# 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<br>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.

BGB-11417-103

# 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 | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | 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) |
| **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.
[a]As 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.

BGB-11417-103

# 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.
[a]Neutropenia includes the terms *neutropenia*, *febrile neutropenia*, *neutrophil count decreased*, and *neutropenic sepsis*. [b]Thrombocytopenia includes the terms *thrombocytopenia* and *platelet count decreased*. [c]Grade 4 neutropenia, n=1; grade 4 thrombocytopenia, n=2. [d]Grade 4 thrombocytopenia. [e]Hospital-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.

BGB-11417-103

# 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) |

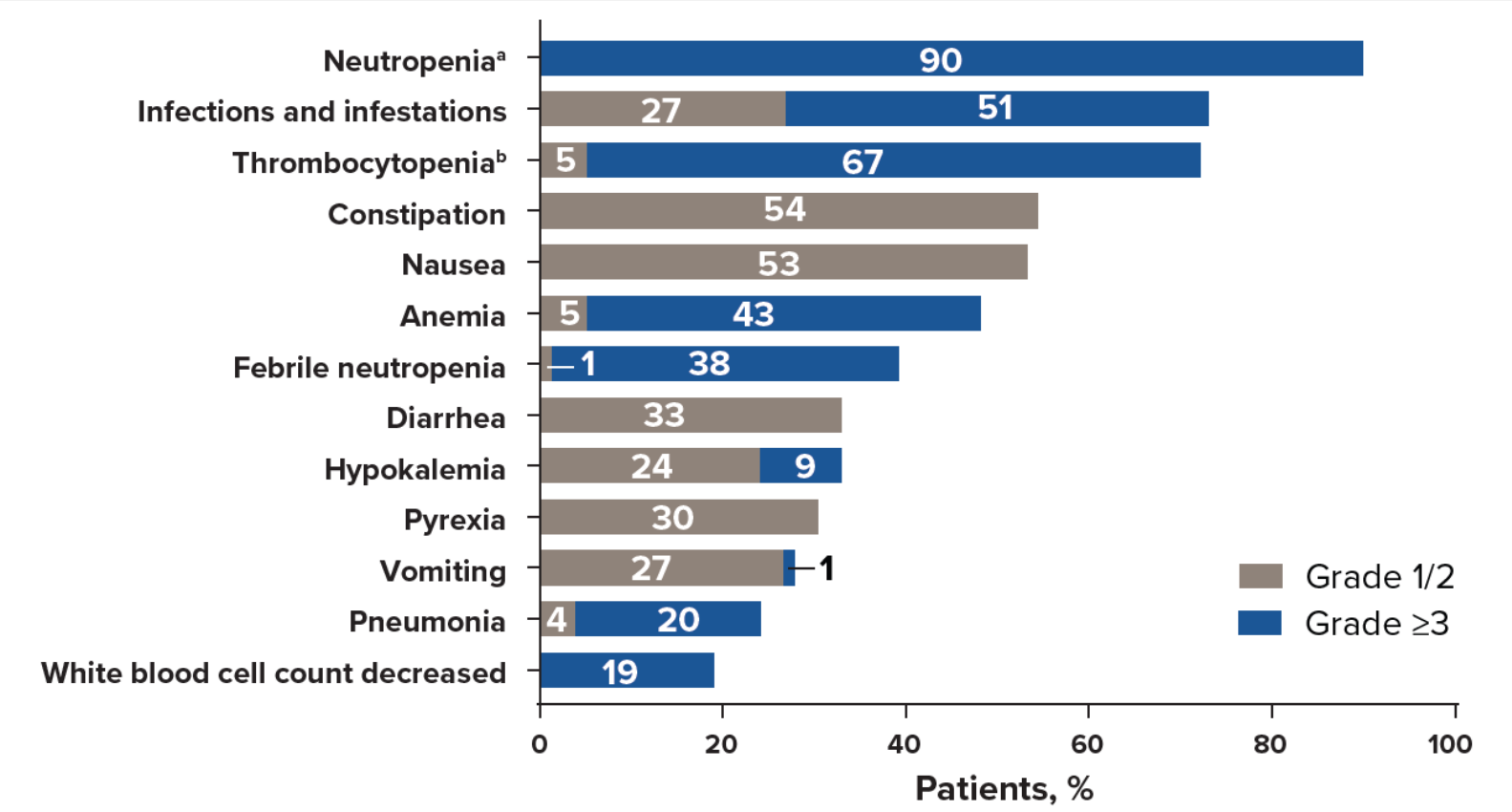
Data cutoff: January 10, 2025.
[a]Hospital-acquired pneumonia (80 mg × 10 d), neutropenic sepsis (160 mg × 10 d; related to disease), bronchopulmonary aspergillosis (80 mg × 10 d; related to disease), pulmonary sepsis without preceding confirmed pneumonia (40 mg × 10 d), metastatic squamous cell carcinoma (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.

BGB-11417-103

# TEAEs in ≥20% (All Grades) or ≥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



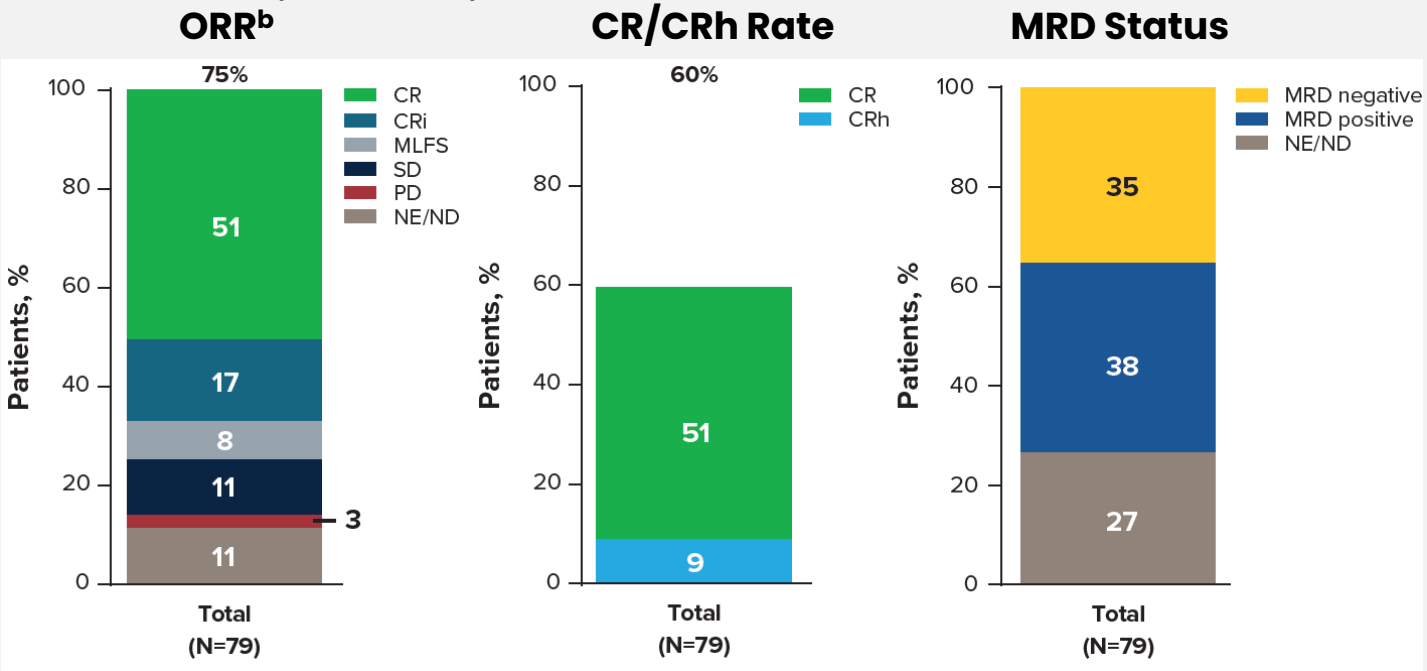

Data cutoff: January 10, 2025.
[a]Neutropenia includes the terms *neutropenia, febrile neutropenia, neutrophil count decreased,* and *neutropenic sepsis.* [b]Thrombocytopenia includes the terms *thrombocytopenia* and *platelet count decreased.*
AML=acute myeloid leukemia, TEAE=treatment-emergent adverse event, TN=treatment naïve.
Shortt J, et al. Poster Presentation at EHA 2025; PF477.

BGB-11417-103

# 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.
[a]Responses were determined using the ELN 2017 criteria and partial hematology recovery criteria for AML. [b]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, SD=stable disease, TN=treatment naïve.
Shortt J, et al. Poster Presentation at EHA 2025; PF477.

BGB-11417-103

# Summary of Disease Responses (Cont'd)[a]

## TN AML

| | 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) |
| **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) |

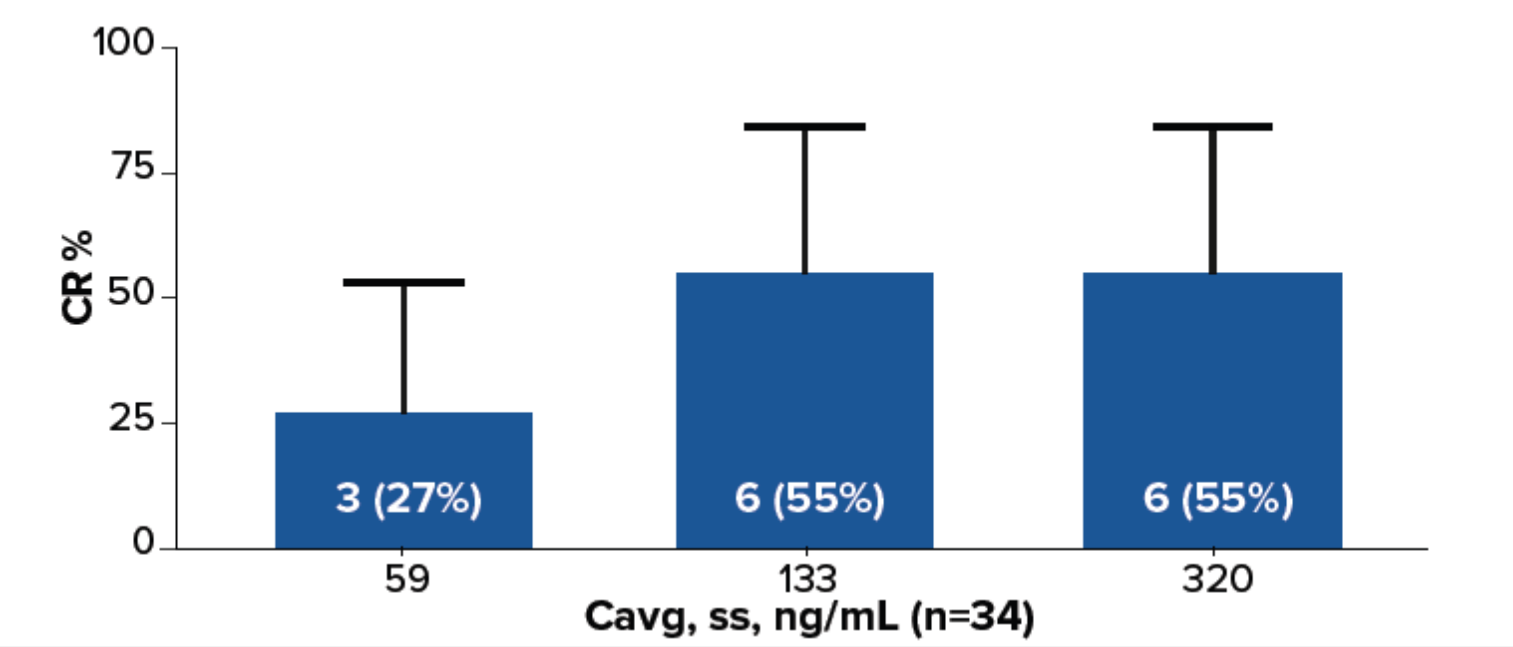
Data cutoff: January 10, 2025.
[a]Responses were determined using the ELN 2017 criteria and partial hematology recovery criteria for AML.
AML=acute myeloid leukemia, aza=azacitidine, CR=complete response, CRh=CR with partial hematologic recovery, CRi=CR with incomplete hematologic recovery, MRD=minimal residual disease, ND=not done, NE=not evaluable, Sonro=sonrotoclax, TN=treatment naïve.
Shortt J, et al. Poster Presentation at EHA 2025; PF477.

BGB-11417-103

# 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.
[a]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.
Shortt J, et al. Poster Presentation at EHA 2025; PF477.