Health-related Quality of Life and Pain in the MAGNITUDE Study of Niraparib With Abiraterone Acetate and Prednisone in Patients With Metastatic Castration-resistant Prostate Cancer and Homologous Recombination Repair Gene Alterations

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INTRODUCTION

- The results from the phase 3, international, randomized, double-blind MAGNITUDE study (ClinicalTrials.gov Identifier: NCT03748641) demonstrated that NIRA + AAP significantly improved the primary endpoint, with a 27.1% reduction in the risk of radiographic progression or death (hazard ratio [HR], 0.73; 95% confidence interval [CI], 0.56-0.96; *P* = 0.022)
- NIRA + AAP also improved secondary endpoints of time to cytotoxic chemotherapy by 41.2% (HR, 0.59; 95% CI, 0.39-0.89; *P* = 0.011) and time to symptomatic progression by 31.4% (HR, 0.69; 95% CI, 0.47-0.99; *P* = 0.044), with manageable toxicity in patients with mCRPC and HRR gene alterations (9-gene panel)[1,2]
- Here, we report HRQoL and pain in patients with mCRPC and HRR gene alterations in the MAGNITUDE study

METHODS

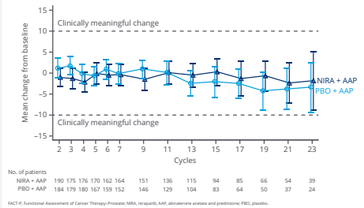
- Eligible patients with mCRPC and HRR gene alterations were randomized 1:1 to receive, orally, either NIRA + AAP or placebo (PBO) + AAP daily in 28-day cycles
- To be eligible to participate in the study, patients needed to have an Eastern Cooperative Oncology Group performance status (ECOG PS) score ≤1 and a Brief Pain Inventory–Short Form (BPI-SF) worst pain score ≤3 in screening
- HRQoL assessments on Day 1 of specified cycles included the FACT-P and the BPI-SF (see **Supplemental Table** for details on meaningful change threshold)
- FACT-P and BPI-SF score changes from baseline were compared between treatment arms using repeated-measures analysis
- Proportional hazards regression models were used to compare time to deterioration (TTD) in worst pain intensity between arms

PROSTATE CANCER

RESULTS

- Compliance for FACT-P and BPI-SF assessments was >80% through Cycle 23
- At baseline, median (range) age was 69 (45-100) in the NIRA + AAP arm and 69 (43-88) in the PBO + AAP arm
  - There were several imbalances in baseline characteristics between the treatment arms; more patients in the NIRA + AAP arm had visceral metastases (24.1% vs 18.5%), bone metastases (86.3% vs 80.6%), and ECOG PS scores of 1 (38.7% vs 30.8%) compared with patients in the PBO + AAP arm
- HRQoL was maintained with NIRA + AAP treatment, with no clinically meaningful differences in FACT-P total score change from baseline over time or between arms (**Figure 1**)

FIGURE 1: Change from baseline over time in FACT-P total score



FACT-P, Functional Assessment of Cancer Therapy-Prostate; NIRA, niraparib; AAP, abiraterone acetate and prednisone; PBO, placebo.

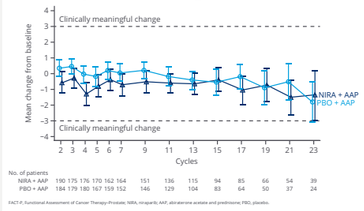
- There was worsening of side effect bother, lack of energy, and nausea (items within the FACT-P physical well-being subscale) in early cycles with NIRA + AAP relative to PBO + AAP, likely driven by events within the known safety profile of NIRA + AAP; however, overall, most patients reported minimal side effect burden (**Table 1**)
- There were no clinically meaningful differences in change from baseline on FACT-P physical well-being scores or over time within treatment arms (**Figure 2**)

TABLE 1: Change in FACT-P categories from baseline

FACT-P item median (range), %	Change from baseline				Percentage of patients with minimal side effect burden*	
	Improved/stable		Worsened			
	NIRA + AAP	PBO + AAP	NIRA + AAP	PBO + AAP	NIRA + AAP	PBO + AAP
Side effect bother	68.6 (60.8-74.1)	79.7 (74.0-86.5)	31.5 (25.8-39.2)	20.4 (13.5-26.0)	85.4 (81.5-90.8)	92.2 (89.1-94.1)
Lack of energy	67.4 (56.4-75.0)	75.2 (66.7-82.2)	32.6 (25.0-43.6)	24.8 (17.8-33.3)	65.5 (56.4-71.4)	75.9 (69.2-79.0)
Nausea	80.8 (73.2-90.2)	90.9 (88.0-93.1)	19.3 (9.7-26.9)	9.2 (6.9-12.0)	93.9 (89.1-95.9)	96.8 (94.7-100.0)

FACT-P, Functional Assessment of Cancer Therapy-Prostate; NIRA, niraparib; AAP, abiraterone acetate and prednisone; PBO, placebo.
*Response of "not at all" or "a little bit" on respective items across cycles.

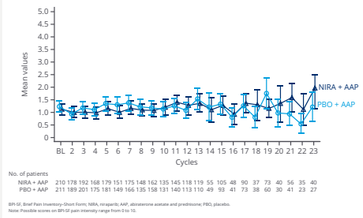
FIGURE 2: Change from baseline over time in FACT-P physical well-being



FACT-P, Functional Assessment of Cancer Therapy-Prostate; NIRA, niraparib; AAP, abiraterone acetate and prednisone; PBO, placebo.

- Mean BPI worst pain intensity score remained stable over time (**Figure 3**)

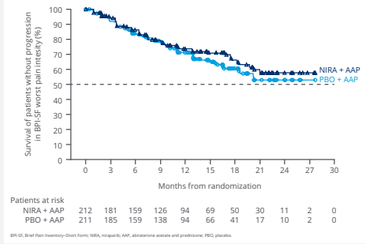
FIGURE 3: Mean BPI-SF worst pain intensity score over time



BPI-SF, Brief Pain Inventory–Short Form; NIRA, niraparib; AAP, abiraterone acetate and prednisone; PBO, placebo.
Note: Possible scores on BPI-SF pain intensity range from 0 to 10.

- There was no difference in TTD for pain intensity with NIRA + AAP treatment versus PBO + AAP (HR, 0.87; 95% CI, 0.61-1.24)
  - At the 25th percentile, the TTD was 11.1 versus 10.1 months for NIRA + AAP and PBO + AAP, respectively (**Figure 4**)
  - The median time to pain progression for each group was not reached at the time of the clinical cutoff (**Figure 4**)

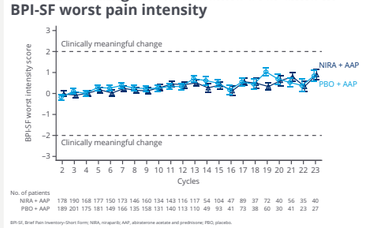
FIGURE 4: Time to BPI-SF worst pain intensity progression



BPI-SF, Brief Pain Inventory–Short Form; NIRA, niraparib; AAP, abiraterone acetate and prednisone; PBO, placebo.

- Repeated-measures analyses showed no clinically meaningful differences in BPI worst pain intensity change from baseline over time or between arms (**Figure 5**)

FIGURE 5: Change from baseline over time in BPI-SF worst pain intensity



BPI-SF, Brief Pain Inventory–Short Form; NIRA, niraparib; AAP, abiraterone acetate and prednisone; PBO, placebo.

KEY TAKEAWAYS

In MAGNITUDE, the combination of niraparib (NIRA) plus abiraterone acetate and prednisone (AAP) was associated with significant clinical benefit based on the primary endpoint, with reduction in the risk of radiographic progression or death, as well as benefit in the secondary endpoints of time to cytotoxic chemotherapy and time to symptomatic progression, without compromising health-related quality of life (HRQoL)

NIRA + AAP was generally well tolerated. Although more patients on NIRA + AAP reported worsening side effect burden, most patients had low pain levels and maintained good HRQoL

CONCLUSIONS

In MAGNITUDE, most patients maintained low pain levels and positive HRQoL over time, with no clinically meaningful differences between treatment arms, further supporting the use of NIRA + AAP as a first-line treatment option in patients with metastatic castration-resistant prostate cancer (mCRPC) and homologous recombination repair (HRR) gene alterations

Side effect burden was low in both arms. The symptoms were generally mild, despite the fact that more patients on NIRA + AAP reported worsening of side effects on the Functional Assessment of Cancer Therapy–Prostate (FACT-P)

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DISCLOSURES

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