

Safety and Efficacy Results of a Phase 1 Study of the Novel BCL2 Inhibitor Sonrotoclax (BGB-11417) for Relapsed/Refractory Waldenström Macroglobulinemia

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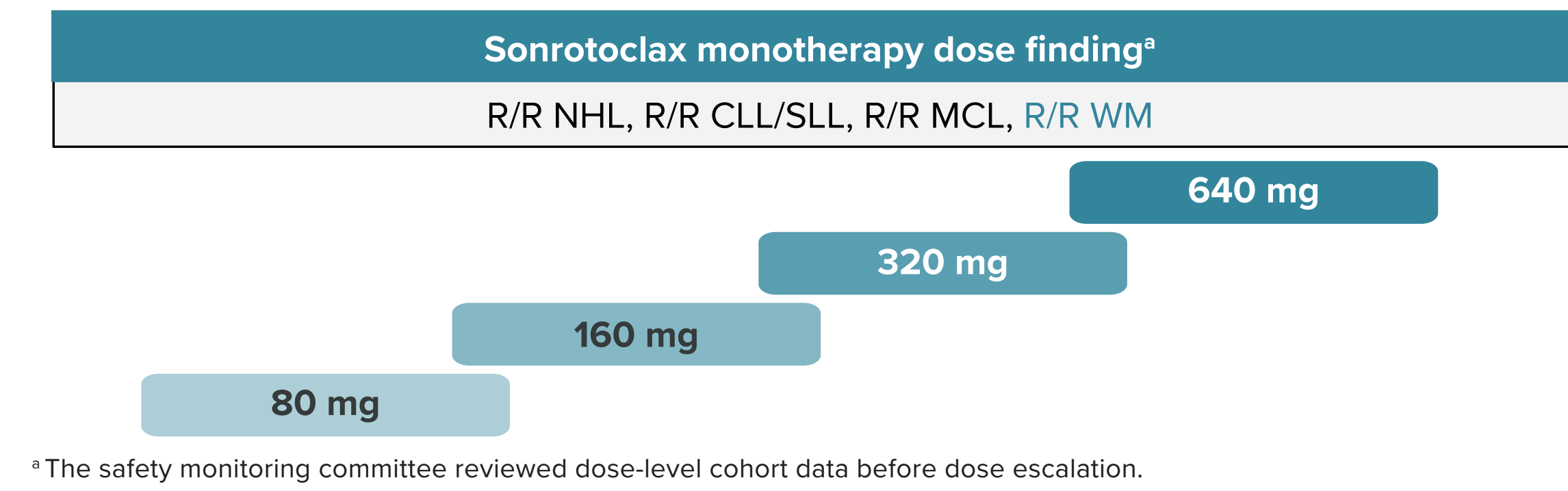
INTRODUCTION

- Waldenström macroglobulinemia (WM) is a rare, incurable, B-cell lymphoma, and more tolerable and effective treatments are needed for patients who experience progression on standard treatments¹
- Inhibition of BCL2 has demonstrated antitumor activity in patients with WM; however, no BCL2 inhibitors are currently approved²
- Sonrotoclax (BGB-11417), a next-generation BCL2 inhibitor, is a more selective and pharmacologically potent inhibitor of BCL2 than venetoclax with a shorter half-life and no accumulation³
- Here, updated safety and efficacy data are presented for patients with relapsed/refractory (R/R) WM treated with sonrotoclax monotherapy in the ongoing BGB-11417-101 study

METHODS

- BGB-11417-101 (NCT04277637) is a first-in-human, phase 1, open-label, multicenter, dose-escalation and -expansion study in patients with B-cell malignancies (Figure 1)
- Eligible patients had R/R WM (disease that relapsed after or was refractory to ≥1 prior systemic therapy) and required treatment per IWWM-7 criteria
- The primary objectives of the study were to assess safety/tolerability, evaluate the ramp-up dosing schedule, define the MTD, and determine the RP2D of sonrotoclax monotherapy in patients with B-cell malignancies, including R/R WM
- Responses were assessed per modified Owens 2013 criteria
- Sonrotoclax was administered orally QD with a ramp-up schedule to mitigate potential risk of TLS

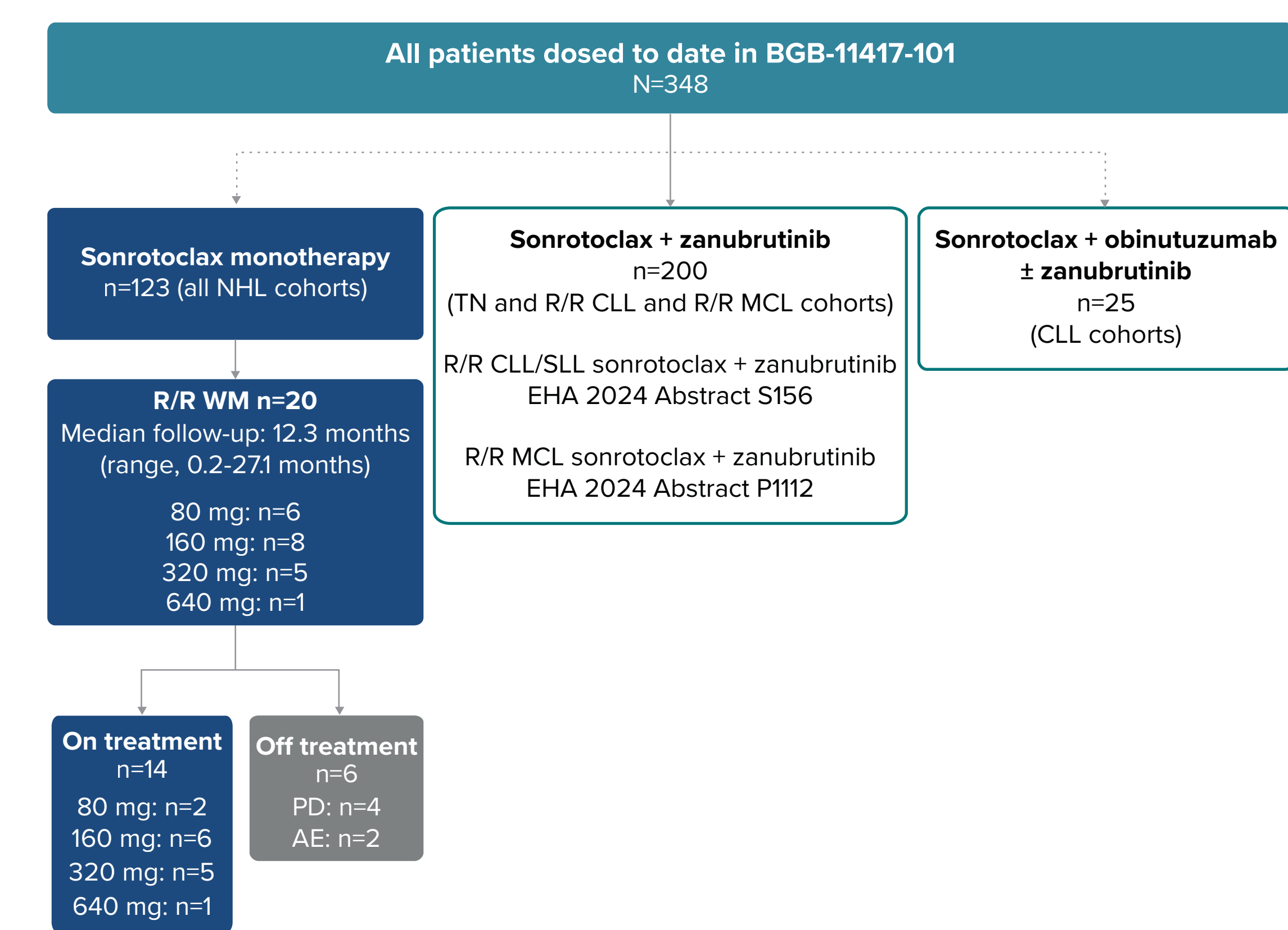
Figure 1. BGB-11417-101 Study Design



RESULTS

- As of February 4, 2024, a total of 20 patients with R/R WM had received sonrotoclax (80, 160, 320, or 640 mg), and 14 remained on treatment (Figure 2)
- Six patients (30%) discontinued treatment due to progressive disease (PD; n=4) and AEs of multifocal neurological syndrome (n=1) and COVID-19 (n=1); neither AE was considered related to sonrotoclax by the investigator

Figure 2. Patient Disposition



- Across dose cohorts, the median age was 68.5 years and the median number of prior treatments was 2.5 (Table 1)
- Twelve patients (60%) received prior BTK inhibitor therapy, nine (45%) of whom had it as their last prior therapy

Table 1. Baseline Patient Characteristics

Characteristic	80 mg (n=6)	160 mg (n=8)	320 mg (n=5)	640 mg (n=1)	All (N=20)
Study follow-up, median (range), months	23.4 (7.6-27.1)	13.1 (2.1-20.0)	4.1 (2.7-8.5)	0.2 (0.2-0.2)	12.3 (0.2-27.1)
Age, median (range), years	65.5 (48-79)	69.5 (61-87)	65.0 (61-77)	84.0 (84-84)	68.5 (48-87)
Male sex, n (%)	6 (100)	5 (63)	4 (80)	1 (100)	16 (80)
ECOG PS					
0	3 (50)	2 (25)	1 (20)	0	6 (30)
1	3 (50)	5 (63)	4 (80)	1 (100)	13 (65)
2	0	1 (13)	0	0	1 (5)
MYD88 mutation, n/tested (%)	4/4 (100)	4/4 (100)	2/2 (100)	1/1 (100)	11/11 (100)
CXCR4 mutation, n/tested (%)	1/4 (25)	1/4 (25)	1/2 (50)	0/1 (0)	3/11 (27)
Prior therapy					
No. of lines of prior systemic therapy, median (range)	3 (1-8)	2.5 (1-9)	1 (1-8)	3 (3-3)	2.5 (1-9)
No. of lines of prior systemic therapy, n (%)					
1	1 (17)	3 (38)	4 (80)	0	8 (40)
2	1 (17)	1 (13)	0	0	2 (10)
≥3	4 (67)	4 (50)	1 (20)	1 (100)	10 (50)
Prior BTK inhibitor, n (%)	4 (67)	4 (50)	3 (60)	1 (100)	12 (60)
BTK inhibitor as last therapy, n (%)	-	-	-	-	9 (45)
Prior BTK inhibitor duration, median (range), months	60.7 (55.3-85.4)	48.4 (19.4-54.5)	13.1 (1.1-25.1)	68.5 (68.5-68.5)	53.7 (1.1-85.4)

LDI, longest diameter; PS, performance status.

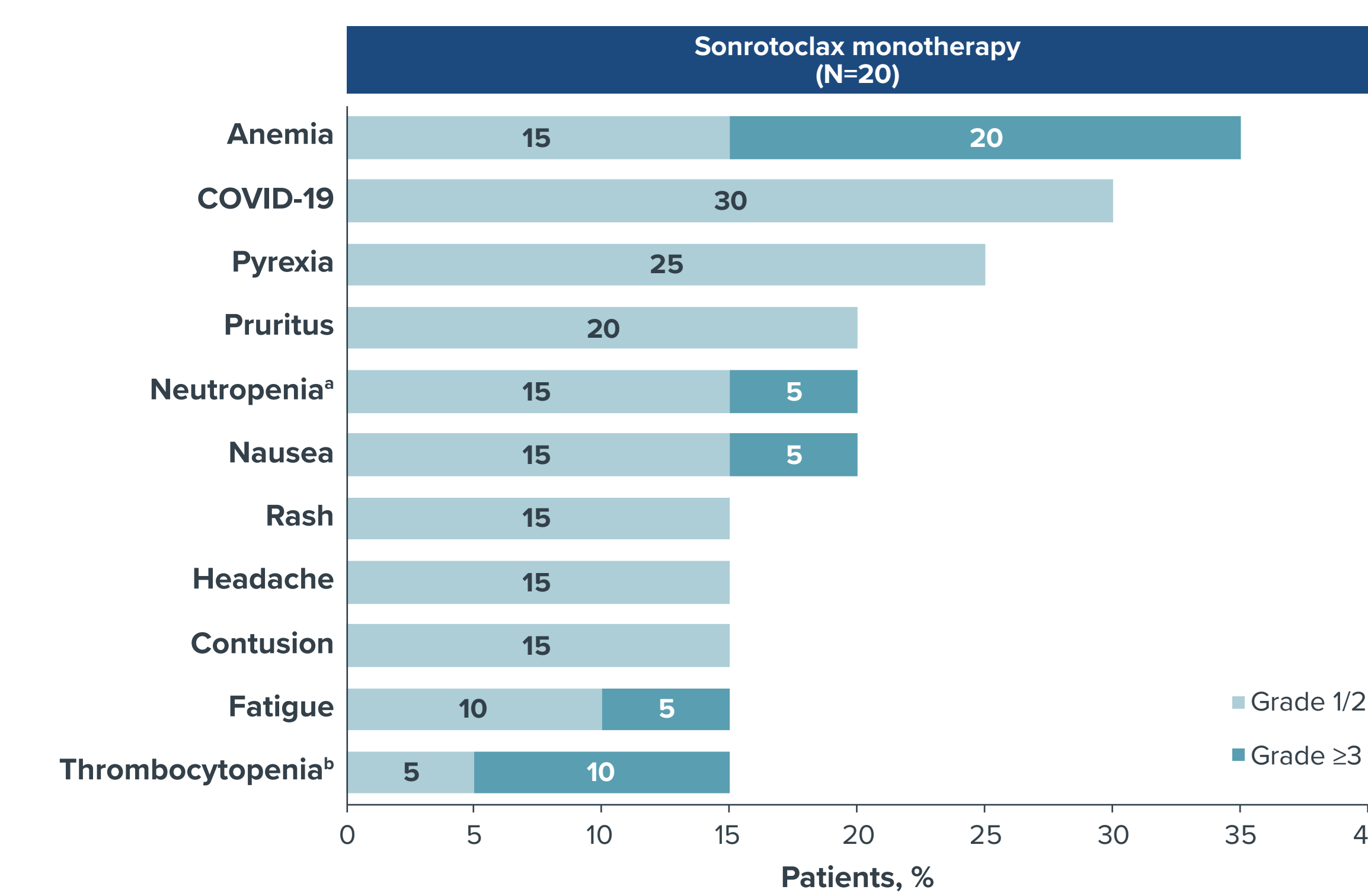
- An overall summary of TEAEs in patients with R/R WM is shown in Table 2
- Four patients died while on study due to PD (n=2), COVID-19 pneumonia (n=1), and multi-organ failure (n=1); neither TEAE was related to sonrotoclax
- The most common any-grade TEAEs across cohorts were anemia (35%), COVID-19 (30%), and pyrexia (25%) (Figure 3)
- The most common grade ≥3 TEAE was anemia (20%)
- No laboratory or clinical TLS was seen regardless of target dose
- One patient in the 160-mg dose group experienced a DLT of grade 3 febrile neutropenia which resolved after 2 days without dose reduction during ramp-up day 2 on 10 mg of sonrotoclax
- Dose escalation is ongoing at 640 mg, with no MTD reached at the time of data cut-off

Table 2. TEAE Summary

Patients, n (%)	80 mg (n=6)	160 mg (n=8)	320 mg (n=5)	640 mg (n=1)	All (N=20)
Any TEAE	5 (83)	8 (100)	5 (100)	0	18 (90)
Grade ≥3	3 (50)	3 (38)	1 (20)	0	7 (35)
Serious TEAEs	3 (50)	2 (25)	1 (20)	0	6 (30)
Deaths	1 (17)	1 (13)	0	0	2 (10) ^a
Led to sonrotoclax discontinuation	1 (17)	1 (13)	0	0	2 (10) ^b
Led to sonrotoclax dose interruption	2 (33)	3 (38)	0	0	5 (25)
Led to sonrotoclax dose reduction	0	0	0	0	0

^a COVID-19 pneumonia, pneumonia. ^b COVID-19, multifocal neurological syndrome (no further information).

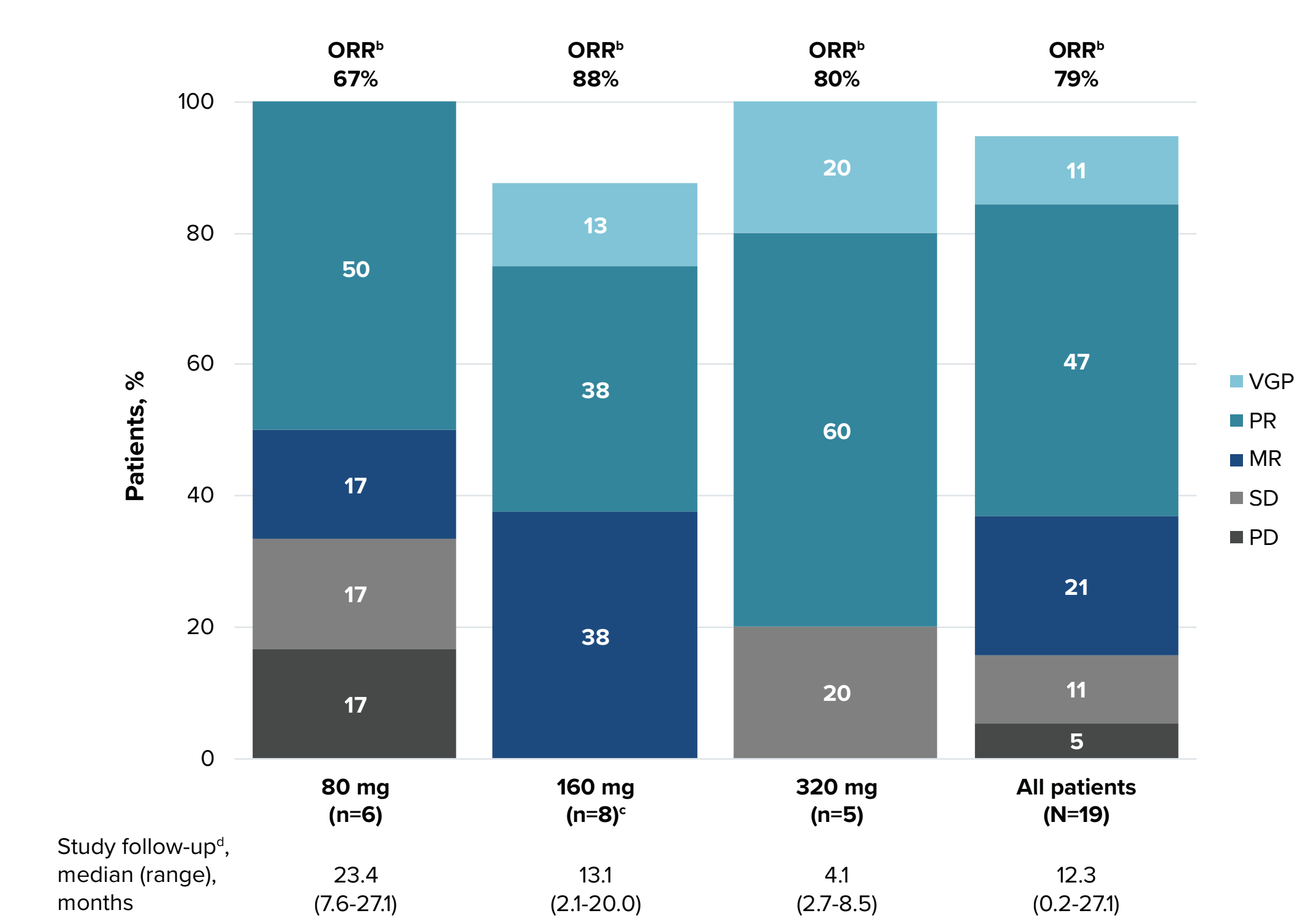
Figure 3. TEAEs in ≥3 Patients



^a Neutropenia combines preferred terms neutrophil count decreased and neutropenia. ^b Thrombocytopenia combines preferred terms platelet count decreased and thrombocytopenia.

- Response rates are shown in Figure 4; the 1 patient in the 640-mg cohort was not yet response evaluable

Figure 4. Response Rates^a

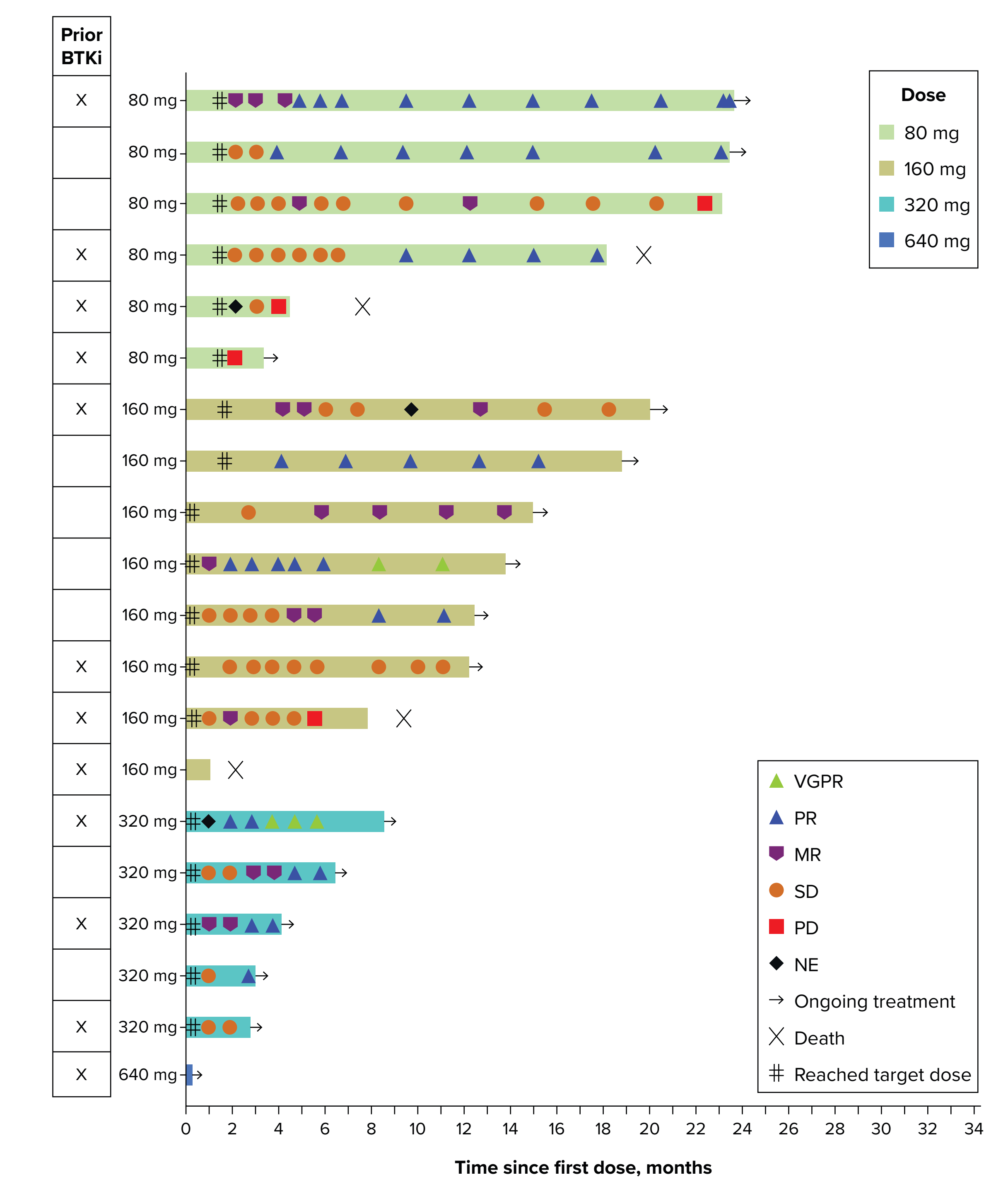


^a Responses were assessed per modified Owens 2013 criteria. ^b ORR was defined as response of MR or better. ^c One patient died due to a COVID-19 infection before a post-baseline response assessment. ^d For all patients as treated (N=20). MR, minor response; NA, not assessable; VGPR, very good partial response.

CONCLUSIONS

- Sonrotoclax monotherapy was well tolerated in patients with R/R WM; the MTD was not reached
- No laboratory or clinical TLS events were observed
- Preliminary antitumor activity was encouraging in this heavily pretreated population, with high and durable responses across all tested dose levels
- Further evaluation of sonrotoclax monotherapy in patients with R/R WM is ongoing in a pivotal study (BGB-11417-203)

Figure 5. Treatment Duration and Investigator-Assessed Responses



BTKi, BTK inhibitor; MR, minor response; NE, not evaluable; VGPR, very good partial response.

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DISCLOSURES

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