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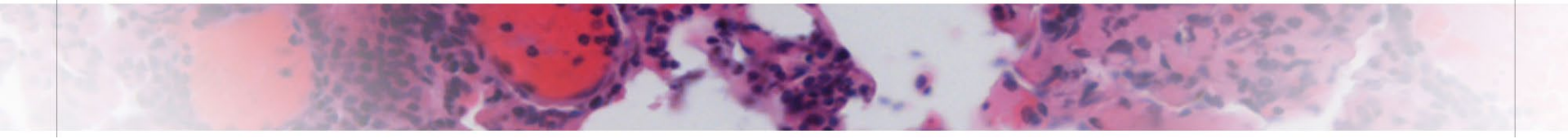

Initial Phase 1b/2 Study Results of Sonrotoclax (BGB-11417) in Combination With Carfilzomib and Dexamethasone in Patients With t(11;14)-Positive Relapsed/Refractory Multiple Myeloma

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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 features[1]
- Although BCL2 inhibitors have shown clinical activity in patients with MM harboring t(11;14), no BCL2-targeted treatments are currently approved for treating MM[2]
- Combining a BCL2 inhibitor with agents such as dexamethasone or carfilzomib that promote BCL2 dependency may further potentiate therapeutic efficacy in MM[3]
- Sonrotoclax (BGB-11417), a next-generation BCL2 inhibitor, is more selective and pharmacologically potent than venetoclax, with a shorter half-life and no drug accumulation[4]
- 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) MM[5]
- 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

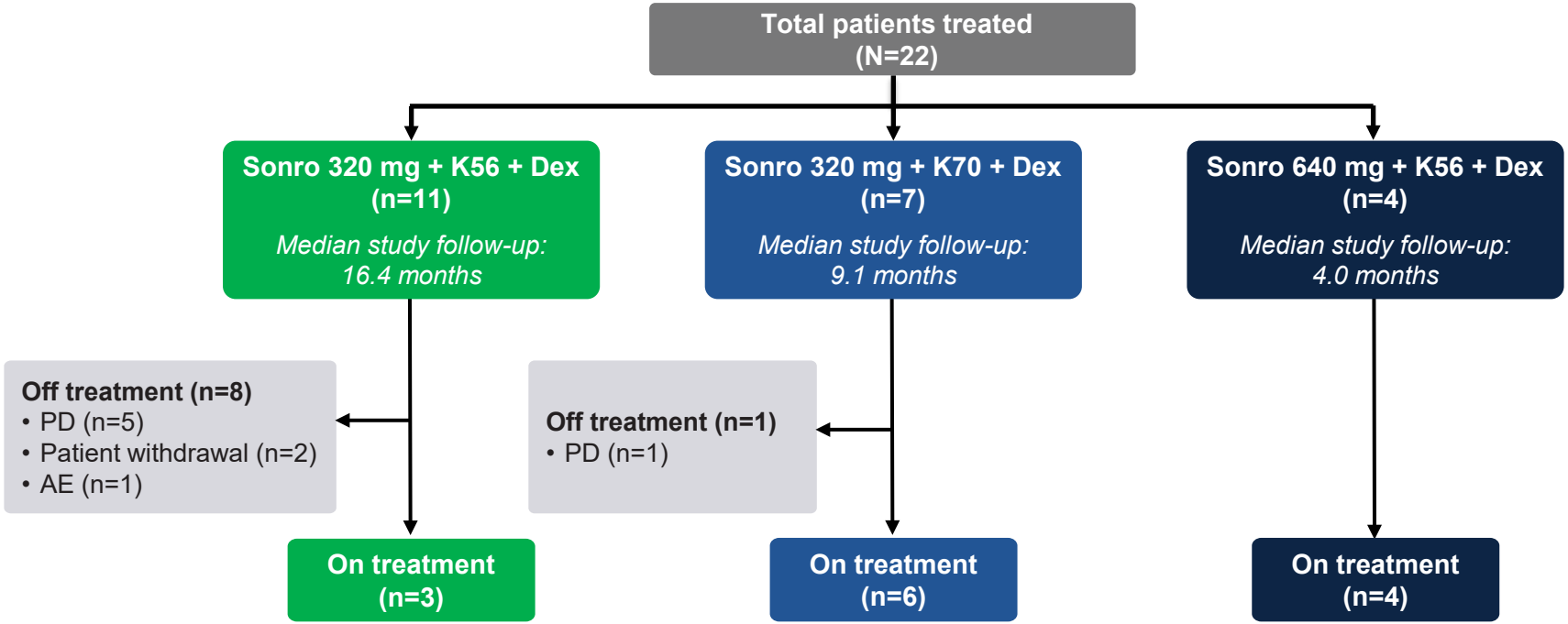
Triple drug combination dose levels

- **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]

[a]Prior anti-CD38 treatment is not required for patients in Australia, New Zealand, and Brazil. [b]Carfilzomib 56 mg/m^2 or 70 mg/m^2 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/m^2. [c]At 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



AE, adverse event; dex, dexamethasone; K, carfilzomib; PD, progressive disease; sonro, sonrotoclax.

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)

[a]High risk is defined as genetic subtypes t(4;14), t(14;16), and del(17p13). [b]Two patients with t(4;14) and 1 patient with del(17p13).[c]Defined 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.

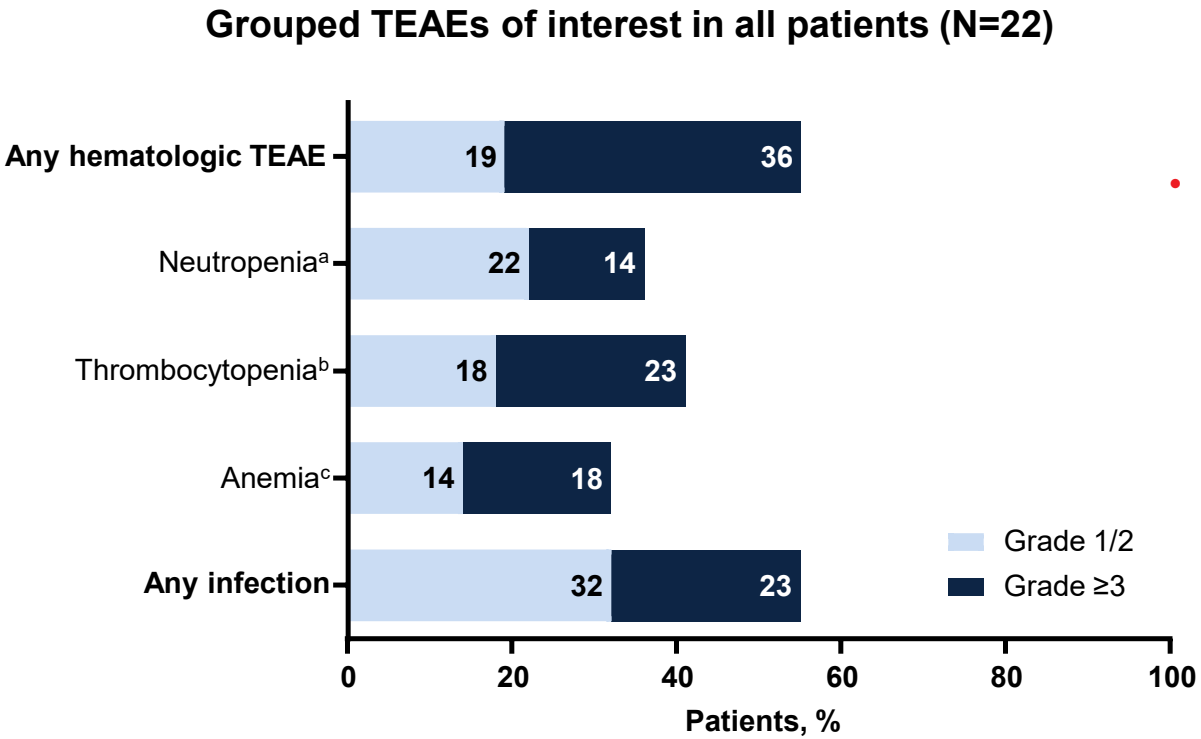
Sonrotoclax + carfilzomib + dexamethasone demonstrated a manageable safety profile

- 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)

[a]One patient had grade 3 coronary artery disease. [b]One patient had grade 2 fatigue that led to sonro dose reduction. [c]One patient had a grade 2 hepatitis B virus infection that led to sonro discontinuation. [d]DLTs 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



- Infections observed in at least 2 patients were upper respiratory tract infections, pneumonia, COVID-19, respiratory tract infections, urinary tract infections, and appendicitis

[a]Includes the PTs *agranulocytosis, febrile neutropenia, neutropenia, neutropenic infection, neutropenic sepsis, and neutrophil count decreased*. [b]Includes the PTs *platelet count decreased* and *thrombocytopenia*. [c]Includes the PTs *anemia* and *hemoglobin decreased*.
PT, preferred term; TEAE, treatment-emergent adverse event.

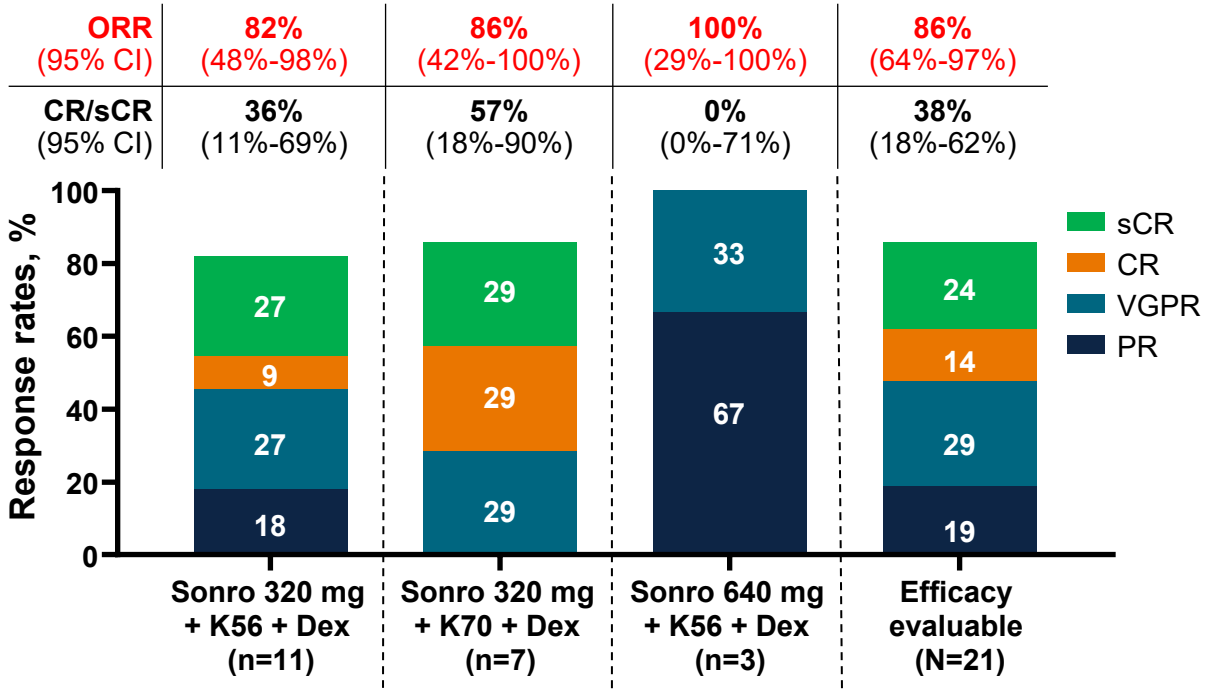
The safety profile of combination therapy has been consistent with the known safety profile of each individual study drug

- 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

	Sonro 320 mg + K56 + Dex (n=11)		Sonro 320 mg + K70 + Dex (n=7)		Sonro 640 mg + K56 + Dex (n=4)		Total (N=22)	
Patients, n (%)	**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

dex, dexamethasone; K, carfilzomib; sonro, sonrotoclax; MM, multiple myeloma; TEAE, treatment-emergent adverse event.

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



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)

- 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%)

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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