

CaDAnCe-302, a phase 3, open-label, randomized study of BGB-16673 compared with idelalisib + rituximab (R), bendamustine + R, or venetoclax + R re-treatment in patients with chronic lymphocytic leukemia/small lymphocytic lymphoma previously exposed to both a BTK and BCL2 inhibitor

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ABSTRACT

Introduction: Novel therapies, including Bruton tyrosine kinase (BTK) inhibitors and B-cell lymphoma 2 (BCL2) inhibitors, have meaningfully improved patient outcomes in chronic lymphocytic leukemia/small lymphocytic lymphoma (CLL/SLL). However, CLL/SLL remains incurable, and most patients will experience disease relapse following a BTK or BCL2 inhibitor. 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 regression. Data from CaDAnCe-101 (BGB-16673-101, NCT05006716), an ongoing phase 1/2 study, demonstrate 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 mutations. Here, CaDAnCe-302, an ongoing phase 3 study that will evaluate the efficacy and safety of BGB-16673 monotherapy vs idelalisib + rituximab (R), bendamustine + R, or venetoclax + R re-treatment in patients with CLL/SLL previously exposed to both BTK and BCL2 inhibitors is described.

Methods: CaDAnCe-302 (BGB-16673-302, NCT06846671) is a global, open-label, randomized, phase 3 clinical study conducted across approximately 101 sites in 14 countries. Eligible patients are ≥18 years of age with a confirmed diagnosis of CLL/SLL and have relapsed after treatment with a covalent BTK inhibitor and a BCL2 inhibitor or are refractory to these treatments. Prior treatment with noncovalent BTK inhibitors is also required in regions where they are approved and available. Patients are excluded if they have prolymphocytic leukemia or history of Richter transformation, have received an autologous stem cell transplant or chimeric antigen receptor T-cell therapy in the last 3 months, or had prior exposure to any BTK protein degraders. Approximately 250 patients are planned to be enrolled and randomized 3:2 to receive either BGB-16673 once daily (arm A) or investigator's choice of idelalisib + R (for CLL only), bendamustine

+ R, or venetoclax + R re-treatment (arm B) until disease progression or intolerance. Patients in arm B will be given the option to cross over to BGB-16673 treatment after confirmation of progressive disease by both the investigator (INV) and independent review committee (IRC). The primary endpoint is progression-free survival (PFS), as determined by IRC per modified 2018 International Workshop on CLL criteria (for CLL) or Lugano classification (for SLL). Secondary endpoints include overall survival, PFS in patients with prior exposure to noncovalent BTK inhibitors by IRC, PFS by INV, overall response rate by IRC and INV, rate of partial response with lymphocytosis or higher by IRC and INV, duration of response by IRC and INV, time to next treatment, and safety/tolerability per National Cancer Institute Common Terminology Criteria for Adverse Events v5.0. Recruitment is ongoing.