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Health-related quality of life (HRQoL) at final analysis of the GALAHAD study of niraparib in patients with metastatic castration-resistant prostate cancer (mCRPC) and DNA-repair defects (DRD)

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Key findings statement

- **Niraparib improved or maintained overall HRQoL, pain intensity, and pain interference in patients with advanced mCRPC, especially in those with *BRCA* gene alterations, in the GALAHAD final analysis**

Conclusions

- Niraparib improved or maintained overall HRQoL measures as assessed by the Functional Assessment of Cancer Therapy-Prostate (FACT-P) total score, and pain intensity and pain interference as measured using the Brief Pain Inventory Short Form (BPI-SF), in patients with advanced mCRPC
- On average, HRQoL improved in the *BRCA* cohort and was maintained in the non-*BRCA* cohort over time
- Both *BRCA* and non-*BRCA* patients experienced rapid reductions in pain and pain interference
- The time to deterioration in FACT-P total scores was longer in *BRCA* patients compared with non-*BRCA* patients (8.31 months vs 3.71 months, respectively)

Additional information can be viewed by scanning the QR code or accessing this link: https://oncologysciencehub.com/congress/presentation. The QR code is intended to provide scientific information for individual reference. The PDF should not be altered or reproduced in any way.

Reference

1. Data on file. Janssen Research & Development. 2021.

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Disclosures

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Introduction

- The phase 2, open-label, multinational GALAHAD study evaluated niraparib monotherapy in patients with mCRPC and biallelic DRD who had progressed on prior taxane-based chemotherapy and androgen-signaling inhibitor therapy
- In the final analysis, niraparib showed meaningful clinical activity, with an overall response rate of 34.2% in the primary efficacy population of patients with germline pathogenic or biallelic somatic *BRCA* mutations and measurable disease[1]
- Here, we report the HRQoL outcomes, which were prespecified study endpoints for the GALAHAD study

Objective

- To evaluate the effect of niraparib on overall HRQoL, pain intensity, and pain interference in patients with advanced mCRPC and biallelic DRD alterations

Methods

- Patients with mCRPC who received at least an androgen-signaling inhibitor therapy and a taxane-based chemotherapy and had either germline *BRCA* or biallelic DRD alterations received niraparib 300 mg capsules once daily
  - DRD alterations included germline pathogenic or biallelic somatic mutations in *BRCA1* or *BRCA2* (*BRCA* cohort) or eligible somatic alterations in non-*BRCA* genes (*ATM*, *FANCA*, *PALB2*, *CHEK2*, *BRIP1*, or *HDAC2* [non-*BRCA* cohort])
- Patient-reported outcomes (PROs) were assessed in all patients who completed the baseline assessment and ≥1 post-baseline assessment
  - All PROs were assessed at baseline; cycles 3, 5, and 7; and then every 3 cycles until the end of treatment
  - The present FACT-P and BPI-SF analyses were conducted with PRO data from baseline and cycles 3, 5, 7, and 10
- The FACT-P provides an assessment of the patient's self-reported functional status, well-being, and prostate cancer–related symptoms
- The BPI-SF allows the patient to identify the location and intensity of their pain
  - The interference items measure how much pain has interfered with recent daily functions (general activity, walking, work, mood, enjoyment of life, relations with others, and sleep)
- Changes from baseline HRQoL were compared for *BRCA* versus non-*BRCA* patients using a mixed-effect model for repeated measures
- Patients were classified as improved, stable, or worsened based on established meaningful change thresholds (**Table 1**)

Table 1. Categorizations of PROs

Categorization	FACT-P	BPI-SF
Improved	CFB ≥ 10	CFB ≤ –0.5 SD
Stable	–10 < CFB < 10	–0.5 SD < CFB < 0.5 SD
Worsened	CFB ≤ –10	CFB ≥ 0.5 SD

PRO, patient-reported outcome; FACT-P, Functional Assessment of Cancer Therapy-Prostate; BPI-SF, Brief Pain Inventory Short Form; CFB, change from baseline; SD, standard deviation.

- Generalized estimating equations were used to calculate odds ratios of HRQoL improvement using non-*BRCA* as the reference category
- Median time to first deterioration in FACT-P total as well as BPI-SF worst pain intensity and interference subscale scores were estimated by a Kaplan-Meier technique and determined by the following meaningful change threshold values:
  - FACT-P total: 10-point reduction from baseline
  - BPI-SF worst pain intensity and pain interference: +0.5 standard deviation from baseline
- Of the 223 patients in the intent-to-treat population (*BRCA*, n = 142; non-*BRCA*, n = 81), 221 completed the HRQoL evaluations at baseline and had ≥1 post-baseline evaluation
  - 84%-98% of the *BRCA* cohort and 88%-100% of the non-*BRCA* cohort completed PRO assessments from baseline through cycle 10

Results

- Patient demographic and baseline characteristics were generally similar in the 2 cohorts as shown in **Table 2**

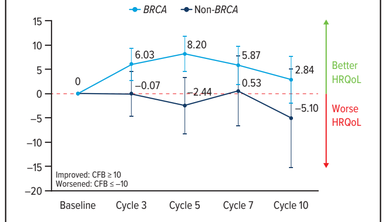
Table 2. Baseline Characteristics of the ITT Population

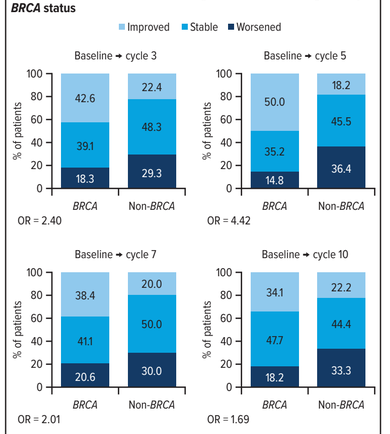
	BRCA (n = 142)	Non-*BRCA* (n = 81)
Age, years Median (range)	67.0 (46-86)	70.0 (52-88)
ECOG-PS score, n (%) 0 1 2	 48 (33.8) 78 (54.9) 16 (11.3)	 18 (22.2) 47 (58.0) 16 (19.8)
Disease status, n (%) Measurable Non-measurable	 76 (53.5) 66 (46.5)	 47 (58.0) 34 (42.0)
FACT-P total score Mean (SD)	96.6 (21.5)	101.3 (22.1)
BPI-SF pain intensity score Mean (SD)	3.2 (2.3)	2.6 (2.3)
BPI-SF pain interference score Mean (SD)	3.5 (2.7)	2.9 (2.5)

ITT, intent-to-treat; *BRCA*, breast cancer gene; ECOG-PS, Eastern Cooperative Oncology Group performance status; FACT-P, Functional Assessment of Cancer Therapy-Prostate; SD, standard deviation; BPI-SF, Brief Pain Inventory Short Form. *BRCA* and non-*BRCA* cohort n values represent total ITT cohorts.

- On average, HRQoL improved in the *BRCA* cohort and was maintained in the non-*BRCA* cohort over time (**Figure 1A**)
  - Notable differences in the proportions of patients demonstrating improved HRQoL were observed between the *BRCA* and non-*BRCA* cohorts at early cycles (cycles 3 and 5), indicating early, detectable HRQoL response in the *BRCA* cohort (**Figure 1B**)
  - Patients in the *BRCA* cohort were more likely to experience clinically meaningful improvements in overall HRQoL than those in the non-*BRCA* cohort
- Both *BRCA* and non-*BRCA* cohorts experienced rapid reduction in pain scores (by cycle 3; **Figure 2A**)
  - On average, the *BRCA* cohort experienced greater early pain relief (by cycle 3) than the non-*BRCA* cohort, with the largest reduction observed between baseline and cycle 3 (**Figure 2A**)
    - Similar mean pain intensity reductions were observed in the 2 cohorts at cycles 7 and 10, but interpretation may be limited by sample size
  - A numerically greater proportion of patients in the *BRCA* cohort demonstrated stable or improved scores (vs those in the non-*BRCA* cohort) through cycle 7 (**Figure 2B**)
- Both *BRCA* and non-*BRCA* cohorts experienced rapid reductions in pain interference (by cycle 3; **Figure 3A**)
  - The largest reduction in pain interference for the *BRCA* cohort was observed between baseline and cycle 5 (**Figure 3A**)
    - Similar mean pain interference reductions were observed in the 2 cohorts at cycle 10, but interpretation may be limited by sample size
  - A numerically greater proportion of patients in the *BRCA* cohort were stable or improved (vs the non-*BRCA* cohort) for most cycles (**Figure 3B**)

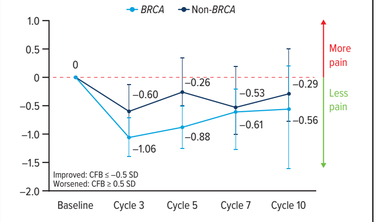
Figure 1. Patients experienced improvements in overall HRQoL by FACT-P MMRM

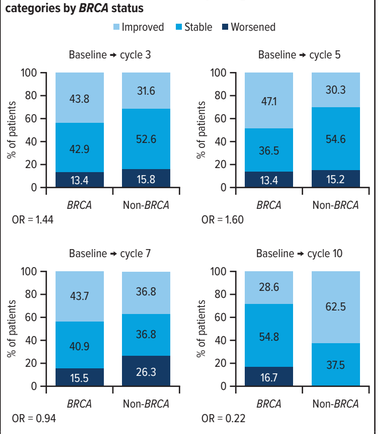




HRQoL, health-related quality of life; FACT-P, Functional Assessment of Cancer Therapy-Prostate; MMRM, mixed-effect model for repeated measures; *BRCA*, breast cancer gene; CFB, change from baseline; OR, odds ratio.
ORs compared rates of "improved" versus "stable/worsened" for *BRCA* patients (non-*BRCA* patients are used as reference); higher OR indicates greater likelihood of improvement in the *BRCA* cohort.

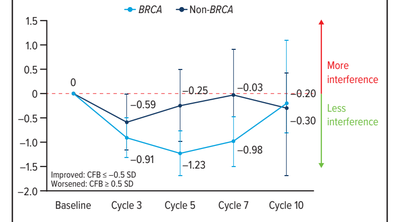
Figure 2. Patients generally demonstrated stable or improved BPI-SF MMRM pain intensity scores

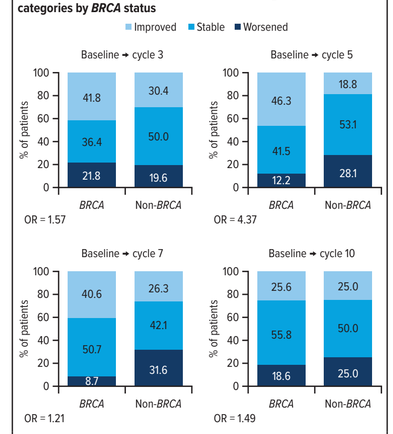




BPI-SF, Brief Pain Inventory Short Form; MMRM, mixed-effect model for repeated measures; *BRCA*, breast cancer gene; CFB, change from baseline; OR, odds ratio.
ORs compared rates of "improved" versus "stable/worsened" for *BRCA* patients (non-*BRCA* patients are used as reference); higher OR indicates greater likelihood of improvement in the *BRCA* cohort.

Figure 3. Patients generally demonstrated stable or improved BPI-SF MMRM pain interference scores

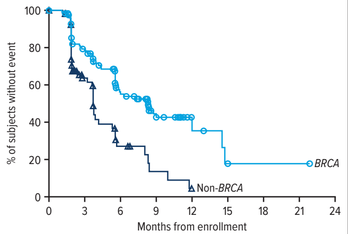




BPI-SF, Brief Pain Inventory Short Form; MMRM, mixed-effect model for repeated measures; *BRCA*, breast cancer gene; CFB, change from baseline; OR, odds ratio.
ORs compared rates of "improved" versus "stable/worsened" for *BRCA* patients (non-*BRCA* patients are used as reference); higher OR indicates greater likelihood of improvement in the *BRCA* cohort.

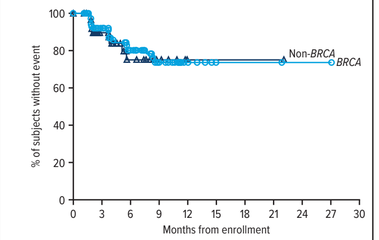
- Median (interquartile range) time to deterioration in the FACT-P total score was numerically longer in the *BRCA* cohort (8.31 [0-21.9] months) compared to the non-*BRCA* cohort (3.71 [0-12.0] months; **Figure 4**)
- Median time to deterioration in pain intensity was not reached in either cohort (**Figure 5**)
- Similarly, median time to deterioration in pain interference was not reached in either cohort (**Figure 6**)

Figure 4. Kaplan-Meier plot of time to deterioration in FACT-P total score



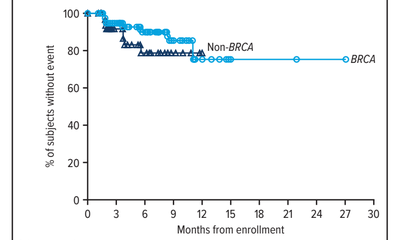
FACT-P, Functional Assessment of Cancer Therapy-Prostate; *BRCA*, breast cancer gene.

Figure 5. Kaplan-Meier plot of time to deterioration in pain intensity subscale score



BRCA, breast cancer gene.

Figure 6. Kaplan-Meier plot of time to deterioration in pain interference subscale score



BRCA, breast cancer gene.

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