Updated Efficacy and Safety Results of the Bruton Tyrosine Kinase Degrader BGB-16673 in Patients With Relapsed/Refractory Indolent Non-Hodgkin Lymphoma From the Ongoing Phase 1 CaDAnCe-101 Study

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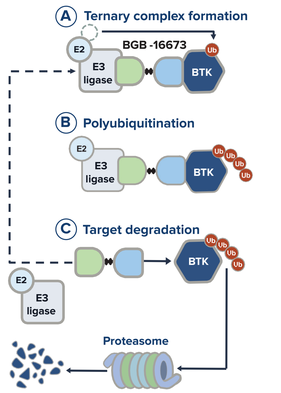
CONCLUSIONS

- Updated data from this ongoing phase 1/2 study show that the novel BTK degrader BGB-16673 was well tolerated, with a low rate of discontinuation due to TEAEs
- BGB-16673 had encouraging efficacy with a short time to response in heavily pretreated patients with NHL, including those with BTK inhibitor-resistant disease
  - The ORR was 55.6% (20/36) in patients with MZL and 37.5% (9/24) in patients with FL
  - Nine patients achieved CR (MZL, n=6; FL, n=3)
- These data support further investigation of the clinical activity of BGB-16673 in patients with MZL and FL

INTRODUCTION

- Bruton tyrosine kinase (BTK) inhibition is effective in indolent non-Hodgkin lymphoma (NHL),[1,2] but disease invariably relapses
- 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 (**Figure 1**)[3]
- 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 inhibitors[4]

Figure 1 . BGB-16673: A BTK-Targeted CDAC



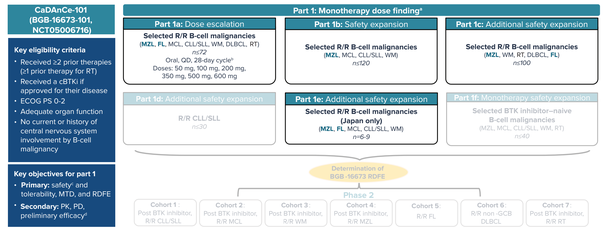
Abbreviations: BTK, Bruton tyrosine kinase; CDAC, chimeric degradation activating compound; ub, ubiquitin

- 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 (CNS) penetration[3,6]
- In a clinical study, BGB-16673 led to substantial reductions in BTK protein levels in peripheral blood and tumor tissue[7]
- Here, updated results in patients with follicular lymphoma (FL) and marginal zone lymphoma (MZL) enrolled in CaDAnCe-101 are presented

METHODS

- CaDAnCe-101 (BGB-16673-101; NCT05006716) is a phase 1/2, open-label, dose-escalation, and dose-expansion study evaluating BGB-16673 in adults with relapsed/refractory B-cell malignancies (**Figure 2**)

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 NCI-CTCAE v5.0 in all patients. [d]Response was assessed per Lugano 2014 criteria after 12 weeks.[8]

Abbreviations: BTK, Bruton tyrosine kinase; cBTKi, covalent Bruton tyrosine kinase inhibitor; CLL/SLL, chronic lymphocytic leukemia/small lymphocytic lymphoma; DLBCL, diffuse large B-cell lymphoma; ECOG PS, Eastern Cooperative Oncology Group performance status; FL, follicular lymphoma; GCB, germinal center B-cell; MCL, mantle cell lymphoma; MTD, maximum tolerated dose; MZL, marginal zone lymphoma; PD, pharmacodynamics; PK, pharmacokinetics; QD, once daily; R/R, relapsed/refractory; RDFE, recommended dose for expansion; RT, Richter transformation; WM, Waldenström macroglobulinemia.

RESULTS

- As of August 22, 2025, 24 patients with FL and 37 with MZL received BGB-16673
- Patients were heavily pretreated, with a median of 3 lines of therapy for both FL (range, 2-9) and MZL (range, 2-15) (**Table 1**)
- The median study follow-up was 6.2 months (range, 1.3-35.6 months) and 7.2 months (range, 0.3-30.8 months) in the FL and MZL groups, respectively

Table 1. Baseline Patient Characteristics

	FL (n=24)	MZL (n=37)
Age, median (range), years	70 (42-86)	73 (33-88)
Male, n (%)	18 (75.0)	19 (51.4)
ECOG PS, n (%)		
0	12 (50.0)	20 (54.1)
1	12 (50.0)	16 (43.2)
Ann Arbor stage III/IV at study entry, n/N (%)[a]	20/23 (87.0)	30/32 (93.8)
Tumor bulk, n (%)		
Longest diameter ≥5 cm	8 (33.3)	8 (21.6)
No. of prior lines of therapy, median (range)	3 (2-9)	3 (2-15)
Prior therapy, n (%)		
cBTK inhibitor	3 (12.5)	30 (81.1)
ncBTK inhibitor	1 (4.2)	4 (10.8)
BCL2 inhibitor	0	6 (16.2)
Anti-CD20–based therapy	24 (100)	37 (100)
Chemotherapy	23 (95.8)	36 (97.3)
Discontinued prior BTK inhibitor due to PD, n/N (%)	4/4 (100)	25/30 (83.3)[b]

[a]Excludes patients with unknown status. [b]Reasons for five discontinuations of BTK inhibitor aside from PD were toxicity (n=4) and other (n=1).
Abbreviations: BCL2, B-cell lymphoma 2; BTK, Bruton tyrosine kinase; cBTK, covalent Bruton tyrosine kinase; ECOG PS, Eastern Cooperative Oncology Group performance status; FL, follicular lymphoma; MZL, marginal zone lymphoma; ncBTK, noncovalent Bruton tyrosine kinase; PD, progressive disease.

Safety

- The overall safety summary is shown in **Table 2**
- The most common treatment-emergent adverse events (TEAEs) are listed in **Table 3**; across both histologies, neutropenia was the most frequently reported grade ≥3 TEAE
- Twelve patients (FL, n=2; MZL, n=10) experienced grade ≥3 infection
- Four patients in the MZL group experienced major hemorrhage (defined as grade ≥3, serious, or any CNS bleeding): intracranial (treatment related in the context of baseline lymphocytosis [376K]), subdural, gastrointestinal, and hemothorax hemorrhage (not related to treatment); n=1 each
- Atrial fibrillation (grade 1) was observed in one patient with MZL
- No patients with FL experienced a TEAE that led to treatment discontinuation or death; one patient with MZL had a TEAE that led to death

Table 2. Overall Safety Summary

Patients, n (%)	FL (n=24)	MZL (n=37)
Any TEAE	24 (100)	36 (97.3)
Any treatment-related	14 (58.3)	30 (81.1)
Grade ≥3	5 (20.8)	19 (51.4)
Treatment-related grade ≥3	2 (8.3)	14 (37.8)
Serious	2 (8.3)	14 (37.8)
Treatment-related serious	1 (4.2)	7 (18.9)
Leading to death	0	1 (2.7)
Treatment-related leading to death	0	1 (2.7)
Leading to treatment discontinuation	0	4 (10.8)
Treatment-related leading to treatment discontinuation	0	4 (10.8)
Leading to treatment modification	8 (33.3)	17 (45.9)
Dose interruption	8 (33.3)	17 (45.9)

Abbreviations: FL, follicular lymphoma; MZL, marginal zone lymphoma; TEAE, treatment-emergent adverse event.

Table 3. TEAEs in ≥4 Patients in Either Group

	FL (n=24)		MZL (n=37)	
Patients, n (%)	Any Grade	Grade ≥3	Any Grade	Grade ≥3
Fatigue	6 (25.0)	0	12 (32.4)	0
Contusion (bruising)	6 (25.0)	0	7 (18.9)	0
Diarrhea	6 (25.0)	0	7 (18.9)	0
Neutropenia[a]	2 (8.3)	2 (8.3)	9 (24.3)	7 (18.9)
Cough	3 (12.5)	0	5 (13.5)	0
Petechiae	1 (4.2)	0	7 (18.9)	0
Upper respiratory tract infection	4 (16.7)	1 (4.2)	4 (10.8)	0
Anemia	1 (4.2)	0	6 (16.2)	2 (5.4)
Thrombocytopenia[b]	2 (8.3)	1 (4.2)	5 (13.5)	2 (5.4)
Myalgia	2 (8.3)	0	4 (10.8)	0
Asthenia	0	0	5 (13.5)	2 (5.4)
Decreased appetite	0	0	5 (13.5)	0
Dyspnea	1 (4.2)	0	4 (10.8)	1 (2.7)
Headache	1 (4.2)	0	4 (10.8)	0
Lipase increased	1 (4.2)	0	4 (10.8)	0
Pyrexia	1 (4.2)	0	4 (10.8)	0

[a]Neutropenia combines preferred terms *neutrophil count decreased* and *neutropenia*. [b]Thrombocytopenia combines preferred terms *platelet count decreased* and *thrombocytopenia*.
Abbreviations: FL, follicular lymphoma; MZL marginal zone lymphoma; TEAE, treatment-emergent adverse event.

Efficacy

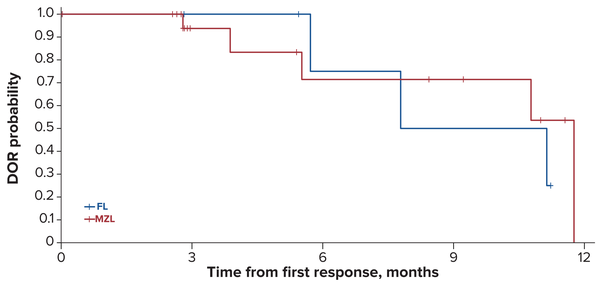
- In 24 patients with FL, the overall response rate (ORR) was 37.5% (n=9) (**Table 4**)
  - Among the nine patients with FL who had a response, three patients maintained a response for ≥6 months; of the remaining patients, five were censored and one experienced events prior to 6 months (**Figure 3**)
- In 36 response-evaluable patients with MZL, the ORR was 55.6% (n=20)
  - Among the 20 patients with MZL who had a response, six patients maintained a response for ≥6 months; of the remaining patients, 11 were censored and three experienced events prior to 6 months (**Figure 3**)
- Nine patients achieved complete response (CR; FL, n=3; MZL, n=6)
- Responses were also seen in patients with MZL who had previously received a covalent BTK inhibitor (15/30)
- Duration of response is presented in **Figure 3**; however, follow-up after response is immature at this time
- As of the data cutoff, 30 patients (FL, n=9; MZL, n=21) remained on treatment; in both groups, progressive disease was the most common reason for treatment discontinuation (FL, n=14 [58.3%]; MZL, n=10 [27.0%])

Table 4. Responses by Histology

	FL (n=24)	MZL (n=36)[a]
Best overall response, n (%)		
CR	3 (12.5)	6 (16.7)
PR	6 (25.0)	14 (38.9)
SD	6 (25.0)	10 (27.8)
PD	8 (33.3)	4 (11.1)
Discontinued prior to first assessment	0	2 (5.6)
NE	1 (4.2)	0
ORR, n (%)[b]	9 (37.5)	20 (55.6)
Time to first response, median (range), months[c]	2.7 (2.6-2.8)	2.8 (2.6-2.9)

[a]Efficacy-evaluable population; one patient was too early in the treatment course to be response-evaluable. [b]Includes best overall responses of PR or CR. [c]In patients with best overall response better than SD.
Abbreviations: CR, complete response; FL, follicular lymphoma; MZL, marginal zone lymphoma; NE, not estimable; ORR, overall response rate; PD, progressive disease; PR, partial response; SD, stable disease.

Figure 3. DOR in Patients With R/R FL or MZL



Abbreviations: DOR, duration of response; FL, follicular lymphoma; MZL, marginal zone lymphoma; R/R, relapsed/refractory.

Study Status

- Enrollment for CaDAnCe-101 phase 1 and phase 2 is ongoing at >100 study sites across the US, Canada, the UK, France, Georgia, Germany, Italy, Moldova, Spain, Sweden, Turkey, Australia, South Korea, Brazil, and Japan

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