CELESTIAL-RRCLL
CLL-RR1

A Phase 3, Randomized, Open-Label, Multicenter Study of Sonrotoclax (BGB-11417) Plus Anti-CD20 Antibody Therapies vs Venetoclax Plus Rituximab in Patients With Relapsed/Refractory Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma

2137

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INTRODUCTION

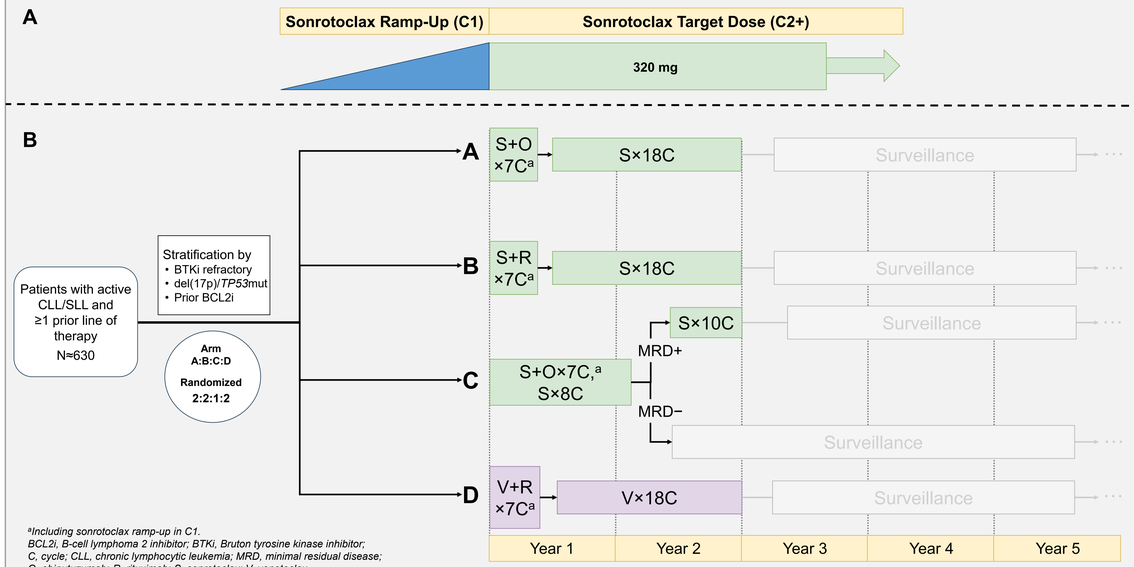
- For patients with relapsed/refractory (R/R) chronic lymphocytic leukemia/small lymphocytic lymphoma (CLL/SLL), treatment options remain limited. Venetoclax plus rituximab (VR) is the only approved fixed-duration regimen, but many patients do not reach deep undetectable minimal residual disease (uMRD) responses and most eventually experience relapse[1]
- The type II anti-CD20 antibody obinutuzumab has shown superior efficacy compared with rituximab in the frontline setting, although randomized data in R/R disease are not yet available and obinutuzumab is not widely accessible for these patients[2]
- 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 drug accumulation. Early data suggest encouraging antitumor activity in R/R CLL[3,4]

STUDY OBJECTIVE

- To investigate whether sonrotoclax in combination with anti-CD20 antibodies can improve clinical outcomes compared with venetoclax-based therapy and to explore MRD-guided vs fixed-duration treatment strategies

STUDY DESIGN

Figure 1. Study Scheme



[a]*Including sonrotoclax ramp-up in C1.*
BCL2i, B-cell lymphoma 2 inhibitor; BTKi, Bruton tyrosine kinase inhibitor; C, cycle; CLL, chronic lymphocytic leukemia; MRD, minimal residual disease; O, obinutuzumab; R, rituximab; S, sonrotoclax; V, venetoclax.

STUDY STATUS

- The study is enrolling at >150 sites across North America, Europe, Asia-Pacific (including Australia, New Zealand, China, and Korea), and Latin America (**Figure 2**)
- Recruitment began in June 2025 and is currently ongoing

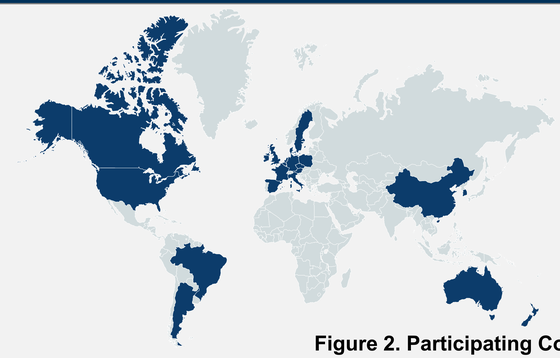


Figure 2. Participating Countries

STUDY DETAILS

- **Patient population**: ≈630 adults with R/R CLL/SLL after ≥1 prior therapy (≥80% previously treated with targeted agents); patients with Richter transformation are excluded
  - Patients with prior BCL2 inhibitor treatment are eligible if they achieved a remission lasting ≥3 years and have been off treatment for ≥2 years
- **Stratification:** by del(17p)/*TP53* mutation status, prior BCL2 inhibitor treatment, and refractoriness to prior BTK inhibitor
- **Treatment:**
  - Oral sonrotoclax and oral venetoclax will be initiated using a ramp-up to the target dose of 320 mg and 400 mg, respectively
  - Rituximab will be administered intravenously at 375 mg/m^2 on day 1 of cycle 2 and at 500 mg/m^2 on day 1 of cycles 3 through 7
  - Obinutuzumab will be administered intravenously at 1,000 mg on days 1/2, 8, and 15 of cycle 2 and on day 1 of cycles 3 through 7
- **Primary endpoint**: progression-free survival (PFS) with sonrotoclax plus obinutuzumab vs VR, assessed by blinded independent review committee (BIRC)
- **Key secondary (powered) endpoint**: PFS with sonrotoclax plus rituximab vs VR by BIRC
- **Other secondary and exploratory endpoints**: uMRD and complete response rates, overall survival, safety, and evaluation of MRD-guided treatment duration and molecular predictors of response

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