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# Tacabrutideg (BGB-16673), a Bruton tyrosine kinase (BTK) degrader, in patients with relapsed/refractory (R/R) chronic lymphocytic leukemia/small lymphocytic lymphoma (CLL/SLL): updated safety and efficacy data from the phase 1 CaDAnCe-101 study

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**Introduction:** BTK is a key mediator of signaling pathways involved in the pathogenesis of CLL/SLL. Tacabrutideg (BGB-16673) is a potential first-in-class oral BTK degrader that induces BTK degradation through the proteasome pathway, leading to tumor

regression. Here we report updated safety and efficacy results for phase 1 of the ongoing open-label, phase 1/2 CaDAnCe-101 trial (BGB-16673-101; NCT05006716) of tacabrutideg monotherapy in patients (pts) with R/R CLL/SLL.

**Methods:** Eligible pts had R/R CLL/SLL with ≥2 prior therapies, an ECOG performance status of 0-2 (EU: 0/1), and adequate organ function. Pts in the US, EU, Japan, and Australia required prior treatment with a covalent BTK inhibitor (BTKi). Tacabrutideg was administered orally once daily. Primary phase 1 study objectives were safety/tolerability (National Cancer Institute Common Terminology Criteria for Adverse Events v5.0; International Workshop on CLL [iwCLL] hematologic toxicity criteria), maximum tolerated dose, and recommended expansion dose. Secondary objectives included the overall response rate (ORR) per iwCLL 2018 criteria with the partial response (PR) with lymphocytosis (PR-L) modification and per the 2014 Lugano criteria (SLL), with the first assessment at 12 weeks on treatment.

**Results:** As of March 25, 2026, 67 pts with R/R CLL/SLL received tacabrutideg (50 mg, n=1; 100 mg, n=22; 200 mg, n=17; 350 mg, n=15; 500 mg, n=12). Median age was 70 (range, 47-91) years, and the median number of prior lines of therapy was 4 (range, 2-10), including covalent BTKi (n=63 [94.0%]), noncovalent BTKi (n=14 [20.9%]), and BCL2 inhibitor (BCL2i; n=55 [82.1%]). At baseline, 43/56 pts (76.8%) had unmutated IGHV, 24/66 (36.4%) had del(17p), 40/67 (59.7%) had *TP53* mutation, and 23/43 (53.5%) had complex karyotype (≥3 abnormalities); among 66 pts with available data, gene mutations were detected in 25 (37.9%) for *BTK*, 10 (15.2%) for *PLCG2*, and 23 (34.8%) for *BCL2*. Median study follow-up was 25.4 (range, 0.3-41.0) months, and 33 pts (49.3%) remained on treatment at data cutoff.

Median tacabrutideg exposure was 19.2 (range, 0.2-37.3) months. Any-grade treatment-emergent adverse events (TEAEs) occurred in 97.0% of pts; those in ≥25% were fatigue (37.3%), contusion (bruising; 32.8%), diarrhea (32.8%), and neutropenia/neutrophil count decreased (29.9%). Examining the frequencies of new or ongoing any-grade TEAEs during the time period of 0 to <12 months compared with 12

to <24 months, the rates of diarrhea (28.4% vs 8.3%) and neutropenia/neutrophil count decreased (26.9% vs 14.6%), respectively, decreased in the second year. Grade ≥3 TEAEs occurred in 64.2% of pts.

All 67 pts were evaluable; the ORR (≥PR-L) was 85.1% (n=57), the ≥PR rate was 80.6% (n=54), and the complete response (CR)/CR with incomplete marrow recovery rate was 3.0% (n=2). At the 200-mg dose, the ORR was 94.1% (16/17), with 1 CR. Median time to first response was 2.8 (range, 2.0-19.4) months, and median duration of response was 20.6 (range, 0-33.1) months. Responses were seen in pts previously treated with covalent BTKi and BCL2i (93.0% [40/43]) and in those treated with covalent BTKi, BCL2i, and noncovalent BTKi (75.0% [9/12]). Pts with disease refractory to both last covalent BTKi and last BCL2i had a response rate of 82.9% (29/35). Of 8 pts refractory to last covalent BTKi, last noncovalent BTKi, and last BCL2i, the ORR was 62.5% (5/8), with 4 PRs and 1 PR-L.

Responses occurred in pts with unmutated IGHV (88.4% [38/43]), del(17p) (70.8% [17/24]), *TP53* mutation (82.5% [33/40]), complex karyotype (73.9% [17/23]), *BTK* mutation (76.0% [19/25]), *PLCG2* mutation (90.0% [9/10]), and *BCL2* mutation (95.7% [22/23]). Median progression-free survival (PFS) was 24.2 (range, 0-35.9) months; 25 pts (37.3%) had PD, and 5 (7.5%) died. The 24-month overall survival (OS) rate was 79.1% (95% CI, 66.6%-87.4%).

**Conclusions:** Tacabrutideg led to durable responses with a manageable safety profile in pts with R/R CLL/SLL, including in pts with difficult-to-treat disease. Disease control was durable with a sustained PFS and promising OS. Tacabrutideg 200 mg daily is being evaluated in ongoing phase 2 and 3 studies in R/R CLL/SLL.