CELESTIAL-TNCLL: An Ongoing, Open-Label, Multiregional, Phase 3 Study of Sonrotoclax (BGB-11417) + Zanubrutinib vs Venetoclax + Obinutuzumab for Treatment-Naive CLL

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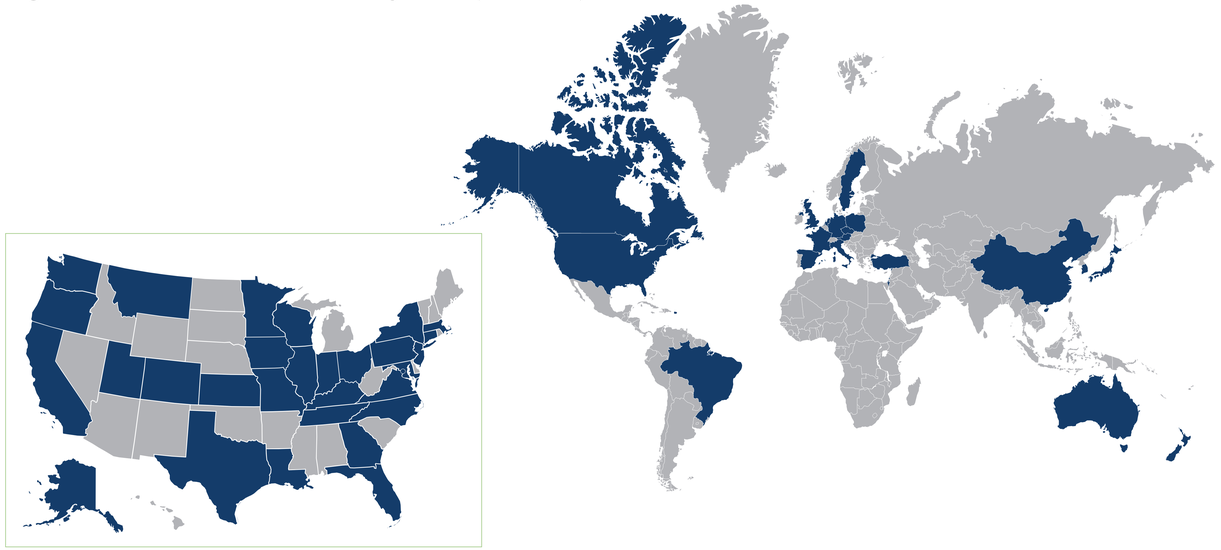
INTRODUCTION

- The combination of venetoclax, the first-generation BCL2 inhibitor, and ibrutinib, a BTK inhibitor, has demonstrated efficacy in patients with CLL[1]
- However, the toxicity profile of this regimen suggests a need for a more tolerable BTK/BCL2 inhibitor combination
- Sonrotoclax, a next-generation BCL2 inhibitor, is a more selective and more pharmacologically potent inhibitor of BCL2 than venetoclax[2]
- Zanubrutinib, a next-generation BTK inhibitor, significantly improved PFS and had a more tolerable safety profile, including fewer cardiac AEs, vs ibrutinib in a randomized, head-to-head study of patients with CLL/SLL[3]
- In a phase 1 study in patients with treatment-naive (TN) CLL, treatment with sonrotoclax + zanubrutinib was generally well-tolerated, with low rates of TEAEs, and resulted in high ORRs and deep responses[4]
- Presented here is the study design of CELESTIAL-TNCLL, a phase 3 trial of sonrotoclax + zanubrutinib in TN CLL

STUDY STATUS

- Enrollment for CELESTIAL-TNCLL began in December 2023, and the study is currently recruiting
- Approximately 230 study sites in 20 countries are planned (**Figure 1**), with an estimated enrollment of 640 patients. In the Americas, there are approximately 50 sites in the US, 6 in Brazil and 15 in Canada

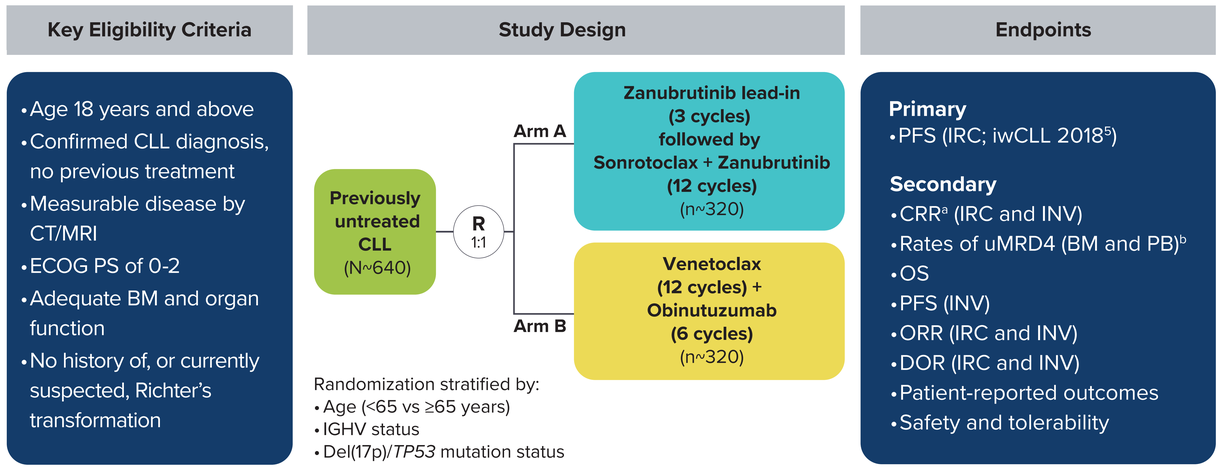
Figure 1. CELESTIAL-TNCLL Study Sites (Planned)



METHODS

- CELESTIAL-TNCLL (BGB-11417-301; NCT06073821) is a randomized, open-label, phase 3 study comparing the efficacy of sonrotoclax + zanubrutinib vs venetoclax + obinutuzumab in patients with TN CLL (**Figure 2**)
- Efficacy will be assessed in accordance with 2018 iwCLL guidelines[5] with modification of treatment-related lymphocytosis for patients with CLL[6]

Figure 2. CELESTIAL-TNCLL Study Design



[a] Defined as CR or CR with incomplete recovery. [b] At $<10^{-4}$ sensitivity at the first post-treatment follow-up based on next-generation sequencing by clonoSEQ® and flow cytometry.
BM, bone marrow; CRR, complete response rate; DOR, duration of response; INV, assessed by investigator; IRC, assessed by independent review committee; PB, peripheral blood; R, randomized; TN, treatment naive; uMRD4, undetectable measurable residual disease.

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