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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Background Eastern Cooperative Oncology Group performance status (ECOG PS) is widely used in hematology trials to determine eligibility and stratify randomization and in routine practice to inform prognosis and treatment tolerability. 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.

Aims To evaluate associations between ECOG PS categories and multidomain PRO profiles in patients with relapsed/refractory chronic lymphocytic leukemia/small lymphocytic lymphoma (R/R CLL/SLL).

Methods Patients gave written informed consent and completed the PRO measures. Baseline (pre-treatment) PRO data were pooled across treatment arms (zanubrutinib vs ibrutinib). Seven domains from the European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire Core 30 (Global Health Status [GHS], physical functioning, role functioning, fatigue, pain, insomnia, nausea/vomiting) and visual analog scale (VAS) scores from the EuroQol 5 dimension 5 level tool were analyzed. PRO scores were oriented such that higher scores indicate higher impairment. Profile analysis was performed using one-way multivariate analysis of variance (MANOVA) with Wilks' lambda to compare PRO profiles across baseline ECOG PS categories (0, 1, 2), including three hierarchical hypothesis tests: (1) *parallelism* (profile shape across domains); (2) *levels* (mean differences between groups); (3) *flatness* (similarity of domain means overall [no difference vs. domain differentiated]). Domain-level pairwise contrasts were evaluated using t-tests. Bivariate logistic regression assessed associations between baseline PRO impairment scores and ECOG PS classification (sensitivity analysis).

Results Among 627 patients, PRO profiles differed significantly by ECOG PS category, rejecting parallelism, equal overall levels, and flatness (all $P<.001$). Physical functioning, role functioning, and fatigue showed most consistent separation, with significant differences in all ECOG PS contrasts (0 vs 1,

0 vs 2, 1 vs 2; all *P*<.001). Other domains showed partial separation, including GHS (0 vs 1, *P*=.001; 0 vs 2, *P*=.001), pain (0 vs 1, *P*=.008; 0 vs 2, *P*=.019), and insomnia (0 vs 1, *P*=.004). VAS scores also differed significantly by ECOG PS (0 vs 1, *P*=.001; 0 vs 2, *P*=.001; 1 vs 2, *P*=.040). No associations were seen for nausea/vomiting. In logistic regression analyses, higher baseline impairment in physical functioning (odds ratio [OR] 1.48, 95% confidence interval [CI] 1.34–1.79), role functioning (OR 1.22, 95% CI 1.22–1.34), and fatigue (OR 1.22, 95% CI 1.10–1.34) was associated with higher odds of worse ECOG PS (all *P*<.001), with additional significant associations for GHS/quality of life (OR 1.34, 95% CI 1.22–1.48; *P*<.001), pain (OR 1.10, 95% CI 1.10–1.22; *P*=.001), insomnia (OR 1.10, 95% CI 1.00–1.22; *P*<.001), and VAS (OR 1.02, 95% CI 1.01–1.03; *P*<.001).

Summary/Conclusion Baseline ECOG PS was strongly associated with multidomain patient-reported symptom and functional profiles, with the most consistent differentiation for physical functioning, role functioning, and fatigue. Using baseline PRO assessment with ECOG PS could provide clinicians with a more patient-centered characterization of functional and symptom burden, supporting improved baseline risk stratification and informing treatment discussions and monitoring in R/R CLL/SLL trials.