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Original Article

# Patient-reported Outcomes in KEYLYNK-010: Pembrolizumab Plus Olaparib Versus Abiraterone or Enzalutamide for Participants with Biomarker-unselected, Previously Treated Metastatic Castration-resistant Prostate Cancer

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**Abstract**

***Background and objective:*** Pembrolizumab plus olaparib did not significantly improve radiographic progression-free survival or overall survival versus a next-generation hormonal agent (NHA) in participants with biomarker-unselected, pretreated metastatic castration-resistant prostate cancer (mCRPC) in the phase 3 KEYLYNK-010 trial. We present prespecified patient-reported outcomes (PROs) from KEYLYNK-010.

***Methods:*** Participants were randomly assigned 2:1 to receive pembrolizumab plus olaparib or an NHA (abiraterone acetate or enzalutamide). PROs were evaluated using the Brief Pain Inventory—Short Form (BPI-SF), Functional Assessment of Cancer Therapy—Prostate Cancer (FACT-P), and EuroQol 5-Dimension 5-Level (EQ-5D-5L) questionnaires. The PRO endpoints included time to pain progression (TTPP) as per BPI-SF and the least squares mean (LSM) change from baseline to week 15 in FACT-P total, BPI-SF, and EQ-5D visual analog scale (VAS) scores.

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Next-generation hormonal agent
Olaparib
Pembrolizumab

***Key findings and limitations:*** The PRO analysis population included 774 participants (pembrolizumab plus olaparib, *n* = 520; NHA, *n* = 254). The median follow-up was 18.7 (range, 6.1–31.7) mo. No meaningful differences were observed in TTPP for pembrolizumab plus olaparib versus NHA (median: 13.5 vs 12.0 mo; hazard ratio 0.95; 95% confidence interval 0.72–1.26). From baseline to week 15, no meaningful LSM differences were observed between the treatment groups in FACT-P total, BPI-SF, and EQ-5D VAS scores. Limitations include no formal hypothesis testing.

***Conclusions and clinical implications:*** No meaningful differences were observed in health-related quality of life (HRQoL) or disease-related symptom scores for pembrolizumab plus olaparib versus NHA in participants with biomarker-unselected, pretreated mCRPC. These findings suggest that pembrolizumab plus olaparib did not negatively impact HRQoL in participants with pretreated mCRPC.

**Clinical trial registry:** NCT03834519.



ADVANCING PRACTICE

**What does this study add?**

Patient-reported outcomes (PROs) provide valuable information on patients' perception of their on-treatment health status and quality of life, which are key considerations for clinicians and patients when making treatment decisions. This prespecified analysis of the KEYLYNK-010 trial of participants with biomarker-unselected, pretreated metastatic castration-resistant prostate cancer (mCRPC) showed that PROs, including health-related quality of life (HRQoL) and disease-related symptoms, were similar between pembrolizumab plus olaparib and a next-generation hormonal agent switch. These findings suggest that the addition of pembrolizumab to olaparib did not negatively impact HRQoL in participants with pretreated mCRPC.

**Clinical Relevance**

In the randomized, open-label, phase 3 KEYLYNK-010 trial of participants with biomarker-unselected mCRPC previously treated with next-generation hormonal agent (NHA) and docetaxel, pembrolizumab plus olaparib did not significantly improve radiographic progression-free survival or overall survival. Treatment-related adverse events of grade 3 or higher occurred in 34.6% and 9.0% of patients treated with pembrolizumab plus olaparib and NHA switch, respectively. In the current analysis of KEYLYNK-010, HRQoL was evaluated using the following validated PRO instruments: Functional Assessment of Cancer Therapy–Prostate; EuroQol 5-Dimensions, 5-Levels; Brief Pain Inventory-Short Form; and an analgesic log. Overall, no meaningful differences in HRQoL or disease-related symptom scores were observed for pembrolizumab plus olaparib versus NHA switch in participants with biomarker-unselected, pretreated mCRPC. Associate Editor: Elena Castro.

**Patient Summary**

In this report, we looked at participants' perception of their health-related quality of life (HRQoL) and disease-related symptoms during treatment with pembrolizumab plus olaparib or a next-generation hormonal agent (NHA) switch for previously treated metastatic castration-resistant prostate cancer (mCRPC). We found that HRQoL and disease-related symptom scores, as reported by the participants, were similar in the pembrolizumab plus olaparib and NHA switch groups. We conclude that HRQoL was not impacted negatively in participants with pretreated mCRPC who received the combination of pembrolizumab and olaparib.

## 1. Introduction

Patients with metastatic castration-resistant prostate cancer (mCRPC) often experience debilitating symptoms that significantly impact health-related quality of life (HRQoL) [1–3]. Therefore, therapies for mCRPC that are tolerable, improve well-being, and maintain overall HRQoL are the key considerations for clinicians and patients when making treatment decisions.

For patients with biomarker-unselected mCRPC whose disease progressed on a next-generation hormonal agent (NHA) and docetaxel, treatment options include radioligand lutetium-177 prostate-specific membrane antigen (PSMA)-617 (for patients with PSMA-positive disease), cabazitaxel,

and NHA switch [4–6]. However, novel treatment regimens that can prolong survival without loss of HRQoL remain an unmet need in this setting.

The combination of the programmed cell death protein 1 inhibitor pembrolizumab and the poly(ADP-ribose) polymerase (PARP) inhibitor olaparib was evaluated versus an NHA switch in participants with biomarker-unselected mCRPC previously treated with an NHA and docetaxel in the randomized, open-label, phase 3 KEYLYNK-010 trial [7]. Pembrolizumab plus olaparib did not significantly improve the dual primary endpoints of radiographic progression-free survival (rPFS; hazard ratio [HR] 1.02 [95% confidence interval {CI} 0.82–1.25], $p = 0.55$) or overall survival (OS; HR 0.94 [95% CI 0.77–1.14], $p = 0.26$) compared with an NHA switch, and the trial was stopped for futility. Treatment-related adverse events of grade $\geq$3 occurred in 34.6% and 9.0% of participants treated, respectively, with pembrolizumab plus olaparib and an NHA. Although KEYLYNK-010 did not meet its dual primary endpoints, patient-reported outcomes (PROs) provide valuable information on patients' perceptions of their HRQoL during treatment. The prespecified secondary and exploratory PRO findings from KEYLYNK-010 are reported herein.

## 2. Patients and methods

### 2.1. Study design and participants

The study design of KEYLYNK-010 (NCT03834519) has been published previously [7]. Briefly, eligible participants were adult males with histologically or cytologically confirmed mCRPC not preselected for homologous recombination repair gene alterations, whose disease progressed on or after abiraterone or enzalutamide (but not both) and docetaxel.

Participants were assigned randomly in a 2:1 ratio to receive pembrolizumab 200 mg intravenously once every 3 wk for $\leq$35 cycles ($\sim$2 yr) plus olaparib 300 mg orally twice daily or an NHA (either abiraterone acetate 1000 mg orally once daily plus 5 mg prednisone/prednisolone orally twice daily if the participant received enzalutamide previously, or enzalutamide 160 mg orally once daily if the participant received abiraterone previously). Randomization was stratified by a prior NHA (abiraterone vs enzalutamide) and the presence of measurable disease at baseline (yes vs no). Treatment continued until confirmed radiographic disease progression, unacceptable toxicity, participant's or investigator's decision to discontinue therapy, or completion of 35 cycles of pembrolizumab.

The study was conducted in accordance with the principles of Good Clinical Practice and was approved by the appropriate institutional review boards and regulatory agencies. Written informed consent was provided by all participants before enrollment.

### 2.2. PRO assessments

Validated PRO instruments were administered by trained site personnel and completed electronically by the participant before all other study procedures in the following order: Functional Assessment of Cancer Therapy—Prostate (FACT-P), EuroQol 5-Dimension, 5-Level (EQ-5D-5L), Brief Pain Inventory—Short Form (BPI-SF), and an analgesic log. The PRO instruments were administered at baseline, every 3 wk until week 21 (FACT-P and EQ-5D-5L) or week 24 (BPI-SF and analgesic log), and then every 6 wk until week 69 (FACT-P and EQ-5D-5L) or week 72 (BPI-SF and analgesic log) and every 12 wk thereafter, until treatment completion or discontinuation, and at the 30-d safety follow-up visit.

BPI-SF is a 15-item domain-specific instrument designed to assess the severity of pain and the impact or interference of pain on daily function [8]. It consists of the pain severity and pain interference domains. A $\geq$2-point change in the average pain severity or the "worst pain" item was considered clinically meaningful. A lower BPI-SF score indicated lower pain.

FACT-P is a multidimensional 39-item questionnaire validated for use in patients with prostate cancer to assess their HRQoL and disease-related symptoms [9–12]. It consists of the 27-item self-reported questionnaire FACT—General subscales (physical well-being, social/family well-being, emotional well-being, and functional well-being) and a 12-item prostate cancer subscale (PCS). A higher FACT-P total or subscale score indicates better HRQoL.

EQ-5D-5L measures general health status and includes the following five domains: mobility, self-care, usual activities, pain/discomfort, and depression/anxiety [13]. EQ-5D-5L also uses a 100-point visual analog scale (VAS), in which participants rate their general health state at the time of the assessment, ranging from 0 (worst health imaginable) to 100 (best health imaginable). The clinically meaningful change threshold for the EuroQol 5-Dimension (EQ-5D) VAS was defined as a $\geq$7-point change from baseline [14].

Additional information on PRO assessments is provided in the Supplementary material.

### 2.3. Outcomes

The dual primary endpoints in KEYLYNK-010 (rPFS and OS) and the key secondary endpoints have been reported [7]. The prespecified secondary PRO endpoint was time to pain progression (TTPP; time from randomization to pain progression) as per item 3 of BPI-SF "worst pain in 24 h" and opiate analgesic use (Analgesic Quantification Algorithm score) [8,15]. Prespecified exploratory endpoints included the least squares mean (LSM) change from baseline to week 15 in BPI-SF (pain interference, pain severity, and worst pain) scores, FACT-P total and subscales scores, and EQ-5D VAS score, and the overall improvement rate and time to deterioration (TTD) in FACT-P total and subscale scores. Time to pain severity progression (time from randomization to the time point at which worsening in pain was observed for asymptomatic and symptomatic participants at baseline) as per BPI-SF was also evaluated.

For the LSM change from baseline analyses, week 15 was selected as the latest time point when the overall questionnaire completion and compliance rates were approximately 60% and 80% per protocol, respectively, based on a blinded

data review prior to the data cutoff date for PRO assessments.

TTD was defined as the time to first onset of deterioration from baseline based on clinically meaningful change thresholds for each FACT-P scale or subscale score (Supplementary Table 1) and was confirmed by a second adjacent deterioration from baseline.

### 2.4. Statistical analysis

The PRO analysis population included all randomly assigned participants who received one or more doses of study treatment and completed one or more PRO assessments. The completion and compliance rates were summarized by treatment group and visit.

TTPP and TTD were estimated using the Kaplan-Meier method. The magnitude of treatment difference was analyzed using a stratified Cox proportional hazards models with the Efron method of handling ties. The LSM change from baseline to week 15 and the between-group differences in LSM were assessed using a constrained longitudinal data analysis model, with the PRO scores as the response variable and the treatment, time, treatment by time interaction, and stratification factors (measurable disease status and prior NHA treatment) as covariates. Participants were categorized as improved, stable, or deteriorated based on the clinically meaningful change threshold from baseline to week 15 in FACT-P and subscale scores (Supplementary Table 1). The proportion of participants in each category was summarized by treatment groups. Empirical mean score changes from baseline and 95% CIs were descriptively summarized at each time point for FACT-P, BPI-SF, and EQ-5D VAS. No formal hypothesis testing was performed.

## 3. Results

### 3.1. Participants

As reported previously, 793 participants were assigned randomly to receive pembrolizumab plus olaparib ($n$ = 529) or an NHA ($n$ = 264) between May 30, 2019 and July 16, 2021 [7]. The PRO analysis population included 774 participants for FACT-P (pembrolizumab plus olaparib, $n$ = 520; NHA, $n$ = 254), 750 participants for BPI-SF (pembrolizumab plus olaparib, $n$ = 506; NHA, $n$ = 244), and 773 participants for EQ-5D VAS (pembrolizumab plus olaparib, $n$ = 520; NHA, $n$ = 253). The median time from randomization to the data cutoff date (January 18, 2022) was 18.7 (range, 6.1–31.7) mo.

### 3.2. Patient-reported outcomes

The completion rates for the FACT-P, BPI-SF, and EQ-5D-5L questionnaires were >84.0% at baseline and >57.0% at week 15 (Supplementary Fig. 1). The compliance rates for all three questionnaires were >84.0% at baseline and >81.0% at week 15.

The median TTPP in the pembrolizumab plus olaparib group versus the NHA group was 13.5 mo (95% CI 9.7–not reached [NR]) versus 12.0 mo (95% CI 10.1–NR; HR 0.95 [95% CI 0.72–1.26]; Fig. 1). The 6-mo pain progression-free rate was 63.0% (95% CI 57.4–68.0) versus 61.1% (95% CI 52.7–68.5). The median time to pain severity progression in the pembrolizumab plus olaparib group versus the NHA group was 16.0 mo (95% CI 12.6–NR) versus 12.0 mo (95% CI 10.1–NR; HR 0.84 [95% CI 0.62–1.13]; Supplementary Fig. 2). The 6-mo pain severity progression-free rate was 68.7% (95% CI 63.3–73.5) versus 64.5% (95% CI 56.0–71.8).

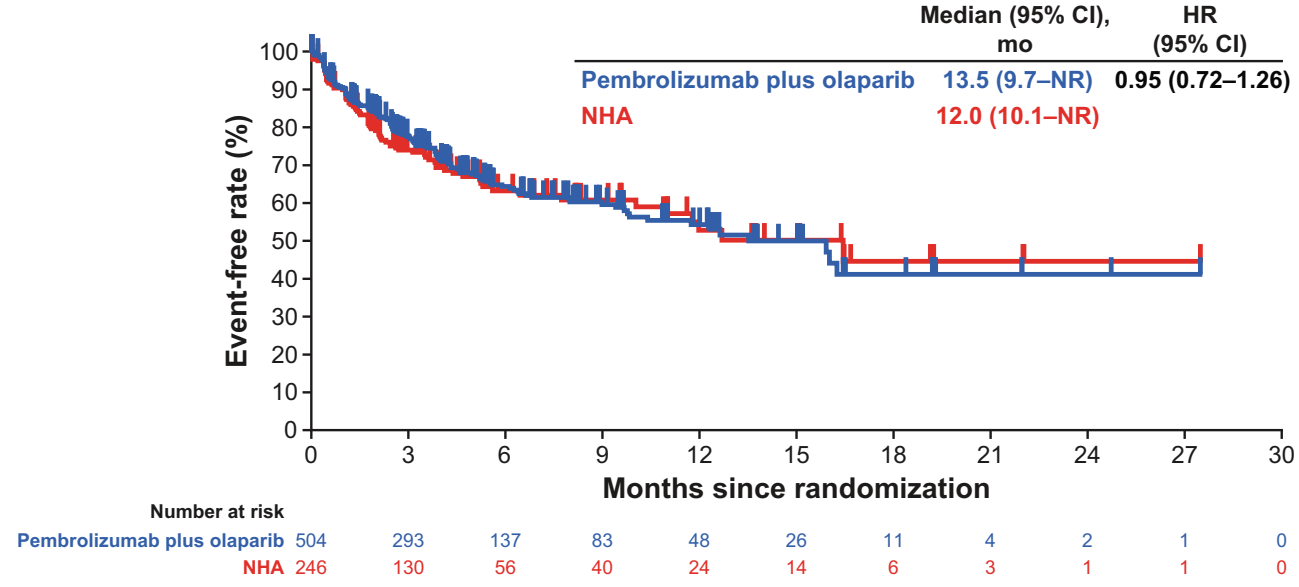


**Fig. 1 – Kaplan-Meier estimates of TTPP. CI = confidence interval; HR = hazard ratio; NHA = next-generation hormonal agent; NR = not reached; TTPP = time to pain progression.**

**Table 1 – Change from baseline to week 15 in the FACT-P total and EQ-5D VAS scores**

| | FACT-P total | | EQ-5D VAS | |
|---|---|---|---|---|
| | Pembrolizumab plus olaparib | NHA | Pembrolizumab plus olaparib | NHA |
| Baseline | | | | |
| *n* | 495 | 244 | 491 | 239 |
| Mean (SD) | 107.00 (21.4) | 104.16 (22.40) | 66.16 (19.47) | 63.24 (20.81) |
| Week 15 | | | | |
| *n* | 350 | 147 | 350 | 147 |
| Mean (SD) | 105.83 (21.69) | 105.38 (22.76) | 68.6 (18.83) | 68.2 (20.58) |
| Change from baseline to week 15 | | | | |
| *n* | | | | |
| LSM (95% CI) | −4.62 (−6.47 to −2.77) | −5.86 (−8.58 to 3.13) | 0.03 (−1.86 to 1.92) | −1.15 (−3.88 to 1.58) |
| Difference in LSM (95% CI) | 1.24 (−1.98 to 4.45) | | 1.18 (−1.98 to 4.34) | |

CI = confidence interval; EQ-5D VAS = EuroQol 5-Dimension visual analog scale; FACT-P = Functional Assessment of Cancer Therapy—Prostate; LSM = least squares mean; SD = standard deviation.

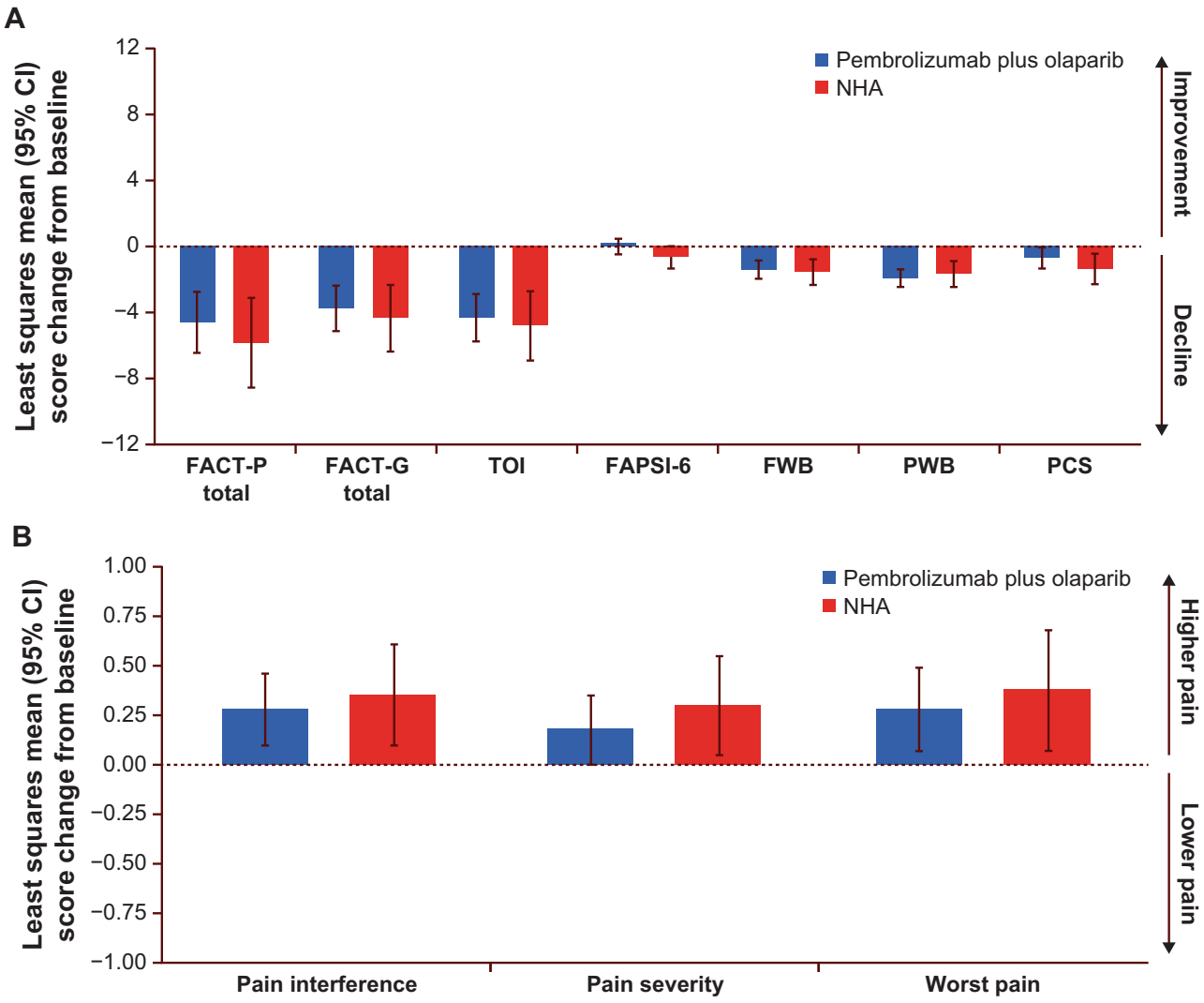


**Fig. 2 – LSM change from baseline to week 15 in (A) FACT-P and (B) BPI-SF scores. BPI-SF = Brief Pain Inventory—Short Form; CI = confidence interval; FACT-G = Functional Assessment of Cancer Therapy—General; FACT-P = Functional Assessment of Cancer Therapy—Prostate; FAPSI-6 = FACT Advanced Prostate Symptom Index—6; FWB = Functional Well-being; LSM = least squares mean; NHA = next-generation hormonal agent; PCS = Prostate Cancer Subscale; PWB = Physical Well-being; TOI = Trial Outcome Index.**

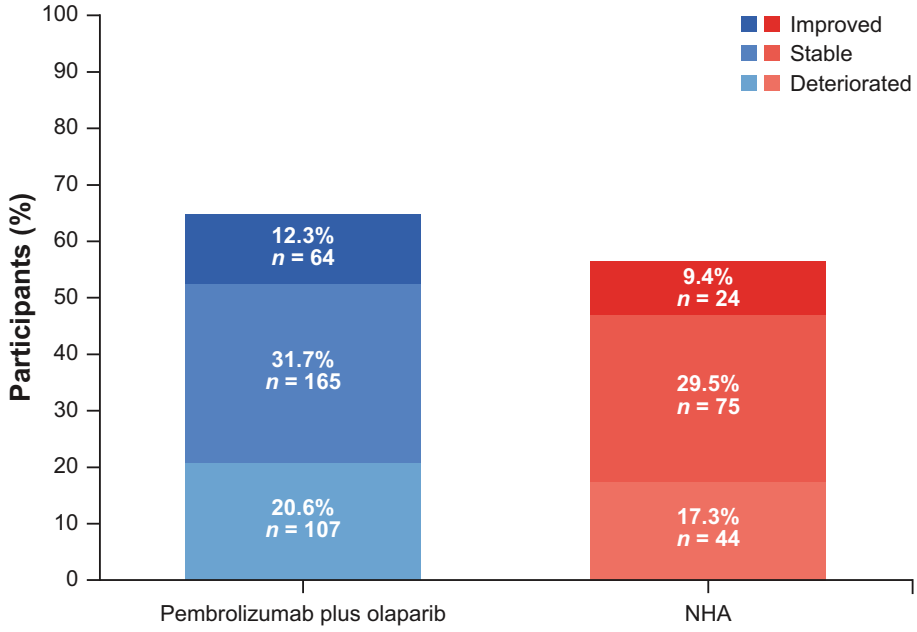


**Fig. 3 – Proportion of participants with improved, stable, and deteriorated FACT-P total scores from baseline to week 15. Participants were categorized as improved, stable, or deteriorated based on the clinically meaningful threshold change from baseline of 10 points (improved, ≥10 points; stable, greater than −10 points and <10 points; and deteriorated, greater than or equal to −10 points), with confirmation at the next consecutive visit. In total, 184 participants in the pembrolizumab plus olaparib group and 111 participants in the NHA group had no assessment. FACT-P = Functional Assessment of Cancer Therapy—Prostate; NHA = next-generation hormonal agent.**

The mean FACT-P total scores were similar between the pembrolizumab plus olaparib and NHA groups at baseline and week 15 (Table 1). No meaningful difference in LSM change from baseline to week 15 was observed in the pembrolizumab plus olaparib group versus the NHA group for FACT-P total (difference, 1.24; 95% CI −1.98 to 4.45) and FACT-P subscale scores (Table 1, Fig. 2A, and Supplementary Table 2). A similar proportion of participants in the pembrolizumab plus olaparib group versus the NHA group had an improved or a stable FACT-P total score from baseline to week 15 (improved: 12.3% vs 9.4%; stable: 31.7% vs 29.5%; Fig. 3). A similar proportion of participants in the pembrolizumab plus olaparib group versus the NHA group had improved or stable scores from baseline to week 15 for all FACT-P subscales, except for PCS (44.4% vs 38.2%; Supplementary Fig. 3).

No meaningful differences in LSM change from baseline to week 15 was observed in the pembrolizumab plus olaparib group versus the NHA group for BPI-SF pain interference (difference, −0.07; 95% CI −0.37 to 0.23), pain severity (difference, −0.12; 95% CI −0.42 to 0.17), and worst pain (difference, −0.10; 95% CI −0.45 to 0.26) scores (Fig. 2B and Supplementary Table 3).

The mean EQ-5D VAS scores were similar between the pembrolizumab plus olaparib and NHA groups at baseline and week 15 (Table 1). No meaningful differences in LSM change from baseline to week 15 was observed in the pembrolizumab plus olaparib group versus the NHA group (difference, 1.18; 95% CI −1.98 to 4.34).

In both the treatment groups, PRO scores were generally maintained across all evaluated time points (Fig. 4). The median TTD in FACT-P total scores for pembrolizumab plus olaparib versus NHA therapy was 7.6 mo (95% CI 4.9–11.7) versus 6.3 mo (95% CI 4.9–11.8; HR 1.04 [95% CI 0.82–1.31]); no meaningful between-group differences were observed for TTD in FACT-P total and subscale scores (Fig. 5).

## 4. Discussion

In this prespecified analysis of the KEYLYNK-010 trial of participants with pretreated mCRPC, PROs were similar between pembrolizumab plus olaparib and NHA therapy, and HRQoL and disease-related symptom scores were generally maintained relative to baseline across all analyzed time points in both the treatment groups. The median TTPP and TTD were generally similar between the pembrolizumab plus olaparib and NHA groups. Additionally, from baseline to week 15, no clinically meaningful changes were observed in PROs with either treatment; the improvement, stability, or deterioration rates for FACT-P total and subscale scores and changes in BPI-SF domains scores and EQ-5D VAS scores were generally similar between treatment groups.

The similar HRQoL and disease-related symptom scores with pembrolizumab plus olaparib, relative to an NHA switch, suggest that the addition of pembrolizumab to olaparib did not impact HRQoL negatively. Consistent with these findings, no meaningful difference in HRQoL and disease-related symptoms between the treatment groups was observed in the randomized phase 3 KEYNOTE-921 trial of pembrolizumab plus docetaxel versus placebo plus docetaxel in participants with chemotherapy-naive mCRPC [16]. In KEYNOTE-921, TTPP and TTD in FACT-P total score were comparable between the groups (HR 1.05 [95% CI

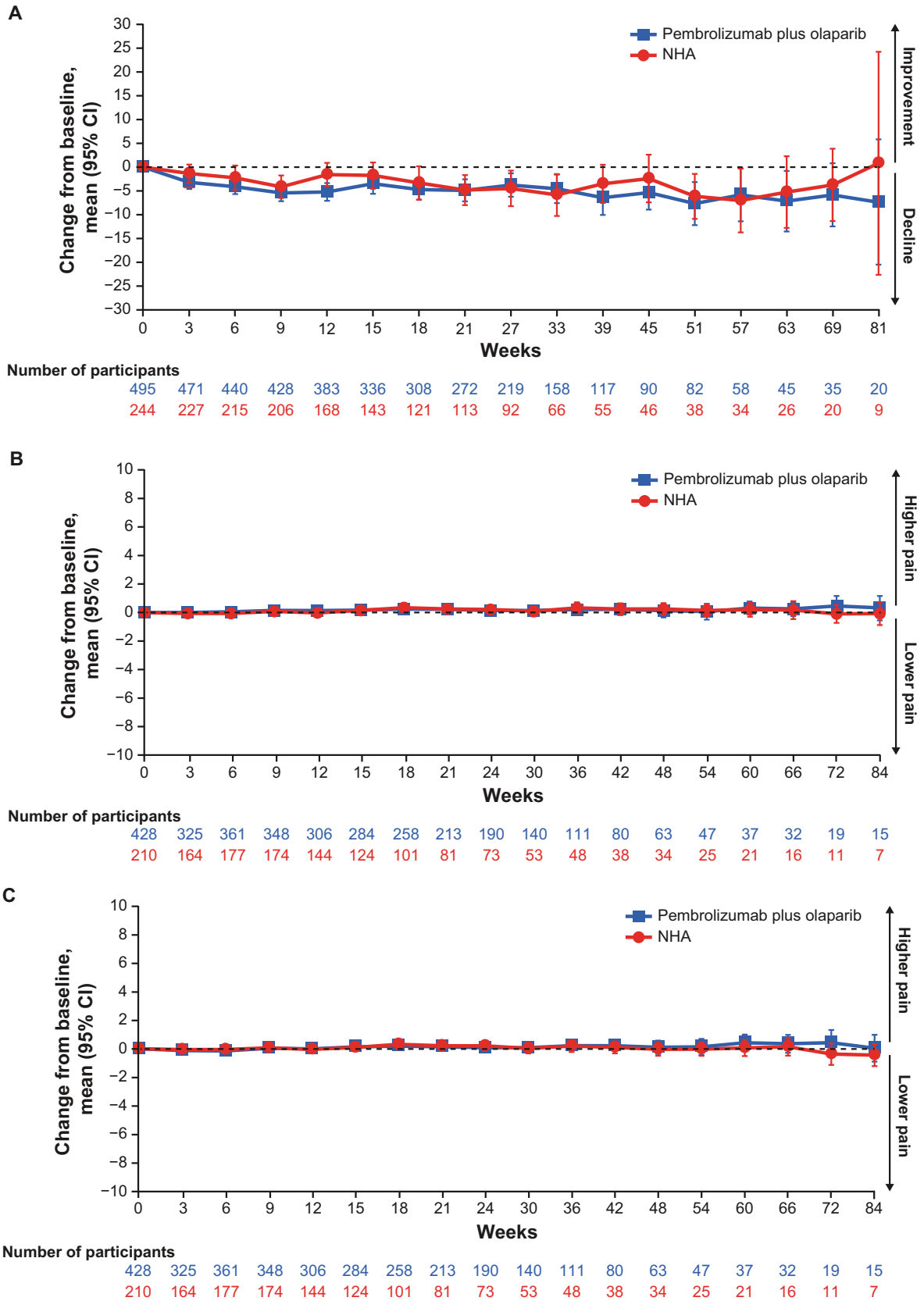


**Fig. 4 – Change from baseline over time in (A) FACT-P total score; BPI-SF (B) pain interference, (C) pain severity, and (D) worst pain scores; and (E) EQ-5D VAS score. BPI-SF = Brief Pain Inventory—Short Form; CI = confidence interval; EQ-5D VAS = EuroQol 5-Dimension visual analog scale; FACT-P = Functional Assessment of Cancer Therapy—Prostate; NHA = next-generation hormonal agent.**

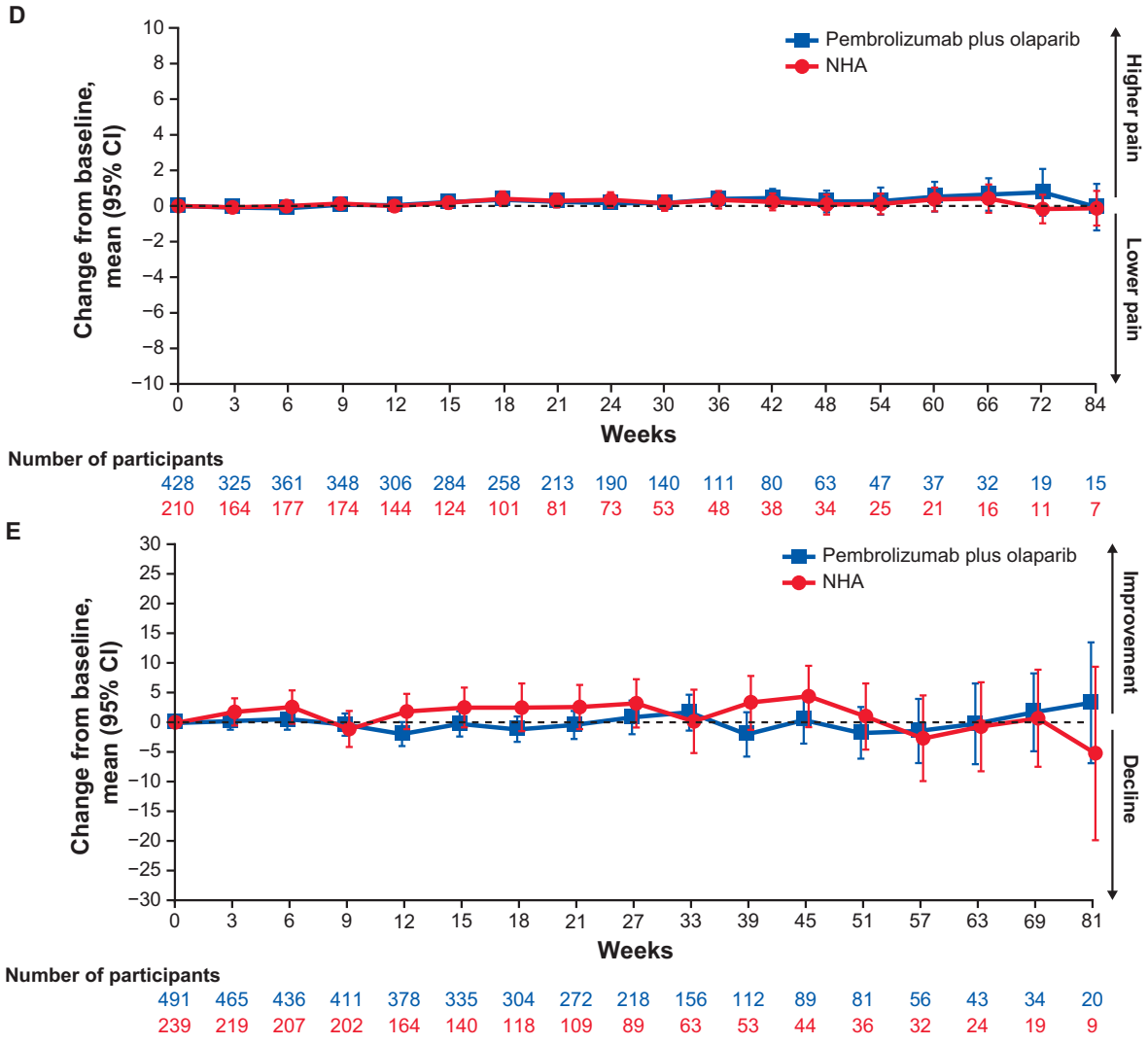


**Fig. 4** (*continued*)

| | Events/participants, *n*/*N* | | Median (95% CI), mo | | |
|---|---|---|---|---|---|
| | Pembrolizumab plus olaparib | NHA | Pembrolizumab plus olaparib | NHA | HR (95% CI) |
| FACT-P total | 219/520 | 103/254 | 7.6 (4.9–11.7) | 6.3 (4.9–11.8) | 1.04 (0.82–1.31) |
| FACT-G total | 224/520 | 101/254 | 6.4 (4.8–11.7) | 6.2 (4.2–NR) | 1.08 (0.86–1.37) |
| TOI | 210/520 | 88/254 | 9.0 (6.2–12.0) | 13.1 (6.2–NR) | 1.18 (0.92–1.51) |
| FAPSI-6 | 161/520 | 75/254 | NR (11.8–NR) | NR (12.0–NR) | 0.99 (0.75–1.30) |
| FWB | 235/520 | 96/254 | 6.9 (4.3–10.6) | 6.6 (4.2–NR) | 1.22 (0.96–1.54) |
| PWB | 248/520 | 95/254 | 4.9 (3.5–6.4) | 9.4 (5.0–NR) | 1.36 (1.07–1.72) |
| PCS | 227/520 | 101/254 | 6.2 (4.4–10.8) | 6.2 (4.4–NR) | 1.09 (0.86–1.38) |

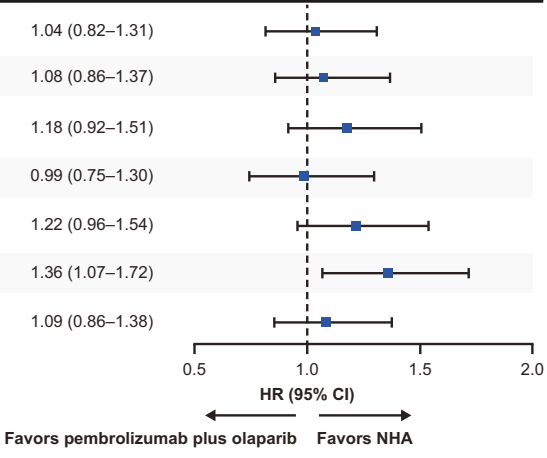


**Fig. 5 – TTD in FACT-P total and subscale scores. CI = confidence interval; FACT-G = Functional Assessment of Cancer Therapy—General, FACT-P = Functional Assessment of Cancer Therapy—Prostate; FAPSI-6 = FACT Advanced Prostate Symptom Index—6; FWB = Functional Well-being; HR = hazard ratio; LSM = least squares mean; NHA = next-generation hormonal agent; NR = not reached; PCS = Prostate Cancer Subscale; PWB = Physical Well-being; TOI = Trial Outcome Index; TTD = time to deterioration.**

0.77–1.43] and 1.09 [95% CI 0.88–1.35], respectively) [16]. Additionally, no meaningful between–treatment group differences were observed in LSM score change from baseline in the FACT-P total and BPI-SF domains, and the mean change from baseline over time in FACT-P total scores, BPI-SF domains, and EQ-5D VAS scores remained relatively similar between the treatment groups [16].

Although combination therapy with pembrolizumab and olaparib in molecularly unselected participants with mCRPC did not show meaningful differences in HRQoL and disease-related symptoms compared with an NHA in the KEYLYNK-010 trial, olaparib as monotherapy has been associated with reduced pain burden and better-preserved HRQoL in participants with mCRPC with DNA damage repair alterations [17]. In cohort A of the phase 3 PROfound trial of participants with mCRPC with *BRCA1*, *BRCA2*, or *ATM* alterations, olaparib provided more favorable HRQoL and disease-related symptoms over the physician's choice of NHA (enzalutamide or abiraterone plus prednisone; TTPP: HR 0.44 [95% CI 0.22–0.91], $p = 0.019$; time to progression of pain severity: HR 0.56 [95% CI 0.25–1.34], nominal $p = 0.17$; and improvement in FACT-P total score: odds ratio 8.32 [95% CI 1.64–151.84], nominal $p = 0.0065$) [17]. However, in the phase 3 TRITON3 trial of the PARP inhibitor rucaparib versus physician's choice of docetaxel or NHA (abiraterone acetate or enzalutamide) in participants with mCRPC with *BRCA1*, *BRCA2*, or *ATM* alterations, similar results for change from baseline in FACT-P, BPI-SF, and EQ-5D VAS were observed between the treatment groups [18]. In the phase 3 PROpel trial of molecularly unselected participants with mCRPC, the addition of olaparib to abiraterone resulted in no meaningful differences in TTPP (HR 1.06 [95% CI 0.75–1.50], nominal $p = 0.75$) and change from baseline in BPI-SF domains and FACT-P total scores throughout the study, compared with abiraterone alone [19,20].

In the post-NHA and docetaxel treatment setting, delayed TTPP or time to worsening in HRQoL has been reported for cabazitaxel versus an NHA (phase IV CARD trial) and lutetium-177-PSMA-617 plus standard of care versus standard of care alone (phase 3 VISION trial) in participants with biomarker-unselected mCRPC [21,22]. These PRO results from the CARD and VISION trials, which showed efficacy benefits with cabazitaxel and lutetium-177-PSMA-617 plus standard of care, respectively [23,24], are consistent with the positive relationship often observed between PROs and tumor response to treatment [25–27]. Notably, in the KEYLYNK-010 trial, pembrolizumab plus olaparib did not improve the dual primary endpoints of rPFS and OS significantly over an NHA switch [7]; thus, the observation of no between-group differences in HRQoL and disease-related symptoms in the current analysis is not unexpected. While pembrolizumab has been shown to be a tolerable combination partner in mCRPC regimens [7,16,28], modest to no improvements in efficacy preclude it from being deployed in biomarker-unselected patients with mCRPC.

The decreasing number of participants with available PRO data over time is a limitation of the study; however, this is a common challenge in HRQoL studies. Other limitations include the mostly exploratory nature of the PRO endpoints, the lack of formal power calculations or multiplicity controls, the lack of sensitivity of the PRO instruments to capture some of the common or specific toxicities of the individual drugs, and the consistently lower completion and compliance rates for the BPI-SF questionnaire than the FACT-P and EQ-5D-5L questionnaires, probably due to the completion of the BPI-SF questionnaire at home versus on-site completion of the FACT-P and EQ-5D-5L questionnaires at each treatment visit. The disparity in the compliance rates for BPI-SF compared with FACT-P and EQ-5D-5L may have affected the estimation of TTPP. Nevertheless, the completion and compliance rates for the BPI-SF questionnaires were similar between the treatment groups. Despite these limitations, PROs were consistently similar between the treatment groups.

## 5. Conclusions

This prespecified analysis of the KEYLYNK-010 trial showed no meaningful differences in HRQoL or disease-related symptoms with either pembrolizumab plus olaparib or an NHA. PRO scores were generally similar between the pembrolizumab plus olaparib and NHA groups at all analyzed time points. These findings suggest that pembrolizumab plus olaparib did not negatively impact HRQoL in participants with heavily pretreated mCRPC.

***Author contributions*:** Niven Mehra had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

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***Data sharing statement*:** Merck Sharp & Dohme LLC, a subsidiary of Merck & Co., Inc., Rahway, NJ, USA (MSD), is committed to providing qualified scientific researchers access to anonymized data and clinical study reports from the company's clinical trials for the purpose of conducting legitimate scientific research. MSD is also obligated to protect the rights and privacy of trial participants, and as such, has a procedure in place for evaluating and fulfilling requests for sharing company clinical trial data with qualified external scientific researchers. The MSD data sharing website (available at: https://externaldatasharing-msd.com) outlines the process and requirements for submitting a data request. Applications will be assessed promptly for completeness and policy compliance. Feasible requests will be reviewed by a committee of MSD subject matter experts to assess the scientific validity of the request and the qualifications of the requestors. In line with data privacy legislation, submitters of approved requests must enter into a standard data sharing agreement with MSD before data access is granted. Data will be made available for request after product approval in the USA and the European Union, or after product development is discontinued. There are circumstances that may prevent MSD from sharing requested data, including country or region-specific regulations. If the request is declined, it will be communicated to the investigator. Access to genetic or exploratory biomarker data requires a detailed, hypothesis-driven statistical analysis plan that is collaboratively developed by the requestor and MSD subject matter experts; after approval of the statistical analysis plan and execution of a data sharing agreement, MSD will either perform the proposed analyses and share the results with the requestor, or construct biomarker covariates and add them to a file with clinical data that are uploaded to an analysis portal so that the requestor can perform the proposed analyses.

## Appendix A. Supplementary material

Supplementary data to this article can be found online at https://doi.org/10.1016/j.euo.2025.04.018.

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