Updated Interim Results of Sonrotoclax + Dexamethasone in Patients With t(11;14)-Positive Relapsed/Refractory Multiple Myeloma: An All-Oral Treatment

PF721

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CONCLUSIONS

- The all-oral combination of sonrotoclax + dexamethasone continued to show a tolerable safety profile, with low rates of grade ≥3 infection and hematologic toxicity
- Efficacy was promising, with an overall response rate of 80.6% and very good partial response or better rate of 55.6% in the 640-mg cohort, in patients with t(11;14)-positive relapsed/refractory MM
- With a median study follow-up of 12 months, the median PFS was 12.9 months (95% CI, 9.0-19.6 months) for the sonrotoclax 640-cohort, in which most patients had triple class exposed/refractory disease
- Enrollment in BGB-11417-105 is ongoing; additional treatment combinations with sonrotoclax are being investigated

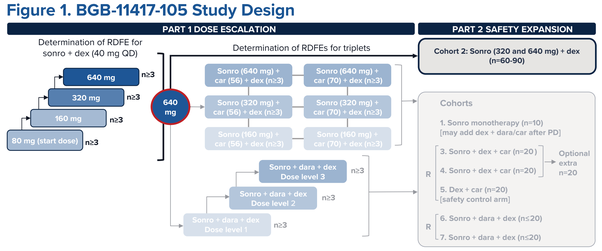
INTRODUCTION

- Multiple myeloma (MM) with t(11;14), found in approximately 15% to 20% of patients at first diagnosis, represents a unique disease subset with distinct features[1]
- Although B-cell lymphoma 2 (BCL2) inhibitors in monotherapy or combination regimens have shown clinical activity in patients with MM, no BCL2-targeted treatments are currently approved for treating MM[2]
- 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[3]
- Initial data from the BGB-11417-105 study indicated that sonrotoclax + dexamethasone is well tolerated and can induce deep and durable responses in heavily pretreated patients with t(11;14) MM[4]
- Presented here are updated safety and efficacy data for sonrotoclax + dexamethasone combination therapy from BGB-11417-105

METHODS

- BGB-11417-105 (NCT04973605) is an ongoing, open-label, phase 1b/2, dose-escalation and dose-expansion study evaluating sonrotoclax as mono- or combination therapy in patients with t(11;14)-positive relapsed/refractory MM (**Figure 1**)
- Key eligibility criteria included
  - Centrally-confirmed t(11;14)
  - At least 3 prior lines of therapy for all dose-escalation cohorts + safety expansion cohorts per protocol amendment 5.0 or later (for safety expansion cohorts per protocol amendment 4.1 or earlier, only 1 prior line of therapy was required)
  - Exposure to a proteasome inhibitor (PI), an immunomodulatory drug (IMiD), and an anti-CD38 antibody
- Sonrotoclax is administered orally once daily; dexamethasone 40 mg is administered orally or intravenously once weekly
- Study endpoints include safety/tolerability, recommended dose for expansion (RDFE; part 1), and antimyeloma activity of sonrotoclax + dexamethasone combination therapy

Figure 1. BGB-11417-105 Study Design

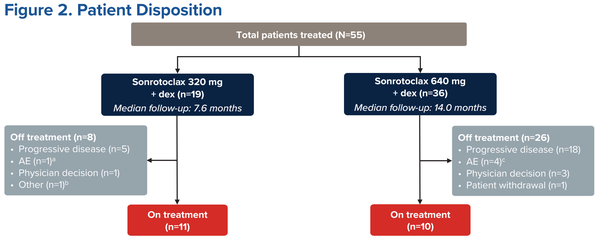


Abbreviations: car, carfilzomib; dara, daratumumab; dex, dexamethasone; R, randomized; RDFE, recommended dose for expansion; sonro, sonrotoclax.

RESULTS

- As of March 20, 2025, 55 patients have received sonrotoclax 320 mg or 640 mg once daily + dexamethasone in part 1 or part 2 and were evaluable; median follow-up time was 12.0 months (range, 0.1-36.4 months; **Figure 2**)
  - 21 patients remain on treatment
- Patients had a median of 3 prior therapy lines (range, 1-12), and 65.5% had ≥3 prior lines (**Table 1**)
  - All patients had prior PI and IMiD exposure, and 72.7% had prior anti-CD38 therapy
  - Many patients were refractory to PI (54.5%), IMiD (65.5%), or anti-CD38 (54.5%), and 40.0% were refractory to all 3 drug classes

Figure 2. Patient Disposition



[a]COVID-19. [b]Death due to pneumonia respiratory syncytial virus. [c]Hematuria, lung carcinoma, diarrhea, metastatic pancreatic cancer.
Abbreviations: AE, adverse event; dex, dexamethasone.

Table 1. Baseline Demographics and Clinical Characteristics

Characteristic	Sonro 320 mg + dex (n=19)	Sonro 640 mg + dex (n=36)	Total (N=55)
Age, median (range), years	70 (44-86)	69 (48-80)	70 (44-86)
Male sex, n (%)	8 (42.1)	19 (52.8)	27 (49.1)
ECOG PS, n (%)			
0	11 (57.9)	17 (47.2)	28 (50.9)
1	6 (31.6)	17 (47.2)	23 (41.8)
2	2 (10.5)	2 (5.6)	4 (7.3)
R-ISS stage at initial diagnosis, n (%)			
I	3 (15.8)	7 (19.4)	10 (18.2)
II	8 (42.1)	17 (47.2)	25 (45.5)
III	2 (10.5)	6 (16.7)	8 (14.5)
Unknown	6 (31.6)	6 (16.7)	12 (21.8)
Time from most recent R/R episode to first dose, median (range), months	1.8 (0.5-23.7)	1.9 (0.4-93.8)[a]	1.9 (0.4-93.8)
Cytogenic risk, n (%)			
High[b]	6 (31.6)	5 (13.9)	11 (20.0)
Not High	12 (63.2)	31 (86.1)	43 (78.2)
Unknown	1 (5.3)	0	1 (1.8)
Prior lines of systemic therapy, median (range)	3 (1-7)	3 (1-12)	3 (1-12)
Prior lines of systemic therapy, n (%)			
1	1 (5.3)	8 (22.2)	9 (16.4)
2	2 (10.5)	8 (22.2)	10 (18.2)
≥3	16 (84.2)	20 (55.6)	36 (65.5)
Prior exposure, n (%)			
PI	19 (100)	36 (100)	55 (100)
IMiD	19 (100)	36 (100)	55 (100)
Anti-CD38 antibody[c]	16 (84.2)	24 (66.7)	40 (72.7)
≥1 PI + ≥1 IMiD + ≥1 anti-CD38 antibody[c]	16 (84.2)	24 (66.7)	40 (72.7)
Refractory status, n (%)			
PI	10 (52.6)	20 (55.6)	30 (54.5)
IMiD	12 (63.2)	24 (66.7)	36 (65.5)
Anti-CD38 antibody[c]	12 (63.2)	18 (50.0)	30 (54.5)
≥1 PI + ≥1 IMiD + ≥1 anti-CD38 antibody[c]	7 (36.8)	15 (41.7)	22 (40.0)
Prior autologous transplant, n (%)	10 (52.6)	23 (63.9)	33 (60.0)

[a]Data for 1 patient are missing. [b]High-risk disease was defined as genetic subtype t(4;14), t(14;16), and del(17p13). [c]Anti-CD38 treatment was not required for study patients in Australia, New Zealand, or Brazil in cohort 2 of part 2.
Abbreviations: dex, dexamethasone; ECOG PS, Eastern Cooperative Oncology Group performance status; IMiD, immunomodulatory drug; PI, proteasome inhibitor; R-ISS, Revised International Staging System; R/R, relapsed/refractory; sonro, sonrotoclax.

- The safety profile was tolerable and manageable for both dose cohorts (**Table 2**)
- Two patients in each cohort died due to treatment-emergent adverse events (TEAEs; 320 mg: pneumonia respiratory syncytial virus and COVID-19; 640 mg: hypoventilation related to lung-involved progressive disease and metastatic pancreatic cancer); none of these TEAEs was considered related to study treatment
  - In the 640-mg cohort, 4 additional deaths occurred >30 days after the last dose; 2 deaths were attributed to the disease under study, and 2 were attributed to other reasons that were unrelated to TEAEs

Table 2. Overall Safety Summary

Patients, n (%)	Sonro 320 mg + dex (n=19)	Sonro 640 mg + dex (n=36)	Total (N=55)
Any TEAE	18 (94.7)	36 (100)	54 (98.2)
Grade ≥3	8 (42.1)	17 (47.2)	25 (45.5)
Serious	4 (21.1)	10 (27.8)	14 (25.5)
Leading to death	2 (10.5)	2 (5.6)	4 (7.3)
TEAE leading to dose interruption	5 (26.3)	17 (47.2)	22 (40.0)
Sonro	5 (26.3)	16 (44.4)	21 (38.2)
Dex	4 (21.1)	11 (30.6)	15 (27.3)
TEAE leading to dose reduction	6 (31.6)	15 (41.7)	21 (38.2)
Sonro	0	3 (8.3)	3 (5.5)
Dex	6 (31.6)	15 (41.7)	21 (38.2)
TEAE leading to treatment discontinuation	3 (15.8)	8 (22.2)	11 (20.0)
Sonro	1 (5.3)	4 (11.1)	5 (9.1)[a]
Dex	3 (15.8)	8 (22.2)	11 (20.0)[b]

[a]n=1 each: COVID-19, hematuria, lung adenocarcinoma, metastatic pancreatic cancer, and diarrhea. [b]n=2 each: mental agitation and insomnia; n=1 each: worsening insomnia, COVID-19, hematuria, lung adenocarcinoma, metastatic pancreatic cancer, diarrhea, and proximal myopathy.
Abbreviations: dex, dexamethasone; sonro, sonrotoclax; TEAE, treatment-emergent adverse event.

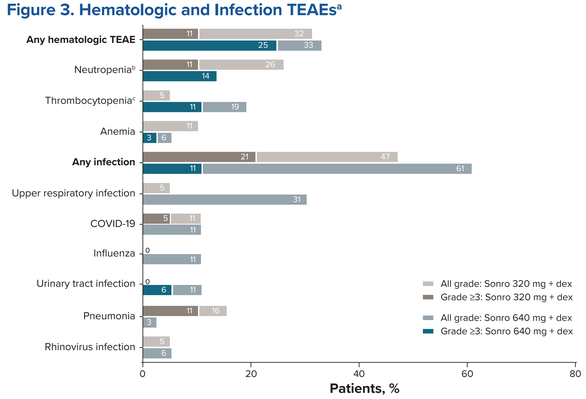
- The most common all-grade TEAEs were insomnia (36.8%) and fatigue (31.6%) for the 320-mg cohort and insomnia (38.9%) and diarrhea (38.9%, all grade 1 or 2) for the 640-mg cohort; across both cohorts, the most common grade ≥3 TEAE was neutrophil count decreased (**Table 3**)
- Hematologic and infection TEAEs of any grade were seen in 32.7% and 56.4% of all patients, respectively (**Figure 3**)
- Grade 3 or higher hematologic and infection TEAEs were seen in 20.0% and 14.5% of all patients, respectively

Table 3. TEAEs in >10% of All Patients

	Sonro 320 mg + dex (n=19)		Sonro 640 mg + dex (n=36)		Total (N=55)	
Patients, n (%)	All grade	Grade ≥3	All grade	Grade ≥3	All grade	Grade ≥3
Insomnia	7 (36.8)	1 (5.3)	14 (38.9)	1 (2.8)	21 (38.2)	2 (3.6)
Fatigue	6 (31.6)	0	11 (30.6)	2 (5.6)	17 (30.9)	2 (3.6)
Diarrhea	0	0	14 (38.9)	0	14 (25.5)	0
Upper respiratory tract infection	1 (5.3)	0	11 (30.6)	0	12 (21.8)	0
Nausea	3 (15.8)	0	7 (19.4)	0	10 (18.2)	0
Contusion	1 (5.3)	0	7 (19.4)	1 (2.8)	8 (14.5)	1 (1.8)
Dyspnea	3 (15.8)	0	5 (13.9)	0	8 (14.5)	0
Arthralgia	2 (10.5)	0	5 (13.9)	0	7 (12.7)	0
Dizziness	2 (10.5)	0	5 (13.9)	0	7 (12.7)	0
Neutrophil count decreased	4 (21.1)	2 (10.5)	3 (8.3)	3 (8.3)	7 (12.7)	5 (9.1)
Constipation	0	0	6 (16.7)	0	6 (10.9)	0
Fall	1 (5.3)	0	5 (13.9)	1 (2.8)	6 (10.9)	1 (1.8)
COVID-19	2 (10.5)	1 (5.3)	4 (11.1)	0	6 (10.9)	1 (1.8)

Abbreviations: dex, dexamethasone; sonro, sonrotoclax; TEAE, treatment-emergent adverse event.

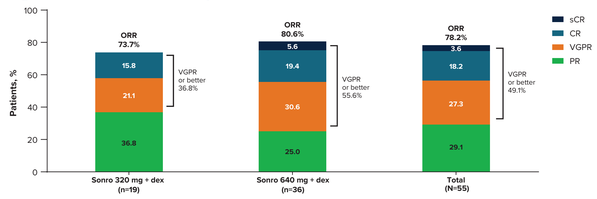
Figure 3. Hematologic and Infection TEAEs[a]



[a]Infections listed in the figure are those that occurred in ≥5% of all patients. [b]Includes the preferred terms *agranulocytosis, febrile neutropenia, neutropenia, neutropenic infection, neutropenic sepsis,* and *neutrophil count decreased.* [c]Includes the preferred terms *platelet count decreased* and *thrombocytopenia.*
Abbreviations: dex, dexamethasone; sonro, sonrotoclax; TEAE, treatment-emergent adverse event.

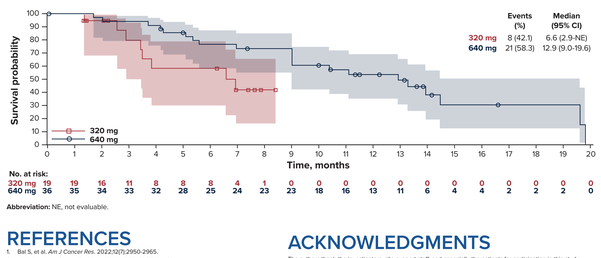
- Among all patients in the 320-mg and 640-mg cohorts, overall response rates were 73.7% and 80.6%; very good partial response or better rates were 36.8% and 55.6%, and complete response or better rates were 15.8% and 25.0%, respectively (**Figure 4**)
- The median time to response was 0.7 months for each cohort; the median duration of response was not reached (range, 1.8 months to not evaluable) for the 320-mg cohort and 12.2 months (range, 8.3-18.9 months) for the 640-mg cohort
- Median progression-free survival was 6.6 months (95% CI, 2.9 months to not evaluable) for the 320-mg cohort and 12.9 months (95% CI, 9.0-19.6 months) for the 640-mg cohort (**Figure 5**)

Figure 4. Best Overall Response



Abbreviations: CR, complete response; dex, dexamethasone; ORR, overall response rate; PR, partial response; sCR, stringent complete response; sonro, sonrotoclax; VGPR, very good partial response.

Figure 5. Progression-Free Survival



Abbreviation: NE, not evaluable.

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DISCLOSURES

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