Patient-Reported Outcomes (PRO) among Patients with Previously Treated Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma (CLL/SLL) receiving Pirtobrutinib: Final Analysis from the BRUIN Phase 1/2 Study

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OBJECTIVE

The final patient-reported outcome (PRO) endpoint analyses are presented here from patients enrolled in the BRUIN study with relapsed or refractory (R/R) CLL treated with at least two prior regimens, including a covalent BTKi (cBTKi).

CONCLUSION

- The final analysis of the BRUIN Phase 1/2 trial demonstrated that each PRO endpoint evaluated remained consistently stable or improved over time in more than 80% of patients with R/R CLL/SLL
- Results are consistent with the interim findings as well as the BRUIN-321 results[1,2,3] demonstrating the consistent benefits from the patient perspective on these outcomes
- Data are limited by the number of patients available to complete PRO instrument limiting the ability to evaluate outcomes beyond Cycle 31.
- While this is a single arm trial, the data demonstrate that patients report clinically meaningful favorable outcomes during treatment with pirtobrutinib.

International Workshop on Chronic Lymphocytic Leukemia; Krakow, Poland; Sept 12-15 – 2025

BACKGROUND

- Pirtobrutinib is a highly selective, non-covalent Bruton tyrosine kinase inhibitor (BTKi) and is approved in the US for the treatment of patients with chronic lymphocytic leukemia/small lymphocytic lymphoma (hereafter, CLL) after at least two prior lines of therapy that includes a BTKi and a BCL-2i.
- BRUIN 18001 (NCT03740529) was an open-label, multi-center phase 1/2 study that investigated the safety and efficacy of pirtobrutinib for the treatment of B-cell malignancies, including CLL.
- Interim results from the July 2022 data cut demonstrated that HRQoL and symptoms were stable or improved for over 70% of patients with pretreated R/R CLL/SLL during the first 24 cycles of pirtobrutinib treatment[1].

METHODS AND ANALYSIS

- The data analyzed in this study were from a January 2025 data cut of the BRUIN trial.
- PRO data were collected at each in-person clinic visit using paper forms.
- Patient-reported physical functioning (PF) and Global Health Status/Quality of Life (GHS/QoL) were measured using the European Organization for Research and Treatment of Cancer (EORTC) Quality of Life Questionnaire Core-30 (QLQ-C30).
- CLL/SLL-related symptoms were assessed using the EORTC Item Library (IL) 87 and fatigue was evaluated using 3 fatigue items from the QLQ-C30 plus the IL63 item set.
- All scales are scored 0-100
- Higher scores represent better PF and GHS/QoL; while lower scores represent fewer CLL/SLL-related symptoms and fatigue.
- Predefined thresholds for meaningful change are presented in **Table 1**

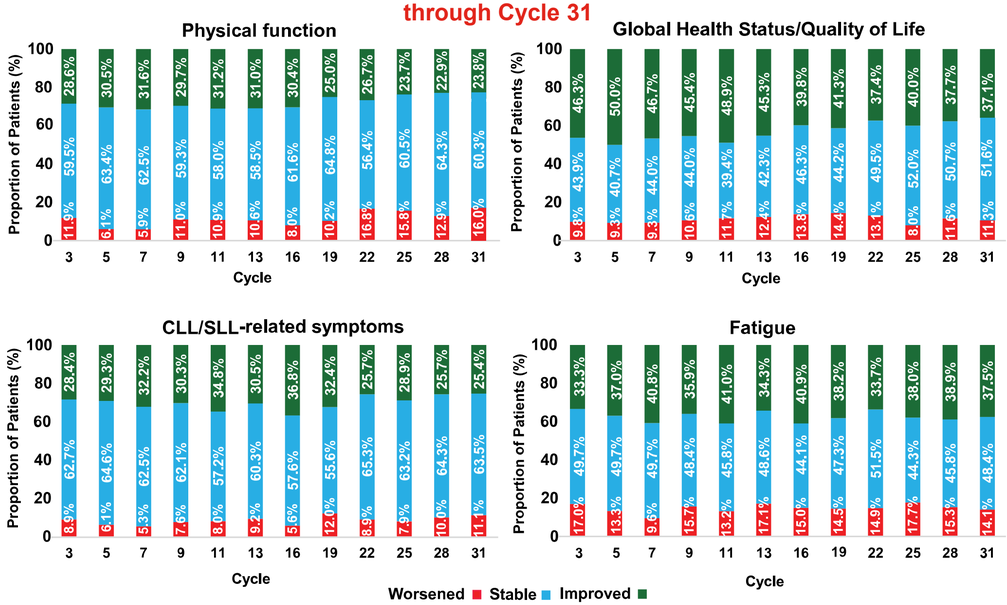
Table 1. Thresholds of minimal clinically important difference (MCID)

	MCID for patient-level changes[a]		MCID for within-group changes[b,4]
PRO	**Improvement**	**Worsening**	**Improvement**
CLL/SLL-related Symptoms	-15.38	+10.25	-4.0
Fatigue	-16.66	+11.11	-4.0
Physical function	+13.33	-13.33	+2.0
GHS/QoL	+16.66	-16.66	+5.0
Role function	+16.66	-16.66	+6.0

[a]Time to event analyses, [b]Longitudinal analyses

RESULTS

Figure 1. Proportion of Patients who improved, remained stable, or worsened from Baseline through Cycle 31



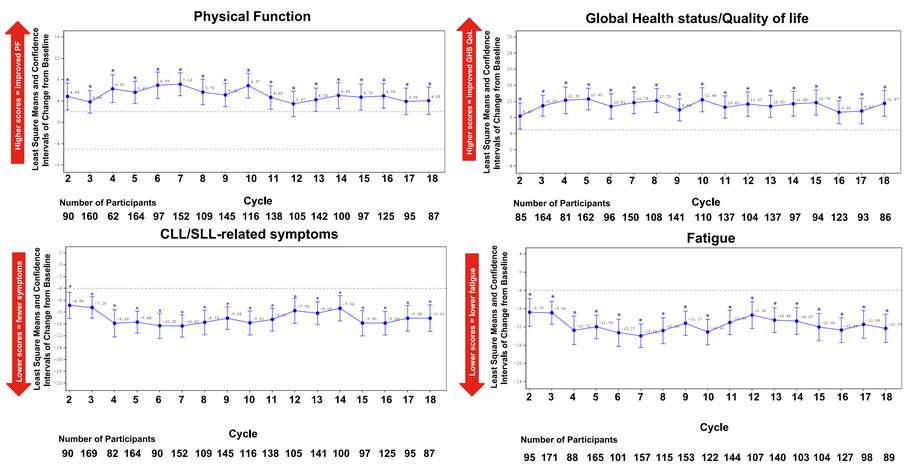
- Most patients reported stable or clinically improved PROs at each of the post-baseline visits through Cycle 31 **(Fig 1).**
- Results from longitudinal analysis show consistent clinically meaningful and statistically significant improvement ($p<0.05$) from baseline in patient-reported PF, CLL/SLL-related symptoms, fatigue and GHS/QoL over time **(Fig 2).**

Table 2. Patient demographics and clinical characteristics

Variable	Total N=263
Median (IQR) Age at baseline, years	68 (62.0-74.0)
Male	68.1%
Median (IQR) Follow-up duration, mos	46.5 (35.5-54.7)
Region, n (%)	
Europe	64 (24.3)
North America	186 (70.7)
Other	13 (5.0)
IGHV status, n (%)	
Mutated	30 (11.4)
Unmutated	181 (68.8)
Failed Test	8 (3.0)
Missing	44 (16.7)

- 263 patients with R/R CLL treated with at least two prior regimens, including a covalent BTKi (cBTKi) were included in this analysis.
- Median duration of study follow up was 46.5 months.

Figure 2. Longitudinal analysis of change from baseline through Cycle 18



Upper dotted line represents clinically-meaningful improvement; lower dotted line represents clinically-meaningful worsening (for CLL, only the improvement line is shown as none of the data reached any worsening value); figures presented through Cycle 18 for ease of visualization.

References

1. Coombs, C., et. al., *Blood* 2023; 2.Ghia P., et al., *EHA* 2025; 3. Hess LM., *ISPOR* 2025; 4. Cocks, K., et al., *European Journal of Cancer*, 2012.

Acknowledgments: We thank the BRUIN clinical trial participants and their caregivers, without whom this work would not be possible. We also thank the BRUIN trial investigators and study staff. Aislinn Richardson, employee of Eli Lilly and Company, provided medical writing support.