A Novel Multivariate Application of Profile Analysis to Characterize Multidomain Patient-Reported Outcome Patterns in Patients With Gastric or Gastroesophageal Junction Adenocarcinoma

MSR3

Marcia Cruz-Correa,[1] Joselyn Angeles-Figueroa, [2,3] Timothy Victor,[2,3] Afsaneh Barzi,[2] Bryant Barnes[2]

[1]University of Puerto Rico, San Juan, Puerto Rico; [2]BeOne Medicines, Ltd, San Mateo, CA, USA; [3]University of Pennsylvania, Philadelphia, PA, USA

CONCLUSIONS

- Patients with an ECOG PS of 1 demonstrated greater symptom burden and reduced functioning, consistent with clinical expectations
- GC/GEJC-specific symptom burden varied meaningfully across domains but did not differentiate ECOG PS groups, suggesting that disease-specific PROs capture dimensions of patient experience that ECOG PS, by design, cannot detect
- These findings establish profile analysis as a rigorous yet intuitive framework for PRO evidence generation, producing integrated, multidomain characterizations of patient experience that are interpretable to clinicians, meaningful to patients, and actionable for health technology assessment stakeholders

BACKGROUND

- Patient-reported outcomes (PROs) in oncology trials are traditionally analyzed domain by domain, producing isolated *P*-values rather than a cohesive characterization of patient experience
- Profile analysis offers a visually intuitive multivariate framework to evaluate patterns and group differences simultaneously, giving clinicians a single, integrated picture of symptoms and functioning profiles[1]
- Baseline functional status as measured by Eastern Cooperative Oncology Group performance status (ECOG PS) compresses multidimensional health into a single ordinal scale; profile analysis can determine whether PROs characterize disease burden beyond PS alone
- The objective of these analyses was to illustrate the application of profile analysis to assess how baseline ECOG PS meaningfully differentiates multidomain PRO profiles in patients with gastric or gastroesophageal junction adenocarcinoma (GC/GEJC) from the RATIONALE-305 trial

METHODS

Study Design and Patients

- RATIONALE-305 was a randomized, open-label, multicenter, multiregional phase 3 study in adults (aged ≥18 years) with previously untreated, locally advanced, unresectable or metastatic GC/GEJC
- Patients were randomized 1:1 to receive tislelizumab or placebo intravenously once every 3 weeks plus investigator's choice of chemotherapy regimen until disease progression, unacceptable toxicity, or patient withdrawal

Measures

- Seven domains were assessed using the European Organization for Research and Treatment of Cancer (EORTC) Quality of Life Questionnaire Core-30 (QLQ-C30)
  - Global health status/quality of life (GHS/QOL), physical and role functioning, fatigue, pain, constipation, and diarrhea
- Four domains were assessed using the EORTC Quality of Life Questionnaire Gastric Cancer Module (QLQ-STO22)
  - Dietary restrictions, dysphagia/odynophagia, pain, and upper gastrointestinal symptoms
- The European Quality of Life 5-Dimension 5-Level (EQ-5D-5L) visual analog scale (VAS) questionnaire was also included

Statistical Analyses

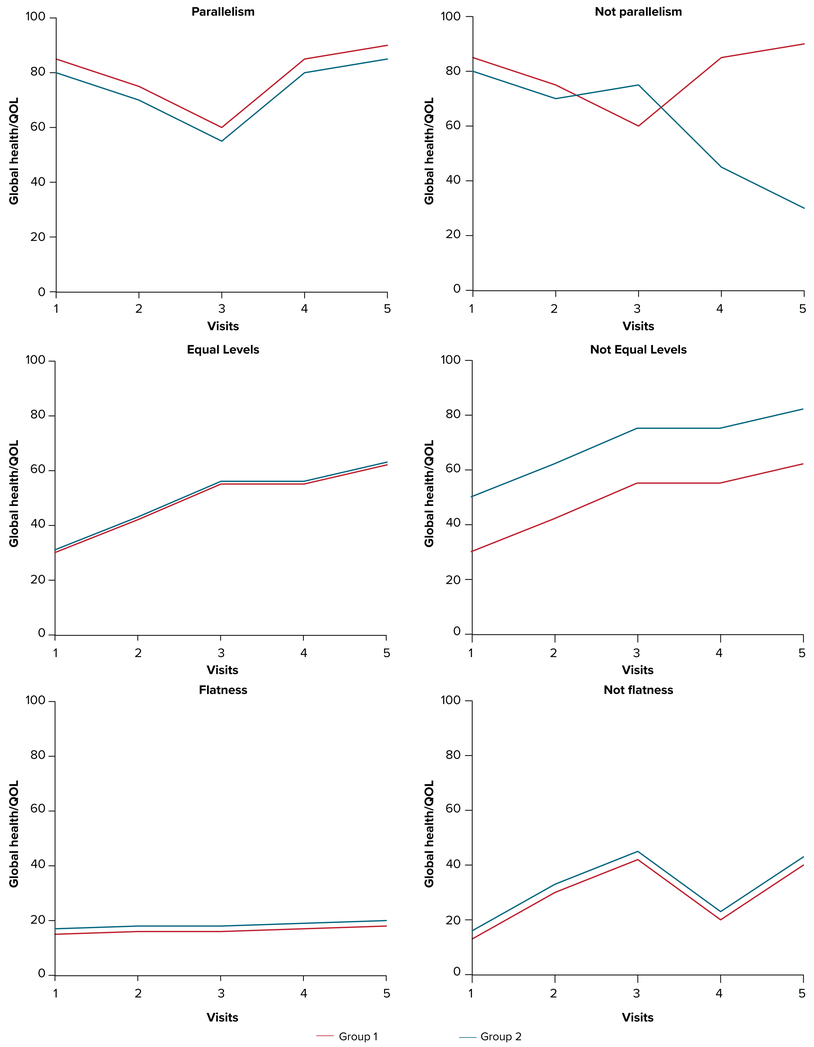
- All analyses were conducted using the data cutoff of February 28, 2023
- Patients who completed baseline QLQ-C30 and EQ-5D-5L VAS and had an ECOG PS of 0/1 were included in the analysis, with data pooled across treatment arms
- A one-way multivariate analysis of variance (MANOVA) was used to first test for overall ECOG PS group differences (0 vs 1)
- Profile analysis evaluated patterns across the seven PRO domains and the EQ-5D-5L VAS by testing three hierarchical hypotheses (**Figure 1 and 2**)

Figure 1. Profile Analysis Hierarchical Hypothesis Testing Sequence

H1	**PARALLELISM**	Do ECOG PS groups follow the same pattern of scores across PRO domains? (Interaction: ECOG PS × PRO domain)
↓	If not rejected (*P*≥.05): proceed to H2	
H2	**EQUAL LEVELS**	Do overall mean PRO scores differ between ECOG PS groups? (Main effect: ECOG PS)
↓	If not rejected (*P*≥.05): proceed to H3	
H3	**FLATNESS**	Are the mean scores similar across all PRO domains? (Main effect: PRO domains)

Hypotheses are tested sequentially: H2 (equal levels) is only tested if H1 (parallelism) is not rejected. H3 (flatness) is only evaluated if H2 is also not rejected.
Abbreviations: ECOG PS, Eastern Cooperative Oncology Group performance status; PRO, patient-reported outcome.

Figure 2. Illustration of Profile Analysis Hypotheses Using Mock Data[a]



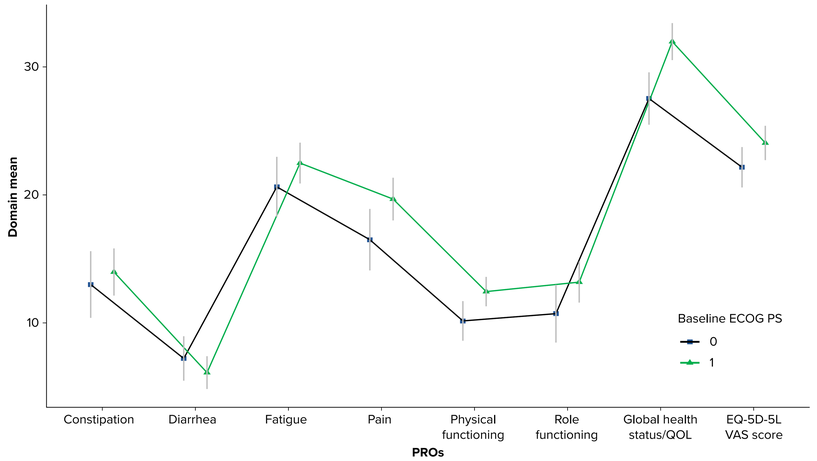
[a]These plots are exclusively illustrative, and all data used to generate these examples are fictitious.
Abbreviation: QOL, quality of life.

- Post hoc sensitivity analyses used *t*-tests and logistic regression to explore domain-specific differences
- The threshold for statistical significance was established at *P*<.05

RESULTS

- The one-way MANOVA demonstrated statistically significant differences between ECOG PS groups in the overall PRO domains (*P*=.021)
- For the QLQ-STO22, one-way MANOVA showed no significant overall difference in PROs between ECOG PS groups (*P*=.355)
- Profile analysis for the QLQ-C30 did not reject the parallelism hypothesis (*P*=.056), which means that the PRO profiles for both groups followed the same pattern across the domains (**Figure 3**)
- The equal levels hypothesis was significant (*P*=.040), indicating that patients with an ECOG PS of 1 reported worse PRO scores than patients with an ECOG PS of 0. Since profile analysis is hierarchical and the equal levels hypothesis was rejected, flatness was not further evaluated

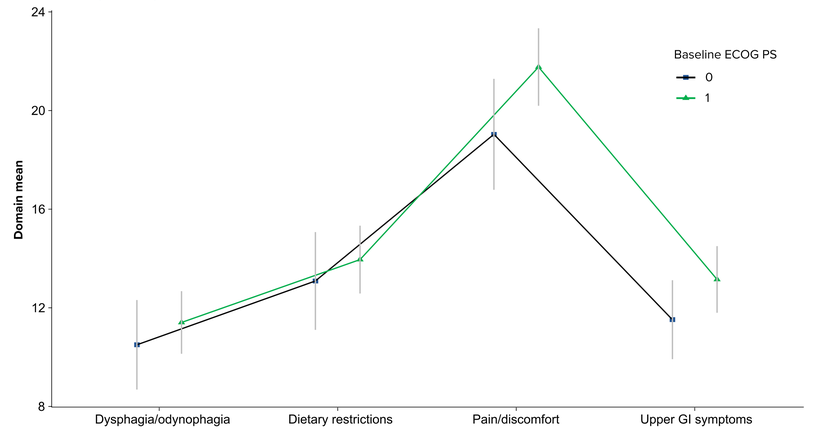
Figure 3. Profile Plot of Domain Means for EORTC QLQ-C30 and EQ-5D-5L VAS Stratified by Baseline ECOG PS (0 vs 1)



Global health status/QOL, EQ-5D-5L VAS score, and physical and role functioning were recoded so that higher values = worse outcomes. EQ-5D-5L VAS score is a separate PRO measure and not a domain of EORTC QLQ-C30.
Abbreviations: ECOG PS, Eastern Cooperative Oncology Group performance status; EORTC QLQ-C30, European Organization for Research and Treatment of Cancer Quality of Life Questionnaire Core-30; EQ-5D-5L, European Quality of Life 5-Dimension 5-Level; PRO, patient-reported outcome; QOL, quality of life; VAS, visual analog scale.

- For QLQ-STO22, no between-group differences were found in the pattern of PRO domains (*P*=.459) or in the overall level of ECOG PS groups (*P*=.135). The flatness test was significant (*P*<.001), which means there was meaningful variation in patients' scores between the four PRO domains (**Figure 4**)

Figure 4. Profile Plot of Domain Means for EORTC QLQ-STO22 Stratified by Baseline ECOG PS (0 vs 1)



Abbreviations: ECOG PS, Eastern Oncology Group performance status; EORTC, European Organization for Research and Treatment of Cancer; GI, gastrointestinal.

- Post hoc sensitivity analyses demonstrated that for the QLQ-C30, patients with an ECOG PS of 1 reported significantly worse GHS/QOL (*P*<.001), physical functioning (*P*=.023), and pain (*P*=.034) compared with those who had an ECOG PS of 0

REFERENCES

1. Bulut O, Desjardins CD. *PsyArXiv Prepr*. 2020.

ACKNOWLEDGMENTS

This study was sponsored by BeOne Medicines, Ltd. Editorial support was provided by Nucleus Global, an Inizio company, and supported by BeOne Medicines.

DISCLOSURES

MC-C: Research funding: BeOne Medicines, Ltd, AbbVie, Genentech, Taiho, Seagen, BMS, Merck, Pfizer, Janssen, Mirati, Tempus, HUYABIO, Regeneron, DELFI; Stock or stock options: Pan American Center for Oncology Trials, University of Puerto Rico Medical Sciences Campus. **JA-F, TV, AB, BB**: Employment and may own stock: BeOne Medicines, Ltd.

CORRESPONDENCE: Joselyn Angeles-Figueroa, joselyn.figueroa@beonemed.com

Presented at ISPOR 2026; May 17-20, 2026; Philadelphia, PA, USA