ASCO® Gastrointestinal Cancers Symposium

Associations Between ECOG Performance Status (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/Objective

- In oncology, ECOG-PS is the predominant clinician-rated tool for assessing trial eligibility and informing prognosis[1,2]
- Misclassification of clinician-rated PS is well documented, which can preclude patients from potentially beneficial therapy or, conversely, expose them to overly aggressive treatment given their condition[3-4]
- PROs capture the patient's direct experience of disease- and treatment-related symptoms and are not subject to clinician interpretation or bias[3]; notably, patient-reported physical functioning is a tumor-agnostic predictor of survival and, in several studies, shown to be more predictive than ECOG-PS
- Here, we evaluated whether baseline (pre-treatment) ECOG-PS meaningfully differentiated PRO-measured symptom burden and functional impairments, irrespective of treatment arm, in patients with 1L locally advanced or metastatic GC/GEJC from the RATIONALE-305 trial

[1]Azam F, et al. *Case Rep Oncol.* 2020;12(3):728-736. [2]Higgins MI, et al. *Cancer.* 2021;127(3):339-341. [3]Scott JM, et al. *J Clin Oncol.* 2020;1;38(25):2824-2829. [4]Chow R, et al. *Support Care Cancer.* 2020;28(5):2071-2078. [5]Quinten C, et al. *Lancet Oncol.* 2009;10:865-871. [6]Mierzynska J, et al. *Lancet Oncol.* 2019;20:e685-e698. **Abbreviations:** ECOG-PS, Eastern Cooperative Oncology Group performance status; GC/GEJC, gastric cancer/gastroesophageal junction cancer; HRQoL, health-related quality of life; PRO, patient-reported outcome; PS, performance status.

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Study Design

RATIONALE-305: randomized, double-blind, phase 3 trial

Key Eligibility Criteria

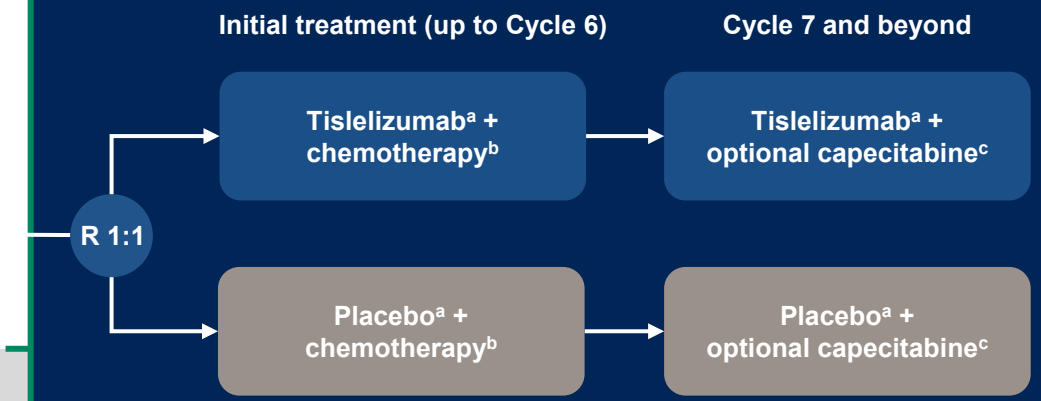
- Locally advanced unresectable or metastatic GC histologically confirmed adenocarcinoma
- No HER2-positive disease
- No prior systemic therapy for advanced disease
- At least one measurable or non-measurable lesion (RECIST v1.1)
- ECOG-PS 0 or 1

Primary endpoints:

- OS in PD-L1 score ≥5%[d] and ITT populations

Secondary endpoints:

- PROs, PFS, ORR, DoR, and safety



Statistical Considerations

- Nine hundred thirty-two randomized patients who completed baseline (pre-treatment) QLQ-C30 and QLQ-STO22 measures were analyzed according to baseline ECOG-PS (0 vs 1), with data pooled across treatment arms (tislelizumab + chemotherapy and placebo + chemotherapy)
- Profile analysis was used to examine whether ECOG-PS groups showed different patterns or overall levels across 11 PRO domains
- Logistic regression was conducted as a sensitivity analysis to identify which PRO domains were associated with ECOG-PS status (0 vs 1)
- The threshold for statistical significance was established at $P < 0.05$

[a]Tislelizumab 200 mg or placebo Q3W (Day 1). [b]Oxaliplatin 130 mg/m² IV (Day 1) and oral capecitabine 1000 mg/m² twice daily (14 consecutive days from Day 1) Q3W (XELOX), or cisplatin 80 mg/m² IV (Day 1) and 5-fluorouracil 800 mg/m²/day IV (Days 1-5) Q3W (FP). [c]Capecitabine as maintenance therapy was optional and only for XELOX-treated patients. [d]PD-L1 score was determined using the VENTANA PD-L1 (SP263) assay by tumor area positivity score. ECOG-PS 0 = fully active, no limitations; ECOG-PS 1 = restricted in physically strenuous activity; mild symptoms impacting activity.
Abbreviations: DoR, duration of response; ECOG PS, Eastern Cooperative Oncology Group performance status; EORTC, European Organisation for Research and Treatment of Cancer; GI, gastrointestinal; HER2, human epidermal growth factor receptor 2; ITT, intent-to-treat; IV, intravenous; ORR, objective response rate; OS, overall survival; PD-L1, programmed death-ligand 1; PFS, progression-free survival; PRO, patient-reported outcome; Q3W, once every 3 weeks; QLQ-C30, Quality of Life Questionnaire Core-30; QLQ-STO22, Quality of Life Questionnaire-Gastric Cancer Module; R, randomized; RECIST v1.1, Response Evaluation Criteria in Solid Tumors version 1.1.

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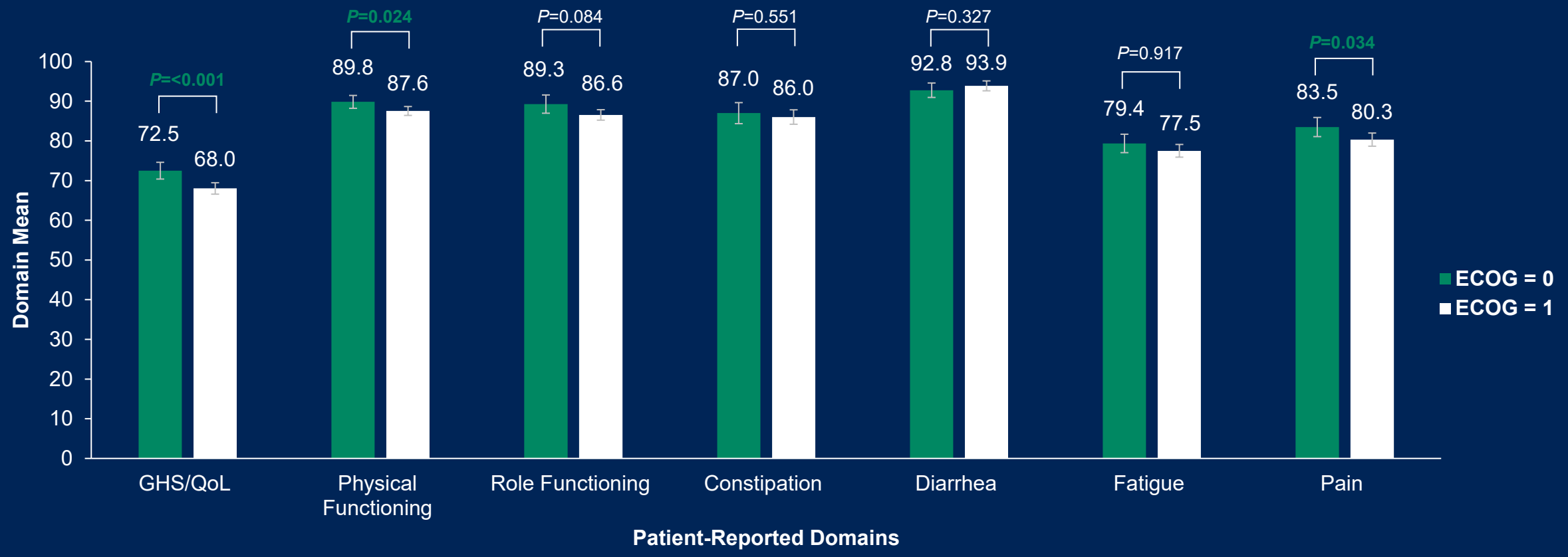
Results: EORTC QLQ-C30 PRO Domains Stratified by ECOG-PS (0 vs 1)

Patients with ECOG-PS 1 reported worse GHS/QoL, lower physical functioning, and greater pain compared with those with ECOG-PS 0



Data cut-off: February 28, 2023. A one-way multivariate analysis of variance (MANOVA) using Wilks' lambda was used to test for overall ECOG-PS group mean differences (0 vs 1). Domain-level t-test was used to explore which specific PRO domains were significantly different between ECOG-PS groups (0 vs 1). Note: Symptom domains (constipation, diarrhea, fatigue, pain, and dietary restrictions) were recoded to align their valence with the other variables. **Abbreviations:** ECOG PS, Eastern Cooperative Oncology Group performance status; EORTC, European Organisation for Research and Treatment of Cancer; GHS/QoL, global health status/quality of life; PRO, patient-reported outcome; QLQ-C30, Quality of Life Questionnaire Core-30; RECIST v1.1, Response Evaluation Criteria in Solid Tumors version 1.1.

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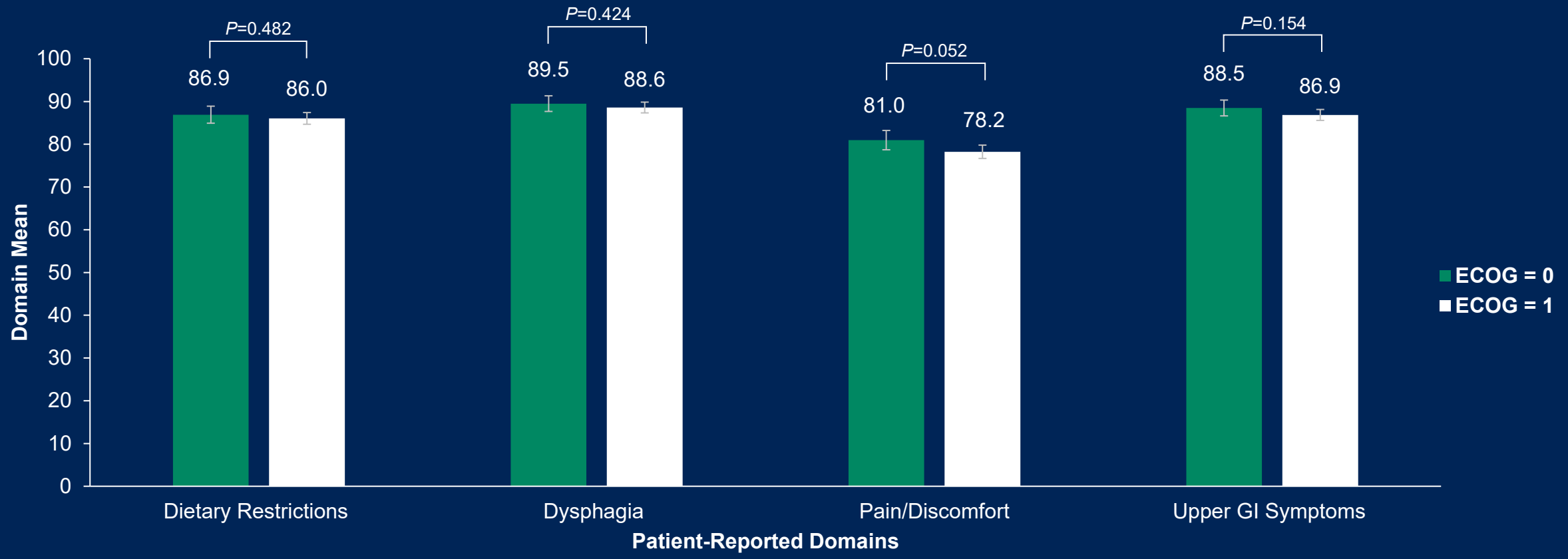
Results: EORTC QLQ-STO22 PRO Domains Stratified by ECOG-PS (0 vs 1)

No differences were observed for QLQ-STO22 GC–specific symptom domains, suggesting that ECOG may not fully capture GC–specific symptom burden at baseline



Data cut-off: February 28, 2023. A one-way multivariate analysis of variance (MANOVA) using Wilks' lambda was used to test for overall ECOG-PS group mean differences (0 vs 1). Domain-level t-test was used to explore which specific PRO domains were significantly different between ECOG-PS groups (0 vs 1). Note: Symptomatic variables (dietary restrictions, dysphagia, pain/discomfort, and upper GI symptoms) were recoded to align their valence with the other variables. **Abbreviations:** ECOG PS, Eastern Cooperative Oncology Group performance status; EORTC, European Organisation for Research and Treatment of Cancer; GHS/QoL, global health status/quality of life; GI, gastrointestinal; PRO, patient-reported outcome; QLQ-STO22, Quality of Life Questionnaire-Gastric Cancer Module; RECIST v1.1, Response Evaluation Criteria in Solid Tumors version 1.1.

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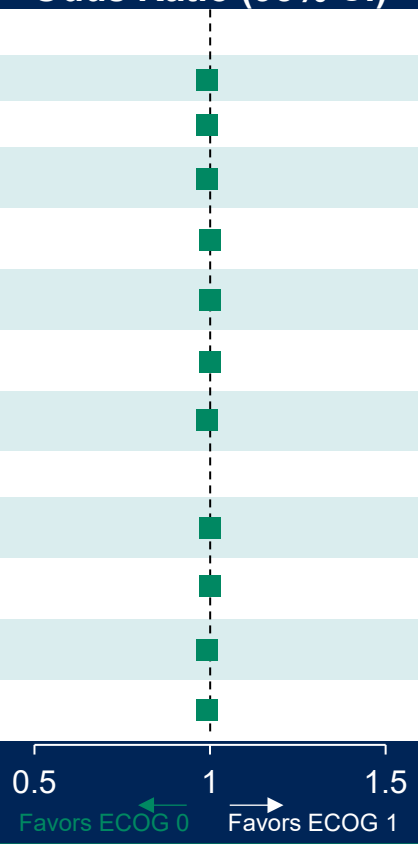
Results: Predictors of ECOG-PS (0 vs 1) Stratified by PRO Domain

The odds of reporting better GHS/QoL, physical functioning, and pain scores were lower for ECOG-PS group 1 vs ECOG-PS group 0

EORTC Measure	Odds Ratio (95% CI)	*P* Value
EORTC QLQ-C30		
GHS/QoL	0.99 (0.98, 0.99)	**<0.001**
Physical functioning	0.99 (0.98, 1.00)	**0.0245**
Role functioning	0.99 (0.99, 1.00)	0.0845
Constipation	1.00 (0.99, 1.00)	0.5509
Diarrhea	1.00 (1.00, 1.01)	0.3273
Fatigue	1.00 (0.99, 1.00)	0.1967
Pain	0.99 (0.99, 1.00)	**0.0343**
EORTC QLQ-STO22		
Dietary restrictions	1.00 (0.99, 1.01)	0.4243
Dysphagia	1.00 (0.99, 1.01)	0.4812
Pain/discomfort	0.99 (0.99, 1.00)	0.0527
Upper GI symptoms	0.99 (0.98, 1.00)	0.1551



Data cut-off: February 28, 2023. Logistic regression analysis was conducted as a sensitivity analysis to identify which PRO domains were associated with ECOG-PS status (1 vs 0). Note: Symptomatic variables (constipation, diarrhea, fatigue, pain, dietary restrictions, dysphagia, and upper GI symptoms) were recoded to align their valence with the other variables. OR<1 = worse outcomes (ECOG 1 patients less likely to report better PROs); OR>1 = better outcomes (ECOG 1 patients more likely to report better PROs). **Abbreviations:** ECOG PS, Eastern Cooperative Oncology Group performance status; EORTC, European Organisation for Research and Treatment of Cancer; GHS/QoL, global health status/quality of life; GI, gastrointestinal; OR, odds ratio; PRO, patient-reported outcome; QLQ-C30, Quality of Life Questionnaire Core-30; QLQ-STO22, Quality of Life Questionnaire-Gastric Cancer Module.

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Conclusions

- Our findings indicate that ECOG-PS captures only part of the patient experience:
  - Among patients with 1L GC/GEJC, those with baseline ECOG-PS 1 reported significantly worse GHS/QoL, physical functioning, and pain than those with ECOG-PS 0, irrespective of treatment arm
  - Multivariable regression analyses confirmed a lower probability of achieving better PRO scores for patients with ECOG-PS 1 compared with ECOG-PS 0
- These results suggest that integrating baseline PROs into eligibility and/or stratification criteria may improve risk stratification, support more patient-centered trial design, and foster more meaningful patient–clinician dialogue at treatment initiation
- On going work in RATIONALE-305 is assessing the extent to which ECOG-PS meaningfully differentiates PRO trajectories over time and by treatment, to further inform how ECOG-PS and PROs can be jointly leveraged in advanced GC/GEJC

Abbreviations: ECOG-PS, Eastern Cooperative Oncology Group performance status; GHS/QoL, global health status/quality of life; PRO, patient-reported outcome.

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