CELESTIAL-RRMCL (BGB-11417-302), a Phase 3, Randomized, Double-Blind Study of Sonrotoclax (BGB-11417) + Zanubrutinib vs Placebo + Zanubrutinib in Patients With Relapsed or Refractory Mantle Cell Lymphoma

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Disclosures for Martin Dreyling

- **Honoraria:** AstraZeneca, BeOne Medicines Ltd, BMS, Gilead/Kite, Janssen, Lilly, Roche
- **Advisory board**: AbbVie, AstraZeneca, AvenCell, BeOne Medicines Ltd, BMS, Genmab, Gilead/Kite, Incyte, Janssen, Lilly/Loxo, Novartis, Roche, Sobi
- **Research support (institution)**: AbbVie, Gilead/Kite, Janssen, Lilly, Roche

Introduction

- MCL is an uncommon, incurable subtype of aggressive B-cell NHL[1]
  - Patients with MCL often experience R/R disease and require novel therapy options[1]
- Venetoclax has demonstrated efficacy in patients with R/R MCL; however, it is not currently approved to treat R/R MCL[2]
- Sonrotoclax (BGB-11417), a next-generation BCL2 inhibitor[3,4]:
  - More selective and pharmacologically potent inhibitor of BCL2 than venetoclax
  - Shorter half-life
  - No drug accumulation
- Zanubrutinib, a next-generation cBTKi, is approved as monotherapy for R/R MCL in the US and China[5]
- In an ongoing phase 1 trial (NCT04277637), sonrotoclax + zanubrutinib was well tolerated and demonstrated high response rates in R/R MCL[6]
- The phase 3 CELESTIAL-RRMCL study was designed to further evaluate sonrotoclax + zanubrutinib in patients with R/R MCL

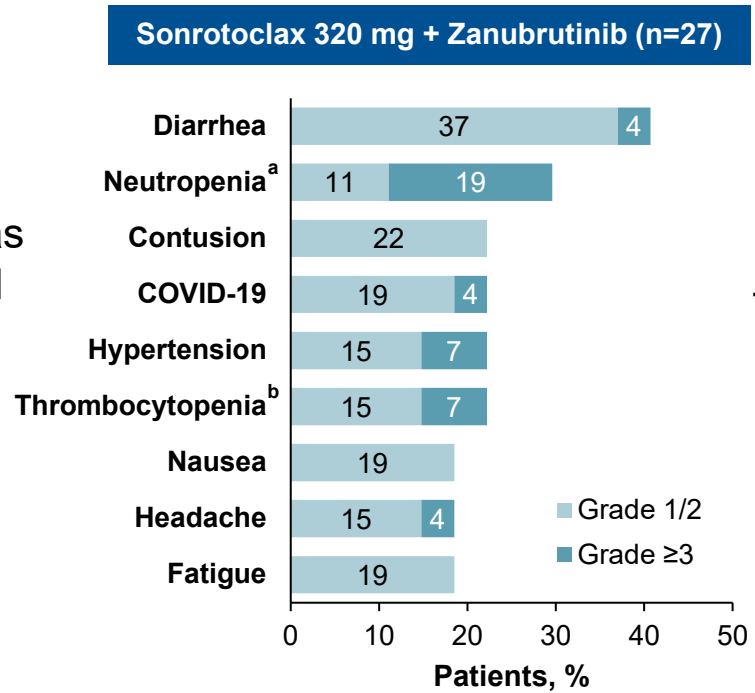
BCL2, B-cell lymphoma 2; BTK, Bruton tyrosine kinase; cBTKi, covalent Bruton tyrosine kinase inhibitor; MCL, mantle cell lymphoma; NHL, non-Hodgkin lymphoma; R/R, relapsed/refractory.

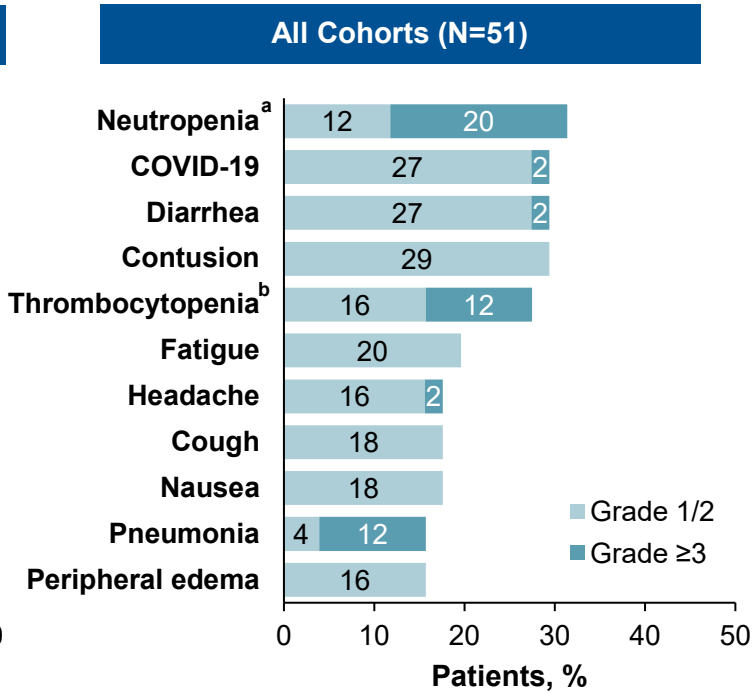
1. Jain P, Wang ML. *Am J Hematol*. 2022;97(5):638-656; 2. Wang M, et al. ASH 2023. Abstract LBA-2; 3. Guo Y, et al. *J Med Chem*. 2024;67(10):7836-7858; 4. Liu J, et al. *Blood*. 2024;143(18):603-608; 5. Brukinsa. Prescribing information. BeiGene, Ltd.; 2024; 6. Tam CS, et al. EHA 2024. Abstract P1112.

Results From the R/R MCL Cohort of the BGB-11417-101 Study[1]:
Most TEAEs Observed With Sonrotoclax + Zanubrutinib Were Low Grade and Transient

- No laboratory or clinical TLS
- No atrial fibrillation/flutter
- Safety profile was similar across all dose levels

TEAEs in ≥15% of patients at the sonrotoclax RP2D (320 mg) and in all patients

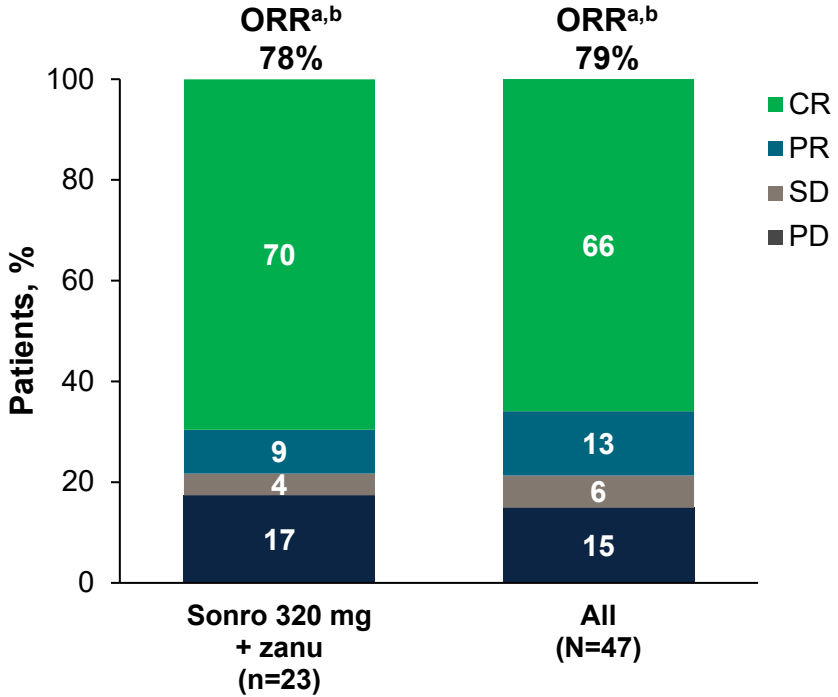




[a]Neutropenia combines preferred terms *neutrophil count decreased* and *neutropenia*. [b]Thrombocytopenia combines preferred terms *platelet count decreased* and *thrombocytopenia*.
MCL, mantle cell lymphoma; RP2D, recommended phase 2 dose; R/R, relapsed/refractory; TEAE, treatment-emergent adverse event; TLS, tumor lysis syndrome.
1. Tam CS, et al. EHA 2025. Abstract S234.

Results From the R/R MCL Cohort of the BGB-11417-101 Study[1]:
Sonrotoclax + Zanubrutinib Demonstrated Deep Responses Across All Dose Levels

- Median study follow-up was 16.4 months
  - All doses: ORR[a,b] was 79%; CR rate was 66%
  - **320-mg dose: ORR was 78%; CR rate was 70%**
  - **All patients who had a BOR of PD, progressed during zanubrutinib lead-in (4 patients in the 320-mg cohort)**
- The median time to CR was 6.7 months (range, 1.5-28.2 months)

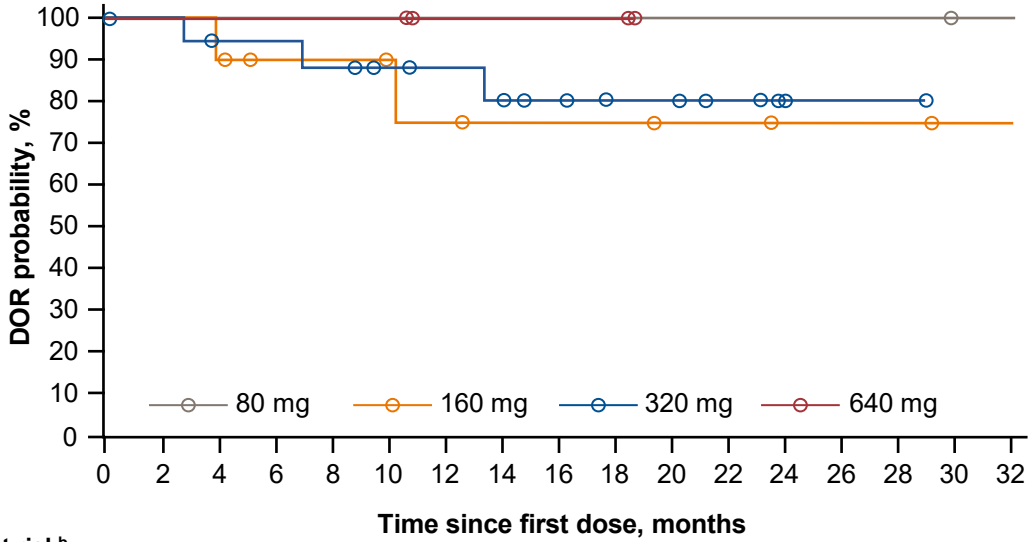


	Sonro 320 mg + zanu (n=23)	All (N=47)
Study follow-up,[c] median (range), months	13.2 (0.7-31.6)	16.4 (0.7-42.4)

[a]Responses were assessed per Lugano 2014 criteria and are shown as the percentages of responding patients who had ≥1 post-baseline tumor assessment after dosing with sonrotoclax unless treatment was discontinued due to clinical progression or death prior to tumor assessment. [b]ORR was defined as PR or better. [c]For all patients as treated (N=51).
BTK, Bruton tyrosine kinase; CR, complete response; ORR, overall response rate; PD, progressive disease; PR, partial response; R/R, relapsed/refractory; SD, stable disease.
1. Tam CS, et al. EHA 2025. Abstract S234.

Results From the R/R MCL Cohort of the BGB-11417-101 Study[1]:
Sonrotoclax + Zanubrutinib Demonstrated Durable Responses[a]

- Median DOR in all patients was not reached (95% CI, 34.8-NE)
  - DOR rate at 24 months was 84.0% (95% CI, 65.3%-93.1%; mFU, 17.7 months)
- Median DOR in the 320-mg dose group was not reached (95% CI, 13.3-NE)
  - DOR rate at 24 months was 80.1% (95% CI, 49.4%-93.3%; mFU, 14.8 months)
- Of 18 patients in the 320-mg dose group who achieved CR, 16 remain in CR (mFU, 13 months)
  - DoCR rate at 18 months was 84.4% (95% CI, 50.4%-95.9%; mFU, 10.2 months)



No. at risk[b]:

80 mg	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	4	4	4
160 mg	10	10	10	10	9	8	7	7	7	7	6	5	5	4	4	4	4	4	4	4	3	3	3	3	2	2	2	2	2	2	1	1	1
320 mg	22	18	18	17	15	15	15	14	14	13	12	11	11	11	10	8	8	7	6	6	6	5	4	4	1	1	1	1	1	0	0	0	0
640 mg	4	4	4	4	4	4	4	4	4	4	4	2	2	2	2	2	2	2	2	0	0	0	0	0	0	0	0	0	0	0	0	0	0

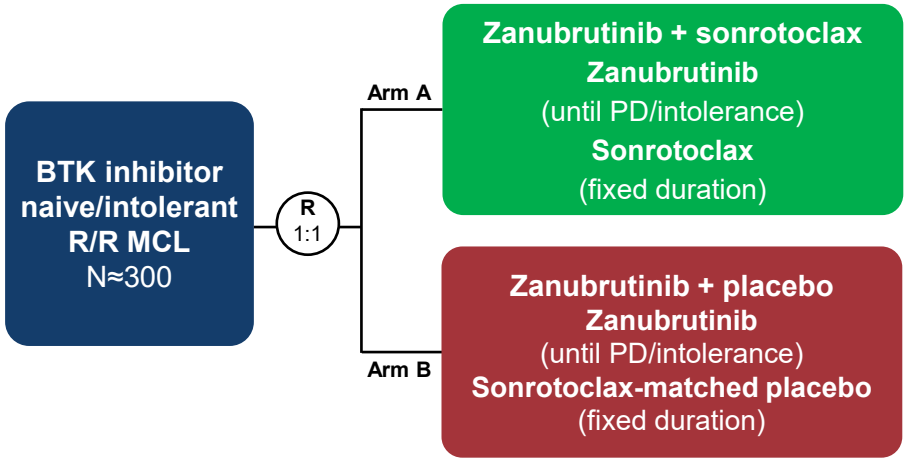
[a]Includes four patients in zanubrutinib lead-in. [b]For all patients as treated (N=51).
CR, complete response; DoCR, duration of complete response; DOR, duration of response; MCL, mantle cell lymphoma; mFU, median follow-up; NE, not evaluable; R/R, relapsed/refractory.
1. Tam CS, et al. EHA 2025. Abstract S234.

CELESTIAL-RRMCL (BGB-11417-302; NCT06742996): A Phase 3, Randomized, Double-Blind Study in Patients With R/R MCL

Key eligibility criteria

- Aged ≥18 years
- Histologically confirmed MCL (WHO-HAEM5 or ICC)
- Received 1-5 prior lines of systemic therapy
- R/R disease after most recent line of therapy
- ECOG PS of 0-2
- No prior BCL2 inhibitor
- No prior cBTKi or ncBTKi[a]

Study design



Endpoints

Primary

- PFS by BIRC

Secondary

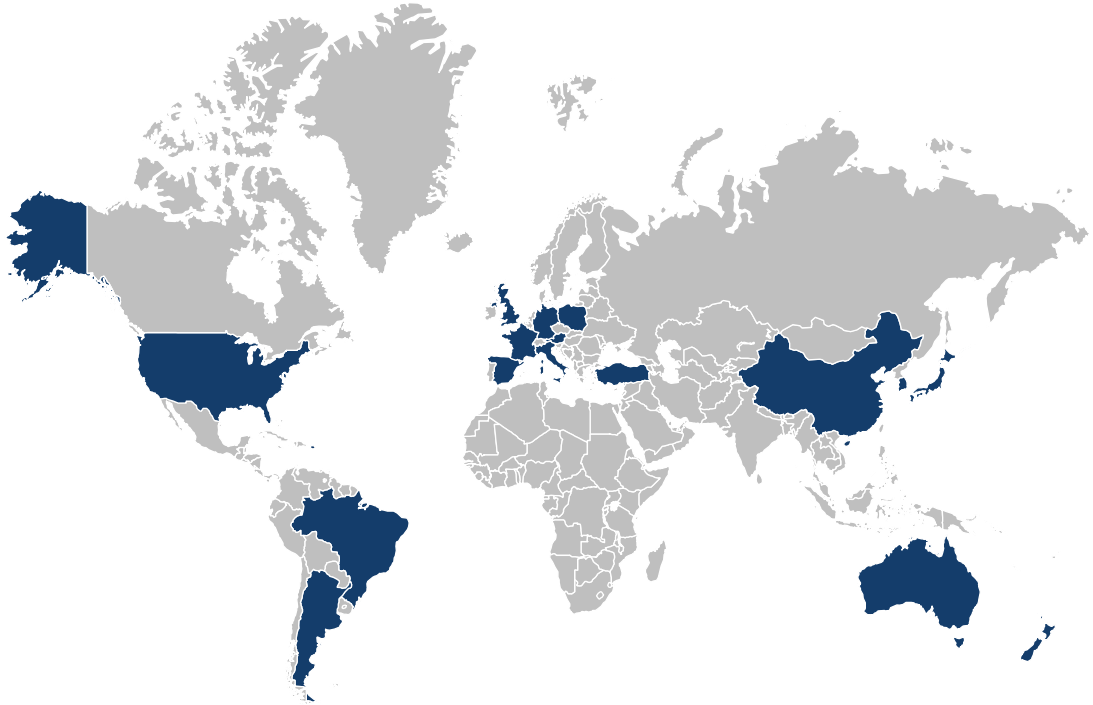
- OS
- PFS by INV
- ORR,[b] CR rate, DOR, and time to first response by BIRC and INV
- Time to next treatment
- HRQOL
- Safety (NCI-CTCAE v5.0)

- No crossover will be allowed between arms

[a]Unless patient was intolerant of the cBTKi (excluding zanubrutinib) or ncBTKi. [b]Proportion of patients who achieved partial response or better per Lugano 2014 criteria.
BCL2, B-cell lymphoma 2; BIRC, blinded independent review committee; cBTKi, covalent Bruton tyrosine kinase inhibitor; CR, complete response; DOR, duration of response; ECOG PS, Eastern Cooperative Oncology Group performance status; HRQOL, health-related quality of life; ICC, International Consensus Classification; INV, investigator; MCL, mantle cell lymphoma; ncBTKi, noncovalent Bruton tyrosine kinase inhibitor; NCI-CTCAE, National Cancer Institute Common Terminology Criteria for Adverse Events; ORR, overall response rate; OS, overall survival; PD, progressive disease; PFS, progression-free survival; R, randomized; R/R, relapsed/refractory; WHO-HAEM5, World Health Organization 2022 Classification of Haematolymphoid Tumours.

CELESTIAL-RRMCL Study Status

- Enrollment for BGB-11417-302 began in March 2025, and recruitment is ongoing, with an estimated enrollment of 300 patients



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