

Title: A Novel Bayesian Approach for Assessing Associations Between ECOG Performance Status (ECOG-PS) and Patient-Reported Outcomes (PROs) in Patients With Gastric or Gastroesophageal Junction (GC/GEJC) Adenocarcinoma: Post Hoc Analysis From the RATIONALE-305 Trial

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Background: Oncology clinicians rely on ECOG-PS to guide trial eligibility and monitor disease impact, yet it provides only a limited, clinician-rated view of a patient’s functional status and is subject to inter-rater variability. We previously demonstrated that, at baseline (pretreatment), patients with ECOG-PS 1 had significantly worse patient-reported GHS/QoL, lower physical functioning, and greater pain compared with those with ECOG-PS 0. Here, we present a novel time-varying Bayesian approach to quantify the probability that longitudinal changes in ECOG-PS track PRO trajectories during treatment in patients with first-line GC/GEJC from the RATIONALE-305 trial.

Methods: Bayesian hierarchical regression models with patient-level trajectories were used to estimate longitudinal ECOG-PS–PRO associations. Seven EORTC QLQ-C30 domains (GHS/QoL, physical and role functioning, fatigue, pain, constipation, and diarrhea) plus the EQ-5D VAS were analyzed. ECOG-PS

was modeled as a continuous, time-varying predictor, with coefficients reflecting the expected PRO change per 1-level ECOG-PS change over time (eg, 0 to 1, 1 to 2, or 1 to 0). Posterior probabilities and 95% credible intervals (CrIs) were estimated for ECOG-PS and for treatment effects comparing tislelizumab + chemotherapy (T+C) versus placebo + chemotherapy (P+C).

Results: 532 patients with longitudinal ECOG-PS and PRO assessments were analyzed. Lower (better) ECOG-PS was strongly and positively associated with better longitudinal PRO scores in five of seven QLQ-C30 domains—GHS/QoL, physical and role functioning, fatigue, and pain—as well as the EQ-5D VAS. For ECOG-PS, the 95% CrIs for fatigue (1.67, 4.46), pain (0.73, 3.15), physical functioning (2.36, 4.40), GHS/QoL (2.92, 5.89), and EQ-5D VAS (2.40, 4.72) were above 0, with corresponding posterior probabilities $\geq 99.9\%$, indicating a very high probability of ECOG-PS–PRO alignment over time independent of treatment. After adjusting for ECOG-PS, treatment effects favored T+C versus P+C for GHS/QoL (95% CrI [-4.88, -0.01]; posterior probability 97.6%) and pain (95% CrI [-5.09, 0.14]; 96.8%), indicating treatment-driven improvements independent of ECOG-PS.

Conclusions: Longitudinal improvements toward lower (better) ECOG-PS levels were strongly associated with more favorable PRO trajectories, while treatment with T+C conferred additional improvements in GHS/QoL and pain beyond what was reflected by ECOG-PS. These empirical findings support incorporating PROs alongside ECOG-PS to give clinicians a more complete view of baseline functional and symptom burden, improve patient-centered monitoring, and strengthen trial eligibility and stratification.

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