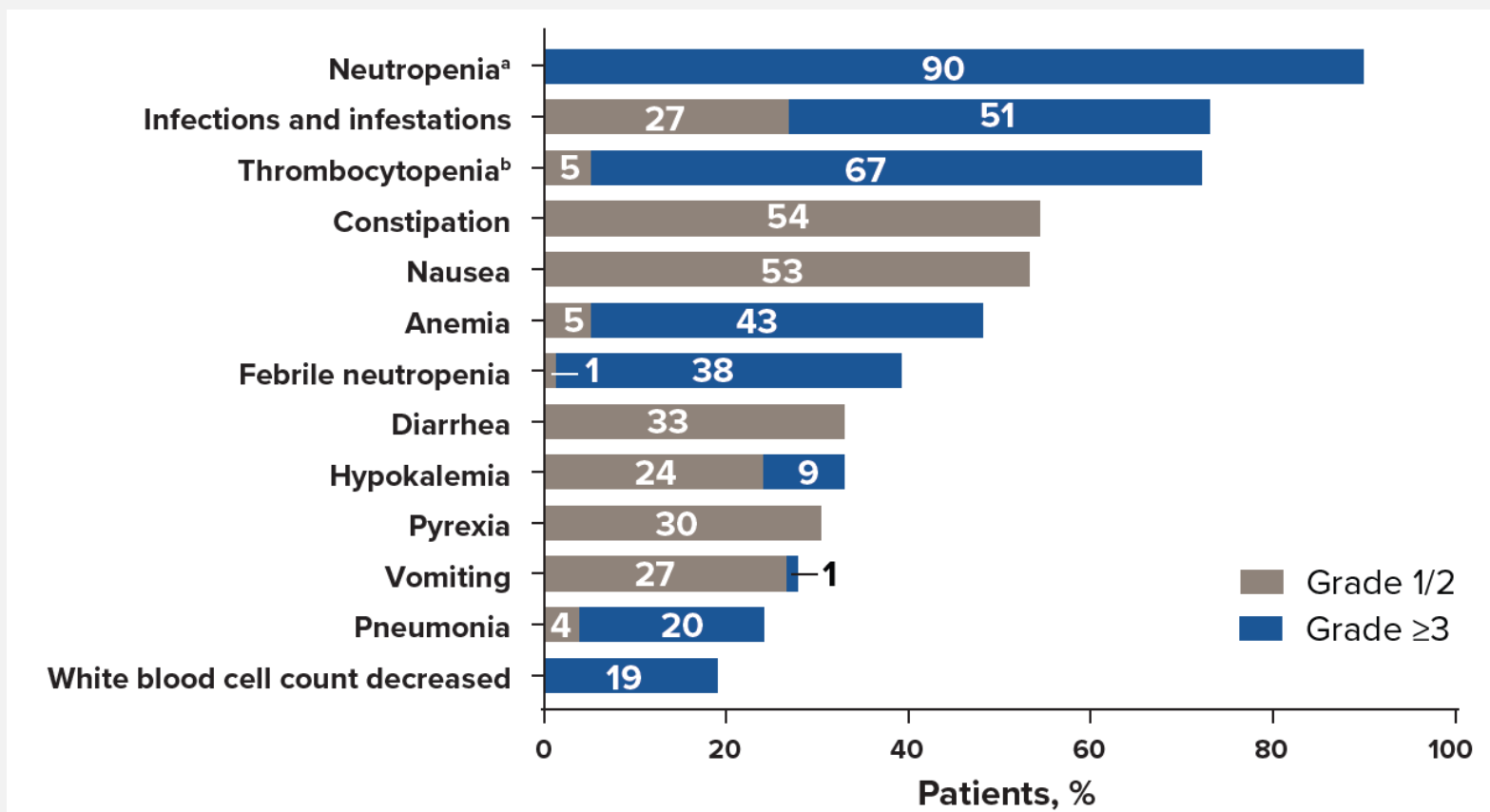
AML=acute myeloid leukemia, aza=azacitidine, DLT=dose-limiting toxicity, RDI=relative dose intensity, Sonro=sonrotoclax, TEAE=treatment-emergent adverse event, TLS=tumor lysis syndrome, TN=treatment naïve.

Shortt J, et al. Poster Presentation at EHA 2025; PF477.

TEAEs in $\geq 20\%$ (All Grades) or $\geq 10\%$ (Grade ≥ 3) of Patients With TN AML

TN AML

- The most common any-grade and grade ≥ 3 TEAEs were neutropenia, infections and infestations, and thrombocytopenia



Data cutoff: January 10, 2025.

^aNeutropenia includes the terms *neutropenia*, *febrile neutropenia*, *neutrophil count decreased*, and *neutropenic sepsis*. ^bThrombocytopenia includes the terms *thrombocytopenia* and *platelet count decreased*.

AML=acute myeloid leukemia, TEAE=treatment-emergent adverse event, TN=treatment naïve.

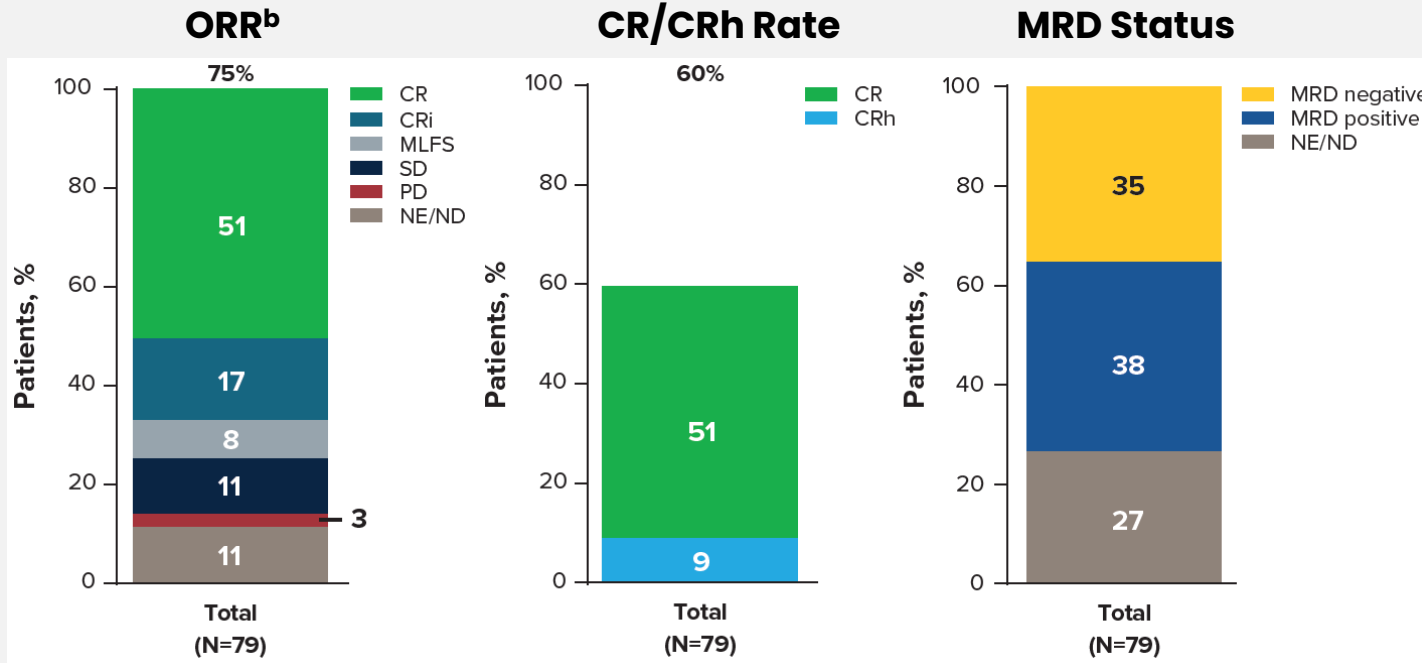
Shortt J, et al. Poster Presentation at EHA 2025; PF477.

Summary of Disease Responses^a



TN AML

- With a median follow-up of 7.7 month, the ORR in all patients was 74.7%
 - CR/CRh was achieved in 59.5% (95% CI, 47.9%-70.4%) by a median of 1.3 months; CR was achieved in 50.6% (95% CI, 39.1%-62.1%) of patients by a median of 1.7 months
 - In cohorts with the longest follow-up (40, 80, and 160 mg x 10 days), 75% of patients who achieved CR/CRh remained alive and progression free at 12 months since the first determination of response
- MRD-negative status was achieved by 35.4% of patients



Data cutoff: January 10, 2025.

^aResponses were determined using the ELN 2017 criteria and partial hematologic recovery criteria for AML. ^bORR 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, SD=stable disease, TN=treatment naïve.

Shortt J, et al. Poster Presentation at EHA 2025; PF477.

Summary of Disease Responses (Cont'd)^a

TN AML

	Sonro dose + aza								Total (N=79)
	Sonro 40 mg × 10 d (n=9)	Sonro 80 mg × 10 d (n=11)	Sonro 80 mg × 14 d (n=13)	Sonro 160 mg × 10 d (n=8)	Sonro 160 mg × 14 d (n=11)	Sonro 160 mg × 28 d (n=9)	Sonro 320 mg × 14 d (n=14)	Sonro 320 mg × 21 d (n=4)	
CR, n (%)	4 (44.4)	8 (72.7)	5 (38.5)	4 (50.0)	5 (45.5)	4 (44.4)	6 (42.9)	4 (100)	40 (50.6)
Time to CR, median (range), months	1.3 (1.3-1.8)	1.8 (0.9-6.5)	1.7 (1.0-2.8)	2.6 (1.0-21.1)	1.2 (0.8-2.7)	3.0 (1.1-7.9)	1.3 (0.9-2.1)	7.6 (2.1-21.7)	1.7 (0.8-21.7)
By end of cycle 2, n (%)	4 (44.4)	6 (54.5)	4 (30.8)	2 (25.0)	5 (45.5)	2 (22.2)	6 (42.9)	1 (25.0)	30 (38.0)
CR/CRh, n (%)	5 (55.6)	8 (72.7)	7 (53.8)	5 (62.5)	6 (54.5)	5 (55.6)	7 (50.0)	4 (100)	47 (59.5)
Time to CR/CRh, median (range), months	1.3 (1.3-5.6)	1.4 (0.9-4.4)	1.7 (1.0-2.8)	1.2 (1.0-4.0)	1.0 (0.8-2.5)	1.2 (1.1-4.9)	1.2 (0.9-2.1)	4.1 (2.1-9.7)	1.3 (0.8-9.7)
CR/CRi, n (%)	6 (66.7)	8 (72.7)	7 (53.8)	6 (75.0)	6 (54.5)	6 (66.7)	10 (71.4)	4 (100)	53 (67.1)
Time to CR/CRi, median (range), months	1.3 (1.1-5.6)	1.4 (0.9-4.4)	1.7 (1.0-2.8)	1.1 (1.0-4.0)	1.0 (0.8-2.5)	1.5 (1.1-4.9)	1.5 (0.8-2.1)	1.8 (1.7-2.1)	1.3 (0.8-5.6)
MRD negative, n (%)	4 (44.4)	4 (36.4)	4 (30.8)	2 (25.0)	3 (27.3)	5 (55.6)	4 (28.6)	2 (50.0)	28 (35.4)
MRD NE/ND, n (%)	3 (33.3)	3 (27.3)	3 (23.1)	3 (37.5)	5 (45.5)	2 (22.2)	2 (14.3)	0	21 (26.6)

Data cutoff: January 10, 2025.

^aResponses were determined using the ELN 2017 criteria and partial hematology recovery criteria for AML.

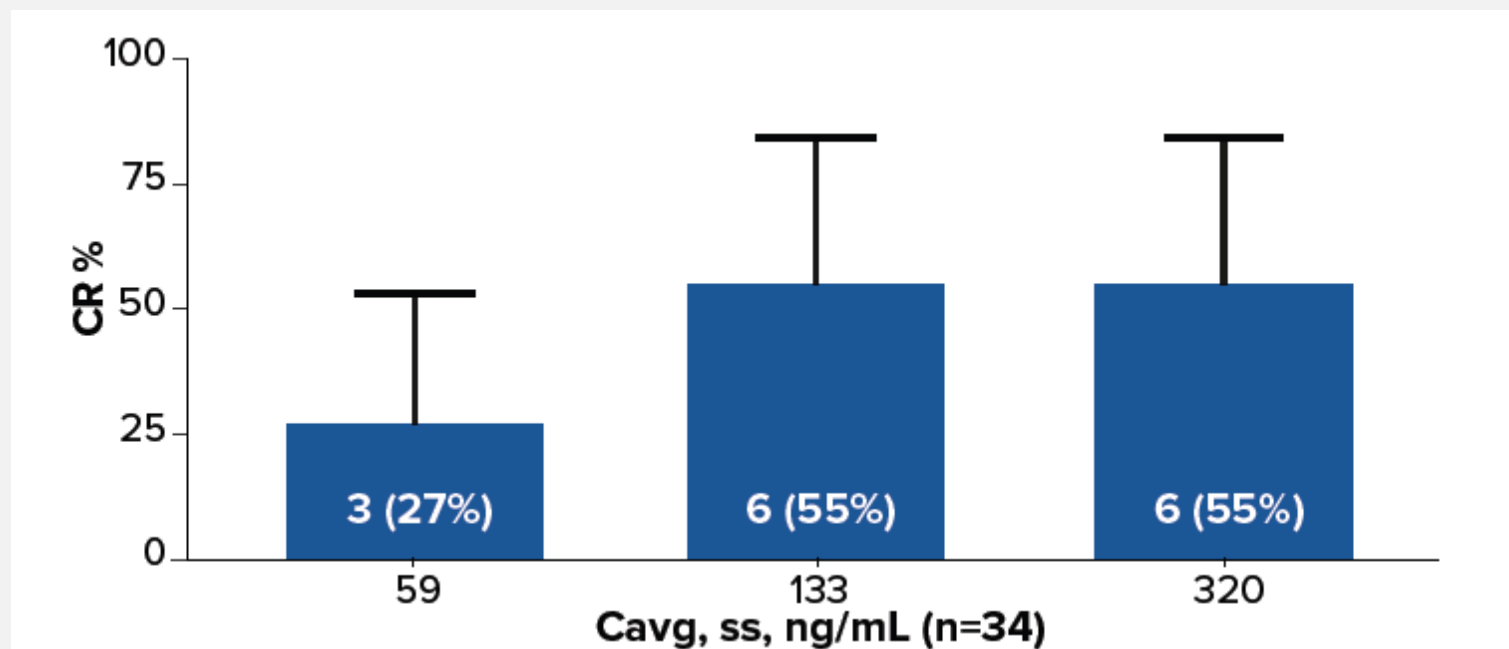
AML=acute myeloid leukemia, aza=azacitidine, CR=complete response, CRh=CR with partial hematologic recovery, CRi=CR with incomplete hematologic recovery, MRD=minimal residual disease, ND=not done, NE=not evaluable, Sonro=sonrotoclax, TN=treatment naïve.

Shortt J, et al. Poster Presentation at EHA 2025; PF477.

CR Rate by Sonrotoclax Exposure in 14-Day Cohorts

TN AML

- Among 14-day cohorts with comparable follow-up, exploratory exposure-response analysis showed that the CR rate for the first tertile corresponding to pharmacokinetic exposure associated with the 80-mg dose was ≈ 2 -fold lower than the CR rate for the second and third tertiles



Data cutoff: January 10, 2025.

^aMedian 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.

Shortt J, et al. Poster Presentation at EHA 2025; PF477.

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/m² 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)	
Follow-up, median (range), months	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)
Age, median (range), years	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)
Male, n (%)	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)
AML type, n (%)										
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)
HMA failure, n (%)^a	0	0	1 (12.5)	0	1 (11.1)	1 (16.7)	1 (11.1)	2 (15.4)	1 (50.0)	7 (10.3)
ELN 2017 AML risk stratification, n (%)										
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)
Positive genetic abnormality, n (%)^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)
Prior therapy										
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)
Treatment exposure										
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.

^aHMA failure received ≥1 cycle of HMA and had PD or no PR or better hematologic improvement after four cycles of >75% of planned dose. ^bAs 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)
Any TEAEs	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 ^a	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 ^b	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)
Serious TEAEs	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)
DLT, n/N (%)	0	0	0	0	0	0	0	1/12 (8.3) ^c	0	1/62 (1.6)

Data cutoff: January 10, 2025.

^aNeutropenia includes the terms *neutropenia*, *febrile neutropenia*, *neutrophil count decreased*, and *neutropenic sepsis*. ^bThrombocytopenia includes the terms *thrombocytopenia* and *platelet count decreased*. ^cAchieved 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.

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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)
Led to death^a	0	0	0	1 (12.5)	1 (11.1)	0	3 (33.3)	1 (7.7)	0	6 (8.8)
Led to discontinuation										
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)
Led to reduction										
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)
Led to interruption										
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.

^aAorto-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).

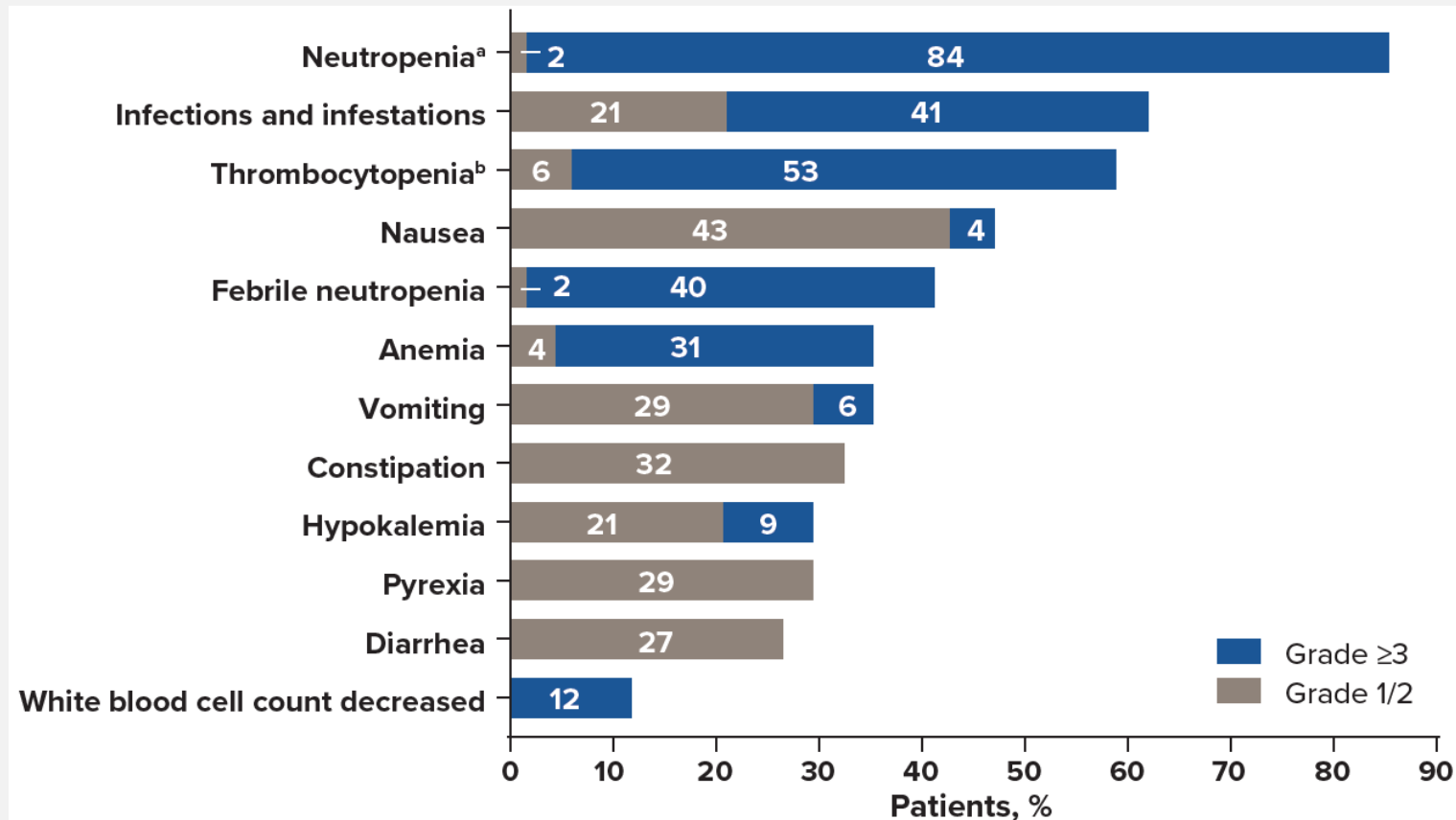
aza=azacitidine, AML=acute myeloid leukemia, CR=complete response, CRh=CR with partial hematologic recovery, CRI=CR with incomplete hematologic recovery, DLT=dose-limiting toxicity, PD=progressive disease, R/R=relapsed refractory, sonro=sonrotoclax, TEAE=treatment-emergent adverse event.

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

R/R AML

- The most common any-grade and grade ≥ 3 TEAEs were neutropenia, infections and infestations, and thrombocytopenia



Data cutoff: January 10, 2025.

^aNeutropenia includes the terms *neutropenia*, *febrile neutropenia*, *neutrophil count decreased*, and *neutropenic sepsis*. ^bThrombocytopenia includes the terms *thrombocytopenia* and *platelet count decreased*.

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

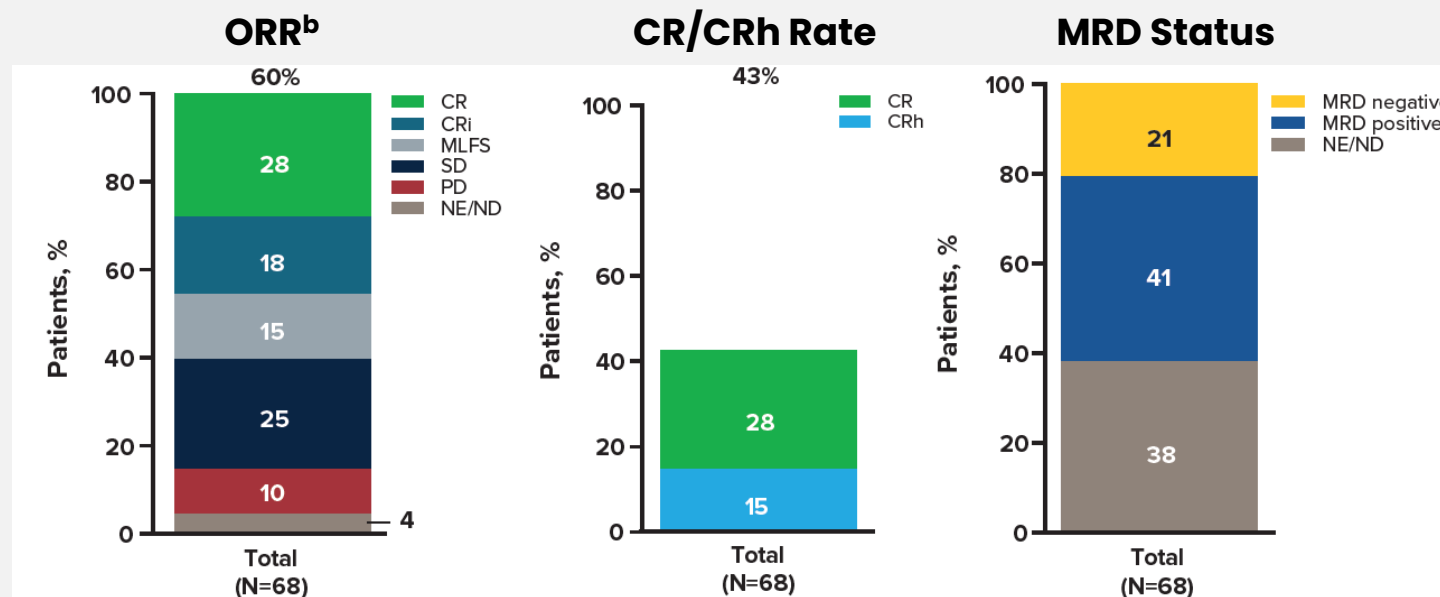
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Summary of Disease Responses^a



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.

^aResponses were determined using the ELN 2017 criteria and partial hematology recovery criteria for AML. ^bORR 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.

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Summary of Disease Responses (Cont'd)^a

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)
CR, n (%)	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)
CR/CRh, n (%)	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)
CR/CRi, n (%)	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)
Proceeded to transplant, n (%)	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)
MRD negative, n (%)	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)
MRD NE/ND, n (%)	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.

^aResponses were determined using the ELN 2017 criteria and partial hematology recovery criteria for AML.

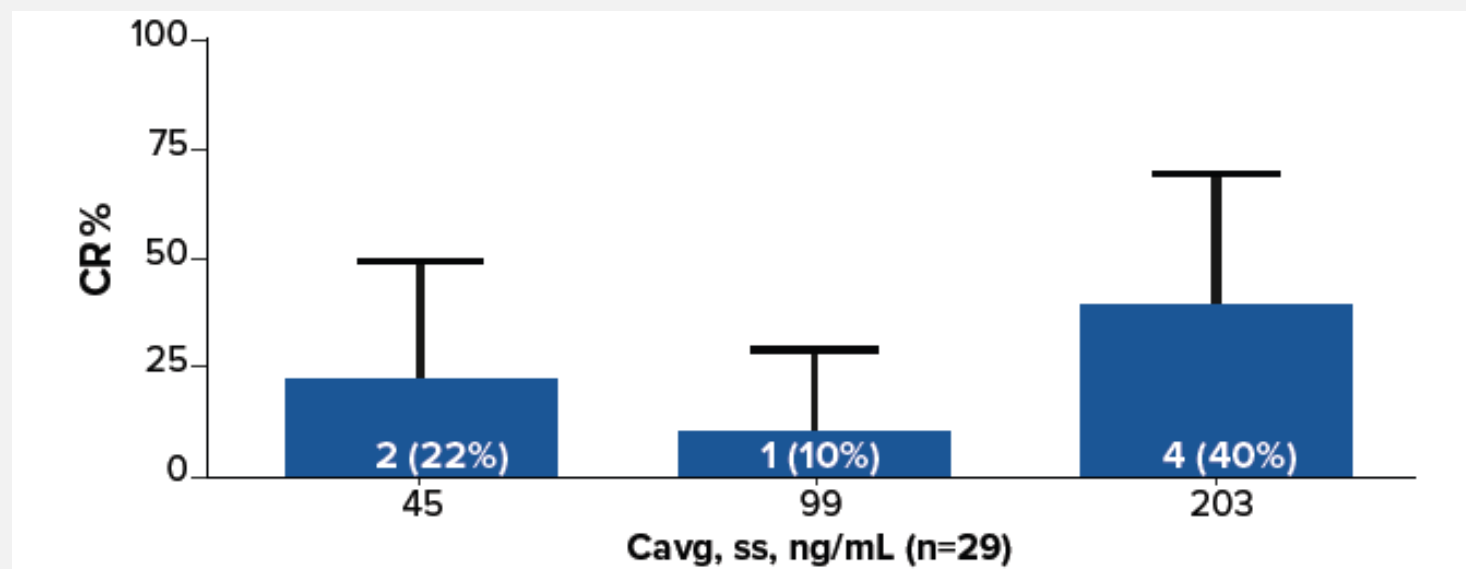
AML=acute myeloid leukemia, aza=azacitidine, CR=complete response, CRh=CR with partial hematologic recovery, CRi=CR with incomplete hematologic recovery, MRD=minimal residual disease, ND=not done, NE=not evaluable, R/R=relapsed refractory, Sonro=sonrotoclax.

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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^a



Data cutoff: January 10, 2025.

^aMedian 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.

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