Sonrotoclax Monotherapy for Treatment of Patients With Relapsed/Refractory Chronic Lymphocytic Leukemia: Data From an Ongoing Phase 1/1b Study (BGB-11417-101)

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Disclosures for Stephen S. Opat

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- **Other relationship (member of safety and data monitoring committee):** Merck

Introduction

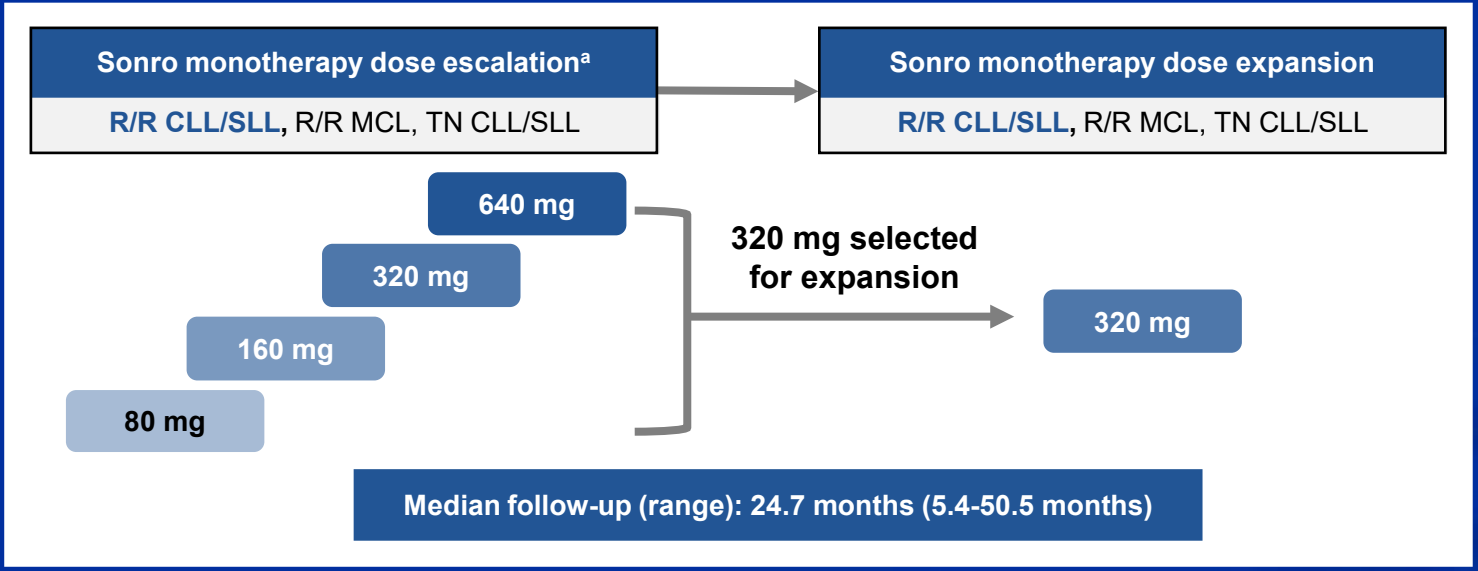
- CLL/SLL remains incurable as many patients experience relapse,[1] necessitating further treatment with novel agents
- Sonro (BGB-11417), a next-generation BCL2 inhibitor, is a more selective and pharmacologically potent inhibitor of BCL2 than venetoclax, with a shorter half-life and no drug accumulation[2]
- Here, updated safety and efficacy data are presented for patients with R/R CLL/SLL treated with sonro monotherapy in the ongoing BGB-11417-101 study

BCL2, B-cell lymphoma 2; CLL/SLL, chronic lymphocytic leukemia/small lymphocytic lymphoma; R/R relapsed/refractory; sonro, sonrotoclax.

1. Hillmen P, et al. *J Clin* Oncol. 2019;37(30):2722-2729; 2. Guo Y, et al. *J Med Chem.* 2024;67(10):7836-7858.

BGB-11417-101 (NCT04277637) Study Design

- BGB-11417-101 is an ongoing phase 1/1b, open-label, multicenter, dose-escalation and -expansion study of sonro as monotherapy or in combination with zanubrutinib or obinutuzumab in patients with various B-cell malignancies
- Eligible patients have CLL/SLL that requires treatment and has relapsed after or was refractory to at least 1 prior line of therapy
- Sonro is administered orally once daily, with a ramp-up to target dose to prevent TLS, continued until disease progression or unacceptable toxicity
- Primary objectives are to assess safety/tolerability, define the MTD, and determine the RP2D of sonro monotherapy
- Secondary objective is to evaluate the ORR per iwCLL 2018 criteria[1]
- Exploratory endpoints include MRD in blood by ERIC flow cytometry assay at week 12 and then every 24 weeks thereafter



[a]The safety monitoring committee reviewed dose-level cohort data before dose escalation.
CLL/SLL, chronic lymphocytic leukemia/small lymphocytic lymphoma; ERIC, European Research Initiative on CLL; iwCLL, international workshop on CLL; MCL, mantle cell lymphoma; MRD, measurable residual disease; MTD, maximum tolerated dose; ORR, overall response rate; RP2D, recommended phase 2 dose; R/R relapsed/refractory; sonro, sonrotoclax; TN, treatment naive; TLS, tumor lysis syndrome.
1. Hallek M, et al. *Blood*. 2018;131(25):2745-2760.

Baseline Patient Characteristics

- Twelve patients (66.7%) remain on treatment
- Six (33.3%) treatment discontinuations due to:
  - PD: n=3
  - Physician decision: n=2
  - Patient withdrawal: n=1

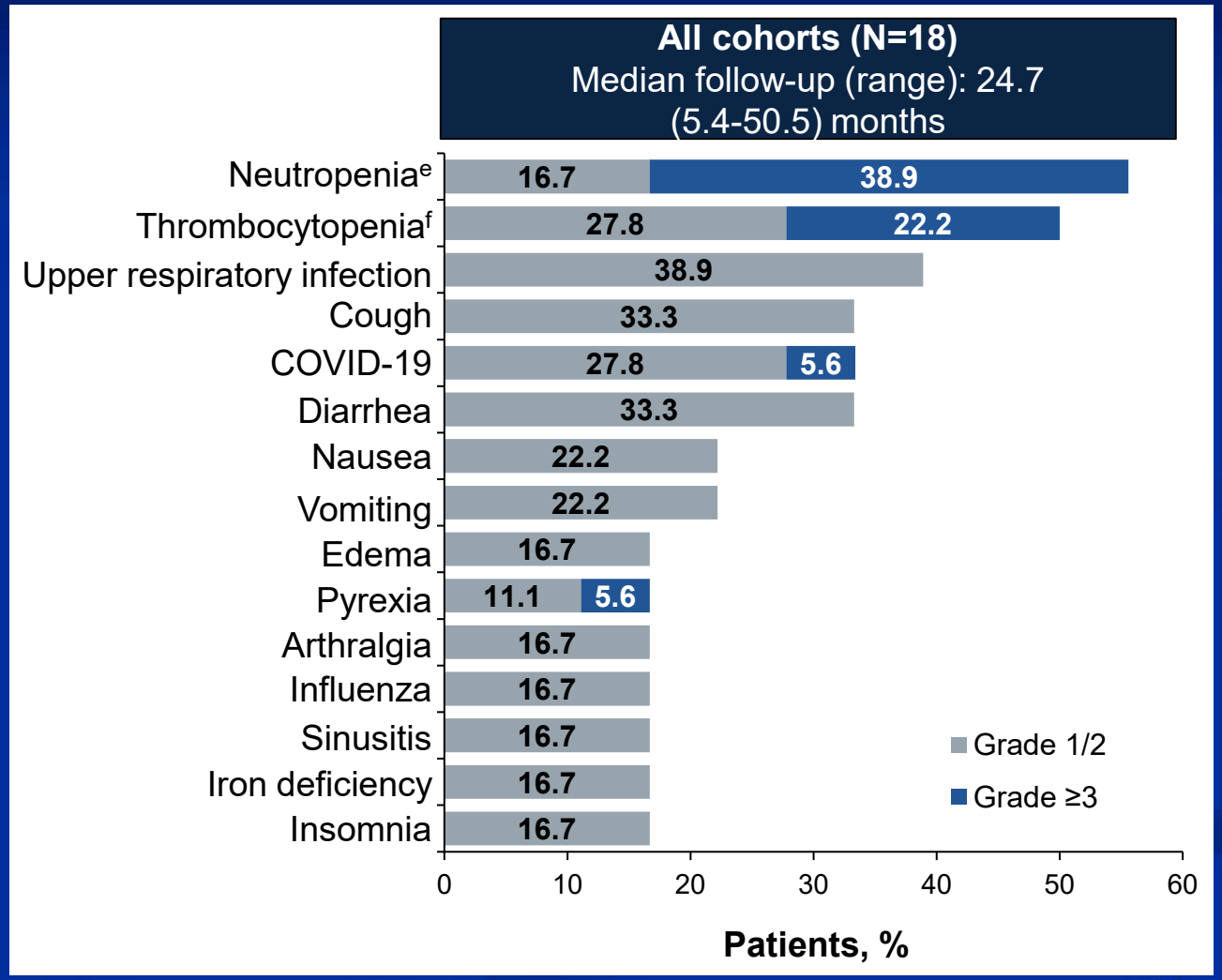
Characteristic	Sonro 80 mg (n=4)	Sonro 160 mg (n=7)	Sonro 320 mg (n=7)	All (N=18)
Follow-up, median (range), months	45.2 (44.0-50.5)	23.2 (5.4-42.7)	22.7 (14.6-28.1)	24.7 (5.4-50.5)
Age, median (range), years	65.5 (55-70)	73.0 (61-84)	65.0 (62-79)	**68.0 (55-84)**
Male, n (%)	4 (100)	3 (42.9)	5 (71.4)	12 (66.7)
ECOG PS, n (%)				
0	2 (50.0)	3 (42.9)	3 (42.9)	8 (44.4)
1	2 (50.0)	4 (57.1)	4 (57.1)	10 (55.6)
del(17p), n/tested (%)	1/3 (33.3)	1/6 (16.7)	2/5 (40.0)	**4/14 (28.6)**
del(17p) and/or *TP53* mutation, n/tested (%)	1/2 (50.0)	3/6 (50.0)	3/4 (75.0)	**7/12 (58.3)**
Unmutated IGHV, n/tested (%)	2/2 (100)	5/6 (83.3)	7/7 (100)	**14/15 (93.3)**
Prior therapy				
No. of lines of prior systemic therapy, median (range)	2.5 (1-3)	2.0 (1-4)	4.0 (1-5)	**3.0 (1-5)**
No. of lines of prior systemic therapy, n (%)				
1	1 (25.0)	1 (14.3)	1 (14.3)	3 (16.7)
2	1 (25.0)	3 (42.9)	1 (14.3)	5 (27.8)
≥3	2 (50.0)	3 (42.9)	5 (71.4)	10 (55.6)
Prior BTK inhibitor, n (%)	3 (75.0)	7 (100)	7 (100)	**17 (94.4)**
Prior BTK inhibitor duration, median (range), months	47.0 (40.9-53.7)	59.6 (33.8-87.3)	78.5 (24.5-113.0)	**61.0 (24.5-113.0)**

Data cutoff: March 1, 2025.
BTK Bruton tyrosine kinase; CLL/SLL, chronic lymphocytic leukemia/small lymphocytic lymphoma; ECOG PS, Eastern Cooperative Oncology Group performance status; IGHV, immunoglobulin heavy chain variable region; PD, progressive disease; R/R, relapsed/refractory; sonro, sonrotoclax.

Safety Summary and TEAEs in ≥3 Patients[a,b]

- No deaths or sonro discontinuations due to TEAEs
- Toxicity comparable across all dose levels with no new safety signals identified; sonro 320 mg selected for expansion
- Neutropenia was manageable with no increase grade ≥3 infections; 8 patients received G-CSF
- TLS, n=2 (11.1%; during sonro ramp-up; 80-mg and 320-mg); both resolved within 24 hours without sequelae or dose changes
- MTD was not reached at 320 mg; 640-mg dose not tested

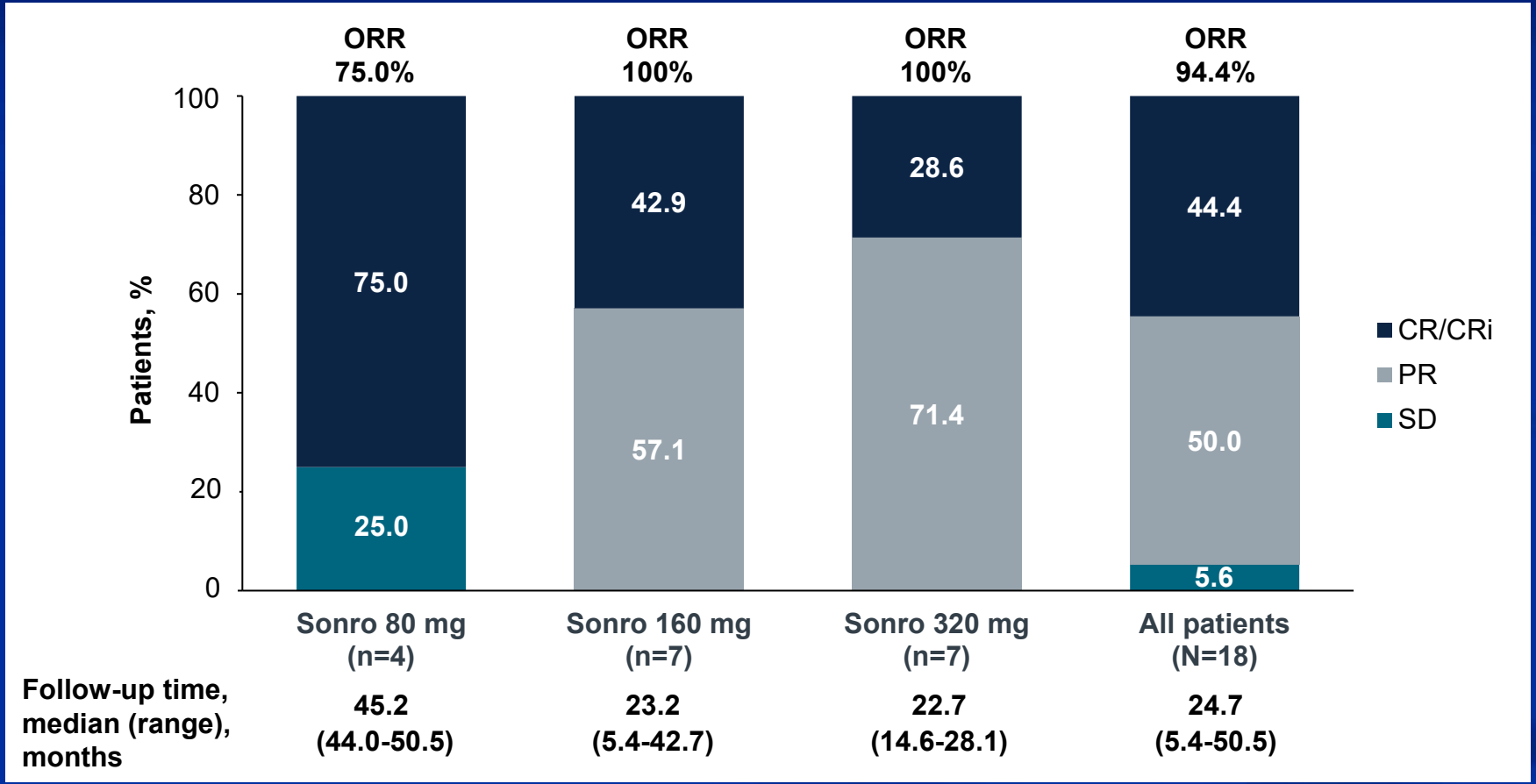
Patients, n (%)	Sonro 80 mg (n=4)	Sonro 160 mg (n=7)	Sonro 320 mg (n=7)	All (N=18)
Any TEAEs	4 (100)	7 (100)	7 (100)	18 (100)
Grade ≥3	2 (50.0)	6 (85.7)	6 (85.7)	14 (77.8)
Serious	3 (75.0)	3 (42.9)	3 (42.9)	9 (50.0)
Led to sonro discontinuation	0	0	0	0
Led to sonro dose interruption	3 (75.0)	5 (71.4)	2 (28.6)	10 (55.6)
Led to sonro dose reduction	0	2 (28.6)[c]	1 (14.3)[d]	3 (16.7)



[a]Grade is listed as worst grade experienced by the patient on any drug. [b]Hematologic TEAEs were graded per iwCLL criteria; nonhematologic TEAEs were graded per CTCAE v5.0 criteria. [c]Grade ≤2 diarrhea (n=2). [d]Grade 2 platelet count decreased (n=1). [e]Neutropenia combines preferred terms *neutrophil count decreased* and *neutropenia*. [f]Thrombocytopenia combines preferred terms *platelet count decreased* and *thrombocytopenia*.
CTCAE, common terminology criteria for adverse events; G-CSF, granulocyte-colony stimulating factor; MTD, maximum tolerated dose; sonro, sonrotoclax; TEAE, treatment-emergent adverse event; TLS, tumor lysis syndrome.

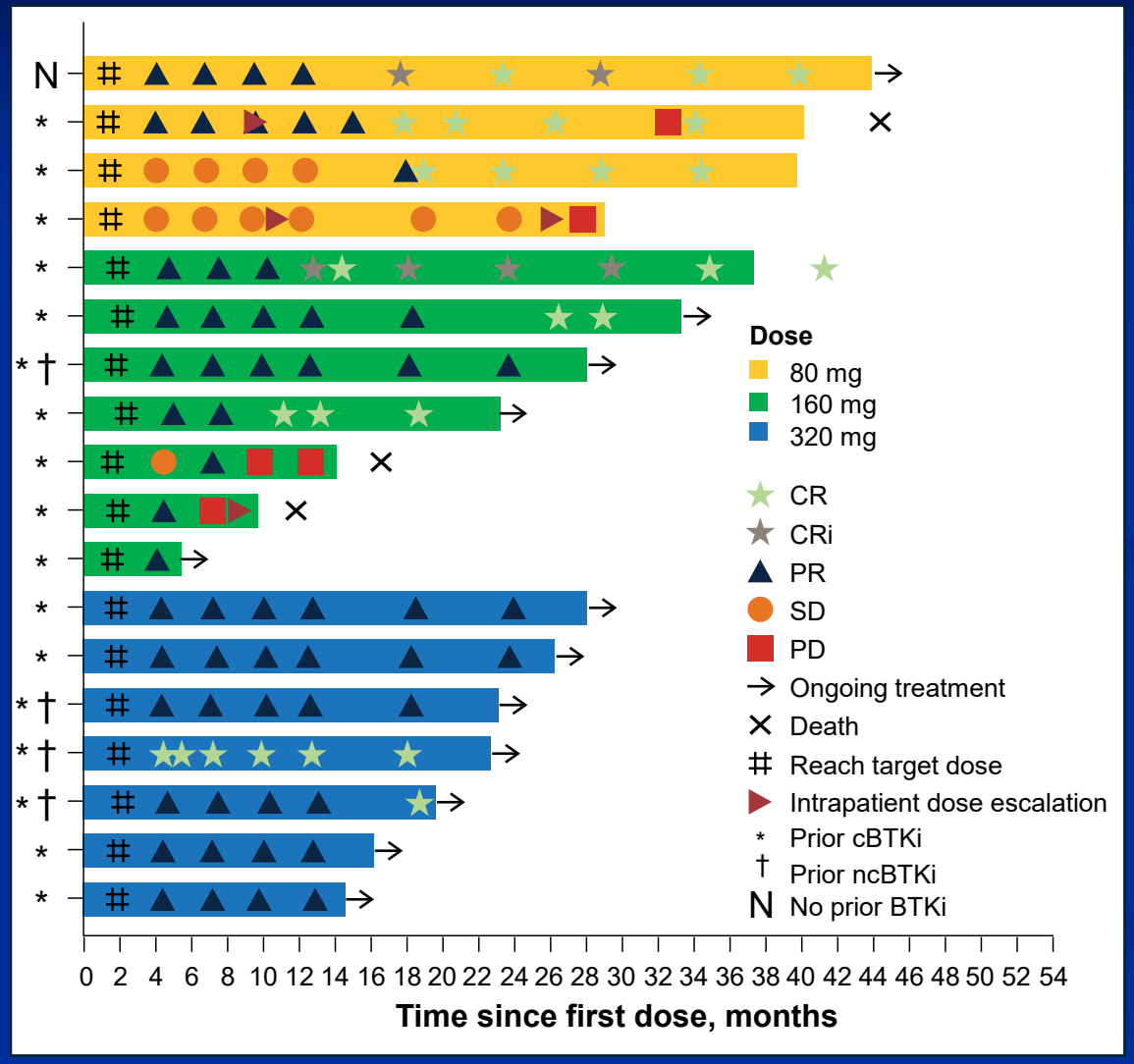
Response Rates

- **Median time to CR:**
  - All patients: 17.8 months (range, 4.4-26.5)
  - 320-mg cohort: 11.6 months (range, 4.4-18.7)
- **Median DoR:** NR
- **Median PFS:** NR after median follow-up time of 23.7 months (range, 4.0-41.2)
- No PFS events in the 320-mg cohort
- All patients remain on treatment



CR, complete response; CRi, complete response with incomplete marrow recovery; DoR: duration of response; NR, not reached; ORR, overall response rate; PFS, progression-free survival; PR, partial response; SD, stable disease; sonro, sonrotoclax.

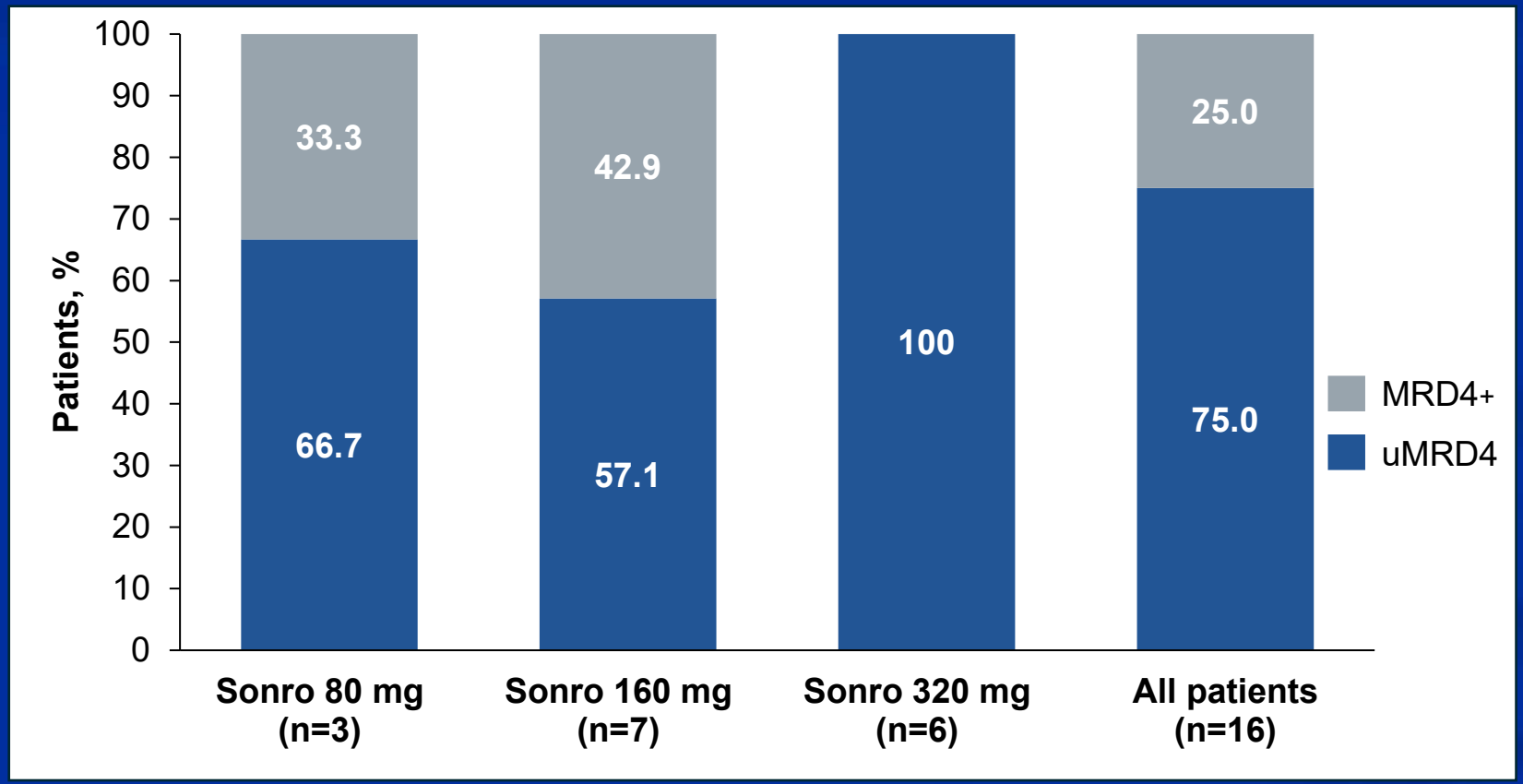
Investigator-Assessed Responses



BTK, Bruton tyrosine kinase; cBTKi, covalent BTK inhibitor; CR, complete response; CRi, complete response with incomplete marrow recovery; ncBTKi, noncovalent BTKi; PD, progressive disease; PR, partial response; SD, stable disease.

Best Overall MRD in Peripheral Blood by Dose Level[a,b]

- The best uMRD rate was 75% across all patients and 100% in the 320-mg cohort



[a]Measured by ERIC-approved flow cytometry method with 10^{-4} sensitivity. uMRD4 defined as $<10^{-4}$ CLL cells of total WBCs. [b]Two patients were excluded from the MRD-evaluable set: 1 patient in the 80-mg cohort had <200,000 total nucleated cells and 1 patient in the 320-mg cohort was missing all MRD samples.
MRD, measurable residual disease; sonro, sonrotoclax; uMRD, undetectable MRD; WBC, white blood cell.

Conclusions

- Sonro monotherapy had a tolerable patient safety profile across all doses tested and demonstrated substantial antitumor activity in a heavily pretreated, high-risk cohort of patients with R/R CLL/SLL, most of whom received prior BTK inhibitors
    - No clinical TLS events were reported
    - Sonro treatment led to deep and durable responses, and median PFS was not reached after a median follow-up of 24.7 months
    - In the 320-mg cohort, the ORR was 100%, the best uMRD rate was 100%, no PFS events had occurred, and all patients remain on treatment as of the data cutoff date
- Based on these results, sonro 320 mg was selected as the RP2D and is being tested as monotherapy or in combinations in potential registrational studies

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