

Association Between Disease Control and Patient-Reported Functioning and Quality of Life in the ASCENT-04/KEYNOTE-D19 Study

Kevin Kalinsky¹, Evandro de Azambuja², Peter Schmid³, Sherene Loi⁴, Sung-Bae Kim⁵, Clinton Yam⁶, Bernardo Rapoport⁷, Seock-Ah Im⁸, Barbara Pistilli⁹, Wassim Mchayleh¹⁰, David W Cescon¹¹, Junichiro Watanabe¹², Manuel Alejandro Lara Bañuelas¹³, Ruffo Freitas-Junior¹⁴, Alain Lortholary¹⁵, Nandita Kachru¹⁶, Ling Shi¹⁷, Shien Guo¹⁷, Maryam Afshari¹⁶, Sara M Tolaney¹⁸

¹Winship Cancer Institute, Emory University, Atlanta, GA, USA; ²Institut Jules Bordet, Hôpital Universitaire de Bruxelles (HUB), Université Libre de Bruxelles (ULB), Brussels, Belgium; ³Centre for Experimental Cancer Medicine, Barts Cancer Institute, Queen Mary University of London, London, UK; ⁴Peter MacCallum Cancer Centre, University of Melbourne, Melbourne, VIC, Australia; ⁵Asan Medical Center, University of Ulsan College of Medicine, Seoul, Republic of Korea; ⁶University of Texas MD Anderson Cancer Center, Houston, TX, USA; ⁷Medical Oncology Centre of Rosebank, Personalised Cancer Care, Saxonwold, South Africa; ⁸Seoul National University Hospital, Cancer Research Institute, Seoul National University College of Medicine, Seoul National University, Seoul, Republic of Korea; ⁹Department of Cancer Medicine, Gustave Roussy, IHU National PReclSion Medicine Center in Oncology, Villejuif, France; ¹⁰AdventHealth Cancer Institute, Orlando, FL, USA; ¹¹Princess Margaret Cancer Centre, University Health Network, Toronto, ON, Canada; ¹²Juntendo University Graduate School of Medicine, Tokyo, Japan; ¹³Oncology Center of Chihuahua, Chihuahua, Mexico; ¹⁴Advanced Center for Diagnosis of Breast Diseases, Federal University of Goiás, Goiás, Brazil; ¹⁵Centre Catherine de Sienne, Nantes, France; ¹⁶Gilead Sciences, Inc., Foster City, CA, USA; ¹⁷Thermo Fisher Scientific, Waltham, MA, USA; ¹⁸Dana-Farber Cancer Institute, Harvard Medical School, Boston, MA, USA

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ASCENT-04/
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Conclusions

- In pooled analyses of the sacituzumab govitecan (SG) plus pembrolizumab (pembro) and chemotherapy (chemo) plus pembro treatment groups in the ASCENT-04 study in participants with triple-negative breast cancer, objective response was associated with favorable changes in role functioning and pain through week 55
- Disease progression was associated with worsening of quality of life (QOL), functioning, pain, and fatigue
- Objective response was associated with clinically favorable patient-reported outcomes (PROs) in role functioning and pain, which were generally maintained over time, with little incremental PRO improvement as duration of response (DOR) increased
- Consistently improved QOL, functioning, pain, and fatigue were observed in participants achieving objective response compared with those with progressive disease
- Findings from these pooled analyses show that disease control is associated with improved PROs; this provides patient-reported context for previously reported improvements in progression-free survival (PFS), DOR, and PROs with SG plus pembro vs chemo plus pembro in ASCENT-04, supporting SG plus pembro as a first-line treatment option in participants with programmed death ligand 1 (PD-L1)-positive metastatic triple-negative breast cancer

Plain Language Summary

- The ASCENT-04 study compared sacituzumab govitecan (SG) plus pembrolizumab (pembro) with chemotherapy plus pembro in participants with advanced triple-negative breast cancer who had not received treatment before; their tumors expressed the programmed death ligand 1 protein
- In the main study, participants receiving SG plus pembro went on to live longer without their cancer getting worse or dying, had a response over a longer length of time, maintained their ability to do everyday work, felt better, and had fewer symptoms compared with participants receiving chemotherapy plus pembro
- 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 preserve this well-being during treatment
- This analysis looked at whether changes in the cancer were related to how participants felt and functioned, using data from participants receiving SG plus pembro and chemotherapy plus pembro
- 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
- A longer response resulted in little additional improvement in how participants felt or functioned, suggesting that keeping the cancer under control may help people maintain these benefits, rather than feel increasingly better over time
- These findings suggest that as long as the cancer stays controlled, participants feel and function better. This provides additional context for improved disease control and patient-reported outcomes seen with SG plus pembro compared with chemotherapy plus pembro in ASCENT-04, supporting SG plus pembro as a front-line treatment option

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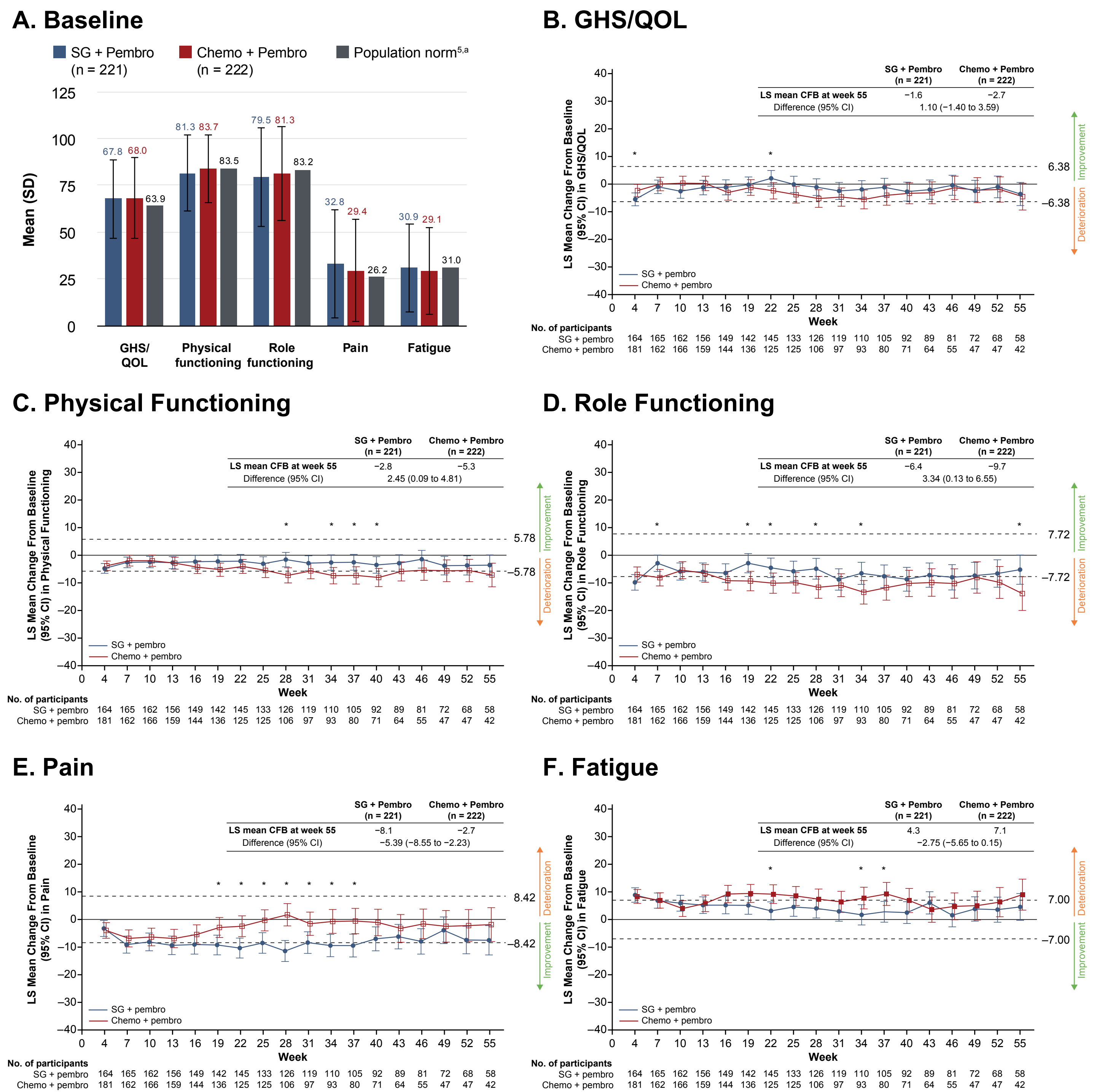
Disclosures: KK reports advisory roles with Daiichi Sankyo, Eli Lilly, Pfizer, Novartis, AstraZeneca, Merck, Seattle Genetics, Puma Biotechnology, Genentech, Gilead Sciences, Menarini Silicon Biosystems, Myovant Sciences, Mersana, ProteinQure, bioTherapeutics, Regor, and Relay Therapeutics; consulting roles with RayzeBio, Bicycle Therapeutics, Jazz Pharmaceuticals, Novartis, Genentech, Eli Lilly, Pfizer, AstraZeneca, Daiichi Sankyo, Myovant Sciences, Takeda, Menarini Silicon Biosystems, and Prelude Therapeutics; being an employee with stock/share in Grail, stock/shares in ADC Therapeutics via a family member; research support from Novartis, Genentech, Eli Lilly, Pfizer, Seattle Genetics, AstraZeneca, Daiichi Sankyo, and Ascentage Pharma; and serving on a steering committee for Immunomedics, AstraZeneca, Ambryx Biotechnology, and Genentech.

Correspondence: Kevin Kalinsky, kevin.michael.kalinsky@emory.edu

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-04 study, first-line treatment with SG + pembro led to a statistically significant and clinically meaningful improvement in PFS vs chemo + pembro in participants with previously untreated programmed death ligand 1 (PD-L1)-positive metastatic triple-negative breast cancer (hazard ratio, 0.65; 95% CI, 0.51–0.84; $P < .001$)³
 - Objective response was numerically higher with SG + pembro (60%) vs chemo + pembro (53%)³
 - Median DOR was numerically longer with SG + pembro (16.5 months) vs chemo + pembro (9.2 months)³
 - The safety profile of SG + pembro was consistent with previous reports of both agents and associated with fewer discontinuations than chemo + pembro³
 - 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; across assessments during the first 55 weeks of treatment, participants receiving SG + pembro had significantly better role and physical functioning with reduced pain vs chemo + pembro; GHS/QOL and fatigue were comparable between treatment groups (Figure 1)⁴
- This post hoc pooled analysis of the SG + pembro and chemo + pembro treatment groups in the ASCENT-04 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 55⁴



¹⁸General population norm scores were re-weighted based on participants' age and gender distributions in the ASCENT-04 ITT analysis set. CFB, change from baseline; chemo, chemotherapy; GHS/QOL, global health status/quality of life; ITT, intent-to-treat; LS, least-squares; pembro, pembrolizumab; PRO, patient-reported outcome; SG, sacituzumab govitecan.

Methods

- Study design, eligibility criteria, and end points 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 = 443) across both treatment groups (Figure 3)
- P values were nominal

Figure 2. ASCENT-04 Study Design

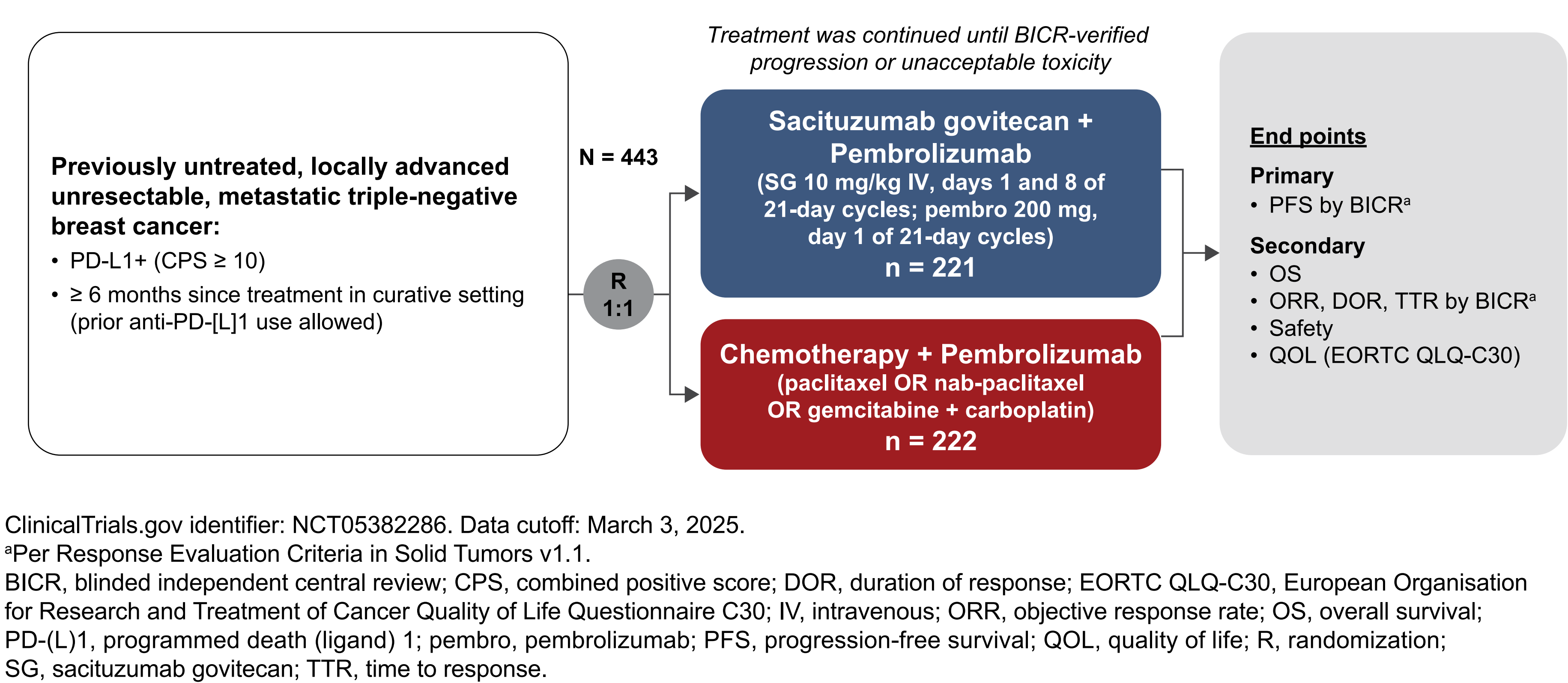
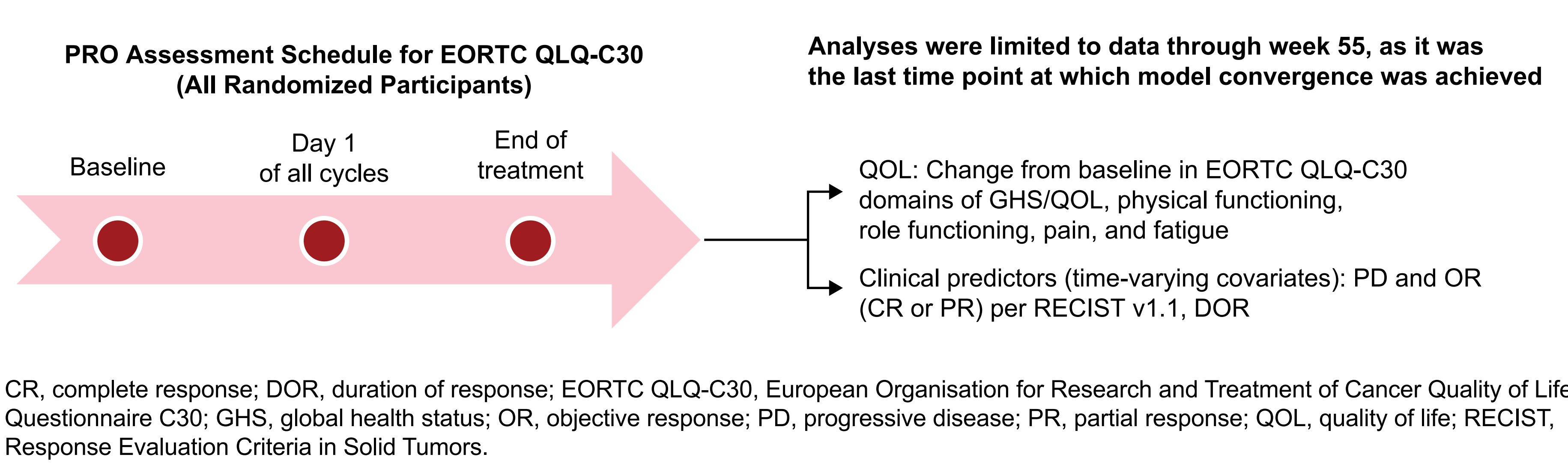


Figure 3. Assessment of Association Between QOL and Clinical Predictors



Results

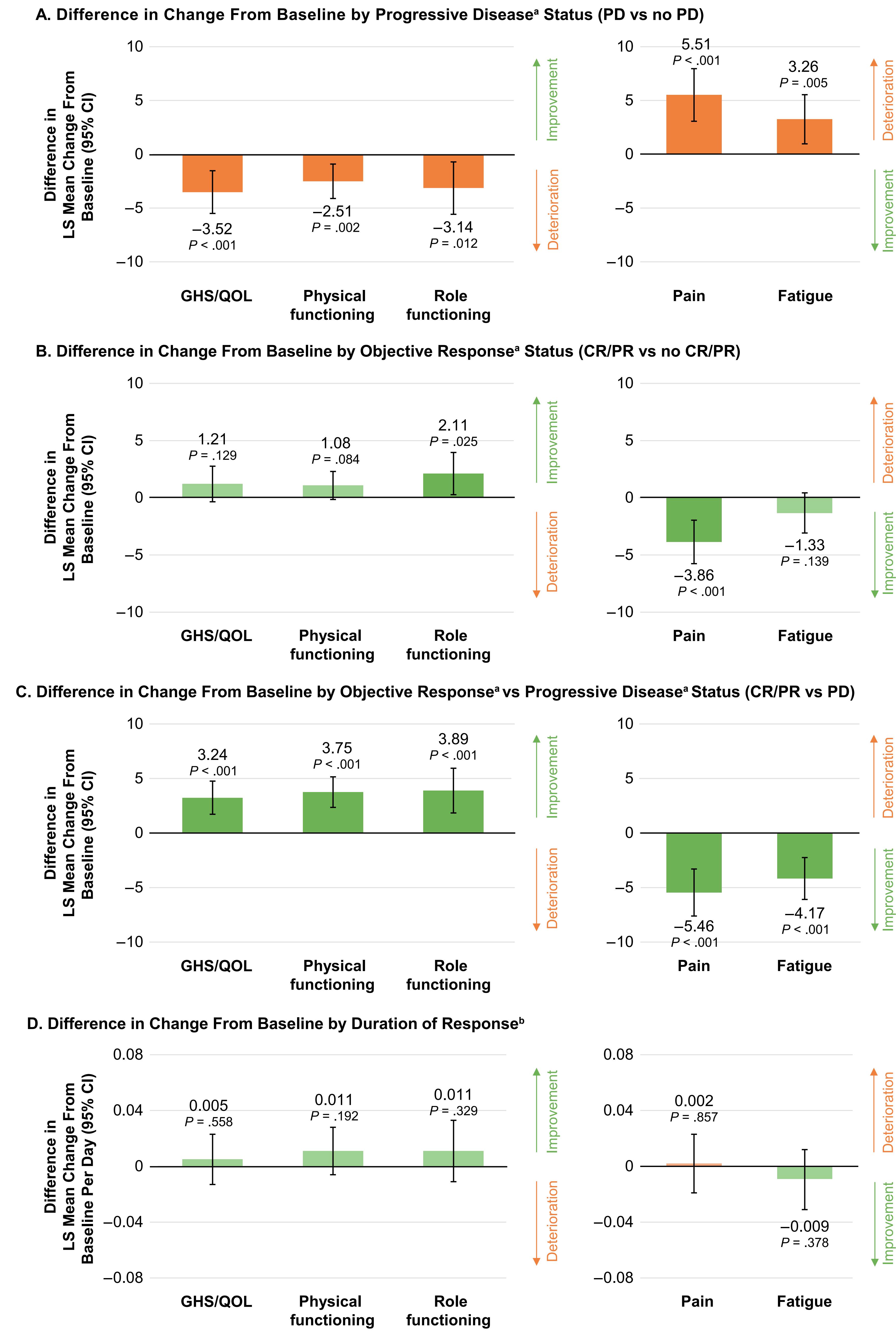
- Progressive disease was associated with worsening in GHS/QOL, physical functioning, and role functioning, and increased pain and fatigue (Figure 4A)
- Objective response was linked with improvements in role functioning and reduction in pain (Figure 4B)
- Consistent improvements in GHS/QOL, physical 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)
- Incremental PRO improvement was not observed as DOR increased (Figure 4D)

Limitations

- PRO reporting may have been impacted by the open-label study design, although published evidence suggests that the absence of blinding has 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 55



^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.