Associations Between ECOG Performance Status and Patient-Reported Outcomes in Relapsed/Refractory Chronic Lymphocytic Leukemia or Small Lymphocytic Lymphoma: Post Hoc Analysis from the ALPINE Trial

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Nicole Lamanna,[1] Timothy Victor,[2,3] Frederick B. Barnes,[2] Rasika Korde,[2] Gisoo Barnes,[2] Jennifer R. Brown,[4] Mazyar Shadman[5]

[1]Herbert Irving Comprehensive Cancer Center, Columbia University, New York, NY, USA; [2]BeOne Medicines, Ltd., San Carlos, CA, USA; [3]University of Pennsylvania, Philadelphia, PA, USA; [4]Dana-Farber Cancer Institute, Department of Medical Oncology, Boston, MA, USA; [5]Fred Hutchinson Cancer Center and University of Washington, Clinical Research Division, Seattle, WA, USA

CONCLUSIONS

- Baseline ECOG performance status was associated with distinct, multidimensional PRO profiles, suggesting that patients with similar clinician-assessed performance status may nonetheless experience substantially different symptom and functional burdens
- Physical functioning, role functioning, and fatigue showed consistent separation across ECOG PS scores, providing the strongest patient-reported corroboration of clinician-rated ECOG PS
  - Nausea/vomiting showed no meaningful separation across ECOG PS scores, suggesting ECOG PS may not fully capture domain-specific symptom burden
- Integrating baseline PRO assessment alongside ECOG PS (at trial initiation and in routine clinical practice) may provide a more patient-centered characterization of baseline risk and symptom burden, support more informed clinician–patient discussions, and help guide future trial design, stratification, and monitoring strategies in CLL/SLL

INTRODUCTION

- Eastern Cooperative Oncology Group performance status (ECOG PS) is widely used in hematology trials for eligibility and stratification, and in routine clinical practice to guide prognosis and treatment decisions
- While patient-reported outcomes (PROs) capture complementary information on patient-reported symptoms and functioning, baseline PROs are not routinely incorporated into stratification or clinical decision-making, and ECOG PS–PRO alignment is underexplored in this setting
- The purpose of this study was to evaluate associations between ECOG PS scores and multidomain PRO profiles in patients with relapsed/refractory chronic lymphocytic leukemia/small lymphocytic lymphoma (R/R CLL/SLL) in the ALPINE trial

METHODS

Study Design and Patients

- ALPINE (NCT03734016; BGB-3111-305) was an open-label, randomized, phase 3 trial comparing the efficacy, safety, and side-effect profiles of zanubrutinib and ibrutinib in patients with R/R CLL/SLL[1]
- Eligible patients were aged ≥18 years, provided written informed consent, and had a confirmed diagnosis of CLL or SLL that met the International Workshop on Chronic Lymphocytic Leukemia criteria[2] for disease and for requiring treatment

Measures

- Health-related quality of life was a protocol-prespecified secondary endpoint assessed using two validated PRO instruments: the European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire – Core 30 (EORTC QLQ-C30) and the EuroQol-5-Dimension-5-Level questionnaire's visual analog scale (EQ-VAS)[3–5]
  - For the EORTC QLQ-C30, seven domains were assessed: global health status/quality of life (GHS/QoL), physical functioning, role functioning, fatigue, pain, insomnia, and nausea/vomiting

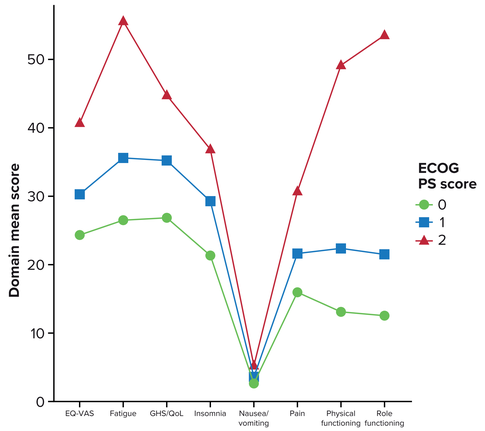
Statistical Analysis

- All analyses were conducted using the data cutoff date of February 28, 2024
- All randomized patients who completed the EORTC QLQ-C30 and EQ-VAS at baseline (pretreatment) were included in the analysis, and the data were pooled across treatment arms (zanubrutinib vs ibrutinib)
- To evaluate patterns across the seven PRO domains (EORTC QLQ-C30) and the EQ-VAS, a profile analysis was performed using one-way multivariate analysis of variance with Wilks' lambda to compare PRO profiles across baseline ECOG PS scores (0, 1, and 2); this included three hierarchical hypothesis tests:
  - Parallelism (Do ECOG PS profile shapes change in the same direction across domains? [Interaction test])
  - Equal overall levels (Are the overall mean scores for PROs the same for both groups? [Main effect of ECOG PS])
  - Flatness (Do domain mean scores differ regardless of ECOG PS score? [Main effect of domain])
- Domain-level pairwise contrasts were evaluated using *t*-tests
- As a sensitivity analysis, bivariate logistic regression assessed associations between baseline PRO impairment scores and ECOG PS scores
- PRO scores were oriented such that the higher the score, the worse the impairment
- The threshold for statistical significance was established to be $P \leq .005$

RESULTS

- Among 627 patients included in the analysis, PRO profiles differed significantly by ECOG PS score, rejecting parallelism, equal overall levels, and flatness (all $P<.001$) (**Figure 1**)
  - The rejection of parallelism meant PRO profile shapes differed by ECOG PS score and differences were not uniform across domains

Figure 1. Profile Plot by ECOG PS Score (0, 1, or 2)

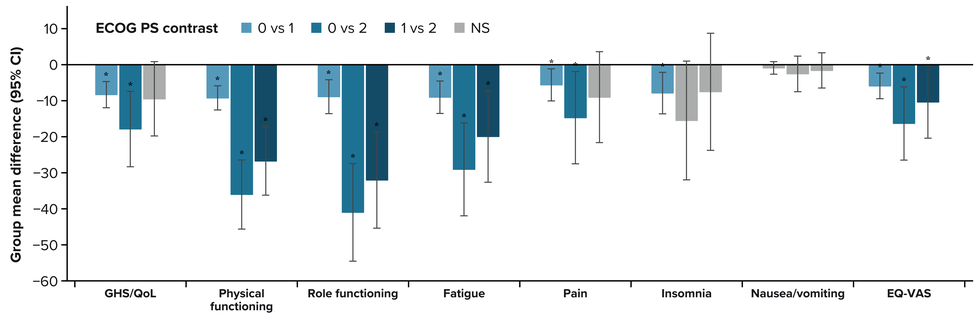


Note: All scales were oriented so that higher scores indicate worse impairment (greater symptom burden or functional limitation). 0: Fully active, no restrictions; 1: Restricted in strenuous activity but fully ambulatory, light work possible; 2: Able to walk and do self-care but unable to work.

Abbreviations: ECOG PS, Eastern Cooperative Oncology Group performance status; EQ-VAS, EuroQol-5-Dimension-5-Level questionnaire's visual analog scale; GHS/QoL, global health status/quality of life

- In multivariate analyses, across all three ECOG PS contrasts (0 vs 1, 0 vs 2, 1 vs 2), physical functioning, role functioning, fatigue, and EQ-VAS showed consistent, statistically significant separation (all $P<.005$) (**Figure 2**)
  - Nausea/vomiting did not significantly separate any ECOG PS contrast
- In multivariable logistic regression, every 10-point worsening in baseline PRO scores was significantly associated with greater odds of having a worse ECOG PS score across all EORTC QLQ-C30 domains except nausea/vomiting (**Figure 3**)
  - The strongest associations were observed for physical functioning (odds ratio [OR] 1.48 [95% confidence interval {CI} 1.34-1.79]; $P<.001$) and GHS/QoL (OR 1.34 [95% CI 1.22-1.48]; $P<.001$), reflecting an increase in odds of 48% and 34%, respectively
- The EQ-VAS demonstrated a 22% increase in odds of having a worse ECOG PS score (OR 1.22 [95% CI 1.10-1.34]; $P<.001$)

Figure 2. Group Mean Differences (95% CIs) Stratified by ECOG PS Score (0, 1, or 2)



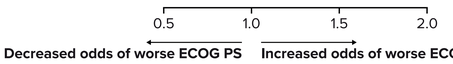
*$P<.005$.

Note: All scales were oriented so that higher scores indicate worse impairment (greater symptom burden or functional limitation). 0: Fully active, no restrictions; 1: Restricted in strenuous activity but fully ambulatory, light work possible; 2: Able to walk and do self-care but unable to work.

Abbreviations: CI, confidence interval; ECOG PS, Eastern Cooperative Oncology Group performance status; EQ-VAS, EuroQol-5-Dimension-5-Level questionnaire's visual analog scale; GHS/QoL, global health status/quality of life; NS, not separated.

Figure 3. Logistic Regression Predictors of ECOG PS Score 0 or 1 by PRO Domain

PRO endpoint	Odds ratio (95% CI)	*P*-value	Odds ratio (95% CI)
EORTC QLQ-C30			
GHS/QoL		**<.001**	1.34 (1.22-1.48)
Physical functioning		**<.001**	1.48 (1.34-1.79)
Role functioning		**<.001**	1.22 (1.22-1.34)
Fatigue		**<.001**	1.22 (1.10-1.34)
Nausea/vomiting		.1129	1.22 (1.00-1.48)
Pain		**<.001**	1.10 (1.10-1.22)
Insomnia		**<.001**	1.10 (1.00-1.22)
EQ-VAS		**<.001**	1.22 (1.10-1.34)



Note: Odds ratios are scaled as per 10-point change on a 0-100 scale.

Abbreviations: CI, confidence interval; ECOG PS, Eastern Cooperative Oncology Group performance status; EORTC QLQ-C30, European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire – Core 30; EQ-VAS, EuroQol-5-Dimension-5-Level questionnaire's visual analog scale; GHS/QoL, global health status/quality of life; PRO, patient-reported outcome.

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DISCLOSURES

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CORRESPONDENCE: Nicole Lamanna: nl2129@cumc.columbia.edu

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