BGB-11417-105

Sonrotoclax in Patients With R/R Multiple Myeloma Harboring t(11,14)

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Phase 1

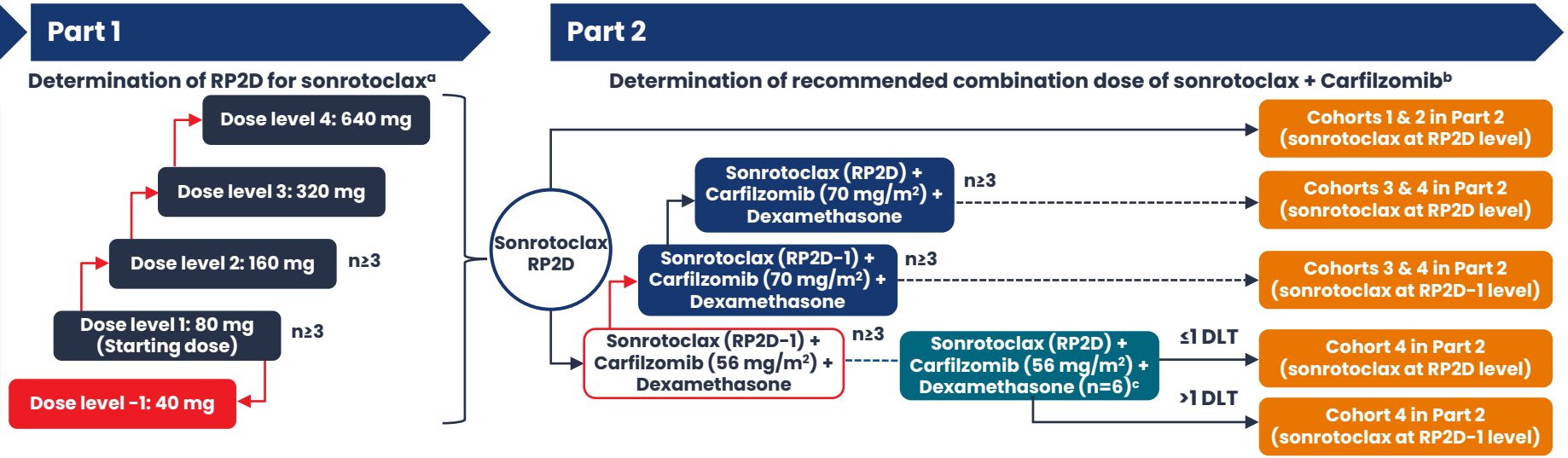
Study Identifier:
BGB-11417-105, NCT04973605

Primary Endpoint: Safety, tolerability, and RP2D of sonrotoclax in combination with dexamethasone with or without carfilzomib; MTD for sonrotoclax in combination with dexamethasone

Key Secondary Endpoints: PK of sonrotoclax in combination with dexamethasone with or without carfilzomib, ORR of sonrotoclax in combination with dexamethasone with or without carfilzomib; PK of dexamethasone in combination with sonrotoclax

Key eligibility criteria

- Confirmed diagnosis of MM (must have an M-component in serum and/or urine)
- ECOG PS 0-2
- Measurable disease[c]
- Documented relapsed or progressive MM on or after any regimen or who are refractory to the most recent line of therapy
- Positivity for t(11;14) by FISH



Dashed arrow indicates the dose combination of sonrotoclax + carfilzomib is selected as the combination MTD or MAD.
[a]Sonrotoclax + dexamethasone (40 mg weekly); dose escalation guided by mTPI-2: target toxicity probability = 0.2, EI = (0.15, 0.25); maximum dose sample size = 18; [b]Sonrotoclax + carfilzomib (56 mg/m² or 70 mg/m² weekly + dexamethasone (40 mg weekly); dose escalation guided by mTPI-2: target toxicity probability = 0.25, EI = (0.2, 0.3); maximum dose sample size = 18 + 6 for sonrotoclax RP2D + carfilzomib 56 mg/m² + dexamethasone; [c]Can open as soon as the dose combination of sonrotoclax (R2PD-1) + carfilzomib (70 mg/m²) + dexamethasone is suggested to be eliminated and data of sonrotoclax (R2PD-1) + carfilzomib (56 mg/m²) + dexamethasone allow for further dose escalation per mTPI-2 decision table. c M-spike ≥ 500mg/dL, or ii. Urine protein M-spike of ≥ 200 mg/day, or iii. Serum free light chains ≥ 10 mg/dL, and an abnormal κ:λ ratio.
DLT=dose-limiting toxicity, ECOG PS=Eastern Cooperative Oncology Group performance status, FISH=fluorescence in situ hybridization, MAD=maximum administered dose, MM=multiple myeloma, MTD=maximum tolerated dose, ORR=overall response rate, PK=pharmacokinetics, PS=performance status, PK=pharmacokinetics, RP2D=recommended phase 2 dose.
Quach H et al. Poster presented at ASH 2022 Abstract 3235; Dhakal B, et al. Poster presentation at EHA 2024;P898.

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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)

Data cut-off: September 3, 2025.
[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, ECOG PS=Eastern Cooperative Oncology Group performance status, IMiD=immunomodulatory drug, K=carfilzomib, PI=proteasome inhibitor, R-ISS=Revised International Staging System; sonro=sonrotoclax.
Quach H, et al. Oral Presentation at ASH 2025;7278.

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Overall Safety Summary

- Sonrotoclax + carfilzomib + dexamethasone demonstrates a manageable safety profile
- No TEAEs led to death
- Sonrotoclax dose reductions and discontinuations were rare – only 1 of each occurred
- To date, MTD has not been reached
- No events of cardiac failure, myocardial infection, 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)

Data cut-off: September 3, 2025.
[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.
Quach H, et al. Oral Presentation at ASH 2025;7278.

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TEAEs in >10% of All Patients

- 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

Data cut-off: September 3, 2025.
Dex=dexamethasone, K=carfilzomib, sonro=sonrotoclax, MM=multiple myeloma, TEAE=treatment-emergent adverse event.
Quach H, et al. Oral Presentation at ASH 2025;7278.

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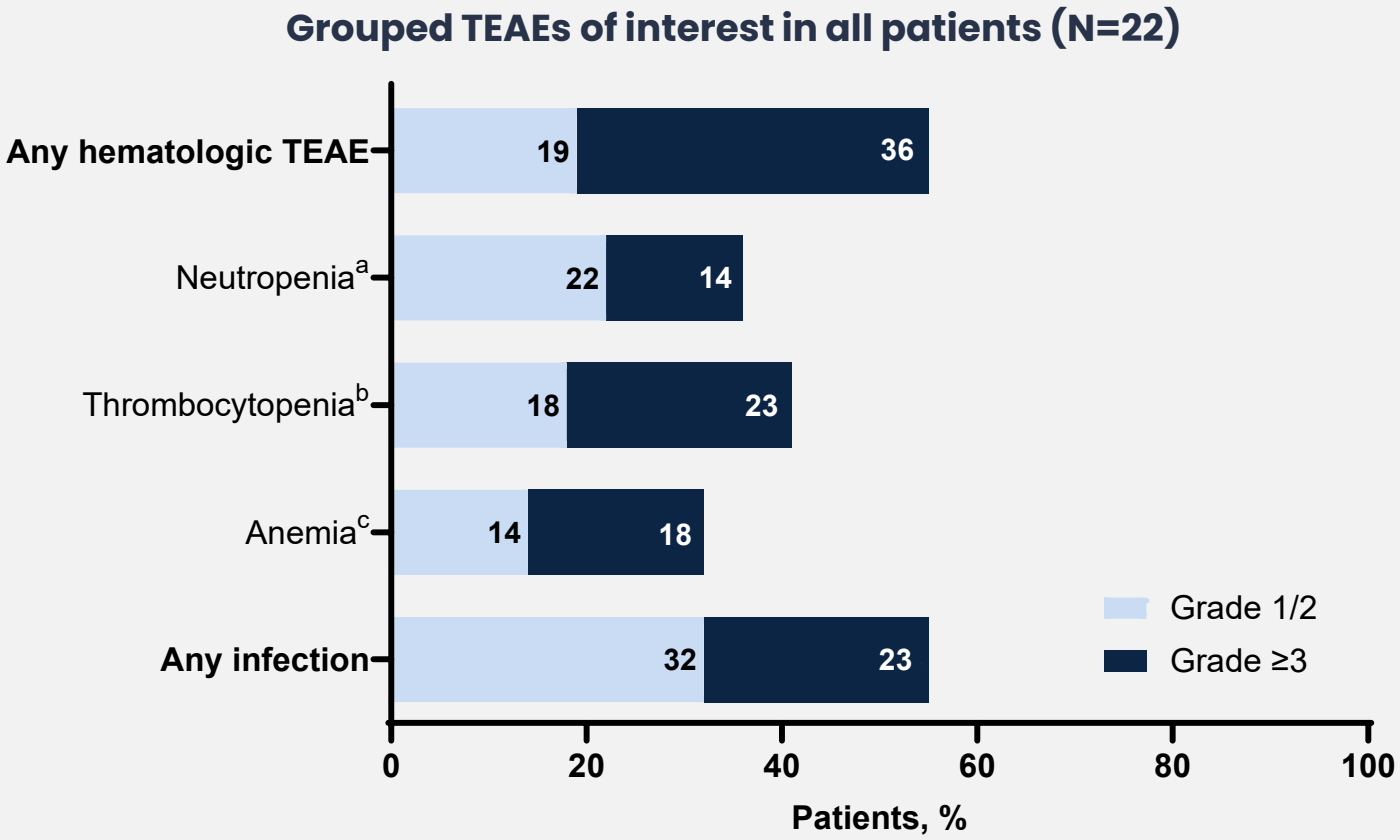
TEAEs of Interest

- The safety profile of combination therapy has been consistent with the known safety profile of each individual study drug
- Infections observed in at least 2 patients were upper respiratory tract infections, pneumonia, COVID-19, respiratory tract infections, urinary tract infections, and appendicitis



Data cut-off: September 3, 2025.
[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.
Quach H, et al. Oral Presentation at ASH 2025;7278.

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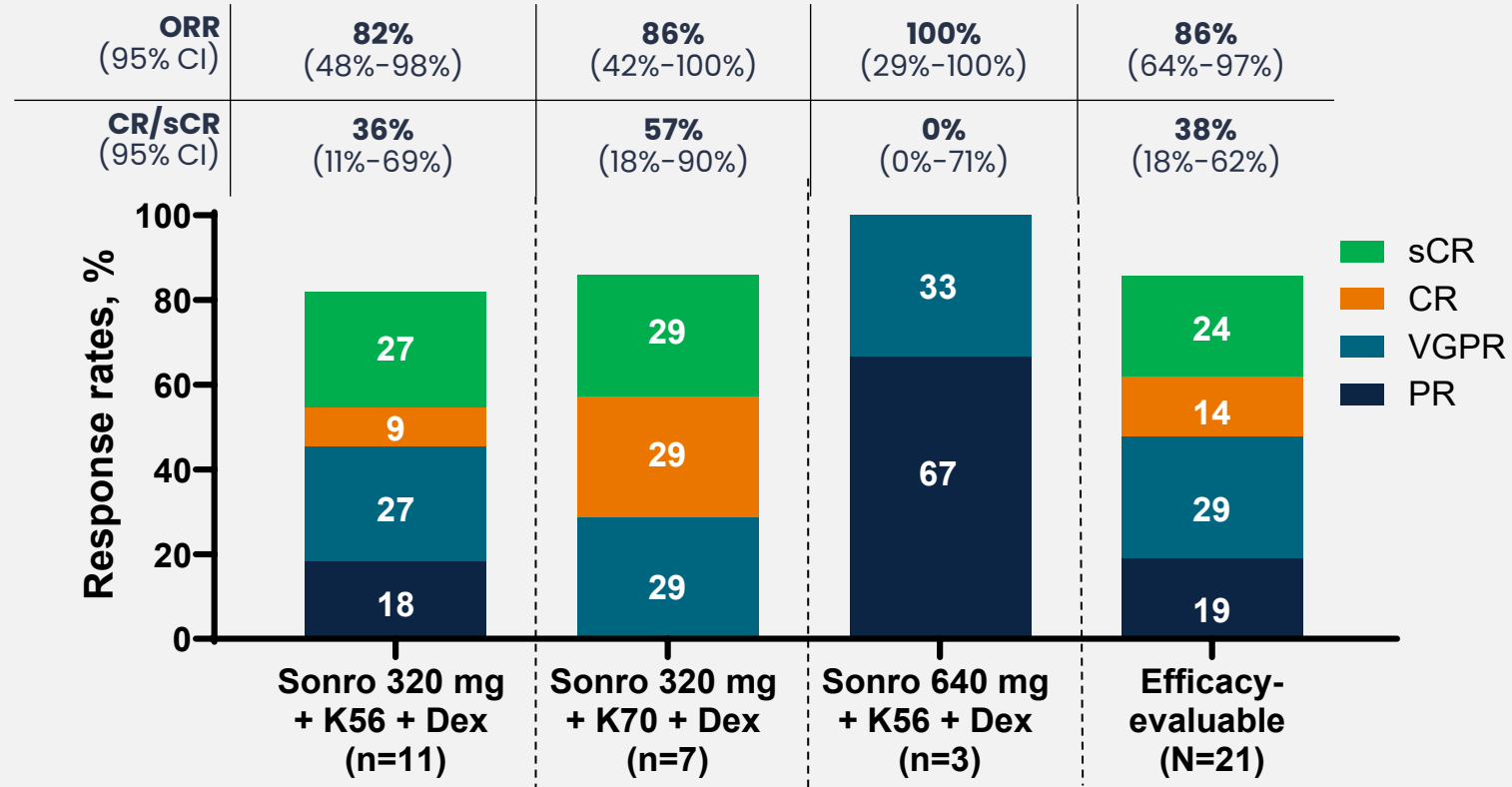
Best Overall Response



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)

- 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%)

Data cut-off: September 3, 2025.
CI=confidence interval, 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.
Quach H, et al. Oral Presentation at ASH 2025;7278.