

CaDAnCe-304, a Phase 3, Open-Label, Randomized Study to Evaluate the Safety and Efficacy of Bruton Tyrosine Kinase Degradator BGB-16673 Compared With Pirtobrutinib in Patients With Relapsed/Refractory Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma

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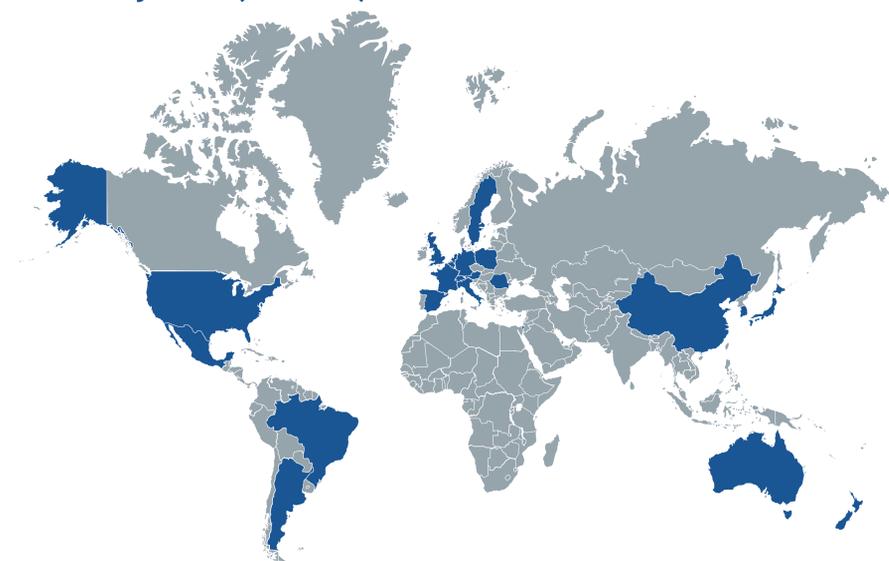
INTRODUCTION

- Targeting Bruton tyrosine kinase (BTK) has revolutionized the treatment of chronic lymphocytic leukemia/small lymphocytic lymphoma (CLL/SLL)¹
- Pirtobrutinib, a noncovalent BTK inhibitor, was recently approved for patients whose disease relapsed following covalent BTK inhibitor therapy such as ibrutinib, acalabrutinib, or zanubrutinib²
- BGB-16673 is an orally available protein degrader that blocks BTK signaling by tagging BTK for degradation through the cell's proteasome pathway, leading to tumor regression³
- By degrading BTK, BGB-16673 disrupts both inherent BTK catalytic activity and its separate protein scaffolding functions, in contrast to small molecule BTK inhibitors that temporarily block BTK catalytic activity alone^{4,5}
- The elimination of BTK by degradation may be effective against treatment-resistant BTK mutants that have been shown to limit the efficacy of current BTK inhibitors⁴
- In preclinical models, BGB-16673 degraded both wild-type BTK and mutant forms of BTK that have shown resistance to covalent and noncovalent BTK inhibitors; additionally, BGB-16673 showed central nervous system penetration^{3,6}
- In a clinical study, BGB-16673 led to substantial reductions in BTK protein levels in peripheral blood and tumor tissue⁷
- Data from CaDAnCe-101 (BGB-16673-101; NCT05006716), an ongoing phase 1/2 study, demonstrated that BGB-16673 has a tolerable safety profile and can achieve responses in heavily pretreated patients with relapsed/refractory (R/R) CLL/SLL, including those with prior BTK inhibitor treatment and BTK resistance mutations⁸
- Here, the study design of CaDAnCe-304 (BGB-16673-304; NCT06973187), an ongoing phase 3 trial in R/R CLL/SLL, is described

STUDY STATUS

- Enrollment for CaDAnCe-304 began in October 2025, and the study is currently recruiting
- Approximately 207 study sites in 23 countries are planned (Figure 1), with an estimated enrollment of 500 patients

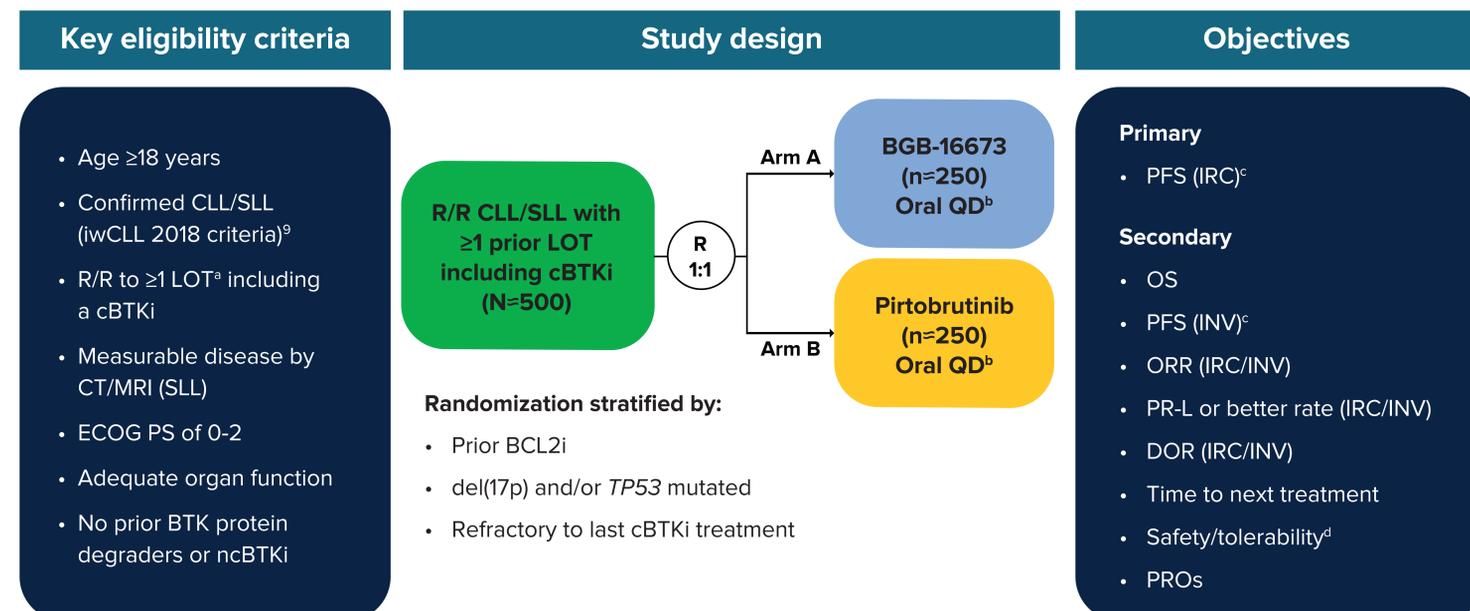
Figure 1. CaDAnCe-304 Study Sites (Planned)



METHODS

- CaDAnCe-304 (BGB-16673-304; NCT06973187) is an open-label, randomized, phase 3 clinical study comparing the efficacy and safety of BGB-16673 vs pirtobrutinib in patients with R/R CLL/SLL previously treated with a covalent BTK inhibitor (Figure 2)

Figure 2. CaDAnCe-304 Study Design



^aDefined as ≥2 consecutive cycles of systemic anticancer regimen. ^bTreatment continued until progressive disease or unacceptable toxicity. ^cPer modified 2018 iwCLL criteria⁹ with modification for treatment-related lymphocytosis¹⁰ for CLL and Lugano classification¹¹ for SLL. ^dPer NCI-CTCAE v5.0.

Abbreviations: BCL2i, B-cell lymphoma-2 inhibitor; BTK, Bruton tyrosine kinase; cBTKi, covalent BTK inhibitor; CLL, chronic lymphocytic leukemia; CT, computed tomography; DOR, duration of response; ECOG PS, Eastern Cooperative Oncology Group performance status; INV, investigator; IRC, independent review committee; iwCLL, International Workshop on Chronic Lymphocytic Leukemia; LOT, line of therapy; MRI, magnetic resonance imaging; ncBTKi, noncovalent BTK inhibitor; ORR, overall response rate; OS, overall survival; PFS, progression-free survival; PR-L, partial response with lymphocytosis; PRO, patient-reported outcome; QD, once daily; R, randomized; R/R, relapsed/refractory; SLL, small lymphocytic lymphoma.

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