

Patient-Reported Outcomes From AMPLITUDE, a Randomized, Placebo-Controlled Phase 3 Trial of Niraparib and Abiraterone Acetate Plus Prednisone in Metastatic Hormone-Sensitive Prostate Cancer With Homologous Recombination Repair Mutations

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Declaration of Interests

Dana E Rathkopf reports advisory/advisory board roles with Astellas Pharma, AstraZeneca, Bayer, Bristol Myers Squibb/Celgene, Curium, Genentech, Janssen, Myovant Sciences, Novartis, and Promontory Therapeutics; trial chair role with Janssen; steering committee member with Janssen and Bristol Myers Squibb; principal investigator role with Bristol Myers Squibb, Janssen, Genentech, Promontory, and Pfizer; and institutional research funding from AstraZeneca, Bristol Myers Squibb/Celgene, Genentech/Roche, Janssen Oncology, Novartis, and Promontory Therapeutics.

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AMPLITUDE: Randomized, Double-Blind, Placebo-Controlled Trial in HRRm mHSPC

Key inclusion criteria:
mHSPC^a, alteration in ≥ 1 HRR-eligible gene^b, ECOG PS 0-2

Key exclusion criteria:
Any prior PARPi or ARPI other than AA + P

Prior allowed treatments in mHSPC:
ADT ≤ 6 months, docetaxel ≤ 6 cycles^c, AA + P ≤ 45 days, palliative radiotherapy

R 1:1
N=696

**Niraparib (200 mg QD)
+ AA (1000 mg QD)
+ P (5 mg QD)
+ ADT
(n=348)**

Primary end point

- radiographic progression-free survival by investigator review

**PBO
+ AA (1000 mg QD)
+ P (5 mg QD)
+ ADT
(n=348)**

Key secondary end points

- Time to symptomatic progression
- Overall survival
- Safety

- ARPI plus ADT \pm docetaxel is standard of care for mHSPC¹⁻⁶
- Patients with HRRm mHSPC have a worse prognosis than those without⁷
- Niraparib, a highly selective and potent inhibitor of PARP-1/2, is approved for treatment with AA + P in *BRCA* mutated mCRPC⁸⁻¹⁰

Clinical data cutoff: January 7, 2025

Median follow-up: 30.8 months

Median number of cycles: 25 in both arms

Stratifications:

- *BRCA2* vs *CDK12* vs all other alterations
- Prior docetaxel (yes vs no)
- Disease volume (high vs low)

AA, abiraterone acetate; ADT, androgen deprivation therapy; ARPI, androgen receptor pathway inhibitor; BL, baseline; ECOG PS, Eastern Cooperative Oncology Group performance status; EQ-5D-5L VAS, Euro-Quality of Life Questionnaire visual analog scale; FACT-G, Functional Assessment of Cancer Therapy-General; FACT-P, Functional Assessment of Cancer Therapy-Prostate; HR, hazard ratio; HRRm, homologous recombination repair gene mutation; mCRPC, metastatic castration-resistant prostate cancer; mHSPC, metastatic hormone-sensitive prostate cancer; PARPi, poly ADP-ribose polymerase inhibitor; PBO, placebo; P, prednisone; PRO, patient-reported outcome; QD, once daily. ^aPatients with lymph node-only disease are not eligible. ^bHRR gene panel was fixed prior to trial initiation based on MAGNITUDE trial and external data from the published literature. HRR eligible genes: *BRCA1*, *BRCA2*, *BRIP1*, *CDK12*, *CHEK2*, *FANCA*, *PALB2*, *RAD51B*, *RAD54L*. ^cLast dose ≤ 3 months prior to randomization. ^dFinal analysis for rPFS. ^eFirst interim analysis. ^fNo imputation for missing data. ^gOverall over treatment phase includes all values from BL to end of treatment. 1. Fizazi, et al. *N Engl J Med*. 2017;377:352-360. 2. James, et al. *N Engl J Med*. 2017;377:338-351. 3. Fizazi, et al. *Lancet*. 2022;399:1695-1707. 4. Smith, et al. *N Engl J Med*. 2022;386:1132-1142. 5. Lowrance et al. *J Urol*. 2023; 209:1082-90. 6. EAU - EANM - ESTRO - ESUR - ISUP - SIOG guidelines on prostate cancer. Accessed: Sept 9, 2025. 7. Olmos, et al. Presented at ASCO 2025. Abstract 5094. 8. Chi, *J Clin Oncol*. 2023;41:3339-3351. 9. Chi, et al. *Ann Oncol*. 2023;34:772-782. 10. AKEEGA. PI. 8/2023. 11. Attard et al. Presented at ASCO 2025. Abstract LBA5006.



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- The AMPLITUDE study investigated niraparib + AA + P versus placebo + AA + P in HRRm mHSPC and met its primary end point of radiographic progression-free survival¹¹
 - Significantly reduced risk of radiographic progression or death by 37% (HR, 0.63; $p=0.0001$)^d
 - Reduced the time to symptomatic progression by 50% (HR, 0.50; $p<0.0001$)^e
- The safety profile of niraparib + AA + P was consistent with prior experience⁸

Stratifications:

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- Prior docetaxel (yes vs no)
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Assessed PRO instruments and subscales

- FACT-G
 - Single item GP5 side-effect bother
- FACT-P
 - FACT-P physical well-being subscale
- EQ-5D-5L VAS

- PRO e-questionnaires were completed at screening, cycles 1-25, then every 4 months up to end of treatment
- PROs were analyzed as least-squares mean change from BL by mixed-effects repeated-measures model^f
- The overall questionnaire completion compliance was $\geq 94.3\%$ ^g

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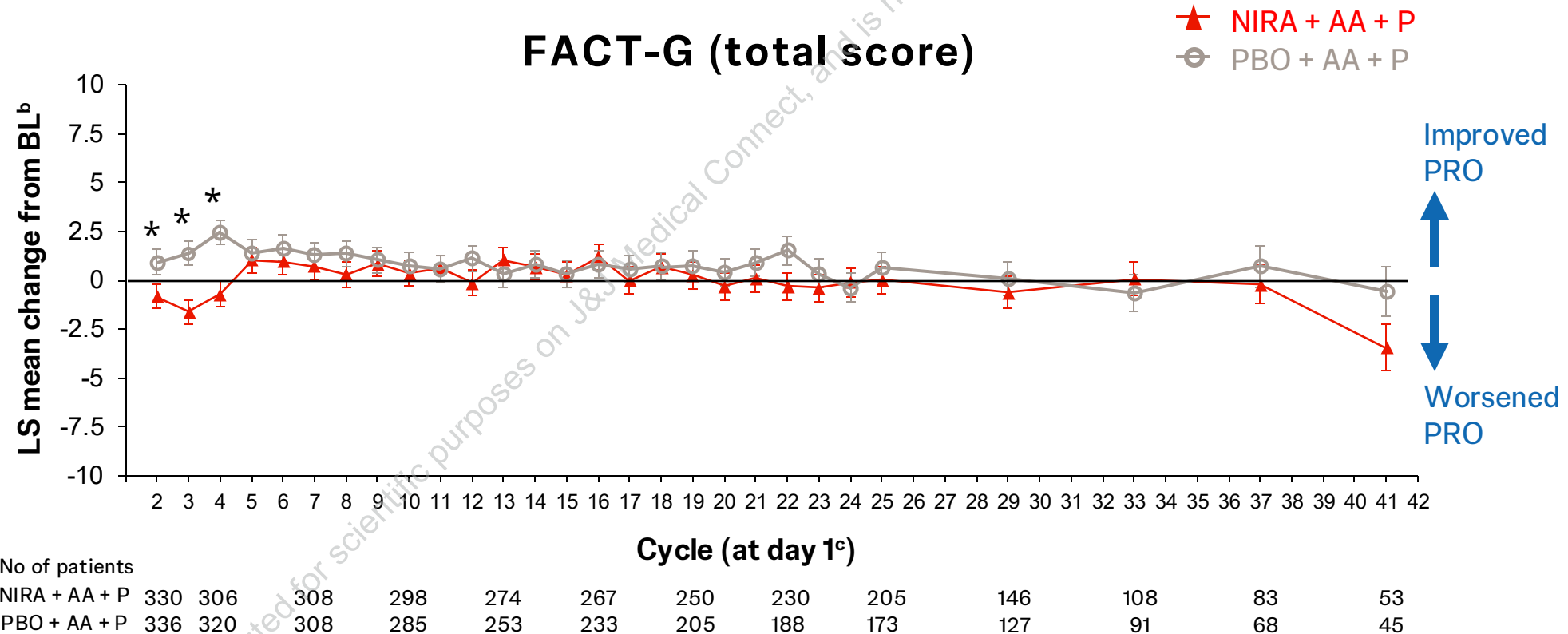


HRQoL FACT-G Was Maintained and Comparable Between Arms After Differences in Initial Cycles

FACT-G score:
0 to 108 points

Mean BL FACT-G (SD)
NIRA + AA + P: 79.7 (14.9)
AA + P: 79.3 (15.2)

Overall LS mean change from BL (SE)
NIRA + AA + P: 0.02 (0.50)
AA + P: 0.77 (0.50)
p=0.289^a



- Initial reduction in HRQoL may be explained by onset of the most frequently observed AEs, hypertension and anemia, within the first 4 cycles

Error bars are SE estimates. Truncation was applied across arms for all subsequent visits at the first visit where $\geq 90\%$ of patients were missing for each end point and from either arm. FACT-G includes physical well-being, social/family well-being, emotional well-being and functional well-being subscales. Responses: 0 "not at all" to 4 "very much". FACT-G total score: A decrease of 9 points or more from baseline in an individual patient's score is considered clinically meaningful deterioration (a decrease in score is worsening in HRQoL). ^aF-test comparing niraparib + AA + P vs AA + P. ^bLS means are derived based on the mixed effects model with baseline, visit, treatment, visit by treatment interactions as fixed effect and individual patients as random effect. ^cCompleted on day 1 of cycle. *p<0.05.

AE, adverse event; HRQoL, health-related quality of life; NIRA, niraparib; SD, standard deviation; SE, standard error.

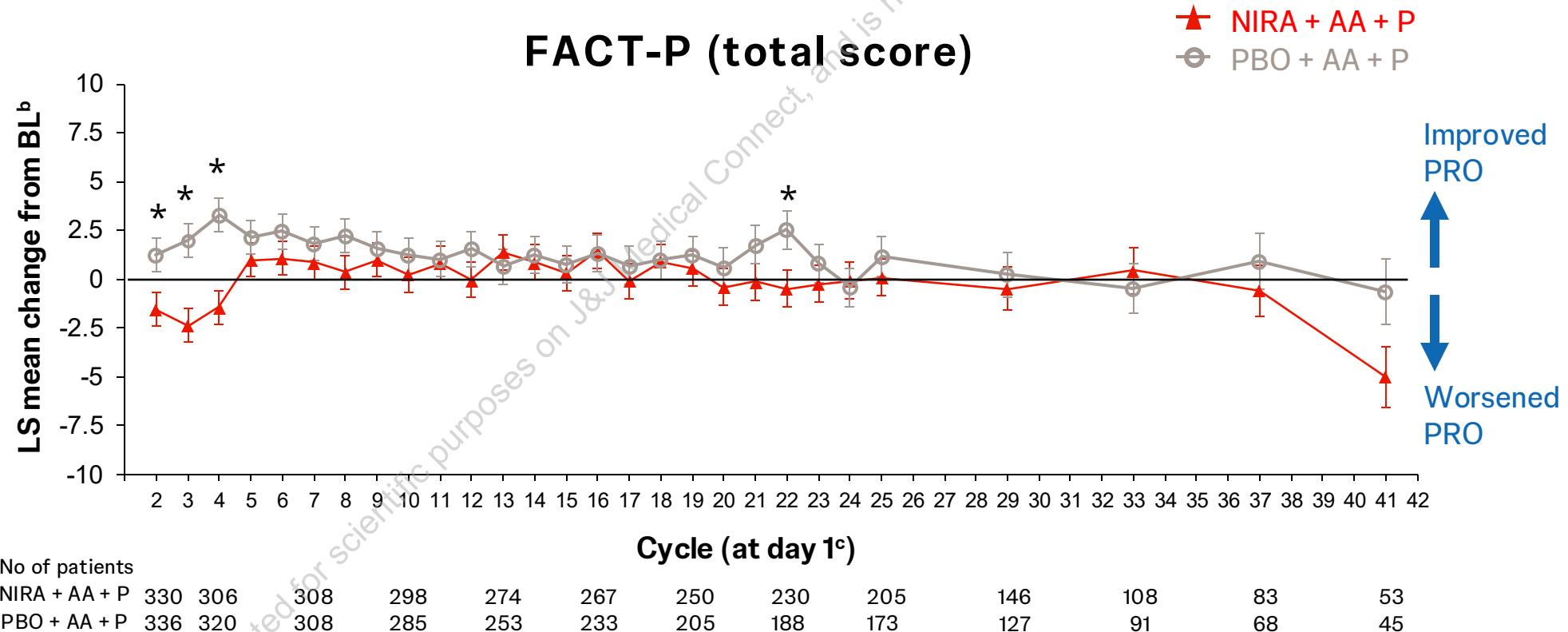


HRQoL FACT-P Was Maintained and Comparable Between Arms After Differences in Initial Cycles

FACT-P score:
0 to 156 points

Mean BL FACT-P (SD)
NIRA + AA + P: 113.3 (20.2)
AA + P: 112.7 (20.4)

Overall LS mean change from BL (SE)
NIRA + AA + P: -0.05 (0.67)
AA + P: 1.22 (0.67)
p=0.181^a



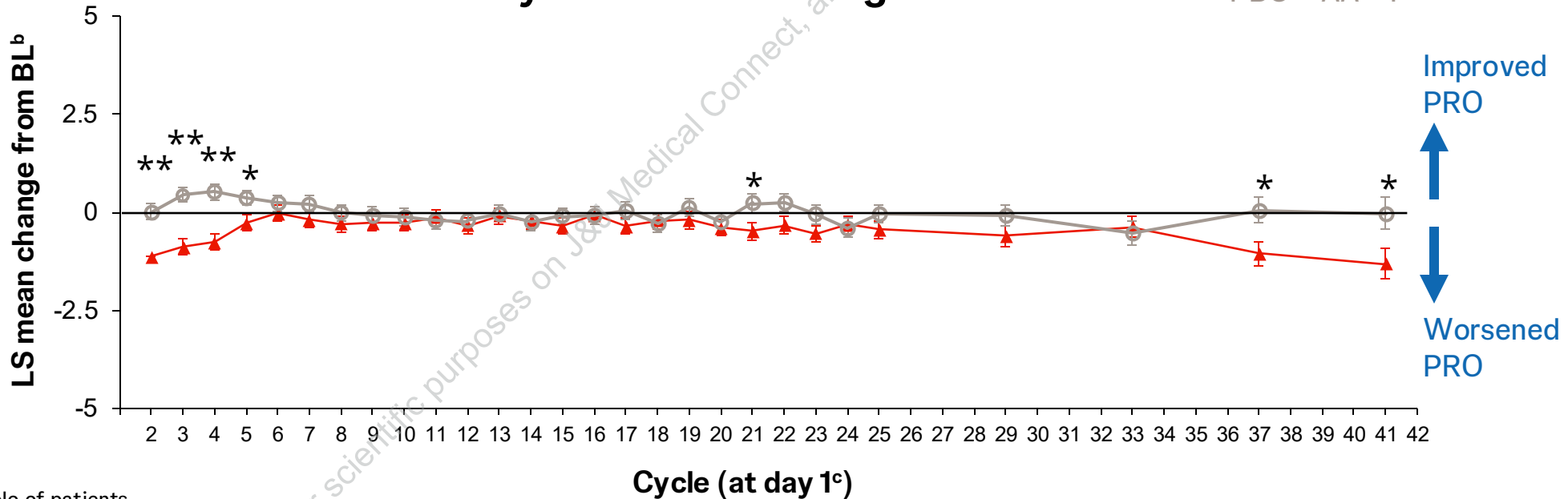
Error bars are SE estimates. Truncation was applied across arms for all subsequent visits at the first visit where $\geq 90\%$ of patients were missing for each end point and from either arm. FACT-P includes FACT-G (physical well-being, social/family well-being, emotional well-being and functional well-being subscales) plus a prostate cancer-specific subscale. Responses: 0 "not at all" to 4 "very much." FACT-P total score: A decrease of 10 points or more from baseline in an individual patient's score is considered clinically meaningful deterioration (a decrease in score is worsening in HRQoL). ^aF-test comparing niraparib + AA + P vs AA + P. ^bLS means are derived based on the mixed effects model with baseline, visit, treatment, visit by treatment interactions as fixed effect and individual patients as random effect. ^cCompleted on day 1 of cycle. *p<0.05.



FACT-P PWB Subscale Was Maintained and Comparable Between Arms After Initial Cycles

FACT-P Physical Well-being Subscale

▲ NIRA + AA + P
 ○ PBO + AA + P



No of patients

NIRA + AA + P	330	306	308	298	274	267	250	230	205	146	108	83	53
PBO + AA + P	336	320	307	285	253	233	205	188	173	127	91	68	45

FACT-P PWB score:
0 to 28 points

Mean BL FACT-P PWB (SD)
 NIRA + AA + P: 23.5 (4.6)
 AA + P: 23.6 (4.4)

Overall LS mean change from BL (SE)
 NIRA + AA + P: -0.43 (0.15)
 AA + P: -0.01 (0.15)
 p=0.0467^a

Error bars are SE estimates. Truncation was applied across arms for all subsequent visits at the first visit where $\geq 90\%$ of patients were missing for each end point and from either arm. The FACT-P PWB is one of the 4 subscales that make up FACT-G and FACT-P. Responses: 0 “not at all” to 4 “very much.” FACT-P PWB subscale: A decrease of 3 points or more from baseline in an individual patient’s score is considered clinically meaningful deterioration (a decrease in score is worsening in health state). ^aF-test comparing niraparib + AA + P vs AA + P. ^bLS means are derived based on the mixed effects model with baseline, visit, treatment, visit by treatment interactions as fixed effect and individual patients as random effect. ^cCompleted on day 1 of cycle. **p<0.0001; *p<0.05.

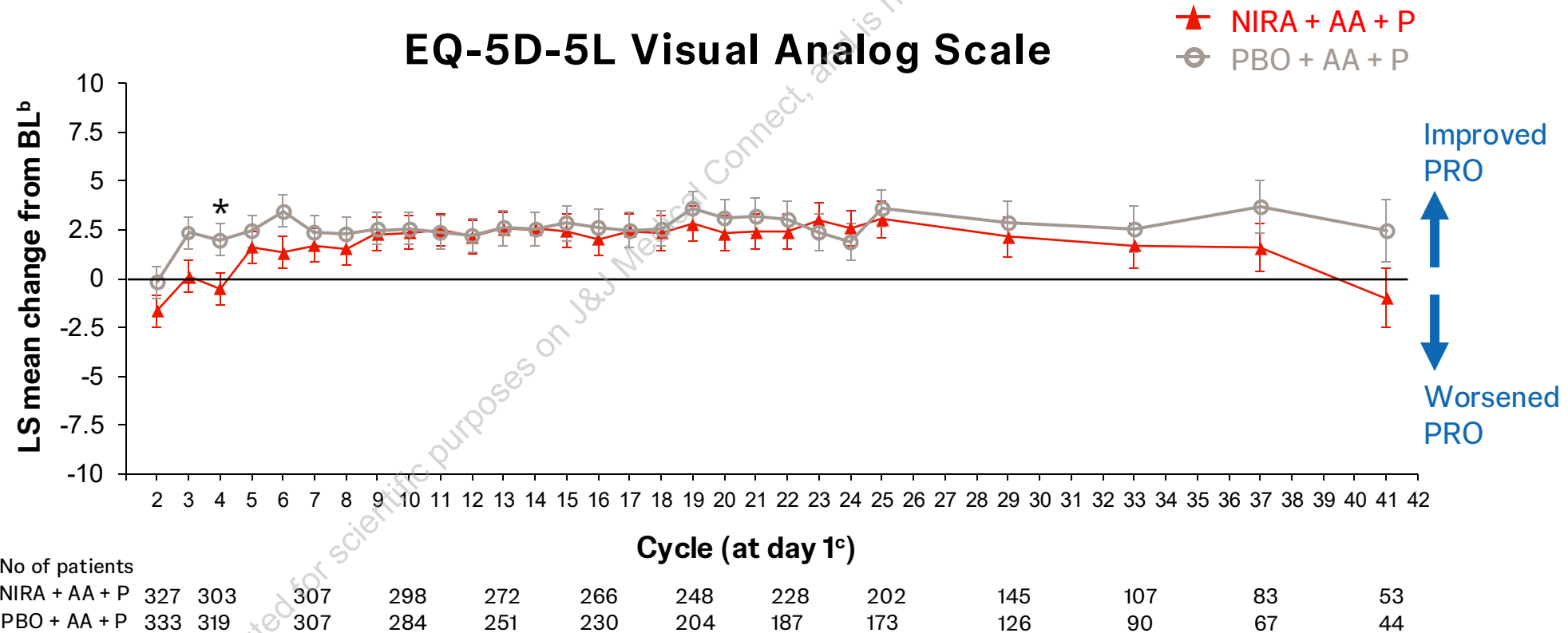


EQ-5D-5L Visual Analog Scale Was Comparable Between Arms

EQ-5D-5L VAS score:
0 to 100 points

Mean BL EQ-5D-5L VAS (SD)
NIRA + AA + P: 74.9 (17.4)
AA + P: 73.9 (18.6)

Overall LS mean change from BL (SE)
NIRA + AA + P: 1.82 (0.63)
AA + P: 2.59 (0.63)
p=0.390^a



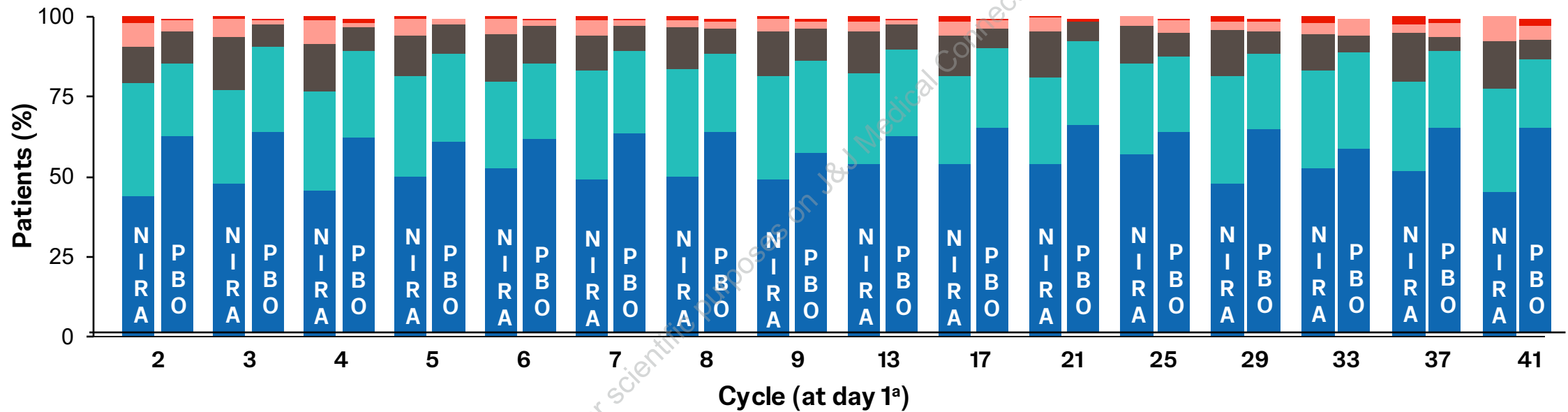
Error bars are SE estimates. Truncation was applied across arms for all subsequent visits at the first visit where $\geq 90\%$ of patients were missing for each end point and from either arm. The EQ-5D-5L VAS is a self-administered, standardized measure of health status; score range: 0 (worst imaginable health state) to 100 (best imaginable health state). EQ-5D-5L VAS score: A decrease of 10 points or more from baseline in an individual patient's score is considered clinically meaningful deterioration. ^aF-test comparing niraparib + AA + P vs AA + P. ^bLS means are derived based on the mixed effects model with baseline, visit, treatment, visit by treatment interactions as fixed effect and individual patients as random effect. ^cCompleted on day 1 of cycle. *p<0.05.



Most Patients Were “Not at All” or “a Little Bit” Bothered by Treatment Side Effects

GP5: Side Effects Bother

“Not at all” “A little bit” “Somewhat” “Quite a bit” “Very Much”



No of patients

NIRA + AA + P	330	320	306	307	302	308	308	299	273	261	234	205	146	108	83	53
PBO + AA + P	337	326	321	324	312	309	302	295	255	223	200	174	128	92	69	46

- Patients “not at all” or “a little bit” bothered: NIRA + AA + P: 76% to 85%, PBO + AA + P: 86% to 93%

Truncation was applied across arms for all subsequent visits at the first visit where $\geq 90\%$ of patients were missing for each end point and from either arm. Side effect bother is the single item GP5 from the FACT-P regarding “bothered by side effects.” *Completed on day 1 of cycle.



Conclusions

- **Niraparib + AA + P significantly delayed radiographic progression or death versus AA + P in patients with HRRm mHSPC, as previously reported¹**
- **Baseline HRQoL was maintained following an initial but not significant reduction with niraparib + AA + P**
- **Initial reduction in HRQoL may be explained by the common AEs observed during initial cycles, which can be managed with dose modifications and supportive care**

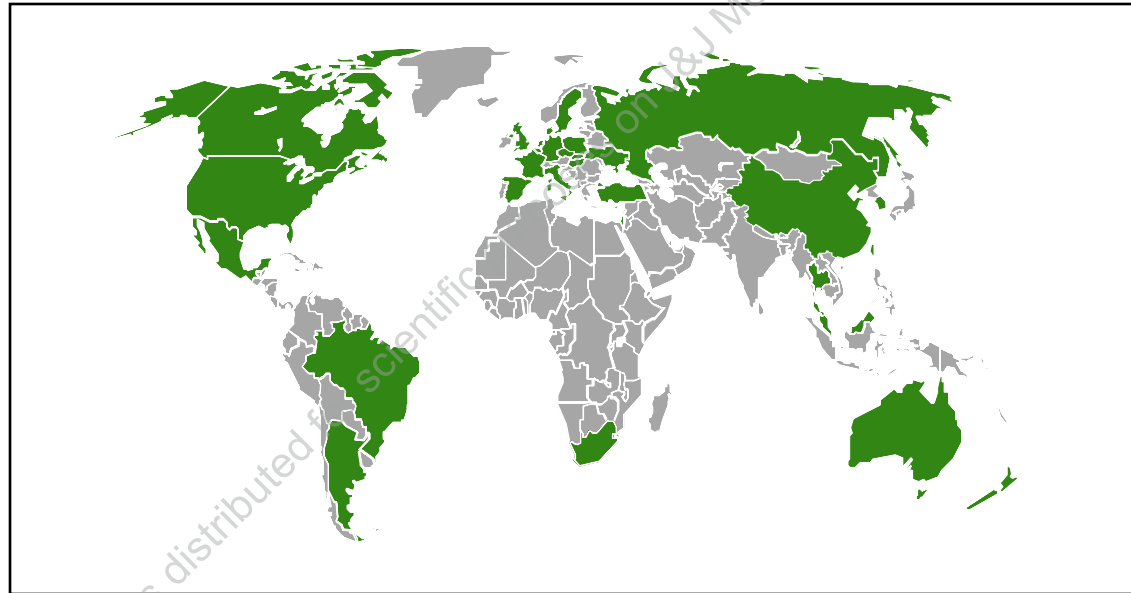
Key Takeaway: The addition of niraparib to AA plus P maintained baseline health-related quality of life while providing clinical benefit, with a safety profile consistent with that previously observed for this combination (niraparib + AA + P)



Acknowledgments

- Thank you to the participants, their families, and the the physicians, nurses, and staff members who provided care for participants and supported the AMPLITUDE trial

A total of 696 patients from 32 countries were randomized in AMPLITUDE



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