Activity of Zanubrutinib in Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma

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Abstract 30056

COI disclosure

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- This study has been approved by the local IRB.

Background

- CLL/SLL is a B-cell malignancy characterized by progressive accumulation of leukemic cells in the peripheral blood, bone marrow, and lymphoid tissues[1]
- The BTK inhibitor zanubrutinib significantly improved PFS vs BR in patients with TN CLL/SLL[2] and has shown superior efficacy and improved safety outcomes compared with ibrutinib in patients with R/R CLL/SLL[3]
- BGB-3111-111 (NCT04172246) is an ongoing, multicenter, open-label phase 1/2 study to assess the safety and efficacy of zanubrutinib in Japanese patients with mature B-cell malignancies

Here, we present efficacy assessed by INV and safety data on zanubrutinib for Japanese patients with CLL/SLL in the BGB-3111-111 study, along with data from global zanubrutinib studies with comparable follow-up times

- Data presented here are updated from the abstract to the 2023 DCO

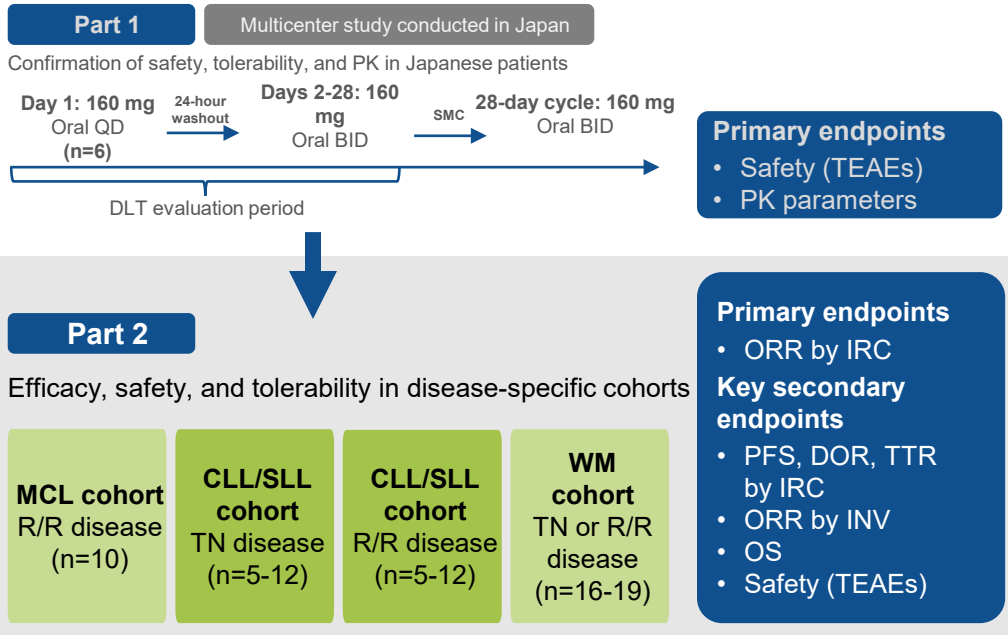
BR, bendamustine and rituximab; BTK, Bruton tyrosine kinase; CLL/SLL, chronic lymphocytic leukemia/small lymphocytic lymphoma; DCO, data cut-off; INV, investigator; PFS, progression-free survival; R/R, relapsed or refractory; TN; treatment naive.

1. Zelenetz AD, et al. *J Natl Compr Canc Netw*. 2015;13(3):326-362; 2. Tam C, et al. *Lancet Oncol*. 2022;23(8):1031-1043;
3. Brown JR. *N Engl J Med*. 2023;388(4):319-332.

Study design

Key eligibility criteria

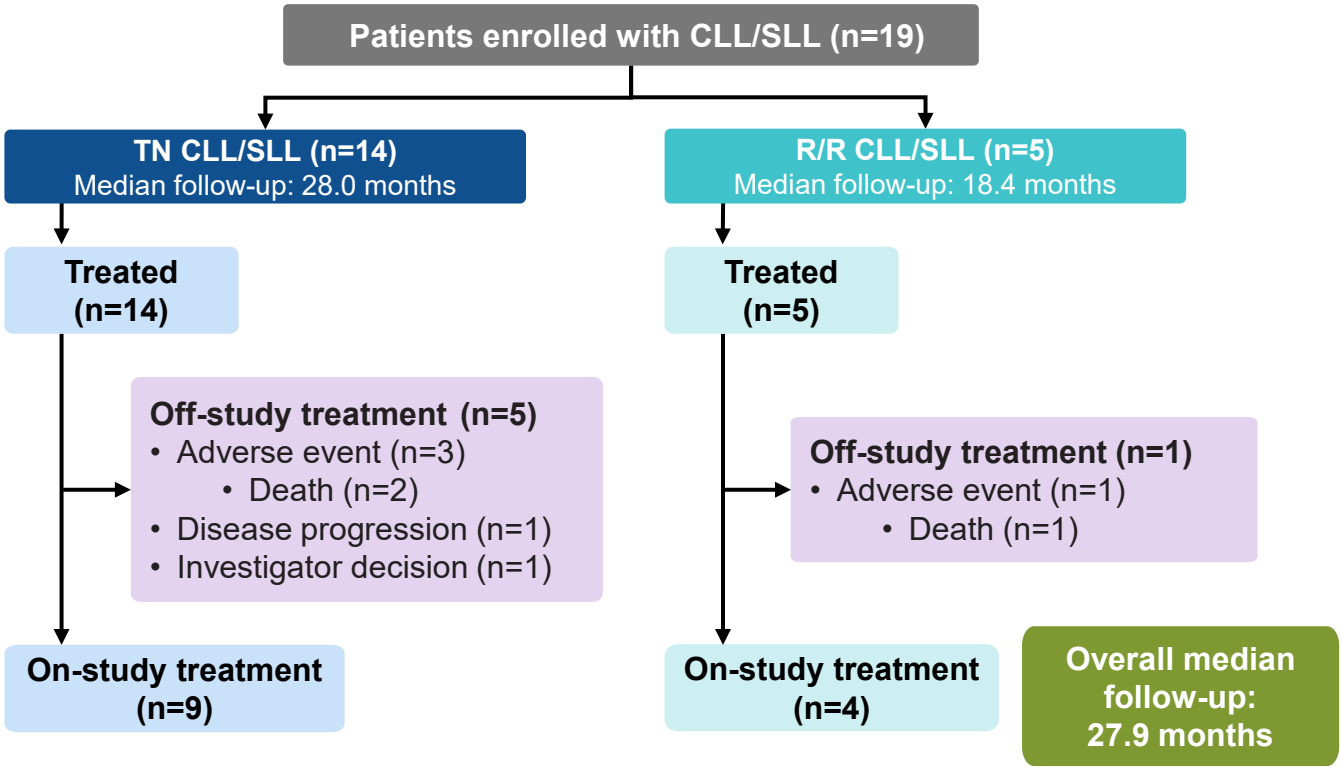
- Japanese
- Age ≥20 years
- ECOG PS of 0-2
- Confirmed diagnosis of mature B-cell neoplasms (CLL/SLL, MCL, FL, MZL, or WM)
- Measurable disease[a]
- No prior systemic chemotherapy or radiation therapy within 2 weeks prior to first dose of zanubrutinib
- No prior alloSCT or therapy with B-cell receptor inhibitor or BCL2 inhibitor



alloSCT, allogeneic stem cell transplant; BCL2, B-cell lymphoma 2; BID, twice daily; DLT, dose-limiting toxicity; CLL/SLL, chronic lymphocytic leukemia/small lymphocytic lymphoma; DOR, duration of response; ECOG PS, Eastern Cooperative Oncology Group performance status; FL, follicular lymphoma; INV, investigator; IRC, independent review committee; MCL, mantle cell lymphoma; MZL, marginal zone lymphoma; ORR, overall response rate; OS, overall survival; PFS, progression-free survival; PK, pharmacokinetics; QD, once daily; R/R, relapsed or refractory; SMC, safety monitoring committee; TEAE, treatment-emergent adverse event; TN, treatment naive; TTR, time to response; WM, Waldenström macroglobulinemia.

[a] MCL, WM, MZL, and FL only

Patient disposition



CLL/SLL, chronic lymphocytic leukemia/small lymphocytic lymphoma; R/R, relapsed or refractory; TN, treatment naive.

Baseline characteristics

Characteristics	Japanese TN (n=14)	SEQUOIA global TN[1] (n=241)[a]	Japanese R/R (n=5)	ALPINE global R/R[2] (n=327)[b]
Age, median (range), years	67.5 (38-77)	70 (40-86)[c]	72.0 (52-77)	67 (35-90)
<65 years, n (%)	6 (42.9)	45 (18.7)	1 (20.0)	126 (38.5)
≥65 years, n (%)	8 (57.1)	196 (81.3)	4 (80.0)	201 (61.5)
Sex, n (%)				
Male	10 (71.4)	154 (63.9)	4 (80.0)	213 (65.1)
Female	4 (28.6)	87 (36.1)	1 (20.0)	114 (34.9)
ECOG PS, n (%)				
0	12 (85.7)	110 (45.6)	5 (100)	129 (39.4)
≥1	2 (14.3)	131 (54.4)	0	198 (60.6)
No. of prior lines of therapy in patients with R/R disease, median (range)	–	–	2.0 (1-4)	1.0 (1-6)

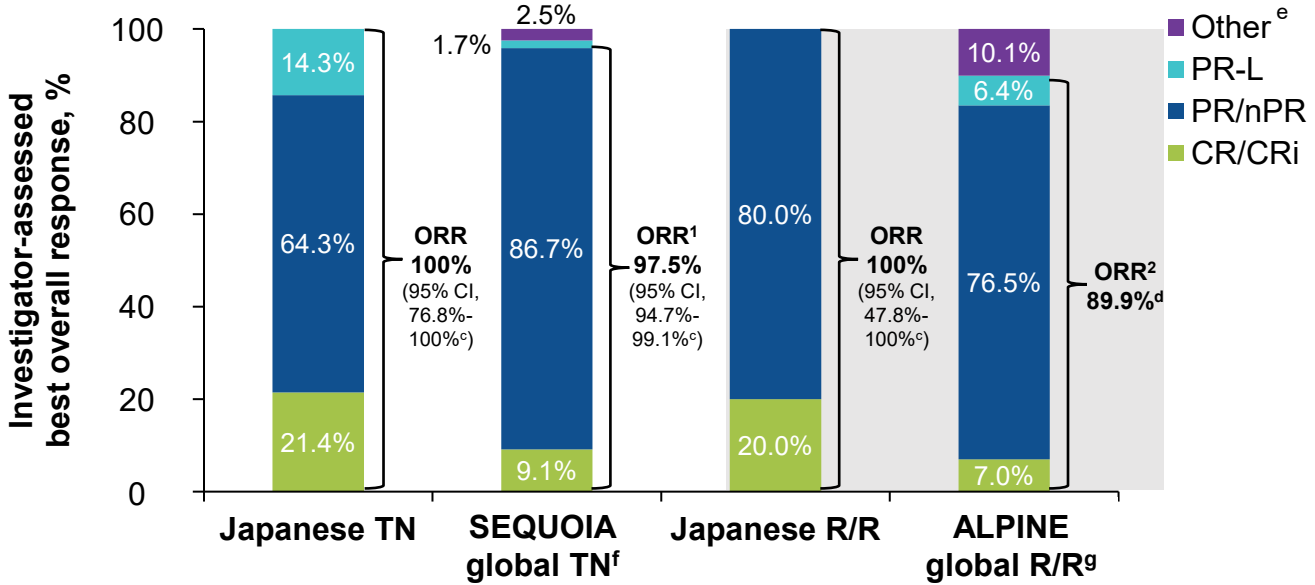
CLL/SLL, chronic lymphocytic leukemia/small lymphocytic lymphoma; ECOG PS, Eastern Cooperative Oncology Group performance status; R/R, relapsed or refractory; TN, treatment naive.

[a] Patients without del(17p) randomized to receive zanubrutinib treatment. [b] Patients randomized to receive zanubrutinib treatment.

[c] Unpublished data.

1. Tam CS, et al. *Lancet Oncol*. 2022;23(8):1031-1043; 2. Brown JR, et al. *N Engl J Med*. 2023;388(4):319-332.

ORR[a] was 100% for both the Japanese TN and R/R cohorts[b]



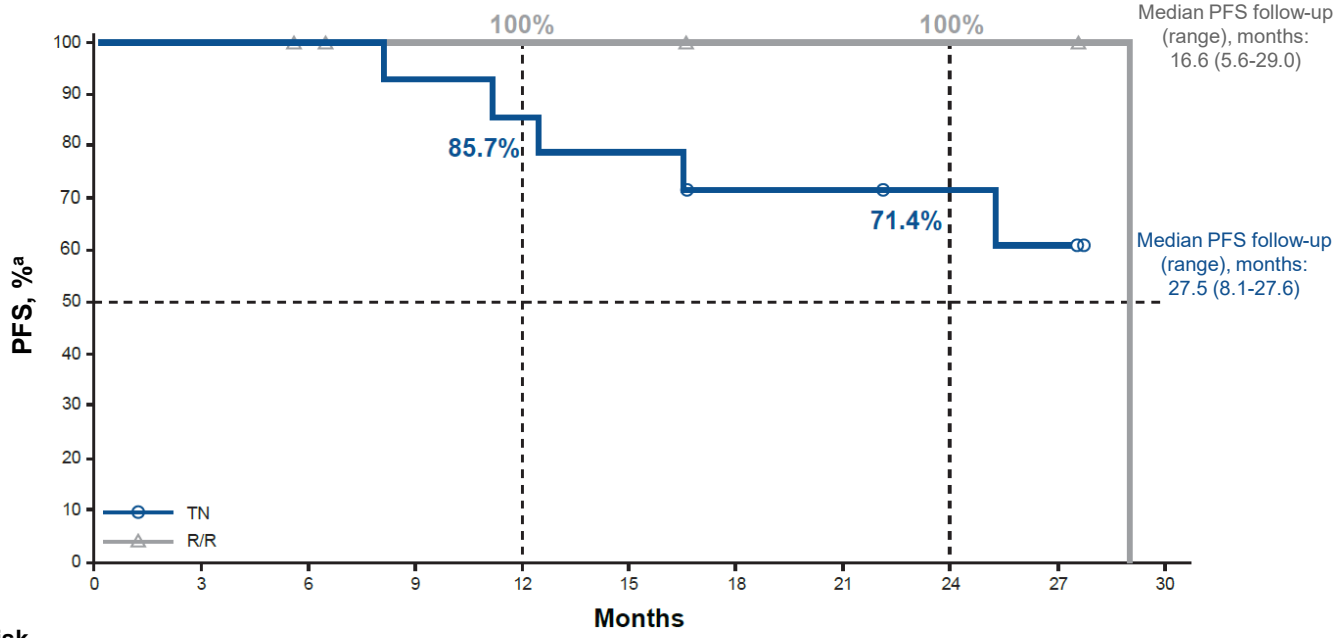
	Japanese TN	SEQUOIA global TN[f]	Japanese R/R	ALPINE global R/R[g]
Sample size	**n=14**	**n=241[h]**	**n=5**	**n=327[i]**
Median follow-up, mo	**28.0**	**26.2[1]**	**18.4**	**29.6[2]**

CLL, chronic lymphocytic leukemia; CR, complete response; CRi, CR with incomplete bone marrow recovery; ORR, overall response rate; PR, partial response; PR-L, partial response with lymphocytosis; PD, progressive disease; R/R, relapsed/refractory; SD, stable disease; TN, treatment naive.

[a] PR-L or better. [b] No CRi, SD, or PD was reported. [c] Estimated using the Clopper-Pearson method. [d] 95% CI not presented in the paper. [e] Other includes patients with SD or PD or regarded as not evaluable or discontinued prior to first assessment. [f] Patients without del(17p) randomized to receive zanubrutinib treatment. [g] Patients randomized to receive zanubrutinib treatment. [h] Includes 3 patients who discontinued before the first assessment. [i] Includes 9 patients who discontinued before the first assessment.

1. Tam CS, et al. *Lancet Oncol*. 2022;23(8):1031-1043; 2. Brown JR, et al. *N Engl J Med*. 2023;388(4):319-332.

50% PFS was not reached in either the TN or R/R subgroup



No. at risk

TN	14	14	14	13	12	11	8	8	7	6	0
R/R	5	5	4	3	3	3	2	2	2	2	0

PFS, progression-free survival; R/R, relapsed or refractory; TN, treatment naive.

[a] PFS rates were estimated by Kaplan-Meier method, with 95% CIs estimated using the Greenwood formula.

The most common (≥15%) TEAEs primarily occurred at lower grades

	TN (n=14)		R/R (n=5)		All (n=19)	
n (%)	Any grade	Grade ≥3	Any grade	Grade ≥3	Any grade	Grade ≥3
≥1 TEAE	14 (100.0)	7 (50.0)	4 (80.0)	1 (20.0)	18 (94.7)	8 (42.1)
COVID-19	4 (28.6)	0	1 (20.0)	0	5 (26.3)	0
Anemia	3 (21.4)	0	1 (20.0)	0	4 (21.1)	0
Constipation	3 (21.4)	0	1 (20.0)	0	4 (21.1)	0
Dental caries	2 (14.3)	0	2 (40.0)	1 (20.0)	4 (21.1)	1 (5.3)
Neutrophil count decreased	2 (14.3)	2 (14.3)	1 (20.0)	1 (20.0)	3 (15.8)	3 (15.8)
Platelet count decreased	3 (21.4)	3 (21.4)	0	0	3 (15.8)	3 (15.8)
Pyrexia	3 (21.4)	0	0	0	3 (15.8)	0

R/R, relapsed or refractory; TEAE, treatment-emergent adverse event; TN, treatment naive.

Rates of atrial fibrillation/flutter were low and similar to those found in the SEQUOIA and ALPINE studies[1,2]

Patients, n (%)	Japanese TN (n=14)	SEQUOIA global TN[1] (n=240)[a]	Japanese R/R (n=5)	ALPINE global R/R[2] (n=324)[b]
Any TEAE of special interest	12 (85.7)	207 (86.3)	4 (80.0)	294 (90.7)
Infections	10 (71.4)	149 (62.1)	3 (60.0)	231 (71.3)
Hemorrhage	6 (42.9)	108 (45.0)	2 (40.0)	137 (42.3)
Anemia	3 (21.4)	11 (4.6)	1 (20.0)	50 (15.4)
Neutropenia	3 (21.4)	38 (15.8)	1 (20.0)	95 (29.3)
Thrombocytopenia	3 (21.4)	11 (4.6)	0	42 (13.0)
Second primary malignancies	2 (14.3)	31 (12.9)	1 (20.0)	40 (12.3)
Atrial fibrillation and flutter	1 (7.1)	8 (3.3)	0	17 (5.2)
Hypertension	0	34 (14.2)	0	76 (23.5)

CLL/SLL, chronic lymphocytic leukemia/small lymphocytic lymphoma; R/R, relapsed or refractory; TEAE, treatment-emergent adverse event; TN, treatment naive.

[a] Zanubrutinib-treated patients without del(17p). [b] Zanubrutinib-treated patients.

1. Tam CS, et al. *Lancet Oncol*. 2022;23(8):1031-1043; 2. Brown JR, et al. *N Engl J Med.* 2023;388(4):319-332.

Conclusions

- Zanubrutinib was safe and effective in Japanese patients with CLL/SLL in the BGB-3111-111 study
- Efficacy results and safety profile were consistent with results from the global SEQUOIA and ALPINE studies in patients with TN CLL/SLL and R/R CLL/SLL, respectively
- These results support the use of zanubrutinib as a treatment option for Japanese patients with CLL/SLL in both the TN and R/R setting

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