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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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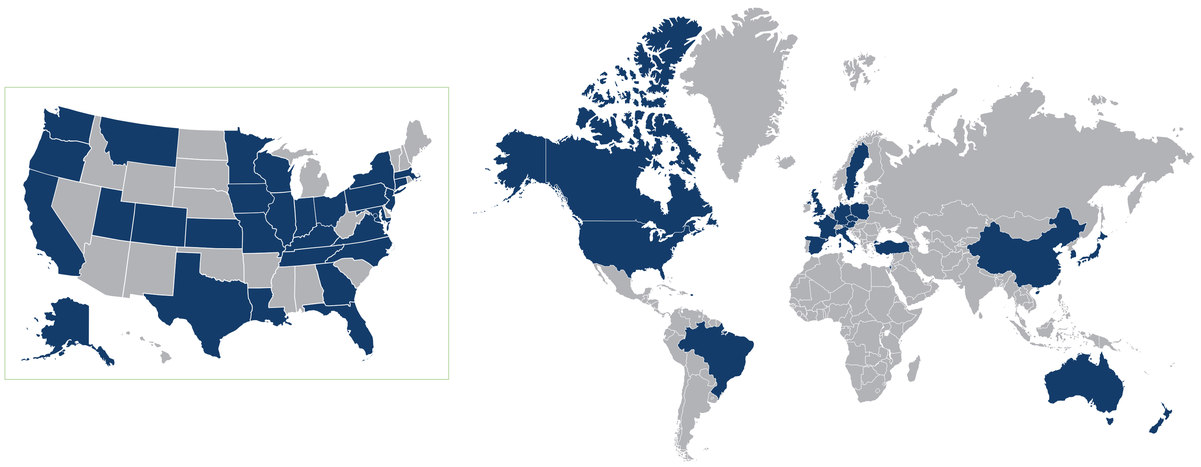
INTRODUCTION

- 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 251 study sites in 19 countries are planned (**Figure 2**), with an estimated enrollment of 640 patients. In the Americas, there are approximately 55 sites in the US, 6 in Brazil and 16 in Canada

Figure 2. 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 1**)
- Efficacy will be assessed in accordance with 2018 iwCLL guidelines[5] with modification of treatment-related lymphocytosis for patients with CLL[6]

Figure 1. CELESTIAL-TNCLL Study Design

Key Eligibility Criteria

- Age 18 years and above
- Confirmed CLL diagnosis, no previous treatment
- Measurable disease by CT/MRI
- ECOG PS of 0-2
- Adequate BM and organ function
- No history of, or currently suspected, Richter's transformation

Study Design

Previously untreated CLL (N~640)

R 1:1

Arm A: **Zanubrutinib lead-in (3 cycles) followed by Sonrotoclax + Zanubrutinib (12 cycles)** (n~320)

Arm B: **Venetoclax (12 cycles) + Obinutuzumab (6 cycles)** (n~320)

Randomization stratified by:
- Age (<65 vs ≥65 years)
- IGHV status
- Del(17p)/*TP53* mutation status

Endpoints

Primary
- PFS (IRC; iwCLL 2018[5])

Secondary
- CRR[a] (IRC and INV)
- Rates of uMRD4 (BM and PB)[b]
- OS
- PFS (INV)
- ORR (IRC and INV)
- DOR (IRC and INV)
- Patient-reported outcomes
- Safety and tolerability

[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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DISCLOSURES

MS: Consulting, advisory boards, steering committees or data safety monitoring committees: AbbVie, Genentech, AstraZeneca, Genmab, Janssen, BeiGene, BMS, Morphosys/Incyte, Kite Pharma, Eli Lilly, Mustang Bio, Fate Therapeutics, Nurix and Merck; Institutional research funding: Mustang Bio, Genentech, AbbVie, BeiGene, AstraZeneca, Genmab, Morphosys/Incyte and Vincerx; Stock options: Koi Biotherapeutics; Employment: BMS (spouse). **AK:** Research funding: Janssen, Roche, Genentech, AbbVie, AstraZeneca, BMS; Honoraria: AbbVie; Consulting role: Janssen, AbbVie, Genentech, AstraZeneca, BMS, Lava Therapeutics; Travel, accommodations, expenses: AbbVie, Janssen. **JW:** Research funding: Janssen, Karyopharm Therapeutics, MorphoSys; Consulting role: Pharmacyclics, Janssen, AstraZeneca, BeiGene, Loxo, Newave Pharmaceutical, Genentech, AbbVie, Merck. **JL:** Nothing to disclose. **TM:** Honoraria: Janssen, AbbVie, Gilead, Alexion, Novartis, Roche; Consulting role: MorphoSys, Sunesis. **TS:** Employment: BeiGene Switzerland GmbH; Equity holder: BeiGene Ltd. **PP, TT:** Employment: BeiGene. **PEMP:** Research funding: AstraZeneca, AbbVie, BeiGene, Janssen, Novartis; Honoraria: AstraZeneca, AbbVie, BeiGene; Travel, accommodations, expenses: AbbVie, BeiGene, Janssen.

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