# Bruton Tyrosine Kinase Degrader BGB-16673 in BTK Inhibitor–Naive Patients With CLL/SLL and Other B-Cell Malignancies: Results From the Phase 1 CaDAnCe-101 Study

PS1693

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CaDAnCe-101

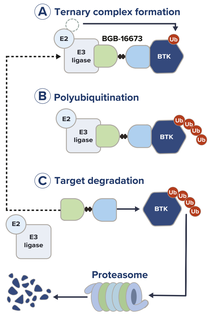
## CONCLUSIONS

- In the first report of BTK degrader clinical activity in a BTK inhibitor–naive population, novel BTK degrader BGB-16673 was well tolerated
  - BTK inhibitor–naive patients had fewer grade ≥3 TEAEs compared with heavily pretreated BTK inhibitor–exposed cohorts[11,12]
  - No cases of major hemorrhage, opportunistic infections (including invasive fungal infections), or febrile neutropenia were reported
- BGB-16673 shows promising antitumor activity in BTK inhibitor–naive patients with CLL/SLL
  - A high response rate was observed and all responses were ongoing at data cutoff
  - Response rates were consistent in patients with high-risk disease features, including del(17p) and/or *TP53* mutation and unmutated IGHV
- These encouraging safety and efficacy results could inform future clinical trials

## INTRODUCTION

- BGB-16673 is a potential first-in-class oral Bruton tyrosine kinase (BTK) degrader that induces BTK degradation through the proteasome pathway, leading to tumor regression[1] (**Figure 1**)
  - Degrades both wild-type and mutant BTK, with the broadest activity among BTK-targeting agents[1,2]
  - Disrupts both BTK kinase activity and its scaffolding-mediated signaling, unlike BTK inhibitors that block kinase activity alone[3,4]
  - Degrades multiple BTK proteins with a single molecule[4]
  - Drives robust clinical responses across several relapsed/refractory (R/R) B-cell malignancies[5]
- These mechanistic advantages support evaluating BGB-16673 in BTK inhibitor–naive patients, with the potential to reduce treatment intolerance and resistance seen with BTK inhibitors[6-9]
- Here we report, for the first time, safety and efficacy results of BGB-16673 in BTK inhibitor–naive patients with B-cell malignancies in the CaDAnCe-101 study

### Figure 1. BGB-16673 Mechanism of Action

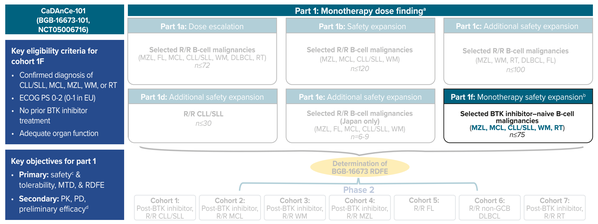



**Abbreviations:** BTK, Bruton tyrosine kinase; ub, ubiquitin.

## METHODS

- CaDAnCe-101 (BGB-16673-101; NCT05006716) is an ongoing open-label, phase 1/2 trial (**Figure 2**)
- BGB-16673 was administered orally at 200 mg once daily

### Figure 2. CaDAnCe-101 Study Design




[a]Data from gray portions of the figure are not included in this presentation. [b]Treatment was administered until progression, intolerance, or other criteria were met for treatment discontinuation. [c]Safety was assessed according to the National Cancer Institute Common Terminology Criteria for Adverse Events v5.0 with iwCLL hematologic toxicity criteria (CLL). [d]Response rates were assessed after 12 weeks per Lugano 2014 criteria for MCL, MZL SLL and RT, per iwCLL 2018 criteria with partial response with lymphocytosis modification for CLL, and after 4 weeks per modified IWWM-11 criteria for WM[10].

**Abbreviations:** BTK, Bruton tyrosine kinase; cBTK, covalent Bruton tyrosine kinase; CLL/SLL, chronic lymphocytic leukemia/small lymphocytic lymphoma; ECOG PS, Eastern Cooperative Oncology Group performance status; IWWM, International Workshop on Waldenström Macroglobulinemia; iwCLL, International Workshop on Chronic Lymphocytic Leukemia; MCL, mantle cell lymphoma; MTD, maximum tolerated dose; MZL, marginal zone lymphoma; PD, pharmacodynamics; PK, pharmacokinetics; QD, once daily; RDFE, recommended dose for expansion; RT, Richter transformation; WM, Waldenström macroglobulinemia.

## RESULTS

- As of December 15, 2025, 54 patients with chronic lymphocytic leukemia/small lymphocytic lymphoma (CLL/SLL; n=29), marginal zone lymphoma (MZL; n=10), mantle cell lymphoma (MCL; n=8), Waldenström macroglobulinemia (WM; n=5), and Richter transformation (RT; n=2) had been enrolled and received BGB-16673
- Patients had a median age of 68 (range, 42-81) years, and a median of 2 (range, 1-9) prior lines of therapy for patients with R/R disease (**Table 1**)
- Median study follow-up was 8.3 (range, 0.4-12.8) months

### Table 1. Baseline Patient Characteristics

| Characteristic | Total (N=54) |
|---|---|
| **Age, median (range), years** | 68 (42-81) |
| **Male, n (%)** | 38 (70.4) |
| **ECOG PS, n (%)** | |
| 0 | 27 (50.0) |
| 1 | 23 (42.6) |
| 2 | 4 (7.4) |
| **Disease status, n (%)** | |
| Treatment naive | 13 (24.1) |
| Treatment-naive CLL/SLL | 11 (37.9) |
| Relapsed or refractory | 41 (75.9) |
| Relapsed or refractory CLL/SLL | 18 (62.1) |
| **Disease type, n (%)** | |
| CLL/SLL | 29 (53.7) |
| MCL | 8 (14.8) |
| MZL | 10 (18.5) |
| WM | 5 (9.3) |
| RT | 2 (3.7) |
| **Bulky disease LDi ≥5 cm, n (%)** | 16 (29.6) |
| **No. of prior lines of therapy, median (range)** | 2 (1-9) |
| **Prior therapy in previously treated patients, n/N (%)** | |
| Anti-CD20 monoclonal antibodies | 41/41 (100) |
| Chemotherapy | 40/41 (97.6) |
| BCL2 inhibitors | 4/41 (9.8) |
| **CLL/SLL risk features, n/N (%)[a,b]** | |
| Binet stage C (CLL) | 6/26 (23.1) |
| Unmutated IGHV | 6/6 (100) |
| del(17p) and/or *TP53* mutation | 8/25 (32.0) |
| Complex karyotype (≥3 abnormalities) | 1/4 (25.0) |

[a]Percentages are calculated based on the number of patients with CLL/SLL. [b]No *BTK* mutations were reported in patients with available *BTK* mutation data.
**Abbreviations:** CLL/SLL, chronic lymphocytic leukemia/small lymphocytic lymphoma; ECOG PS, Eastern Cooperative Oncology Group performance status; IGHV, immunoglobulin heavy chain variable region; LDi, longest diameter; MCL, mantle cell lymphoma; MZL, marginal zone lymphoma; RT, Richter transformation; WM, Waldenström macroglobulinemia.

## Safety

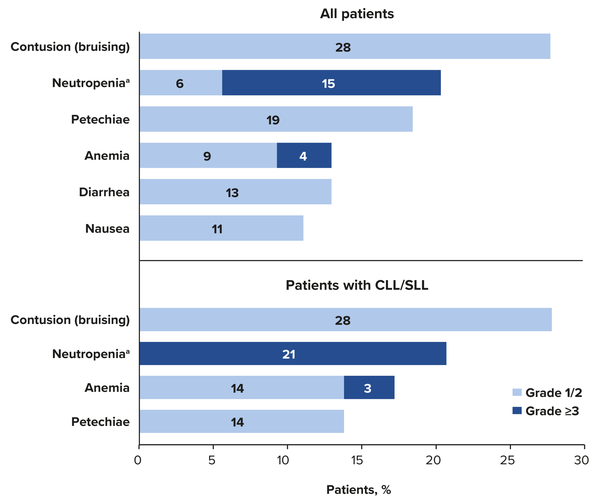
- Overall, 83.3% of patients experienced a treatment-emergent adverse event (TEAE) of any grade, and 33.3% experienced a grade ≥3 TEAE (**Table 2**)
  - Median duration of exposure was 8.1 (range, 0.4-12.8) months
- The most common any-grade TEAEs in all patients were contusion (bruising; 27.8%), neutropenia/neutrophil count decreased (20.4%), and petechiae (18.5%) (**Figure 3**); the most common grade ≥3 TEAE was neutropenia/neutrophil count decreased (14.8%)
  - In patients with CLL/SLL, the most common grade ≥3 TEAE was neutropenia/neutrophil count decreased (20.7%) (**Figure 3**)
  - One patient with MCL developed grade 3 paroxysmal atrial fibrillation, which resolved to sinus rhythm
  - No cases of major hemorrhage, opportunistic infections (including invasive fungal infections), or febrile neutropenia occurred
  - Grade 3 infections were reported in 3 patients (5.6%), and no grade 4 or 5 infections occurred
- One TEAE led to treatment discontinuation and death due to metastatic neoplasm; one additional TEAE led to treatment discontinuation due to exacerbation of chronic back pain

### Table 2. Overall Safety Summary

| Patients, n (%) | Total (N=54) |
|---|---|
| **TEAE** | 45 (83.3) |
| Treatment-related | 35 (64.8) |
| Grade ≥3 | 18 (33.3) |
| Treatment-related | 13 (24.1) |
| Serious | 6 (11.1) |
| Treatment-related | 2 (3.7) |
| Leading to dose interruption | 10 (18.5) |
| Treatment-related | 5 (9.3) |
| Leading to dose reduction | 0 |
| Treatment-related | 0 |
| Leading to treatment discontinuation | 2 (3.7) |
| Treatment-related | 0 |
| Leading to death | 1 (1.9) |
| Treatment-related | 0 |

**Abbreviation:** TEAE, treatment-emergent adverse event.

### Figure 3. TEAEs in ≥10% of Patients




[a]Neutropenia combines preferred terms *neutropenia* and *neutrophil count decreased*. The values of any-grade TEAEs have been calculated from individual grade 1/2 and grade ≥3 values rounded to the nearest whole number.
**Abbreviations:** CLL/SLL, chronic lymphocytic leukemia/small lymphocytic lymphoma; TEAE, treatment-emergent adverse event.

## Efficacy

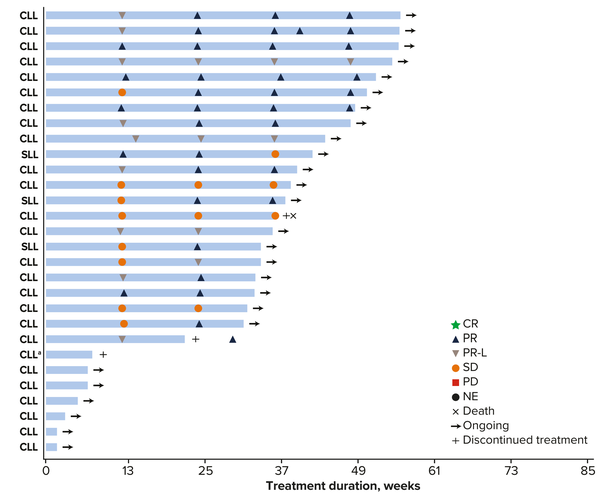
- Efficacy is only reported for patients with CLL/SLL at this time, due to small sample sizes in other cohorts
- In 22 evaluable patients with CLL/SLL, the overall response rate (ORR) was 86.4%, with a median follow-up of 8.2 (range, 0.4-12.8) months (**Table 3**; **Figure 4**)
  - Responses were ongoing in all 19 patients who responded at data cutoff
- Median time to first response was 2.8 (range, 2.7-5.6) months, around the time of first disease assessment, and median time to best response was 5.5 (range, 2.7-6.8) months
- Responses occurred in 4 of 6 evaluable patients (66.7%) with del(17p) and/or *TP53* mutation; the other two patients remain on treatment with stable disease. Responses occurred in all 4 evaluable patients with unmutated IGHV
- No PFS events were observed at 6 months
- BTK degradation data in peripheral blood were available for 44 patients; all showed complete BTK degradation at steady state

### Table 3. Summary of Best Overall Response in Patients With CLL/SLL

| | CLL/SLL (n=22) |
|---|---|
| **Best overall response, n (%)** | |
| CR | 0 |
| PR | 15 (68.2) |
| PR-L | 4 (18.2) |
| SD | 3 (13.6) |
| PD | 0 |
| **Overall response rate, n (%)[a]** | 19 (86.4) |

[a]Proportion of patients who achieved a best overall response of PR-L or better.
**Abbreviations:** CLL/SLL, chronic lymphocytic leukemia/small lymphocytic lymphoma; CR, complete response; PD, progressive disease; PR, partial response; PR-L, partial response with lymphocytosis; SD, stable disease.

### Figure 4. Treatment Duration and Responses in Patients With CLL/SLL




[a]Treatment discontinued due to withdrawal of consent by the patient.
**Abbreviations:** CLL, chronic lymphocytic leukemia; CR, complete response; NE, not estimable; PD, progressive disease; PR, partial response; PR-L, partial response with lymphocytosis; SD, stable disease; SLL, small lymphocytic lymphoma.

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## DISCLOSURES

**AMF**: Honoraria: Janssen, BeOne Medicines, Ltd; Consulting or advisory role: Janssen, BeOne Medicines, Ltd, AstraZeneca, AbbVie, Lilly; Travel, accommodations, expenses: Janssen, BeOne Medicines, Ltd, AstraZeneca, AbbVie, Lilly. **AC**: Honoraria: Johnson & Johnson, AbbVie, Regeneron, AstraZeneca, Knight Therapeutics, Lilly; Consulting or advisory role: Johnson & Johnson, AstraZeneca, Ipsen; Research funding: Johnson & Johnson, AbbVie, Regeneron, AstraZeneca, Roche, BeOne Medicines, Ltd, Pfizer, BMS; Travel, accommodations, expenses: Johnson & Johnson, AbbVie, Takeda, Roche, AstraZeneca. **ML**: Consulting or advisory role: Janssen, BeOne Medicines, Ltd, Sobi; Speakers bureau: Janssen, BeOne Medicines, Ltd, AbbVie. **CS**: Consulting or advisory role: AstraZeneca, MSD, Janssen-Cilag; Speakers bureau: AbbVie, AstraZeneca, Lilly; Travel, accommodations, expenses: AbbVie, AstraZeneca. **CYC**: Consulting, advisory board, honoraria: Roche, Janssen, Gilead, AstraZeneca, Lilly, BeOne Medicines, Ltd, Menarini, Dizal, AbbVie, Genmab, Sobi, CRISPR Therapeutics, BMS, Regeneron; Speakers bureau: Janssen, AstraZeneca, BeOne Medicines, Ltd, Genmab, AbbVie, Roche, MSD; Research funding: BMS, Roche, AbbVie, MSD, Lilly; Travel expenses: Lilly, BeOne Medicines, Ltd. **EM**: Consulting or advisory role: AbbVie. **FM**: Consultant: Roche, BMS, Gilead; Honoraria or speakers bureau: Takeda, Roche, Chugai; Data safety monitoring board or advisory board: Gilead, BMS, AbbVie. **MB-D**: Honoraria and speakers bureau: AbbVie, BMS, Incyte, Kite, Roche, AstraZeneca; Consulting and advisory role: AbbVie, Incyte, Kite, Roche, AstraZeneca; Research funding: AbbVie, Incyte, Kite, Roche; Expert testimony: Incyte, Kite, Roche; Travel, accommodations, expenses: AbbVie, BMS, Incyte, Kite, Roche, AstraZeneca. **NS**: Consulting or advisory role: Amgen, BMS, Foundation Medicine; Speakers bureau: Amgen, Takeda, Jazz Pharmaceuticals, Genentech. **YW**: Research funding (payable to institution): Incyte, InnoCare, LOXO Oncology, Lilly, MorphoSys, Novartis, Genentech, Genmab, AbbVie, BeOne Medicines, Ltd, Merck, AstraZeneca, BMS; Advisory board (payable to institution): Lilly, LOXO Oncology, TG Therapeutics, Incyte, InnoCare, Kite Pharma, Janssen, BeOne Medicines, Ltd, AstraZeneca, Genmab, AbbVie; Consultancy (payable to institution): InnoCare Pharma, AbbVie; Honoraria (payable to institution): Kite Pharma. **SR**: Employment: BeOne Medicines, Ltd, BMS: Stock or other ownership: BeOne Medicines, Ltd, BMS, Celgene. **YZ, LX, KB, SF**: Employment and may own stock: BeOne Medicines, Ltd. **IM, LM**: No disclosures.

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