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

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Disclosures for Binod Dhakal

- **Honoraria**: BMS, Karyopharm
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Introduction

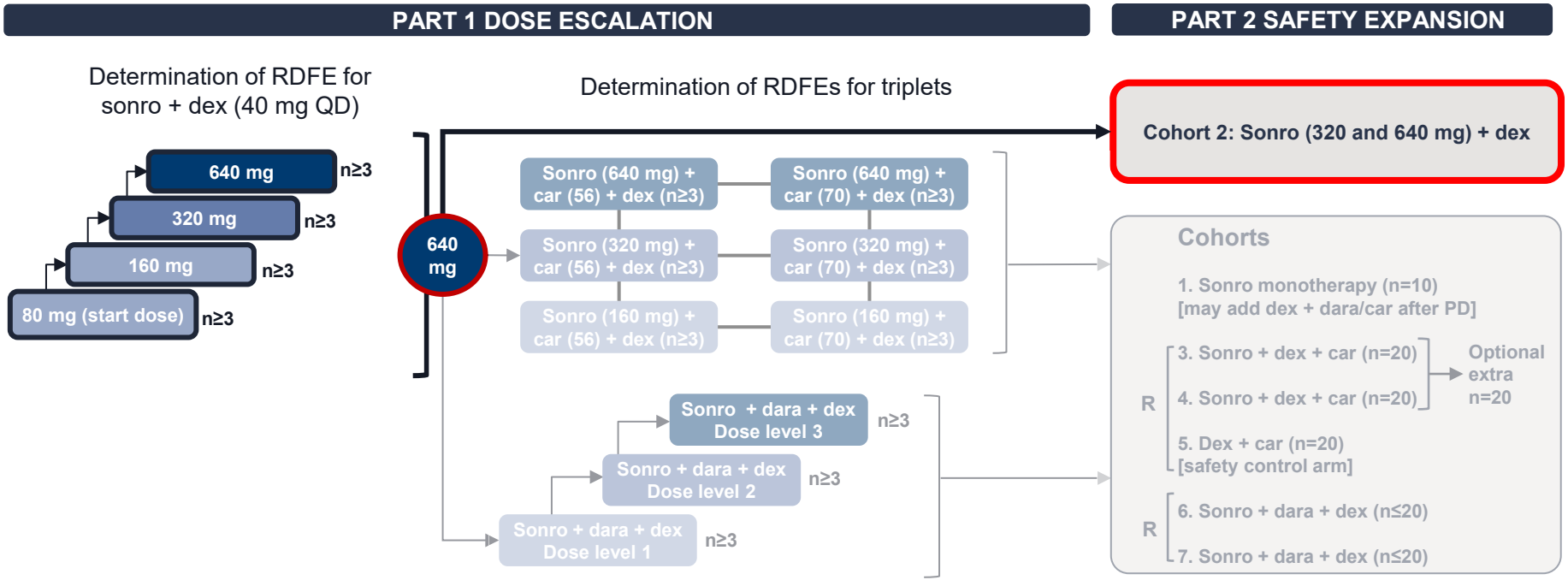
- MM with t(11;14), found in approximately 15% to 20% of patients at first diagnosis, represents a unique disease subset with distinct features[1]
- Although BCL2 inhibitors in monotherapy or combination regimens have shown clinical activity in patients with MM, no BCL2-targeted treatments are currently 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]
- Updated safety and efficacy data are presented for patients treated with sonrotoclax + dexamethasone combination therapy from BGB-11417-105 study

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. Guo Y, et al. *J Med Chem*. 2024;67(10):7836-7858; 4. Dhakal B, et al. ASH 2024. Abstract P898.

BGB-11417-105 (NCT04973605) study design

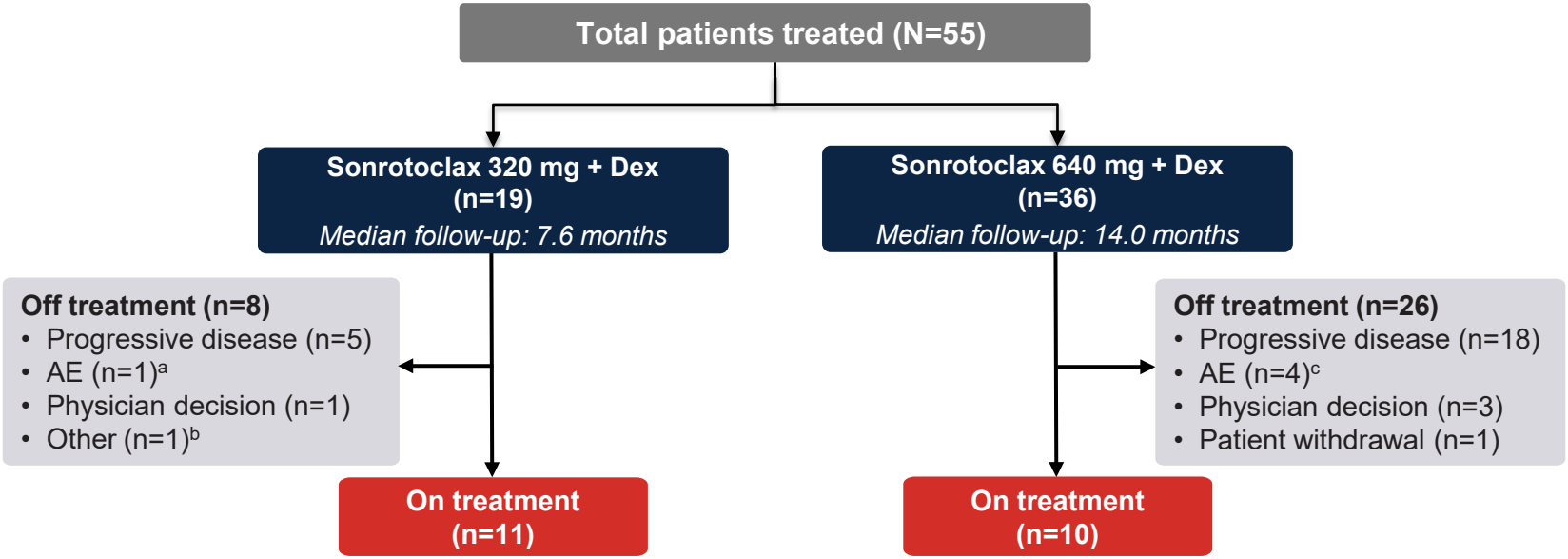
- This is an ongoing, open-label, phase 1b/2, dose-escalation and dose-expansion study evaluating sonrotoclax as a mono- or combination therapy in patients with R/R MM harboring t(11;14)



car, carfilzomib; dara, daratumumab; dex, dexamethasone; MM, multiple myeloma R, randomized; RDFE, recommended dose for expansion; R/R, relapsed/refractory; sonro, sonrotoclax.

Patient disposition

- As of March 20, 2025, a total of 55 patients had received sonrotoclax 320 mg or 640 mg once daily + dexamethasone in part 1 or 2 and were evaluable; median follow-up was 12.0 months (range, 0.1-36.4 months)



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

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			
0 to 1	17 (89.5)	34 (94.4)	51 (92.7)
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)
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)

Characteristic	Sonro 320 mg + dex (n=19)	Sonro 640 mg + dex (n=36)	Total (N=55)
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 to ≥1 PI + ≥1 IMiD + ≥1 anti-CD38 antibody[c], n (%)	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.
dex, dexamethasone; ECOG PS, Eastern Cooperative Oncology Group performance status; IMiD, immunomodulatory drug; PI, proteasome inhibitor; R/R, relapsed/refractory; sonro, sonrotoclax.

Sonrotoclax + dexamethasone demonstrated a tolerable safety profile in patients with t(11;14)-positive MM

- Sonrotoclax + dexamethasone was tolerable and manageable for both dose cohorts
- No patients experienced a DLT (assessed during the first 21 days of part 1)
- Dose reduction or discontinuation of sonrotoclax was rare
- Four patients died due to TEAEs[a], none of which were considered related to study treatment

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)[a,b]
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)
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)
Leading to treatment discontinuation	3 (15.8)	8 (22.2)	11 (20.0)
Sonro	1 (5.3)	4 (11.1)	5 (9.1)[c]
Dex	3 (15.8)	8 (22.2)	11 (20.0)[d]

[a]n=1 each: pneumonia RSV, COVID-19, hypoventilation related to lung-involved PD, metastatic pancreatic cancer. [b]In the 640-mg cohort 4 additional deaths occurred >30 days after the last dose due to disease under study (n=2) and reasons unrelated to TEAEs (n=2). [c]n=1 each: COVID-19, hematuria, lung adenocarcinoma, metastatic pancreatic cancer, and diarrhea. [d]n=2 each: mental agitation and insomnia; n=1 each: worsening insomnia, COVID-19, hematuria, lung adenocarcinoma, metastatic pancreatic cancer, diarrhea, and proximal myopathy.
dex, dexamethasone; sonro, sonrotoclax; PD, progressive disease; RSV, respiratory syncytial virus; TEAE, treatment-emergent adverse event.

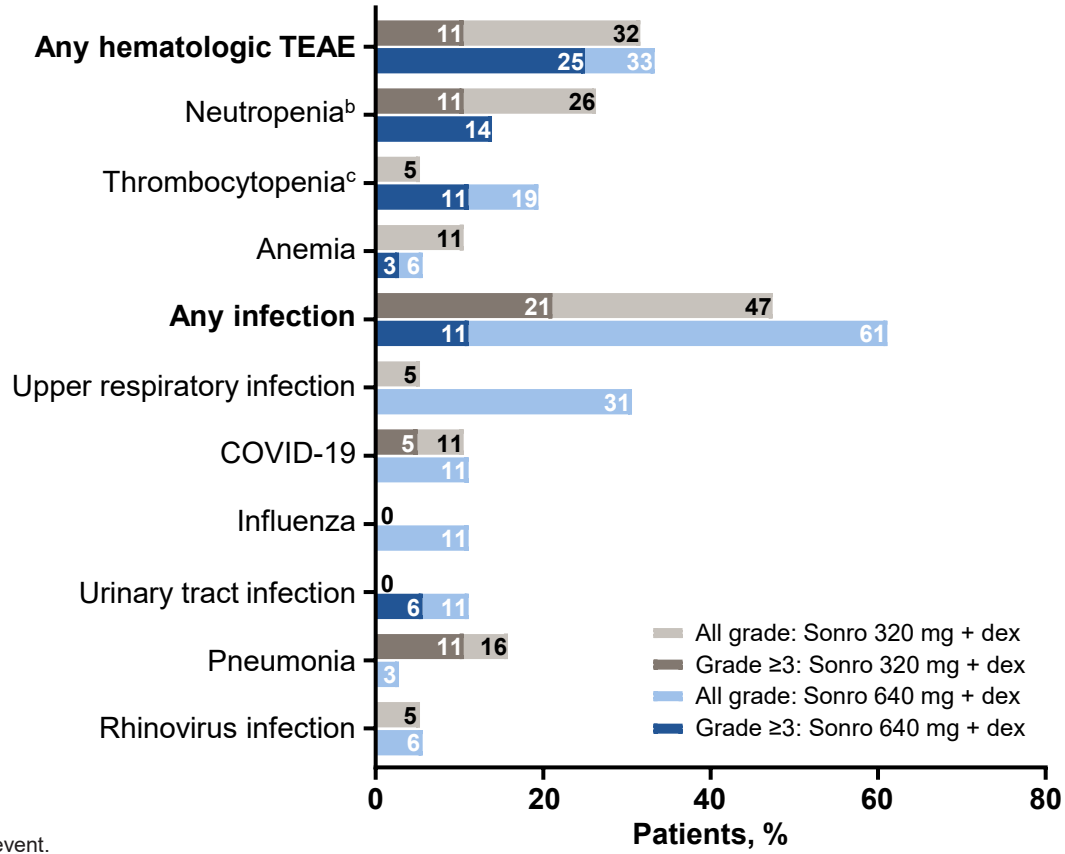
Most common TEAEs (>10% of all patients)

Patients, n (%)	Sonro 320 mg + dex (n=19)		Sonro 640 mg + dex (n=36)		Total (N=55)	
	Any grade	Grade ≥3	Any grade	Grade ≥3	Any 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
URTI	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)

dex, dexamethasone; sonro, sonrotoclax; TEAE, treatment-emergent adverse event; URTI, upper respiratory tract infection.

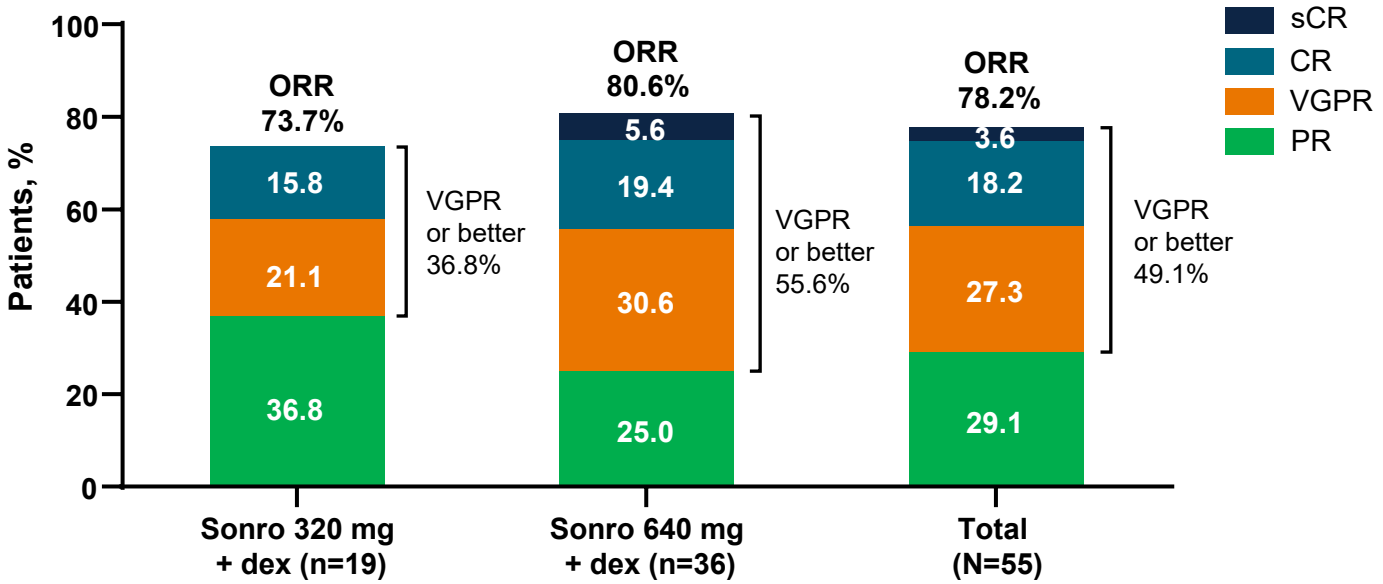
Sonrotoclax + dexamethasone had low rates of grade ≥3 infections[a] and hematologic toxicities in patients with t(11;14)-positive MM

- **Hematologic TEAEs:**
  33% (any-grade) and 20% (grade ≥3)
- **Infection TEAEs:**
  56% (any-grade) and 14.5% (grade ≥3)



[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*.
dex, dexamethasone; sonro, sonrotoclax; TEAE, treatment-emergent adverse event.

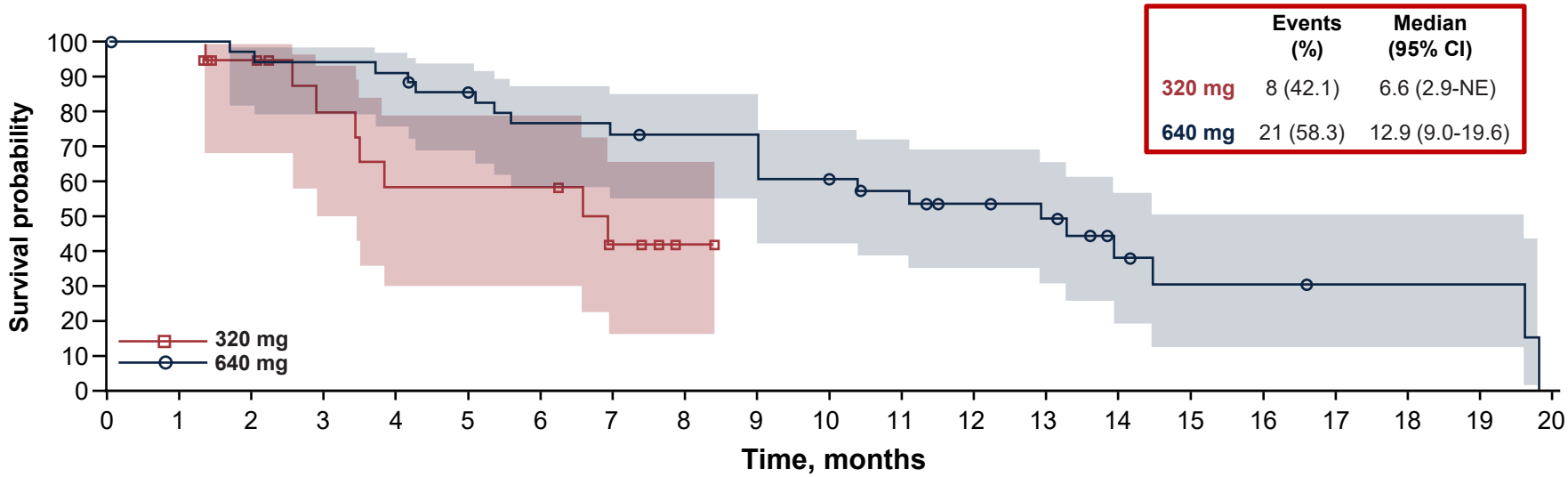
Sonrotoclax + dexamethasone showed a high ORR and VGPR rate in patients with t(11;14)-positive MM



- Median time to response for each cohort was 0.7 months
- Median DOR was not reached (range, 1.8 months-NE) for the 320-mg cohort and was 12.2 months (range, 8.3-18.9 months) for the 640-mg cohort

CR, complete response; dex, dexamethasone; DOR, duration of response; NE, not estimable; ORR, overall response rate; PR, partial response; sCR, stringent complete response; sonro, sonrotoclax; VGPR, very good partial response.

Progression-free survival



No. at risk:

320 mg	19	19	16	11	8	8	8	4	1	0	0	0	0	0	0	0	0	0	0	0
640 mg	36	35	34	33	32	28	25	24	23	23	18	16	13	11	6	4	4	2	2	2	0

- With a median study follow-up of 12 months, the median PFS was 12.9 months for the sonrotoclax 640-cohort, in which patients had heavily pretreated disease

NE, not estimable.

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 ORR of 81% and VGPR or better rate of 56% in the 640-mg cohort, in patients with heavily pretreated, t(11;14)-positive relapsed/refractory MM
- With a median study follow-up of 12 months, the median PFS was 13 months (95% CI, 9-20 months) for the sonrotoclax 640-mg 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

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