

Association Between Disease Control and Patient-Reported Functioning and Quality of Life in the ASCENT-03 Study

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Conclusions

- In pooled analyses of the sacituzumab govitecan (SG) and chemotherapy (chemo) treatment groups in the ASCENT-03 study in participants with triple-negative breast cancer, objective response was associated with better patient-reported quality of life (QOL) and functioning and less pain through week 25
- Disease progression was associated with worsening of QOL, functioning, and pain through week 25
- Longer duration of response (DOR; per additional day) was associated with small favorable changes in global health status (GHS)/QOL and fatigue, with similar directional trends across domains, suggesting that patient well-being is maintained while response is sustained
- Together, findings from these pooled analyses support disease control as an important correlate of how patients feel and function during treatment
- These results help contextualize the previously reported improvements in progression-free survival (PFS), DOR, and patient-reported outcomes (PROs) with SG vs chemo in ASCENT-03, supporting SG as a first-line treatment option

Plain Language Summary

- The ASCENT-03 study compared sacituzumab govitecan (SG) with chemotherapy in participants with advanced triple-negative breast cancer who had not had treatment before
- In the main study, participants receiving SG went on to live longer without their cancer getting worse or dying, had a response over a longer length of time, and generally felt better with improved symptoms compared with participants receiving chemotherapy
- Most participants began treatment with a similar ability to do everyday activities, work, and hobbies as individuals in the general population. An important goal of treatment was to maintain this well-being
- This analysis looked at whether changes in the cancer were related to how participants felt and functioned, using data from participants receiving SG and chemotherapy
- Participants whose tumors shrank or disappeared in response to treatment generally felt better, had a greater ability to stay active and carry out everyday activities, and had less pain and fatigue compared with participants whose tumors grew
- Participants who had a response over a longer length of time also tended to maintain quality of life and experienced less fatigue than those who responded for a shorter length of time
- These findings suggest that as long as the cancer stays controlled, participants are better able to maintain how they feel and function. This provides additional context for improved disease control and patient-reported outcomes seen with SG compared with chemotherapy in ASCENT-03, supporting SG as a front-line treatment option

References: 1. Bellino S, et al. *Drugs R D*. 2024;24:123-7. 2. US Food and Drug Administration. Core patient-reported outcomes in cancer clinical trials. Guidance for industry. Accessed July 14, 2025. <https://www.fda.gov/media/149994/download>. 3. Cortes J, et al. *N Engl J Med*. 2025;393:1912-25. 4. Punie K, et al. Presented at the San Antonio Breast Cancer Symposium; December 9-12, 2025; San Antonio, TX. Oral Presentation RF6-05. 5. Nolte S, et al. *Eur J Cancer*. 2019;107:153-63. 6. Lord-Besson J, et al. *JNCI Cancer Spectr*. 2023;7:pkad002. 7. Mouillet G, et al. *Cancer Med*. 2020;9:7363-74.

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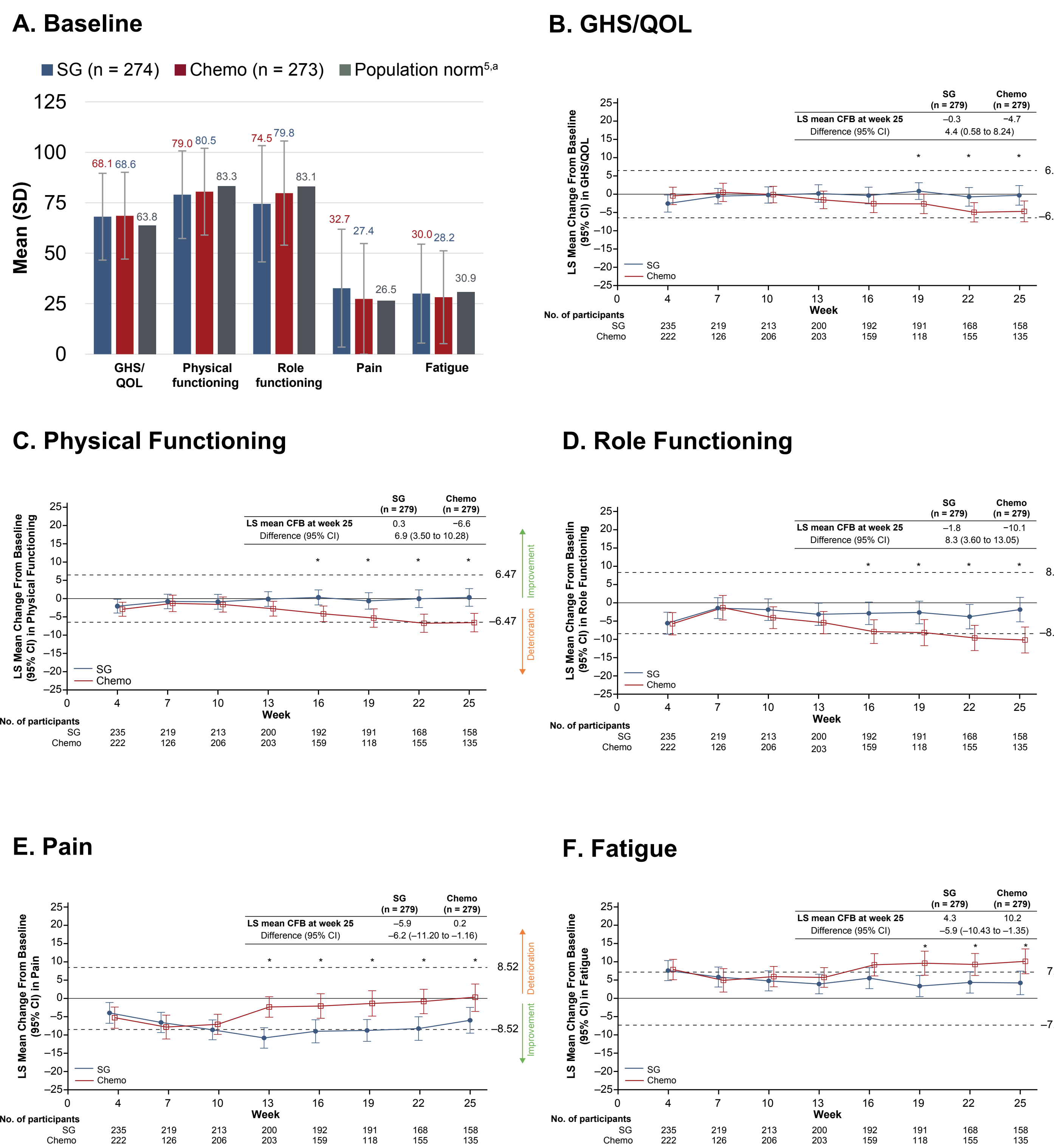
Disclosures: MO reports advisory roles with AstraZeneca, Daiichi Sankyo, Gilead Sciences, Inc., Hoffman-La Roche, Eli Lilly, MSD, Pfizer, ProteinOure, and Novartis; speaking roles with AstraZeneca, Gilead Sciences, Inc., Lilly, and MSD; honoraria from Curio Science and i-One; research support from AstraZeneca, Gilead Sciences, Inc., Pfizer, Roche, and Immunet; a steering committee role for AstraZeneca; membership with AACR, ASCO, and SEOM; a leadership role for SOLTI Cancer Research Group; and travel grants from AstraZeneca, Gilead Sciences, Inc., Roche, and Pfizer.

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Introduction

- PROs and health-related QOL assessments in cancer clinical trials are crucial to evaluating the benefit-risk ratio of a treatment^{1,2}
- In the ASCENT-03 study, first-line treatment with SG led to a statistically significant and clinically meaningful improvement in PFS vs chemo in participants with previously untreated metastatic triple-negative breast cancer who were not candidates for programmed death (ligand) 1 (PD-[L]1) inhibitors (hazard ratio, 0.62; 95% CI, 0.50-0.77; $P < .0001$)³
 - Objective response was similar across treatment arms (SG, 48%; chemo, 46%)³
 - Median DOR was numerically longer with SG (12.2 months) vs chemo (7.2 months)³
 - The safety profile of SG was consistent with previous reports and associated with fewer dose reductions and discontinuations due to adverse events than chemo³
 - Prespecified PROs from the European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire C30 (EORTC QLQ-C30), including physical functioning, role functioning, and symptom burden (fatigue and pain), were assessed⁴
 - At baseline, domain scores were similar between treatment groups and comparable with the general population; at week 25, PRO analysis indicated maintenance of GHS and functioning, and improvement of symptom domains (ie, pain) with SG vs chemo (**Figure 1**)⁴
- This post hoc pooled analysis of the SG and chemo treatment groups in the ASCENT-03 study further evaluated associations between disease control and the assessed PROs

Figure 1. PROs at Baseline and Changes From Baseline Across Scheduled Post-Baseline Visits Through Week 25^a

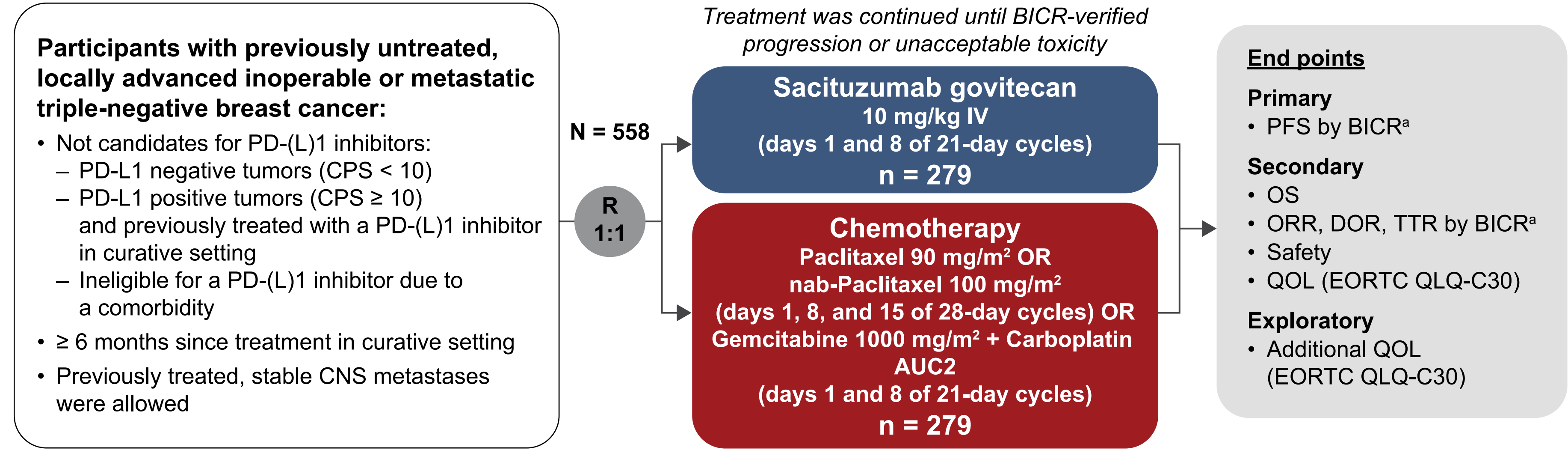


^aGeneral population norm scores were re-weighted based on participants' age and gender distributions in the ASCENT-03 ITT analysis set. CFB, change from baseline; chemo, chemotherapy; GHS/QOL, global health status/quality of life; ITT, intent-to-treat; LS, least-squares; PRO, patient-reported outcome; SG, sacituzumab govitecan.

Methods

- Study design, eligibility criteria, and endpoints are shown in **Figure 2**
- EORTC QLQ-C30 data were collected at baseline, on day 1 of each cycle, and at the end of treatment (**Figure 3**)
- Mixed-effect repeated measure modeling analyses were used to evaluate associations between disease control and change from baseline in EORTC QLQ-C30 domains in the pooled intent-to-treat population (n = 558) across both treatment groups (**Figure 3**)
- P values were nominal

Figure 2. ASCENT-03 Study Design

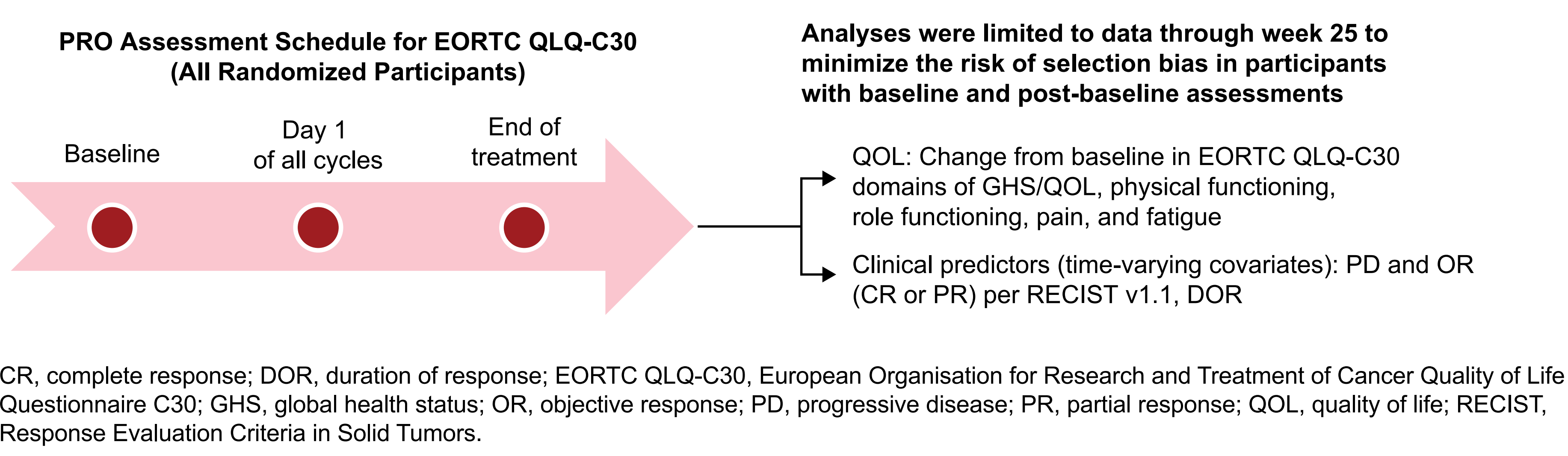


ClinicalTrials.gov identifier: NCT05382299. Data cutoff: April 2, 2025.

^aPer Response Evaluation Criteria in Solid Tumors v1.1.

AUC, area under the curve; BICR, blinded independent central review; CNS, central nervous system; CPS, combined positive score; DOR, duration of response; EORTC QLQ-C30, European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire C30; IV, intravenous; ORR, objective response rate; OS, overall survival; PD-[L]1, programmed cell death (ligand) 1; PFS, progression-free survival; QOL, quality of life; R, randomization; TTR, time to response.

Figure 3. Assessment of Association Between QOL and Clinical Predictors



Results

- Progressive disease was associated with worsening in GHS/QOL, physical functioning, and role functioning, and increased pain (**Figure 4A**)
- Objective response was linked with improvements in GHS/QOL, physical functioning, and role functioning, and reduction in pain (**Figure 4B**)
- Consistent improvements in GHS/QOL, physical functioning, and role functioning, as well as reductions in pain and fatigue, were observed in participants with complete/partial response vs progressive disease (**Figure 4C**)
- Longer DOR was associated with modest improvement in GHS/QOL and less fatigue (**Figure 4D**)

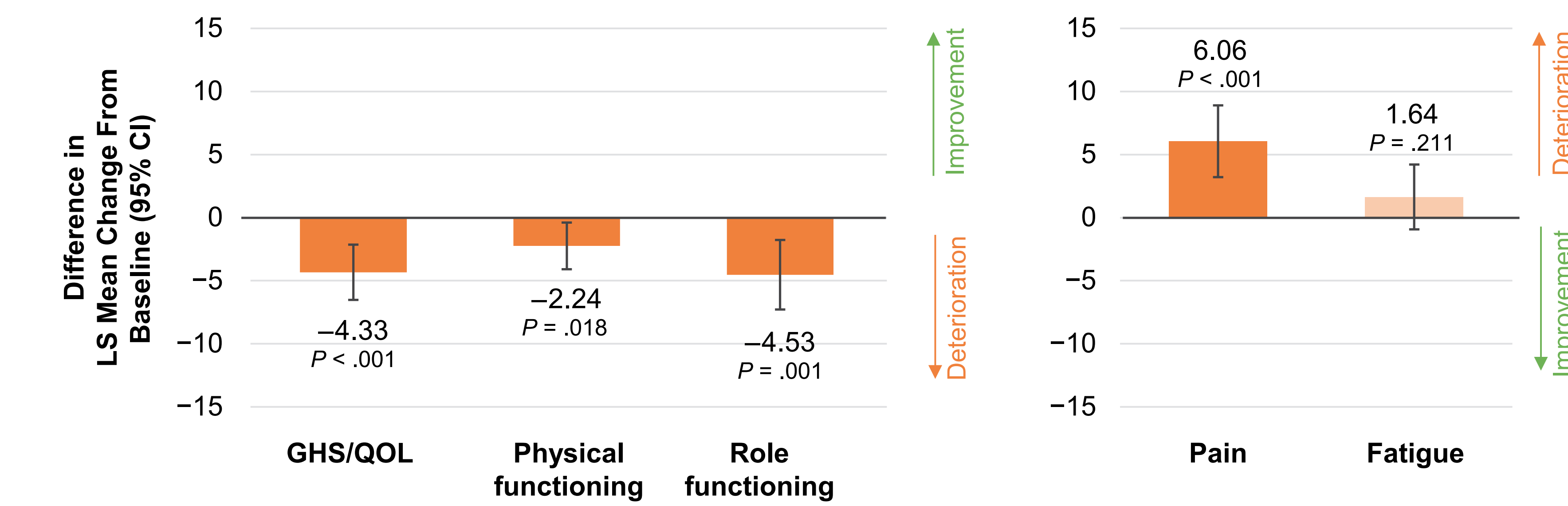
Limitations

- PRO reporting may have been impacted by the open-label study design, although published evidence suggests a limited impact^{6,7}
- Participants were not assessed for PROs after the end of treatment visit; thus, the impact of treatment discontinuation, subsequent therapy, disease progression, or longer-term toxicities on functioning and symptoms could not be assessed
- Confidence intervals and nominal P values were not adjusted for multiplicity and should be interpreted descriptively due to the exploratory nature of these post-hoc analyses

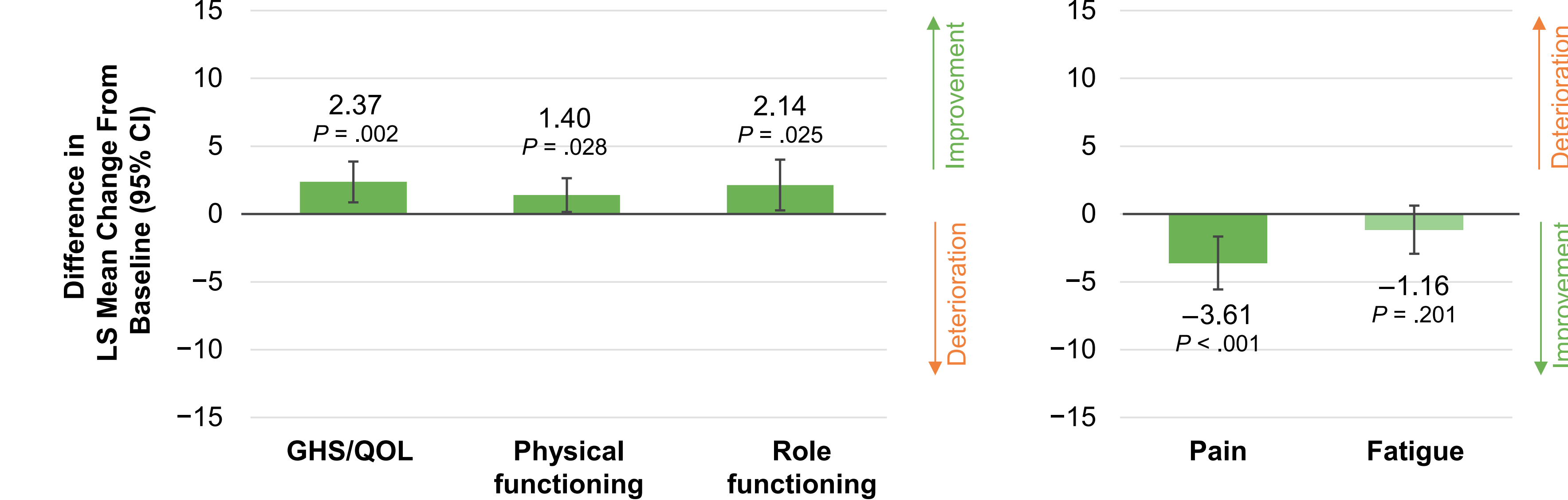
Results

Figure 4. Association Between Clinical Outcomes and PRO Change From Baseline Across Scheduled Post-Baseline Visits Through Week 25

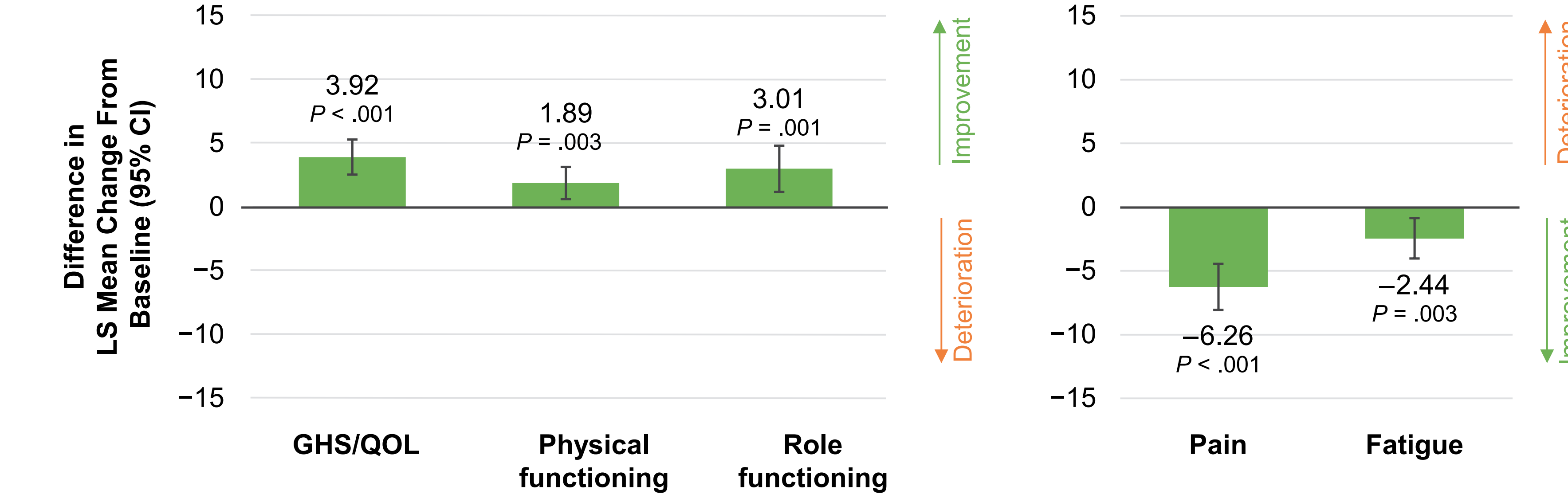
A. Difference in Change From Baseline by Progressive Disease^a Status (PD vs no PD)



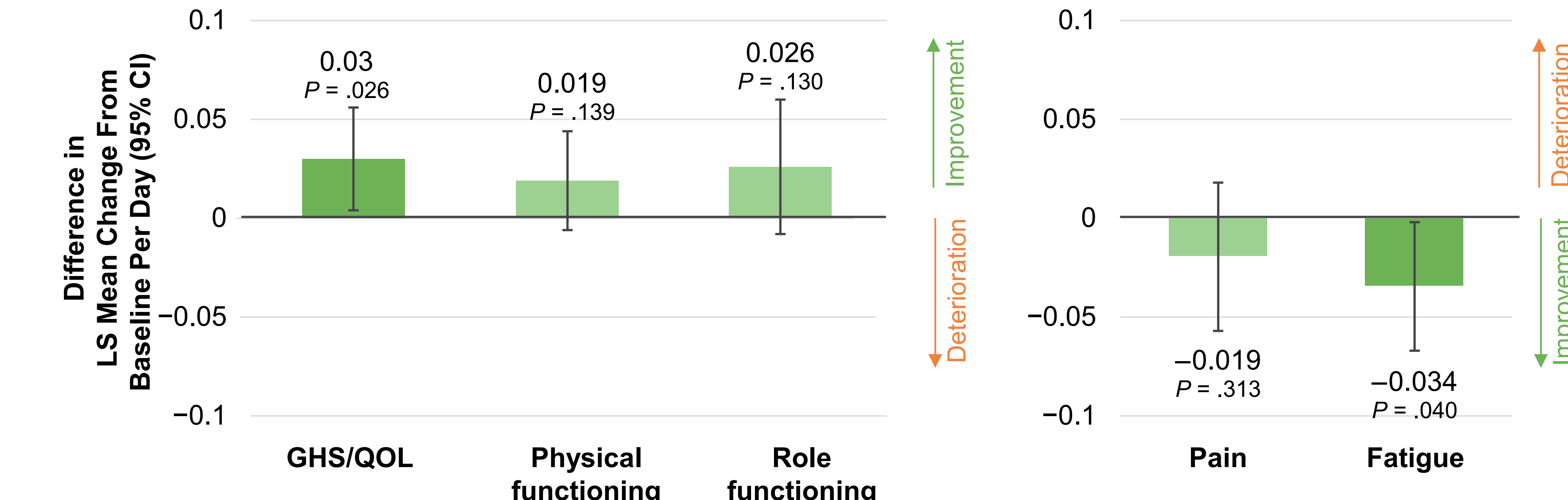
B. Difference in Change From Baseline by Objective Response^a Status (CR/PR vs no CR/PR)



C. Difference in Change From Baseline by Objective Response^a vs Progressive Disease^a Status (CR/PR vs PD)



D. Difference in Change From Baseline by Duration of Response^a



^aPD and OR were modeled as binary time-varying covariates. ^bDOR was modeled as a continuous time-varying covariate, representing cumulative days from first documented CR/PR to PRO assessment. Nonresponders were given a DOR of 0 in this analysis. CR, complete response; DOR, duration of response; GHS/QOL, global health status/quality of life; LS, least-squares; OR, objective response; PD, progressive disease; PR, partial response; PRO, patient-reported outcome.