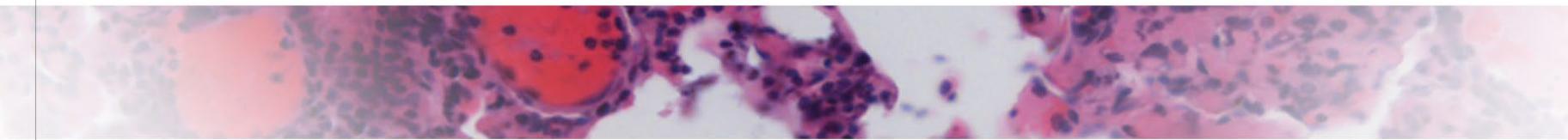




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Initial Phase 1b/2 Study Results of Sonrotoclax (BGB-11417) in Combination With Carfilzomib and Dexamethasone in Patients With t(11;14)-Positive Relapsed/Refractory Multiple Myeloma

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Introduction

- Patients with MM harboring t(11;14), found in approximately 15% to 20% of patients at first diagnosis, represent a unique disease subset with distinct features¹
- Although BCL2 inhibitors have shown clinical activity in patients with MM harboring t(11;14), no BCL2-targeted treatments are currently approved for treating MM²
- Combining a BCL2 inhibitor with agents such as dexamethasone or carfilzomib that promote BCL2 dependency may further potentiate therapeutic efficacy in MM³
- Sonrotoclax (BGB-11417), a next-generation BCL2 inhibitor, is more selective and pharmacologically potent than venetoclax, with a shorter half-life and no drug accumulation⁴
- Preliminary data from the BGB-11417-105 study indicate that sonrotoclax + dexamethasone is well tolerated and can induce deep and durable responses in heavily pretreated patients with t(11;14) MM⁵
- Presented here are initial safety and efficacy data for the sonrotoclax + carfilzomib + dexamethasone combination therapy dose escalation cohorts from study BGB-11417-105

BCL2, B-cell lymphoma 2; MM, multiple myeloma.

1. Bal S, et al. *Am J Cancer Res.* 2022;12(7):2950-2965; 2. Vogler M, et al. *Signal Transduct Target Ther.* 2025;10(1):9; 3. Matulis SM, et al. *Leukemia.* 2016;30(5):1086-1093; 4. Guo Y, et al. *J Med Chem.* 2024;67(10):7836-7858; 5. Dhakal B, et al. EHA 2025. Abstract PF721.

BGB-11417-105 (NCT04973605) study design

- BGB-11417-105 is an ongoing, open-label, phase 1b/2, dose-escalation and dose-expansion study evaluating sonrotoclax in patients with R/R MM harboring t(11;14)

PART 1 DOSE ESCALATION

Key eligibility criteria

- Confirmed MM with t(11;14) translocation
- At least 3 prior lines of therapy including PI, IMiD and anti-CD38 monoclonal antibody^a
- No more available approved therapies



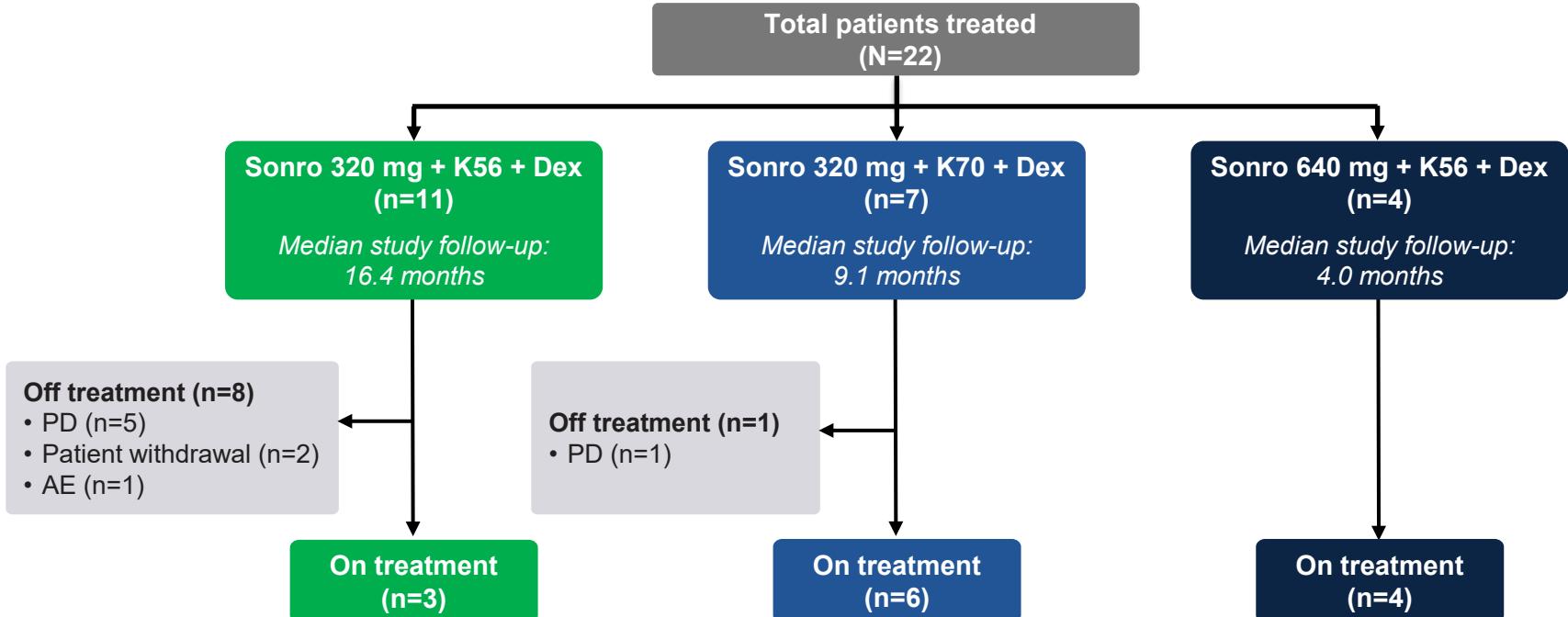
Triple drug combination dose levels

- Sonrotoclax 640 mg QD + K70^b + Dex 40 mg QW (n≥3)^c
- Sonrotoclax 640 mg QD + K56^b + Dex 40 mg QW (n≥3)
- Sonrotoclax 320 mg QD + K70^b + Dex 40 mg QW (n≥3)
- Sonrotoclax 320 mg QD + K56^b + Dex 40 mg QW (n≥3)
- Sonrotoclax 160 mg QD + K70^b + Dex 40 mg QW (n≥3)^c
- Sonrotoclax 160 mg QD + K56^b + Dex 40 mg QW (n≥3)^c

^aPrior anti-CD38 treatment is not required for patients in Australia, New Zealand, and Brazil. ^bCarfilzomib 56 mg/m² or 70 mg/m² per week is administered intravenously on days 1, 8, and 15 of each 28-day cycle, except cycle 1 day 1 on which carfilzomib is administered at 20 mg/m². ^cAt data cutoff, no patients had been enrolled at these dose levels. dex, dexamethasone; IMiD, immunomodulatory drug; K, carfilzomib; MM, multiple myeloma; PI, proteasome inhibitor; QD, once daily; QW, once weekly; R/R, relapsed/refractory.

Patient disposition

- As of September 3, 2025, 22 patients had received sonrotoclax + carfilzomib + dexamethasone across 3 dose levels



Baseline demographics and clinical characteristics

| Parameters | Sonro 320 mg + K56 + Dex (n=11) | Sonro 320 mg + K70 + Dex (n=7) | Sonro 640 mg + K56 + Dex (n=4) | Total (N=22) |
|---|------------------------------------|-----------------------------------|-----------------------------------|-----------------|
| Age, median (range), y | 62.0 (51-77) | 67.0 (60-77) | 69.5 (44-74) | 65.0 (44-77) |
| Male, n (%) | 8 (73) | 6 (86) | 2 (50) | 16 (73) |
| ECOG PS 0 or 1, n (%) | 11 (100) | 7 (100) | 4 (100) | 22 (100) |
| R-ISS stage at initial diagnosis, n (%) | | | | |
| I | 3 (27) | 0 | 0 | 3 (14) |
| II | 4 (36) | 3 (43) | 2 (50) | 9 (41) |
| III | 1 (9) | 1 (14) | 2 (50) | 4 (18) |
| High cytogenetic risk ^a , n (%) | 3 (27) ^b | 0 | 0 | 3 (14) |
| Prior lines of systemic therapy, median (range) | 5.0 (3-8) | 3.0 (2-5) | 3.5 (3-8) | 4.0 (2-8) |
| Prior lines of systemic therapy, n (%) | | | | |
| 2 | 0 | 1 (14) | 0 | 1 (5) |
| 3 | 1 (9) | 4 (57) | 2 (50) | 7 (32) |
| ≥4 | 10 (91) | 2 (29) | 2 (50) | 14 (64) |
| Triple-class ^c exposed, n (%) | 9 (82) | 6 (86) | 4 (100) | 19 (86) |
| Refractory status, n (%) | | | | |
| PI | 9 (82) | 4 (57) | 1 (25) | 14 (64) |
| IMiD | 11 (100) | 5 (71) | 3 (75) | 19 (86) |
| Anti-CD38 antibody | 7 (64) | 3 (43) | 3 (75) | 13 (59) |
| Triple-class ^c refractory | 7 (64) | 1 (14) | 1 (25) | 9 (41) |
| Prior ASCT, n (%) | 7 (64) | 4 (57) | 3 (75) | 14 (64) |

^aHigh risk is defined as genetic subtypes t(4;14), t(14;16), and del(17p13). ^bTwo patients with t(4;14) and 1 patient with del(17p13). ^cDefined as ≥1 PI, ≥1 IMiD, and ≥1 anti-CD38 antibody. ASCT, autologous stem cell transplant; dex, dexamethasone; IMiD, immunomodulatory drug; K, carfilzomib; PI, proteasome inhibitor; R-ISS, Revised International Staging System; sonro, sonrotoclax.

Sonrotoclax + carfilzomib + dexamethasone demonstrated a manageable safety profile

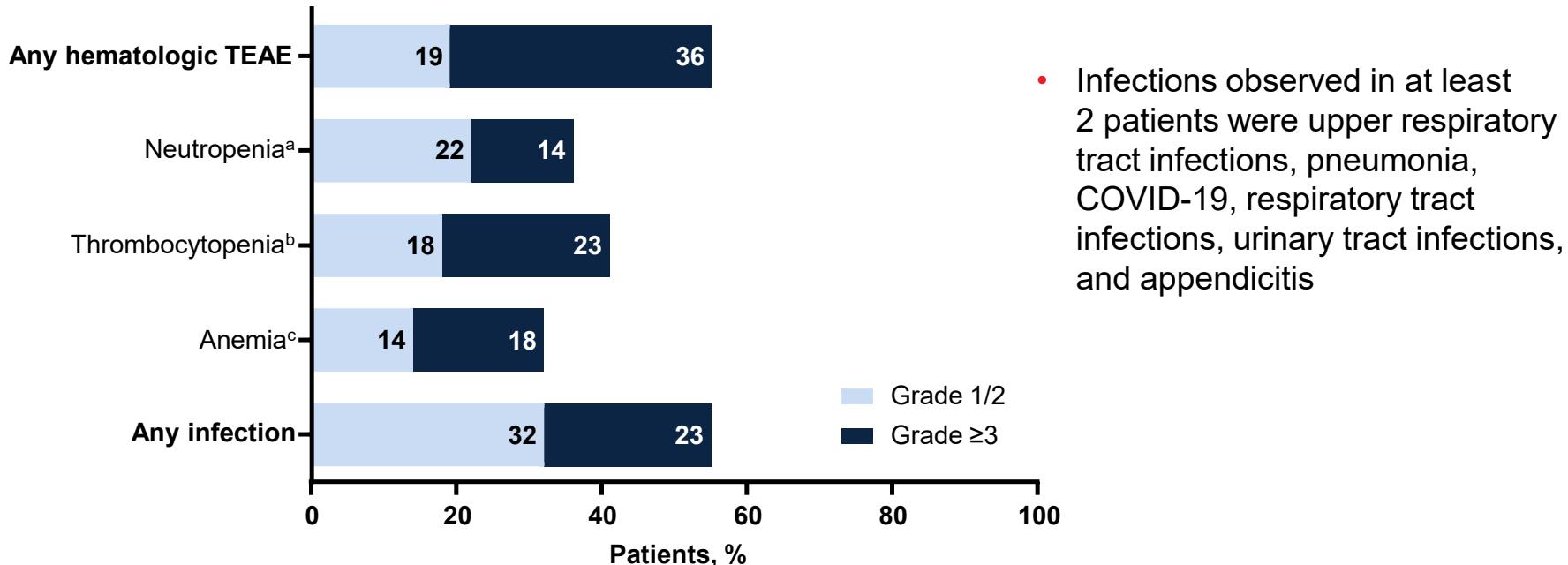
- No TEAEs led to death
- Sonrotoclax dose reductions and discontinuations were rare – only 1 of each occurred
- To date, the MTD has not been reached
- No events of cardiac failure, myocardial infarction, or cardiac arrest were seen at any dose level^a

| Patients, n (%) | Sonro 320 mg + K56 + Dex (n=11) | Sonro 320 mg + K70 + Dex (n=7) | Sonro 640 mg + K56 + Dex (n=4) | Total (N=22) |
|---|---------------------------------|--------------------------------|--------------------------------|--------------------|
| Any TEAE | 11 (100) | 7 (100) | 4 (100) | 22 (100) |
| Grade ≥3 | 9 (82) | 5 (71) | 2 (50) | 16 (73) |
| Serious | 7 (64) | 2 (29) | 1 (25) | 10 (46) |
| Led to death | 0 | 0 | 0 | 0 |
| Led to dose interruption | | | | |
| Sonro | 8 (73) | 5 (71) | 1 (25) | 14 (64) |
| Dex | 6 (55) | 4 (57) | 1 (25) | 11 (50) |
| K | 9 (82) | 4 (57) | 1 (25) | 14 (64) |
| Led to dose reduction | | | | |
| Sonro | 1 (9) ^b | 0 | 0 | 1 (5) ^b |
| Dex | 5 (46) | 3 (43) | 1 (25) | 9 (41) |
| K | 1 (9) | 6 (86) | 1 (25) | 8 (36) |
| Led to treatment discontinuation | | | | |
| Sonro | 1 (9) ^c | 0 | 0 | 1 (5) ^c |
| Dex | 2 (18) | 1 (14) | 0 | 3 (14) |
| K | 2 (18) | 2 (29) | 0 | 4 (18) |
| DLT^d | 1 (9) | 1 (14) | 0 | 2 (9) |

^aOne patient had grade 3 coronary artery disease. ^bOne patient had grade 2 fatigue that led to sonro dose reduction. ^cOne patient had a grade 2 hepatitis B virus infection that led to sonro discontinuation. ^dDLTs included transient grade 3 thrombocytopenia (related to sonro and K) and acute kidney injury (related to K). dex, dexamethasone; DLT, dose-limiting toxicity; K, carfilzomib; MTD, maximum tolerated dose; sonro, sonrotoclax; TEAE, treatment-emergent adverse event.

Sonrotoclax + carfilzomib + dexamethasone was well tolerated

Grouped TEAEs of interest in all patients (N=22)



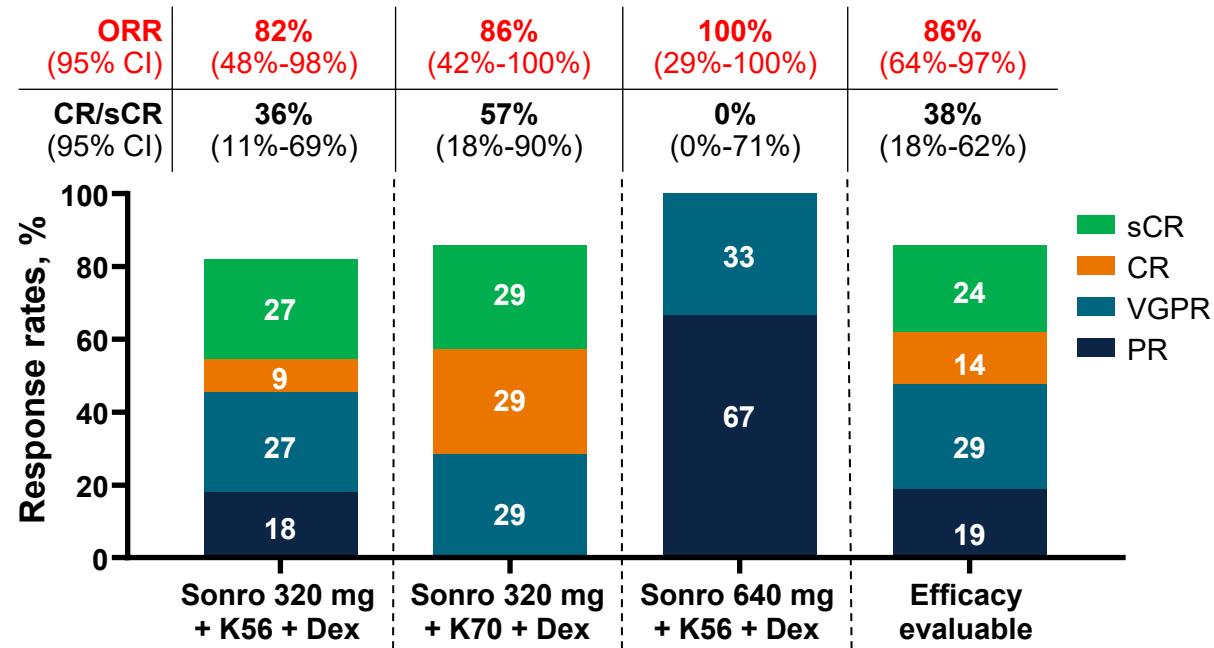
^aIncludes the PTs agranulocytosis, febrile neutropenia, neutropenia, neutropenic infection, neutropenic sepsis, and neutrophil count decreased. ^bIncludes the PTs platelet count decreased and thrombocytopenia. ^cIncludes the PTs anemia and hemoglobin decreased.

The safety profile of combination therapy has been consistent with the known safety profile of each individual study drug

- TEAEs observed in >20% of all patients were consistent with individual study drug components and/or symptoms of MM
 - Most patients had events that were grade 1 or 2 in severity and were transient

| Patients, n (%) | Sonro 320 mg + K56 + Dex (n=11) | | Sonro 320 mg + K70 + Dex (n=7) | | Sonro 640 mg + K56 + Dex (n=4) | | Total (N=22) | |
|-----------------------------------|---------------------------------|-----------|--------------------------------|-----------|--------------------------------|-----------|--------------|-----------|
| | Any grade | Grade 3/4 | Any grade | Grade 3/4 | Any grade | Grade 3/4 | Any grade | Grade 3/4 |
| Fatigue | 4 (36) | 1 (9) | 4 (57) | 2 (29) | 3 (75) | 0 | 11 (50) | 3 (14) |
| Insomnia | 6 (55) | 1 (9) | 2 (29) | 0 | 1 (25) | 0 | 9 (41) | 1 (5) |
| Nausea | 3 (27) | 0 | 3 (43) | 0 | 2 (50) | 0 | 8 (36) | 0 |
| Anemia | 4 (36) | 3 (27) | 2 (29) | 0 | 1 (25) | 1 (25) | 7 (32) | 4 (18) |
| Diarrhea | 3 (27) | 0 | 2 (29) | 0 | 1 (25) | 0 | 6 (27) | 0 |
| Platelet count decreased | 3 (27) | 1 (9) | 3 (43) | 1 (14) | 0 | 0 | 6 (27) | 2 (9) |
| Back pain | 4 (36) | 0 | 2 (29) | 1 (14) | 0 | 0 | 6 (27) | 1 (5) |
| Constipation | 1 (9) | 0 | 2 (29) | 0 | 2 (50) | 0 | 5 (23) | 0 |
| Headache | 2 (18) | 0 | 1 (14) | 0 | 2 (50) | 0 | 5 (23) | 0 |
| Neutrophil count decreased | 2 (18) | 2 (18) | 2 (29) | 0 | 1 (25) | 0 | 5 (23) | 2 (9) |
| Edema peripheral | 2 (18) | 0 | 2 (29) | 0 | 1 (25) | 0 | 5 (23) | 0 |
| White blood cell count decreased | 2 (18) | 1 (9) | 2 (29) | 0 | 1 (25) | 0 | 5 (23) | 1 (5) |
| Upper respiratory tract infection | 3 (27) | 0 | 1 (14) | 0 | 1 (25) | 0 | 5 (23) | 0 |
| Pain in extremity | 2 (18) | 0 | 3 (43) | 0 | 0 | 0 | 5 (23) | 0 |

Promising efficacy was achieved with sonrotoclax + carfilzomib + dexamethasone across dose levels



- Median time to response: ~1 month; similar across doses
- Median time to VGPR: ~2 months; similar across doses
- Median DOR and PFS: NR
 - 12-month DOR rate: 80.4% (95% CI, 50.6%-93.2%)
 - 9-month PFS rate: 69.3% (95% CI, 43.7-85.0%)

| | | | | |
|----------------------------|-----------------|----------------|---------------|-----------------|
| Median study follow-up, mo | 16.4 (6.2-25.8) | 9.1 (3.4-10.4) | 5.4 (2.6-6.7) | 10.4 (2.6-25.8) |
|----------------------------|-----------------|----------------|---------------|-----------------|

CR, complete response; dex, dexamethasone; DOR, duration of response; K, carfilzomib; NR, not reached; ORR, overall response rate; PFS, progression-free survival; PR, partial response; sCR, stringent complete response; sonro, sonrotoclax; VGPR, very good partial response.

Conclusions

- Sonrotoclax + carfilzomib + dexamethasone combination therapy was well tolerated in heavily pretreated patients with t(11;14)-positive R/R MM
 - To date, the MTD has not been reached, and dose escalation is ongoing
 - No TEAEs led to death
 - Sonrotoclax dose reductions and discontinuations were rare (n=1 each)
- Promising antimyeloma activity was observed with an 86% ORR and 38% CR/sCR rate
 - At a median study follow-up of 10.4 months, median PFS and DOR have not been reached
- Enrollment in BGB-11417-105 is ongoing, with additional treatment combinations with sonrotoclax under evaluation in patients with t(11;14)-positive R/R MM

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