ASH: December 12–15 in New Orleans, LA

Abstract Submission Deadline: August 4, 2026, at 11:59 p.m. PT

Title:

Estimating clinically meaningful change thresholds for a European Organisation for Research and Treatment of Cancer IL-409 proxy in relapsed/refractory chronic lymphocytic leukemia/small lymphocytic lymphoma: results from the ALPINE trial

Authors and Affiliations:

Jennifer R. Brown,[1] Timothy Victor,[2] Joselyn Angeles-Figueroa,[2] Bruce Morrison,[2] Nicole Lamanna,[3] Loic Ysebaert,[4] Tommi Salmi,[5] Alan Wu,[2] Rasika Korde,[2] Gisoo Barnes[2]

[1]Department of Medical Oncology, Dana Farber Cancer Institute, Boston, MA, USA; [2]BeOne Medicines Ltd., San Carlos, CA, USA; [3]Department of Medicine, Division of Hematology/Oncology, Herbert Irving Comprehensive Cancer Center, Columbia University, New York, NY, USA; [4]IUCT Oncopole, Toulouse, France; [5]BeOne Medicines Ltd., GmbH, Basel, Switzerland

Presenting Author: Timothy Victor

Background: Shorter patient-reported outcome (PRO) instruments can reduce assessment burden, but their clinical utility depends on validated thresholds for meaningful improvement and worsening. Item libraries offer efficiency and precision and are preferred by regulatory agencies because they reduce patient burden, minimize cultural and gender bias, and focus only on disease- and treatment-related symptoms. The European Organisation for Research and Treatment of Cancer (EORTC) IL-409 is a shortened item library that includes chronic lymphocytic leukemia (CLL) content (17 items) and selected EORTC quality of life questionnaire core 30 (QLQ-C30) domains. The IL-409 is tailored to the clinical and symptomatic profile of the relapsed/refractory (R/R) CLL/small lymphocytic lymphoma (SLL) population, thereby reducing assessment burden and supporting medication adherence. Although validation work has been done for the individual domains, the current study aims to formally validate the full IL-409 proxy using the QLQ-C30 from the phase 3 ALPINE trial (NCT03734016), which evaluated zanubrutinib vs ibrutinib in patients with R/R CLL/SLL. Because the IL-409 was not utilized in the trial, available QLQ-C30 responses were used to create an IL-409 proxy for domains with shared items. The objective of this analysis was to estimate thresholds and interpret meaningful changes in improvement or worsening in PRO scores.

Methods: Patients with baseline EuroQol 5-Dimension visual analogue scale (EQ VAS; a validated measure) and PRO scores and at least one matched post-baseline assessment were included. Six QLQ-C30 domains relevant to IL-409 were evaluated: global health status (GHS), physical and role functioning (fully shared domains), fatigue, pain, and dyspnea (partially shared domains). PRO scores were standardized such that higher scores indicated greater impairment. Meaningful within-patient and between-patient group change thresholds (Osoba D, *J Clin Oncol*, 1998) were estimated using the distribution-based method, longitudinal model-based method, and regulatory-directed anchor-based method. For anchor-based analyses, a 15-point EQ VAS change (ie, 15% of its 0–100 scale range) classified patients as improved, no change, or worsened. The EQ VAS was considered an appropriate anchor where polychoric correlations with PRO domains were ≥0.30.

Results: Of 652 patients enrolled in ALPINE, 606 were eligible for this analysis. These patients had a mean age of 66.7 years, were 68.3% male and 31.7% female, and had an approximately equal distribution across treatment arms (zanubrutinib, 51%; ibrutinib, 49%). The EQ VAS anchor correlated with GHS, physical and role functioning, fatigue, and dyspnea ($|r| \geq 0.30$; all $p<0.001$), supporting the use of the EQ VAS as an anchor for these domains. Pain was not sufficiently correlated with the EQ VAS anchor ($|r| = 0.24$); therefore, it was not included. Across all methods, thresholds were clinically plausible and generally consistent with the published QLQ-C30 guidance. Using physical functioning, for example, the clinically important change (within-patient change) thresholds were –12.34 for improvement and 5.16 for

worsening. Similar results were observed for the GHS, role functioning, fatigue, and dyspnea domains. Results of the current study, and subsequent sensitivity analyses, suggest that any change from baseline on the scales in either direction (improvement or worsening) indicates meaningful change for the selected domains comprising the IL-409 proxy.

Conclusions: This study is the first threshold evaluation of the CLL subset of QLQ-C30 domains, supporting the use of QLQ-C30-derived IL-409 proxy scores for clinical interpretation. IL-409 proxy thresholds were consistent across methods and aligned with established clinically meaningful change for QLQ-C30. Based on the predefined EORTC thresholds, these results may help clinicians interpret whether observed PRO changes reflect clinically meaningful improvement or worsening in their patients with R/R CLL/SLL. IL-409 presents a promising alternative to longer, more burdensome PRO questionnaires within clinical trials. A randomized crossover equivalence study is planned to assess the extent to which the IL-409 alone produces scores equivalent to those derived from the full QLQ-C30.

Character count: 4,157 / 4,500 characters (titles, authors, and affiliations are excluded from the total word count; no tables, figures, graphs, or images are allowed in the abstract submission).

Sponsor: BeOne Medicines, Ltd