

TITAN: Health-related quality of life data

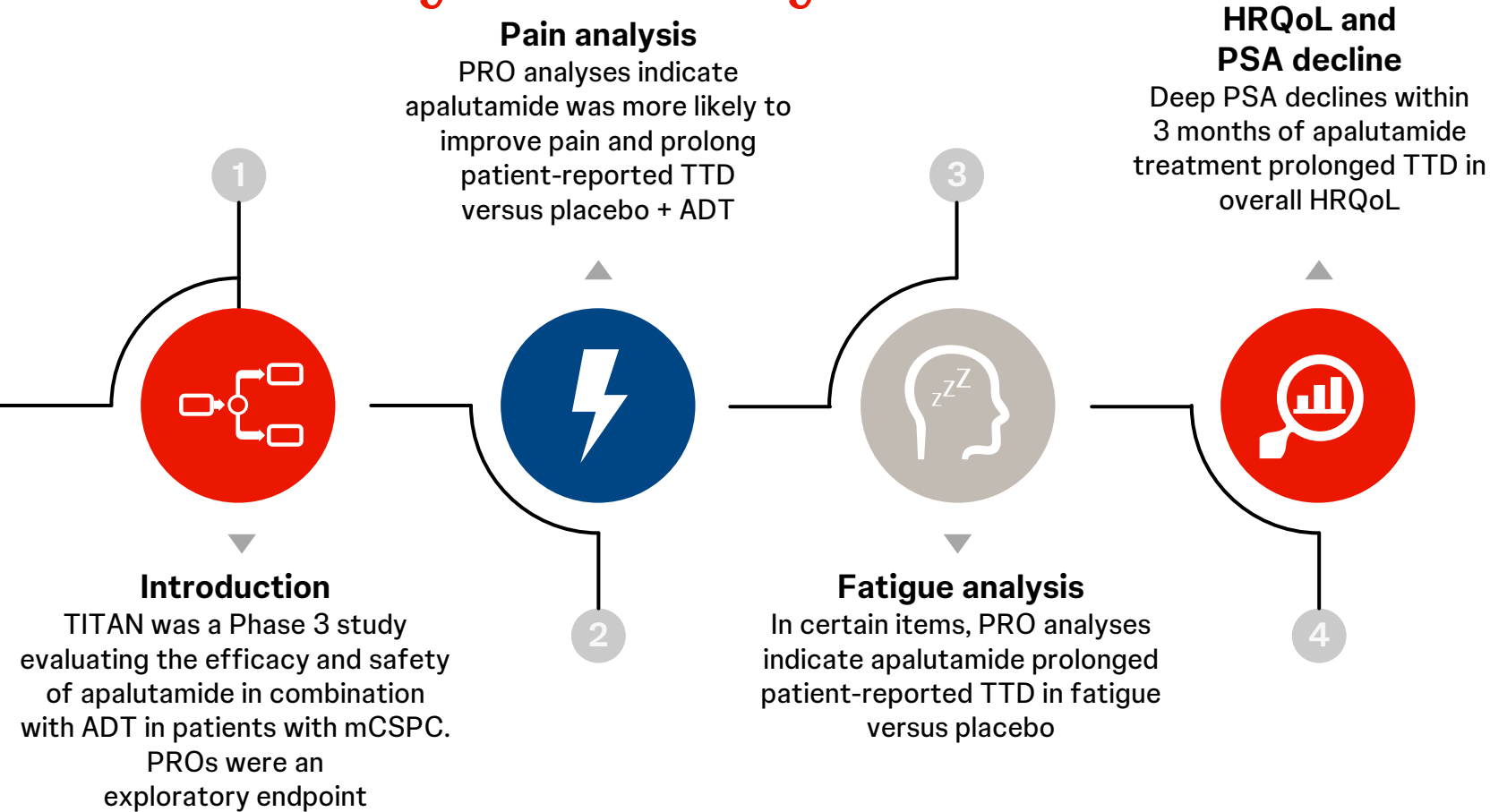
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HRQoL, health-related quality of life; PSA, prostate-specific antigen.



TITAN: Key takeaways



Maintenance of HRQoL taken together with significantly improved OS and rPFS and a tolerable safety profile supports apalutamide as a standard of care for a broad range of patients with mCSPC

ADT, androgen deprivation therapy; HRQoL, health-related quality of life; mCSPC, metastatic castration-sensitive prostate cancer; OS, overall survival; PRO, patient-reported outcome; PSA, prostate-specific antigen; rPFS, radiographic progression-free survival; TTD, time to deterioration.



TITAN: Study design

Broad patient population

Key eligibility criteria

- Castration sensitive
- Distant metastatic disease by ≥ 1 lesion on bone scan
- ECOG PS 0 or 1

On-study requirement

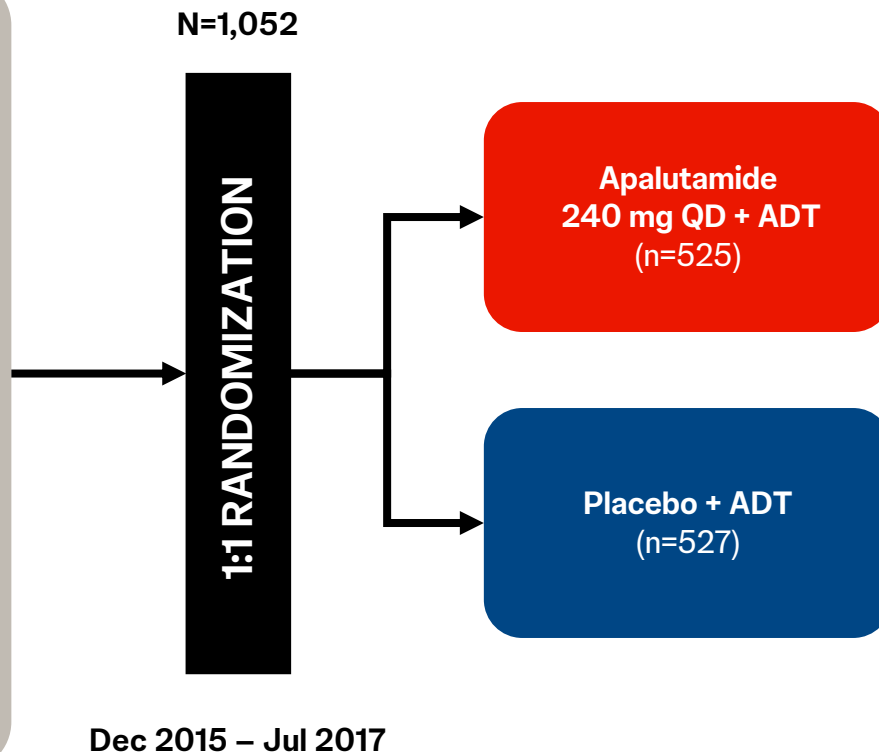
- Continuous ADT

Permitted

- Prior DOC ≤ 6 cycles ended ≤ 2 months
- ADT ≤ 6 months for mCSPC or ≤ 3 years for local disease
- Local treatment completed ≥ 1 year prior

Stratifications

- Gleason score at diagnosis (≤ 7 vs > 7)
- Region (NA and EU vs all other countries)
- Prior DOC (yes vs no)



Dual primary endpoints

- OS
- rPFS

Secondary endpoints

- Time to:
 - Cytotoxic chemotherapy
 - Pain progression
 - Chronic opioid use
 - Skeletal-related event

Exploratory endpoints

- PROs
- Time to PSA progression
- Second PFS
- Time to symptomatic progression

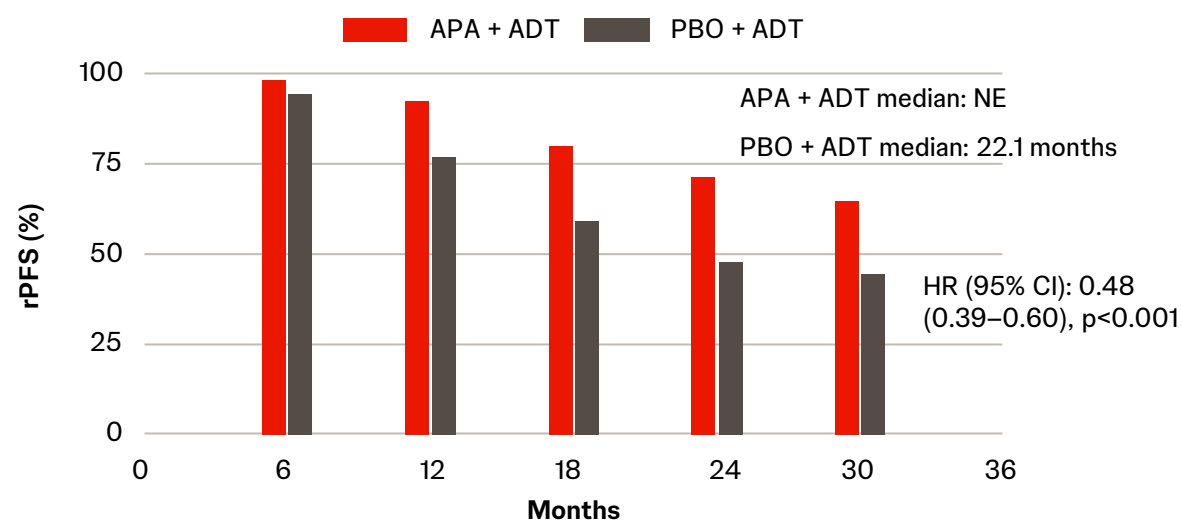
ADT, androgen deprivation therapy; DOC, docetaxel; ECOG PS, Eastern Cooperative Oncology Group performance status; EU, European Union; mCSPC, metastatic castration-sensitive prostate cancer; NA, North America; OS, overall survival; PFS, progression-free survival; PRO, patient-reported outcome; PSA, prostate-specific antigen; QD, once a day; rPFS, radiographic progression-free survival.

Reproduced with permission from Agarwal N, et al. Apalutamide plus androgen deprivation therapy for metastatic castration-sensitive prostate cancer: Analysis of pain and fatigue in the phase 3 TITAN study. J Urol. 2021;206(4):914–923. <https://www.auajournals.org/doi/10.1097/JU.0000000000001841>



TITAN efficacy: Apalutamide significantly reduced radiographic progression and death as compared to ADT

rPFS at primary analysis (primary endpoint)¹

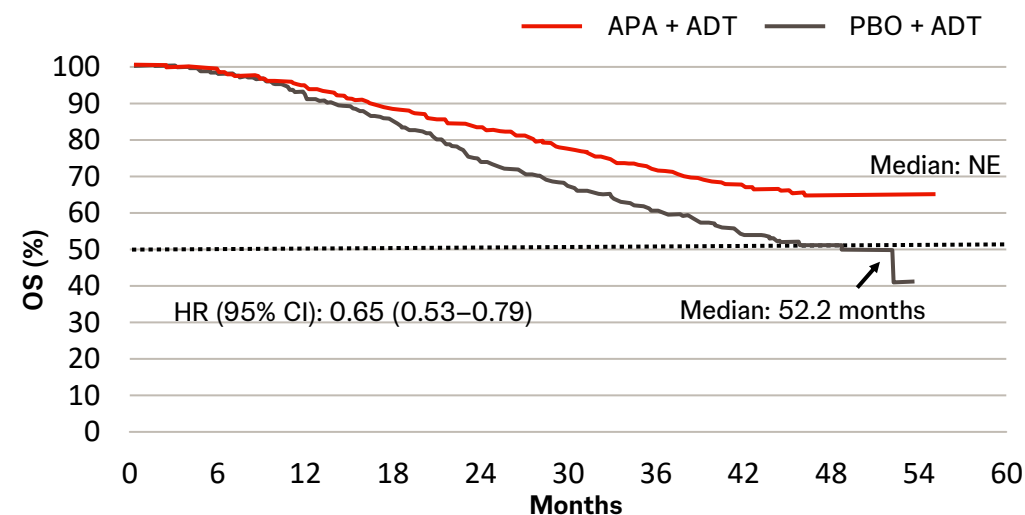


Number at risk

APA + ADT	525	469	389	315	89	2	0
PBO + ADT	527	437	325	229	57	3	0

rPFS was statistically significant based on prespecified p value of p=0.005. At primary analysis, there was a 52% reduction in risk of radiographic progression or death*

OS at final analysis (primary endpoint)²



Number at risk

APA + ADT	525	513	489	452	425	394	362	227	52	3	0
PBO + ADT	527	510	474	436	374	339	301	181	43	0	0

OS was significantly improved at primary analysis and updated at final analysis.[†] At final analysis, there was a 35% reduction in the risk of death[‡]

*Median follow-up of 22.7 months. [†]The primary analysis of TITAN showed significantly improved OS [HR (95% CI): 0.67 (0.51–0.89), p=0.005],¹ with updated HR 0.65 at the final analysis.² [‡]Median follow-up of 44 months.

ADT, androgen deprivation therapy; APA, apalutamide; CI, confidence interval; HR, hazard ratio; NE, not estimable; OS, overall survival; PBO, placebo; rPFS, radiographic progression-free survival.

1. Chi KN, et al. *N Engl J Med*. 2019;381(1):13–24. 2. Reproduced with permission from Chi KN, et al. Apalutamide in Patients with metastatic castration-sensitive prostate cancer: Final survival analysis of the randomized, double-blind, phase III TITAN study. *J Clin Oncol*. 2021;39(20):2294–2303. <https://ascopubs.org/doi/10.1200/JCO.20.03488>.



TITAN: Safety results

	APA + ADT (n=524)		PBO + ADT (n=527)		Crossover group (n=208)*	
Median (range) treatment duration, months [†]	39.3 (0–55.7)		20.2 (0.1–37.0)		15.4 (0.6–18.2)	
Total exposure, patient years	1,358.9		793.3		243.6	
TEAEs by group term, event (event rate/100 patient-years of exposure) [‡]	All grades [§]	Grade 3/4 [§]	All grades	Grade 3/4	All grades	Grade 3/4
Any TEAE of interest	543 (40.0)	103 (7.6)	178 (22.4)	21 (2.7)	102 (41.9)	16 (6.5)
Skin rash	331 (24.4)	40 (2.9)	66 (8.3)	5 (0.6)	44 (18.1)	8 (3.3)
Fracture	83 (6.1)	21 (1.5)	33 (4.2)	4 (0.5)	5 (2.1)	0
Fall	63 (4.6)	9 (0.7)	54 (6.8)	5 (0.6)	14 (5.7)	0
Ischemic heart disease	45 (3.3)	21 (1.5)	13 (1.6)	5 (0.7)	1 (0.4)	1 (0.4)
Ischemic cerebrovascular disorder	18 (1.3)	11 (0.8)	10 (1.3)	2 (0.3)	7 (2.9)	7 (2.8)
Seizure	3 (0.2)	1 (0.1)	2 (0.3)	0	0	0

Grade 3/4 AEs and specific AEs such as rash, fracture, fall, heart diseases, and seizure occurred more commonly in the apalutamide arm than in the placebo + ADT arm

*Of patients in the PBO + ADT arm, 39.5% crossed over to APA + ADT. [†]Patients received treatment until disease progression or unacceptable toxicity. [‡]Event rate per 100 patient-years of exposure is calculated as 100 times the number of distinct events with the group term/total patient-years of exposure (total days of exposure/365.25) for the treatment group. AEs occurred from the time of the first dose of the study intervention through 30 days after the last dose. AEs were graded according to National Cancer Institute Common Terminology Criteria for Adverse Events, version 4.0.3. One patient who was assigned to the apalutamide group withdrew consent before treatment. [§]The worst toxicity grade is included. Patients with missing toxicity grades were counted in the all-grade column.

ADT, androgen deprivation therapy; AE, adverse event; APA, apalutamide; CI, confidence interval; HR, hazard ratio; PBO, placebo; TEAE, treatment-emergent adverse event.

Reproduced with permission from Chi KN, et al. Apalutamide in Patients with metastatic castration-sensitive prostate cancer: Final survival analysis of the randomized, double-blind, phase III TITAN study. J Clin Oncol. 2021;39(20):2294–2303. <https://ascopubs.org/doi/10.1200/JCO.20.03488>.



PRO analyses in TITAN

	BPI-SF	BFI	FACT-P	EQ-5D-5L
Description	Assesses the severity of pain and the impact of pain on daily functions ¹	Assesses the severity of fatigue and the impact of fatigue on daily functioning ²	Assesses overall HRQoL, including physical, social, and emotional impact of prostate cancer and its treatments ³	Assesses overall HRQoL by five dimensions: mobility, self-care, usual activities, pain/discomfort, and anxiety/depression ⁴
Frequency of assessment in TITAN	BL, 7 consecutive days of each treatment cycle and Months 4, 8, 12 in follow-up ⁵	BL, 7 consecutive days of each treatment cycle and Months 4, 8, 12 in follow-up ⁵	BL, cycles 2–7, then every other cycle and Months 4, 8, 12 in follow-up ⁵	BL, cycles 2–7, then every other cycle and Months 4, 8, 12 in follow-up ⁵

BFI, Brief Fatigue Inventory; BL, baseline; BPI-SF, Brief Pain Inventory Short-Form; EQ-5D-5L, EuroQoL 5D questionnaire 5 level; FACT-P, Functional Assessment of Cancer Therapy-Prostate; HRQoL, health-related quality of life; PRO, patient-reported outcome.

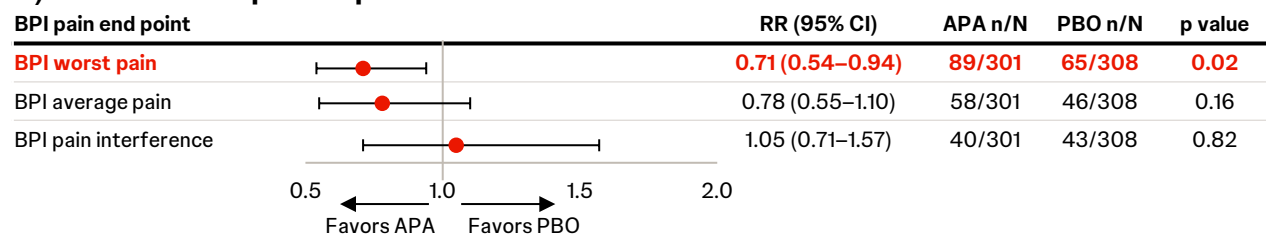
1. Cleeland CS. Brief Pain Inventory (short form). 1991; Available at: http://www.nccrc.org/files/news/briefpain_short.pdf. (Accessed October 6, 2025). 2. The University of Texas M. D. Anderson Cancer Center. Brief Fatigue Inventory. 1999; Available at: https://www.mdanderson.org/content/dam/mdanderson/documents/Departments-and-Divisions/Symptom-Research/BFI_English_SAMPLE.pdf. (Accessed October 6, 2025). 3. Functional Assessment of Cancer Therapy-Prostate Questionnaire (FACT-P): A Full Guide for Researchers and Clinicians. 2025; Available at: <https://resref.com/functional-assessment-of-cancer-therapy-prostate-questionnaire-fact-p-a-full-guide-for-researchers-and-clinicians/>. (Accessed October 6, 2025). 4. eProvide. EuroQoL 5-Dimension 5-Level (EQ-5D-5L). 2025; Available at: <https://eprovide.mapi-trust.org/instruments/euroqol-5-dimension-5-level>. (Accessed September 25, 2025). 5. Agarwal N, et al. *Lancet Oncol*. 2019;20:1518–1530.



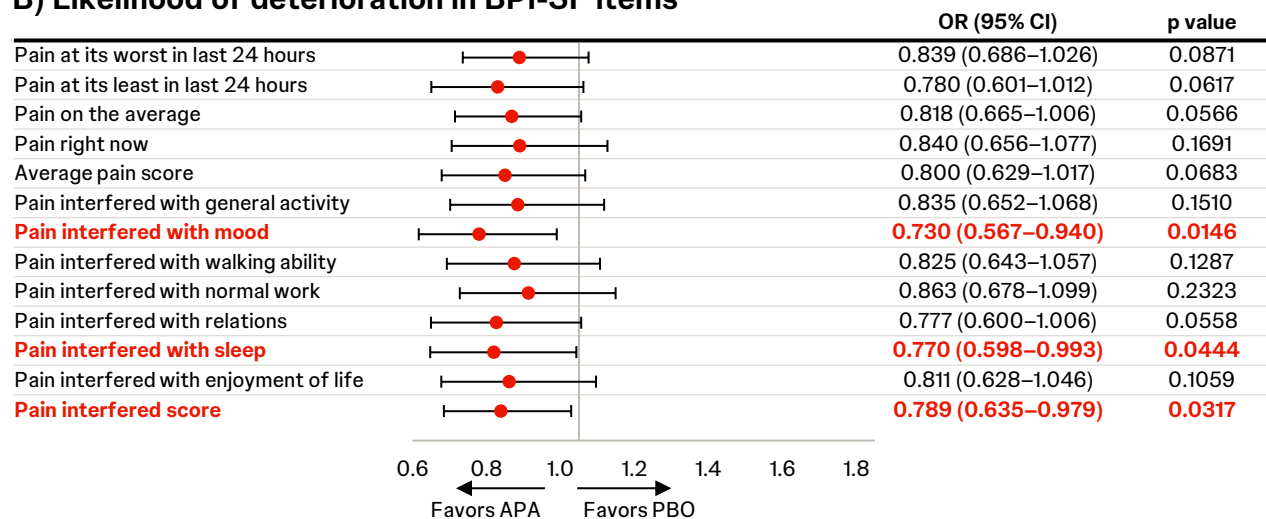
Apalutamide relieved pain, as evident through increased likelihood of improvement for patients with pain at baseline

TITAN: Likelihood of pain improvement or deterioration

A) Likelihood of pain improvement



B) Likelihood of deterioration in BPI-SF items



The risk of deterioration for some BPI-SF pain items was significantly lower with apalutamide + ADT than with placebo + ADT

ADT, androgen deprivation therapy; APA, apalutamide; BPI, Brief Pain Inventory; BPI-SF, Brief Pain Inventory-Short Form; CI, confidence interval; OR, odds ratio; PBO, placebo; RR, risk ratio.

Reproduced with permission from Agarwal N, et al. Apalutamide plus androgen deprivation therapy for metastatic castration-sensitive prostate cancer: Analysis of pain and fatigue in the phase 3 TITAN study. J Urol. 2021;206(4):914–923. <https://www.auajournals.org/doi/10.1097/JU.0000000000001841>

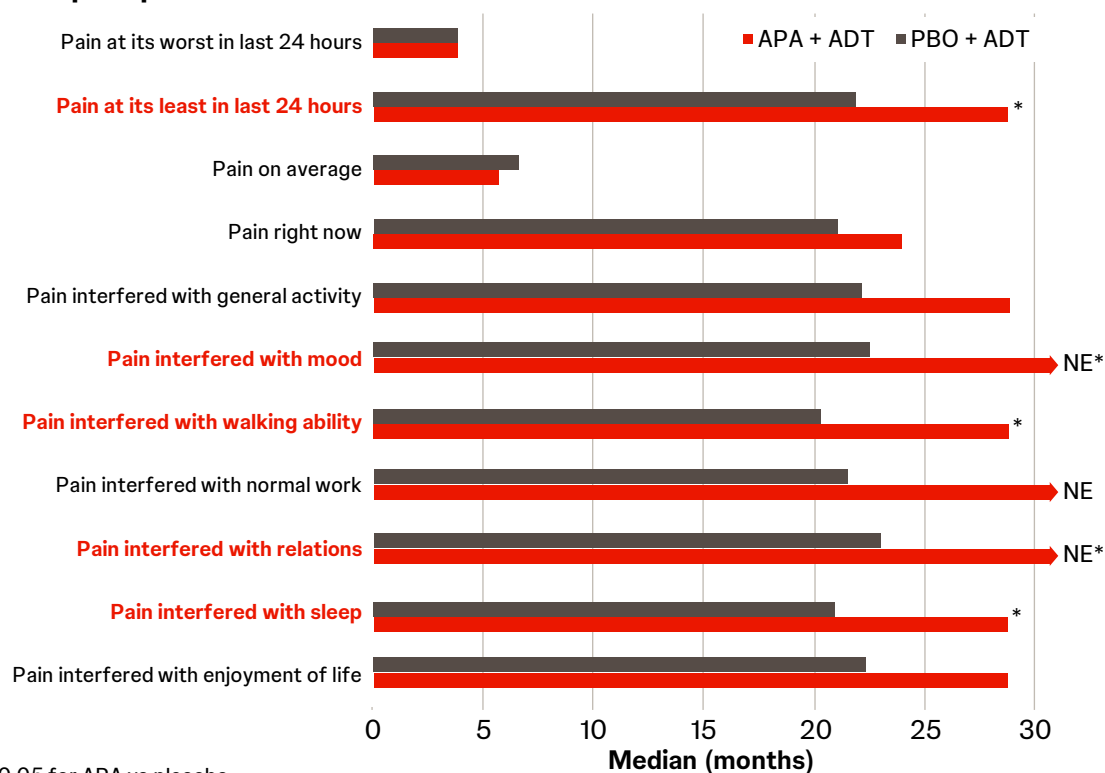


Apalutamide prolonged TTD in pain that interfered with daily activities as compared to placebo

TITAN: TTD in pain

TTD in pain per BPI-SF items

Analysis of BPI results



Median time to deterioration for certain pain items was significantly longer with apalutamide + ADT than with placebo + ADT

*p<0.05 for APA vs placebo.

ADT, androgen deprivation therapy; APA, apalutamide; BPI, Brief Pain Inventory; BPI-SF, Brief Pain Inventory-Short Form; NE, not estimable; PBO, placebo; TTD, time to deterioration.

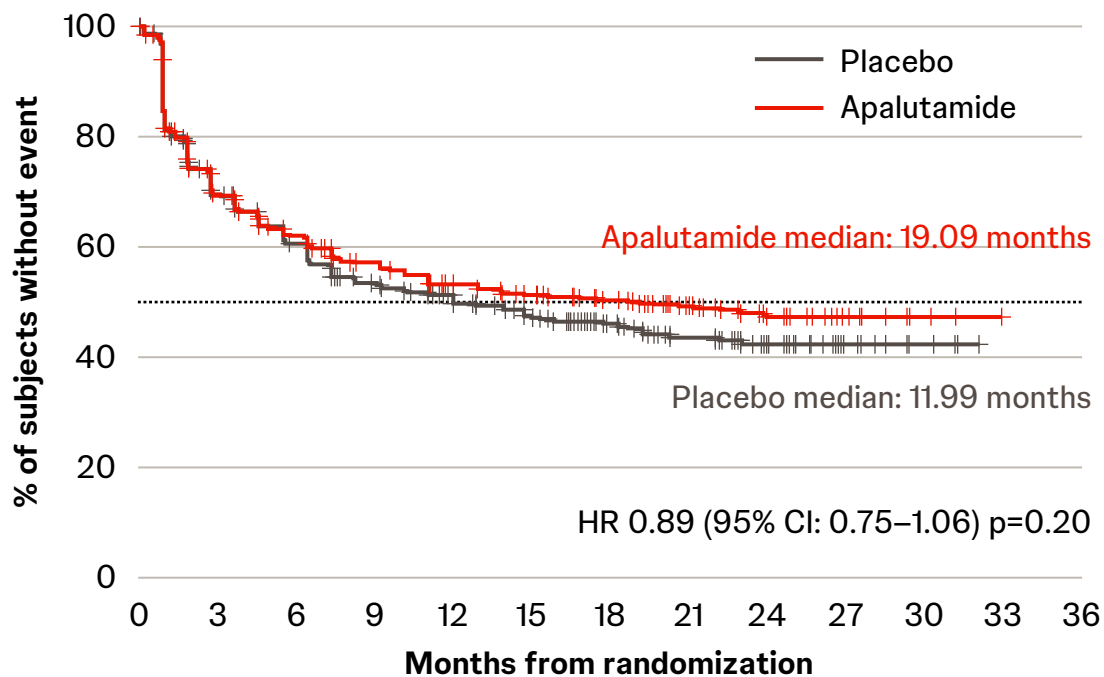
Reproduced with permission from Agarwal N, et al. Apalutamide plus androgen deprivation therapy for metastatic castration-sensitive prostate cancer: Analysis of pain and fatigue in the phase 3 TITAN study. J Urol. 2021;206(4):914–923.

<https://www.auajournals.org/doi/10.1097/JU.0000000000001841>



Trend towards improvement in time to worst pain intensity progression with apalutamide vs placebo

TITAN: Time to worst pain intensity



No. at risk:

Placebo	527	343	289	247	215	184	152	89	43	22	4	0	0
Apalutamide	525	330	285	250	228	210	178	117	62	20	4	1	0

ADT, androgen deprivation therapy; BPI-SF, Brief Pain Inventory-Short Form; CI, confidence interval; HR, hazard ratio.
Data on File. Johnson & Johnson. TITAN Interim Clinical Study Report; April 10, 2019.

7.1 months delay in time to worst pain intensity progression with apalutamide + ADT vs placebo + ADT

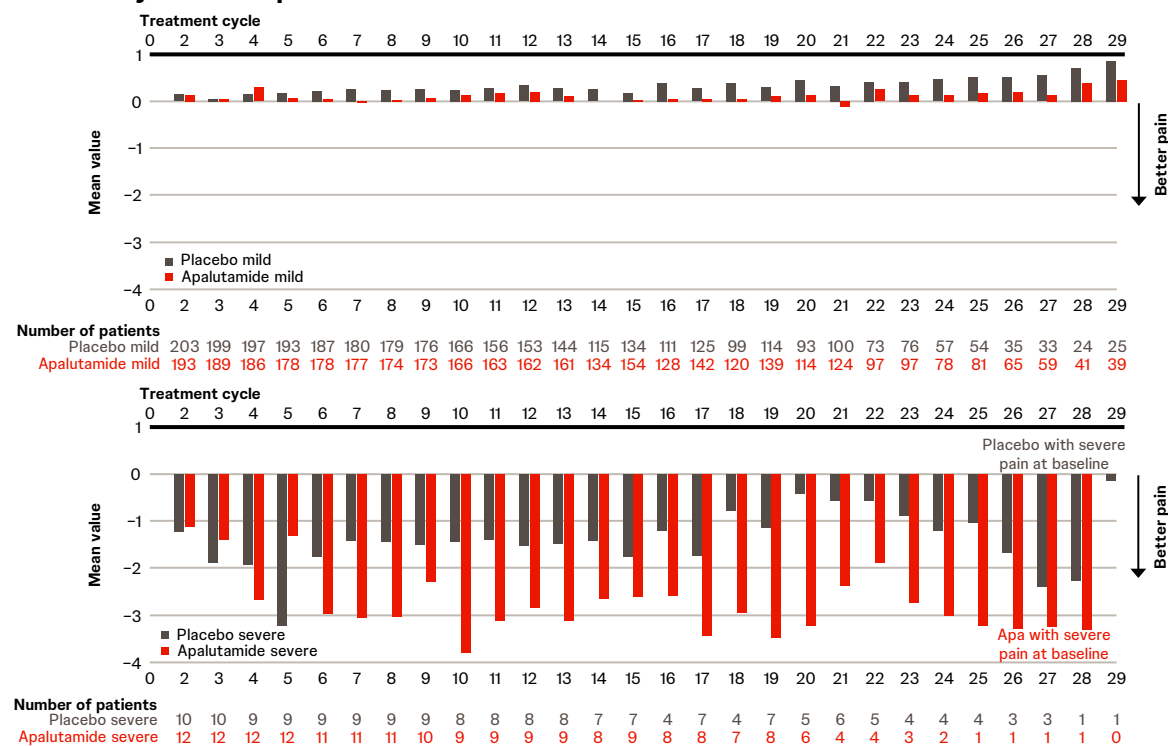
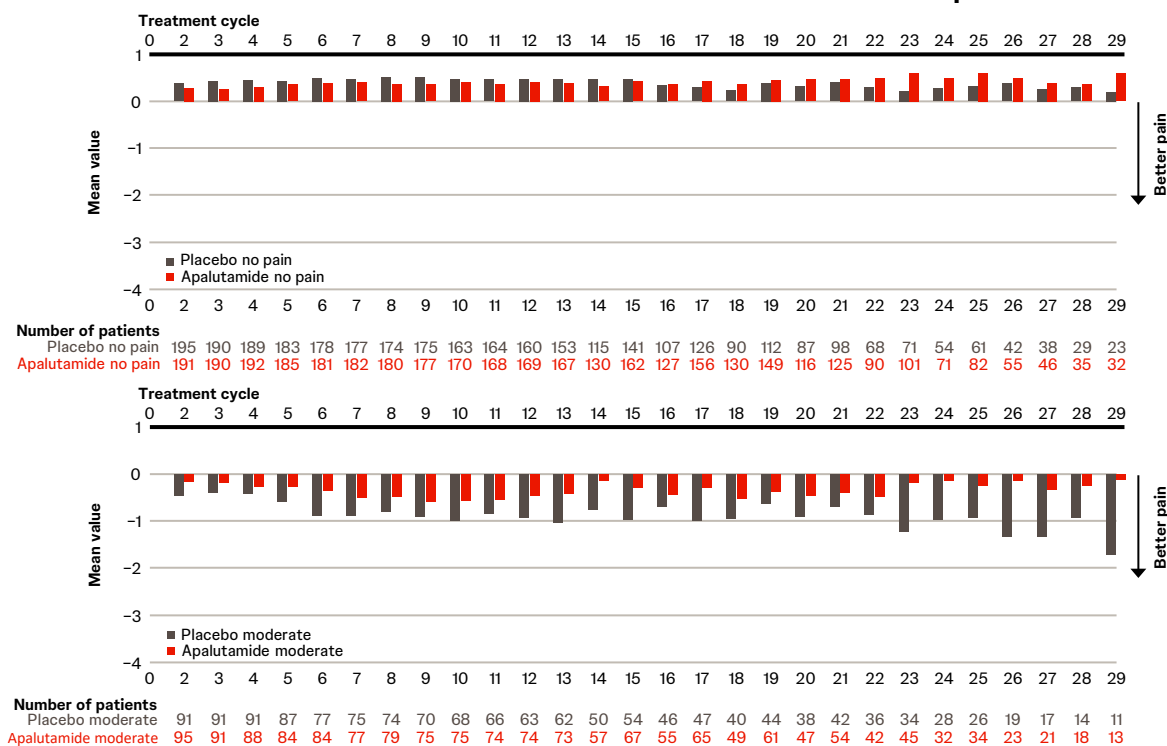


Trend towards improvement in mean pain interference with apalutamide versus placebo in patients with severe baseline pain

TITAN: Patient-reported changes in pain interference

Patient-reported changes in pain interference from baseline by BPI-SF

Mean pain interference as stratified by baseline pain



Data from 29 treatment cycles are presented. Error bars are the standard error of the mean.

APA, apalutamide; BPI-SF, Brief Pain Inventory-Short Form.

Agarwal N, et al. Lancet Oncol. 2019;20:1518–1530.

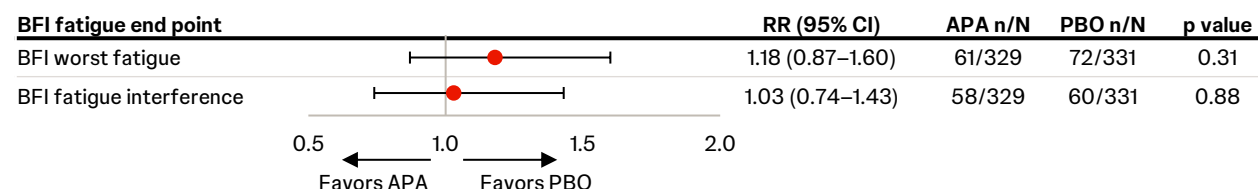


The likelihood of experiencing fatigue was not different between apalutamide and placebo groups

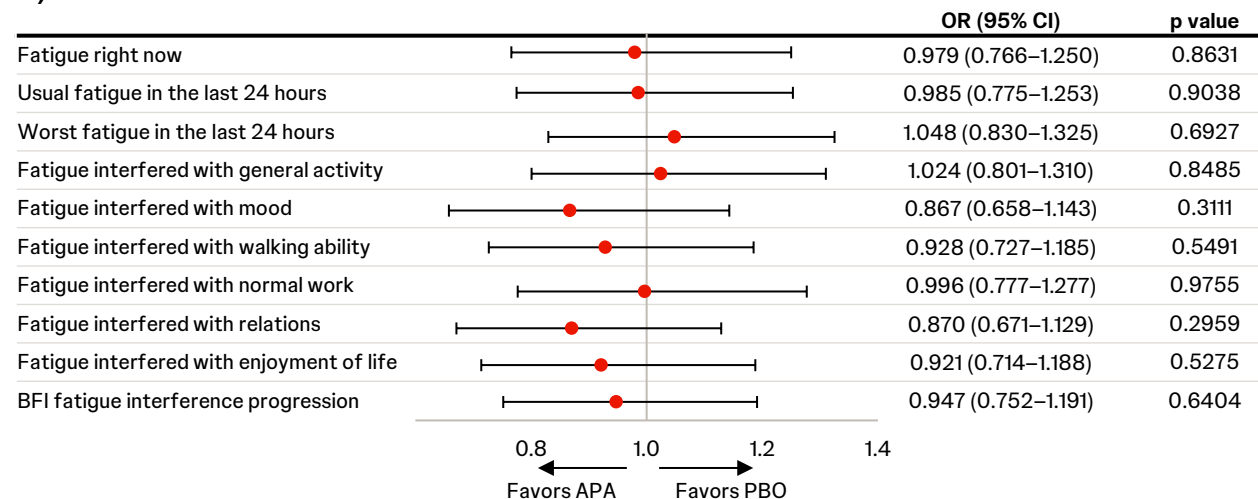
TITAN: Likelihood of fatigue

Analysis of BFI results¹

A) Likelihood of fatigue



B) Model-based likelihood of deterioration in BFI scale items



There were no significant differences between treatment groups on mean BFI domain scores

Of note, as many as 43% of patients treated with ADT have been reported to experience clinically significant fatigue²

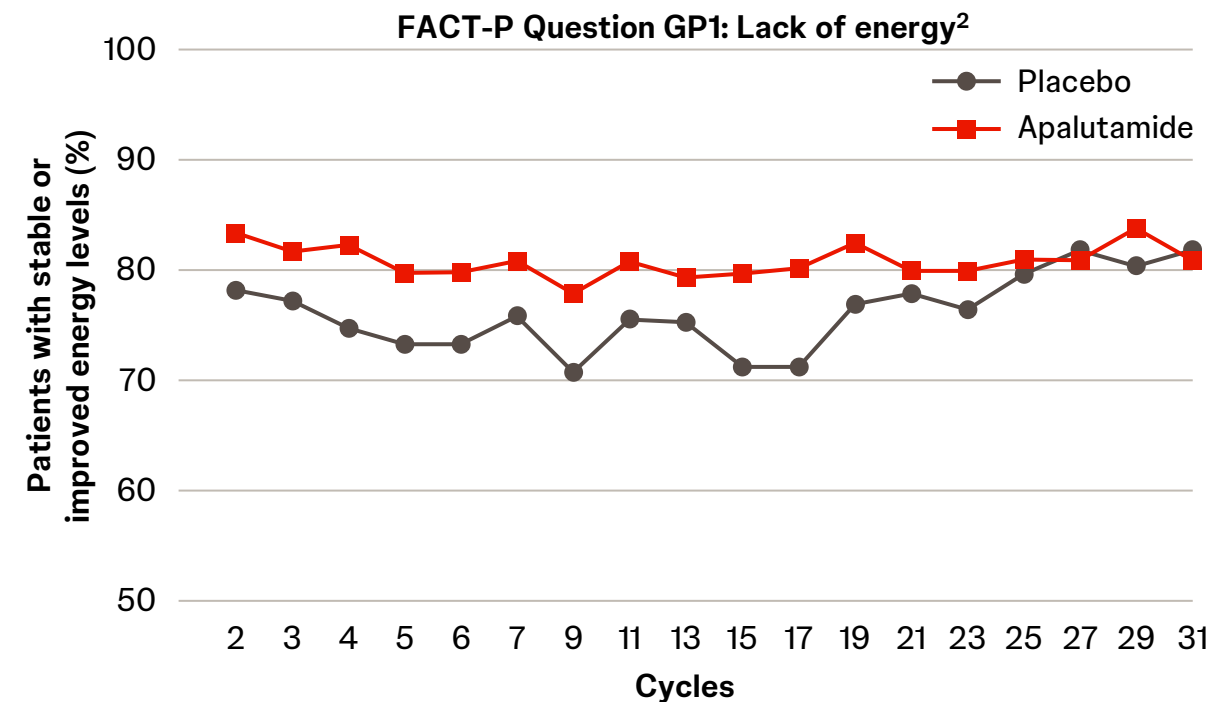
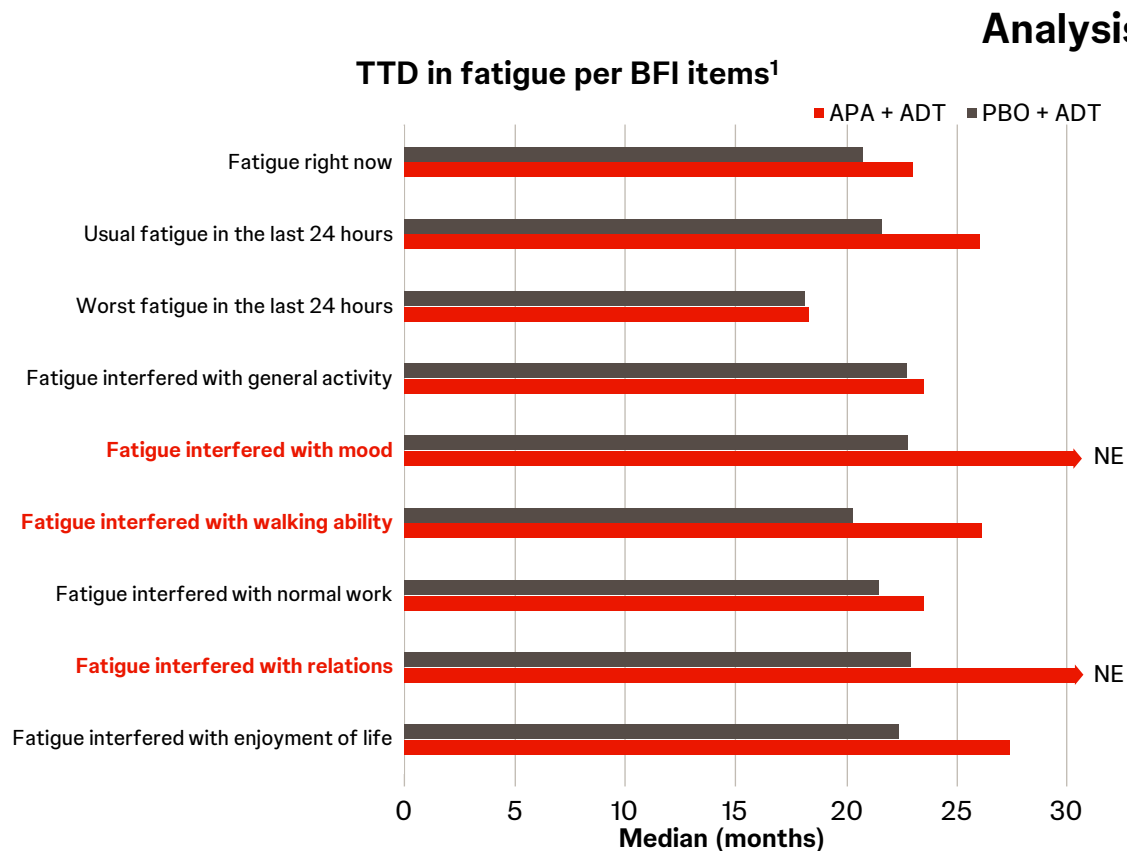
ADT, androgen deprivation therapy; APA, apalutamide; BFI, Brief Fatigue Inventory; CI, confidence interval; OR, odds ratio; PBO, placebo; RR, risk ratio.

1. Reproduced with permission from Agarwal N, et al. Apalutamide plus androgen deprivation therapy for metastatic castration-sensitive prostate cancer: Analysis of pain and fatigue in the phase 3 TITAN study. *J Urol*. 2021;206(4):914–923. <https://www.auajournals.org/doi/10.1097/JU.0000000000001841>. 2. Storey DJ, et al. *Ann. Oncol*. 2012;23(6):1542–1549.



Apalutamide prolonged TTD in fatigue that interfered with daily activities as compared to placebo

TITAN: TTD in fatigue



At each cycle, >78% of apalutamide and >71% of placebo + ADT patients had energy levels that were stable or improved relative to baseline levels

ADT, androgen deprivation therapy; APA, apalutamide; BFI, Brief Fatigue Inventory; FACT-P, Functional Assessment of Cancer Therapy-Prostate; NE, not estimable; PBO, placebo; TTD, time to deterioration.

1. Reproduced with permission from Agarwal N, et al. Apalutamide plus androgen deprivation therapy for metastatic castration-sensitive prostate cancer: Analysis of pain and fatigue in the phase 3 TITAN study. J Urol. 2021;206(4):914–923.

<https://www.auajournals.org/doi/10.1097/JU.0000000000001841>. 2. Agarwal N, et al. ASCO 2021; Abstract 5068 (poster presentation).

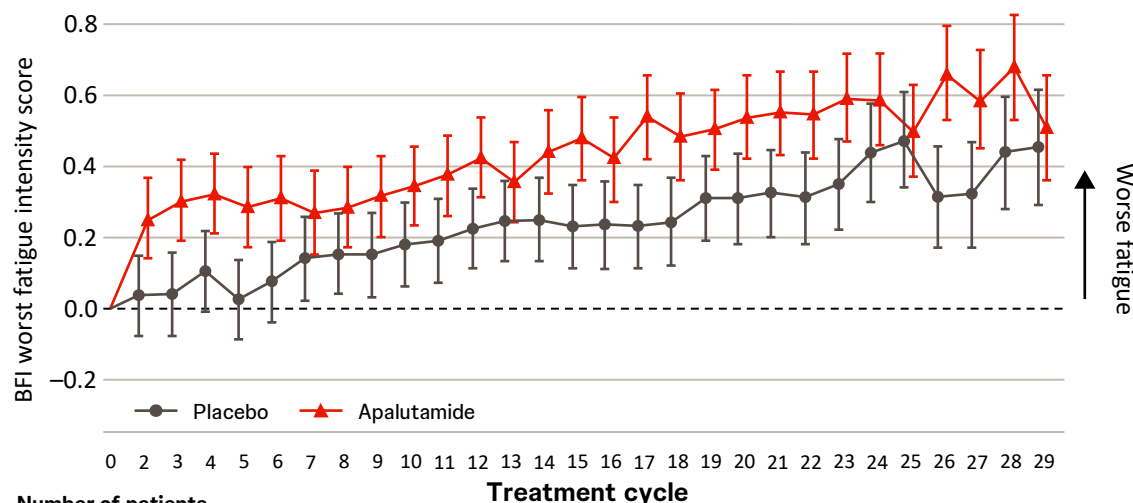


Changes in patient-reported fatigue intensity and interference were similar between apalutamide and placebo groups

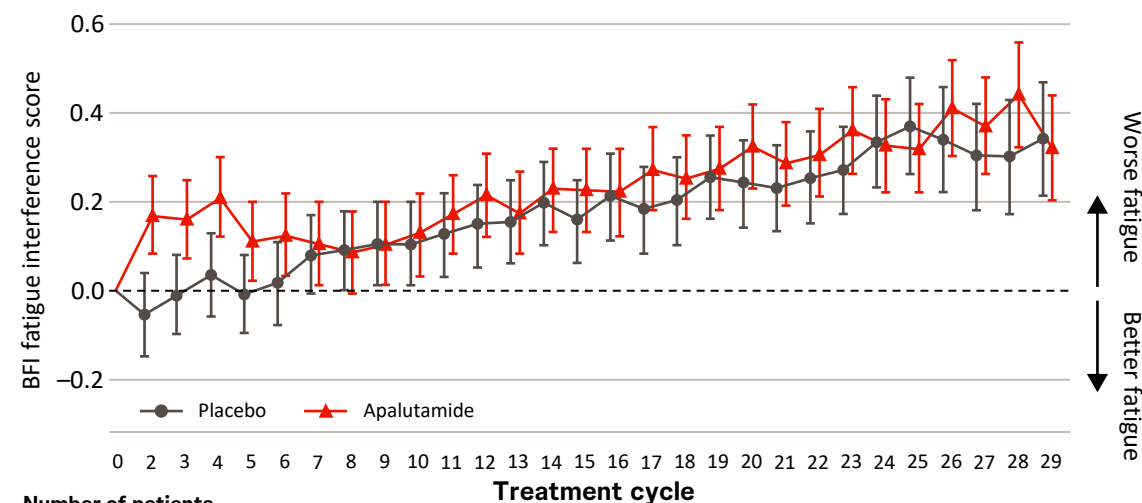
TITAN: Patient-reported changes in fatigue

Patient-reported changes in fatigue from baseline in BFI

(A) Worst fatigue intensity



(B) Fatigue interference



BFI, Brief Fatigue Inventory.

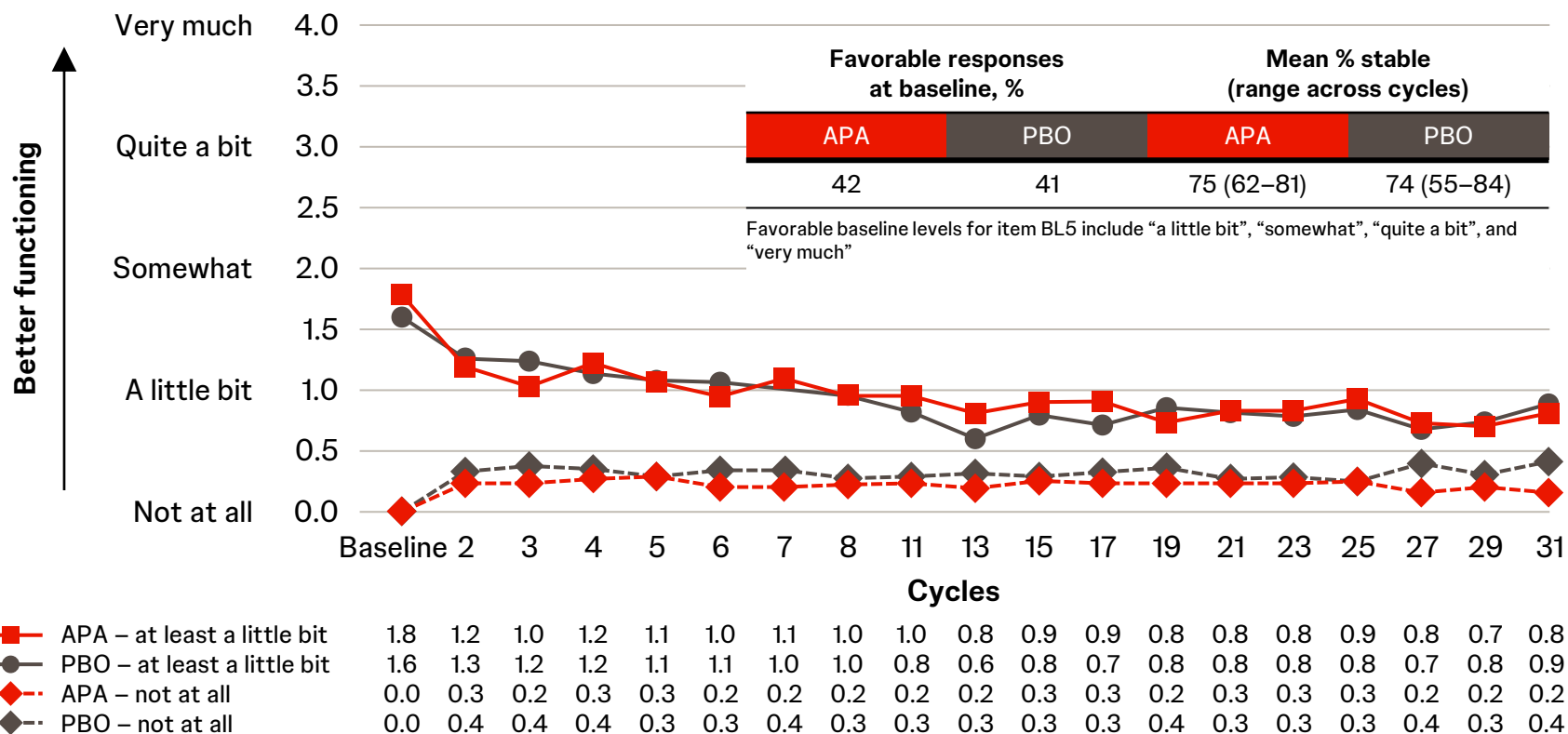
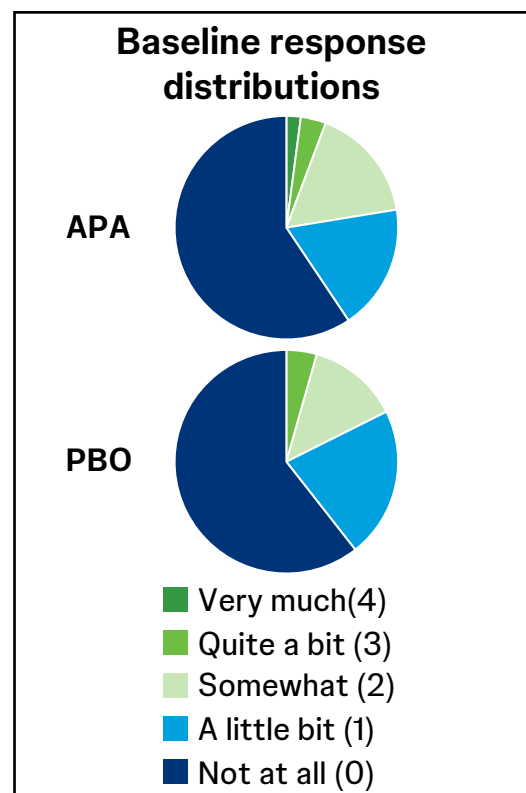
Reprinted from The Lancet Oncology, 20(11). Agarwal N, et al. Health-related quality of life after apalutamide treatment in patients with metastatic castration-sensitive prostate cancer (TITAN): a randomised, placebo-controlled, phase 3 study. 1518–1530, 2019, with permission from Elsevier.



Sexual function was comparable between apalutamide and placebo groups and stable over time

TITAN: Sexual function

FACT-P item BL5: "I am able to have and maintain an erection"

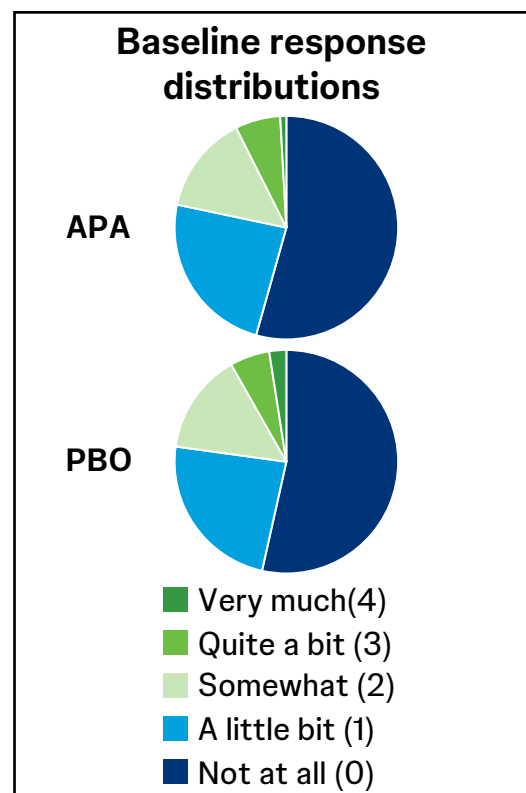


APA, apalutamide; FACT-P, Functional Assessment of Cancer Therapy-Prostate; PBO, placebo.
Saad F, et al. SUO 2021; Abstract 1455 (poster presentation).

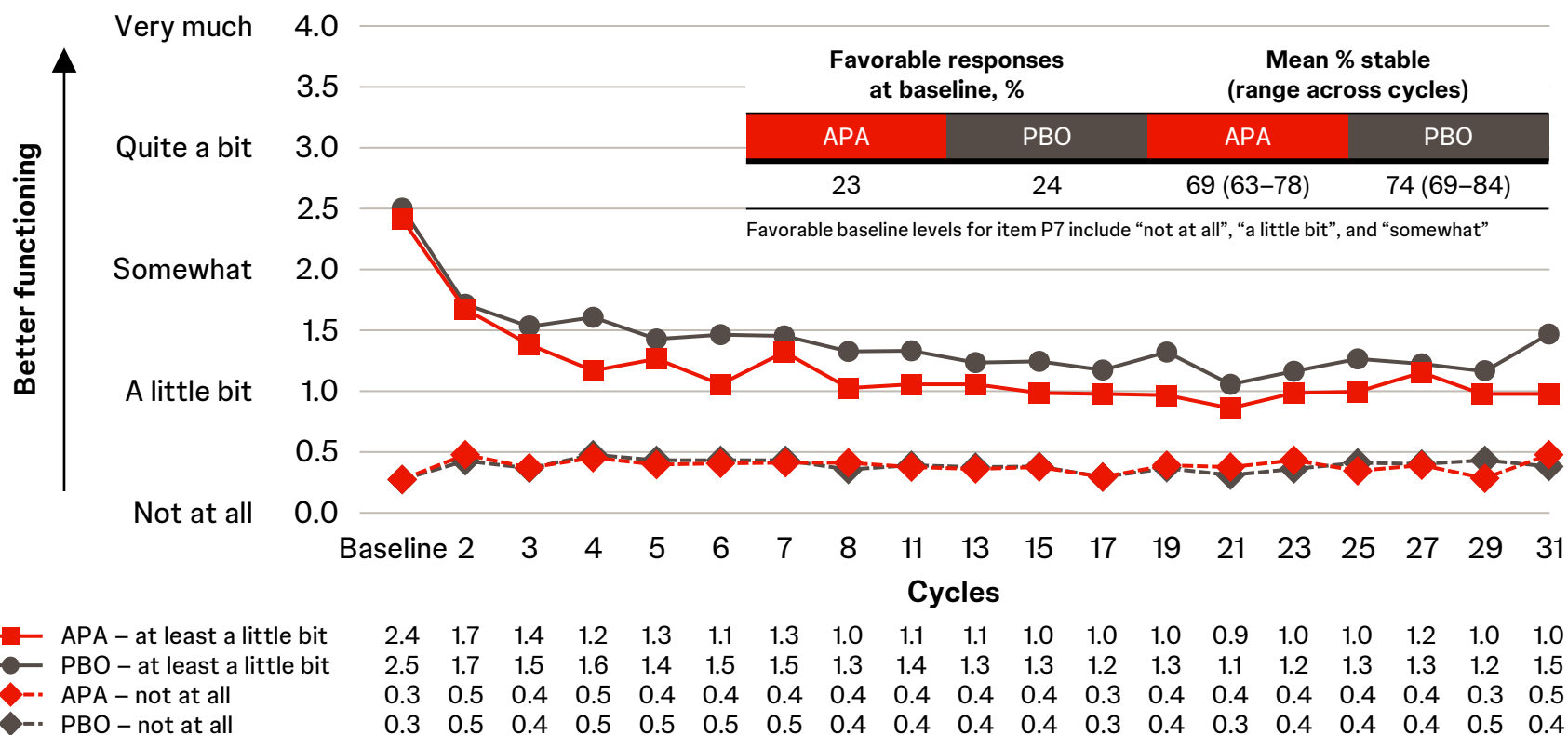


Difficulty urinating was comparable between apalutamide and placebo groups and stable over time

TITAN: Difficulties with urination



FACT-P item P7: "I have difficulty urinating"



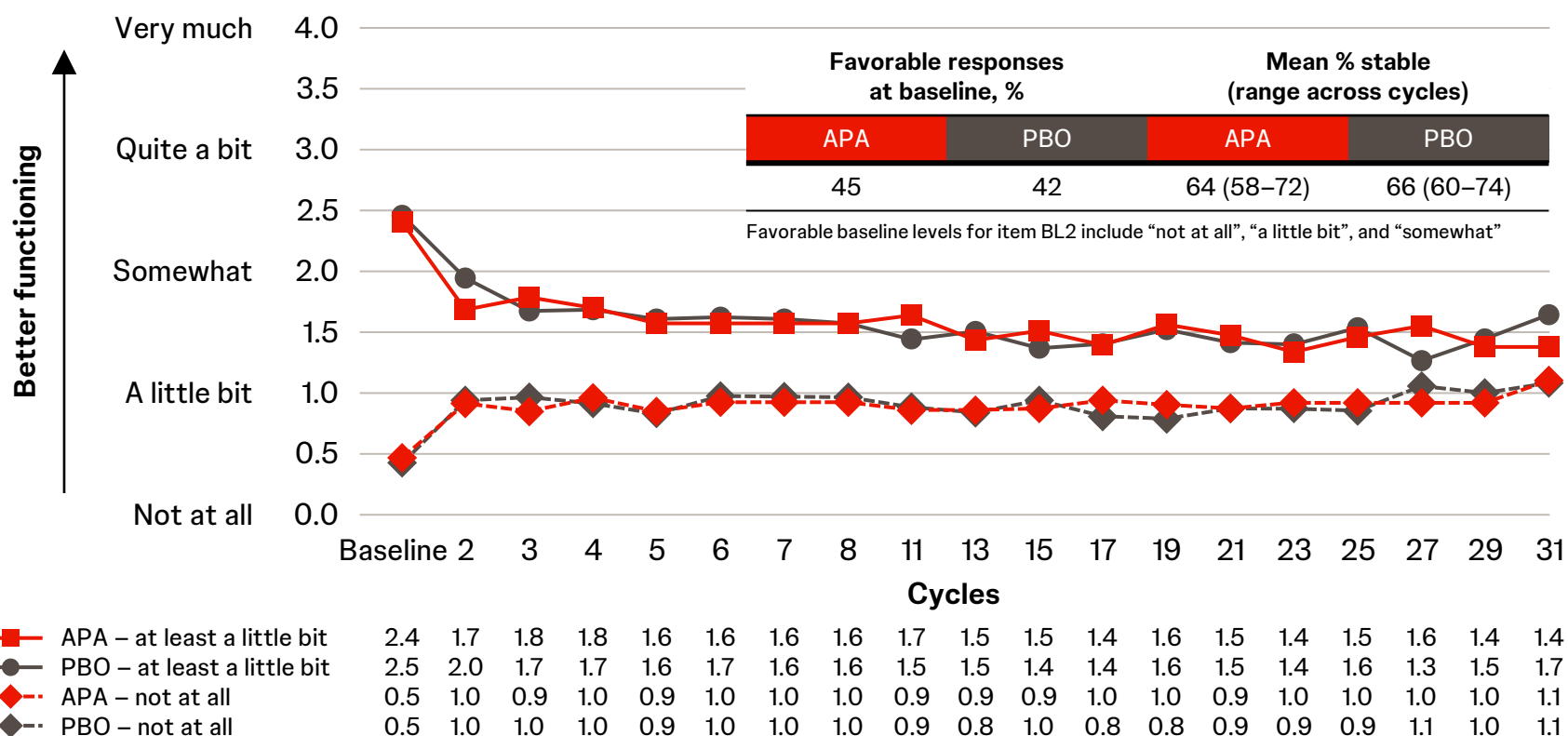
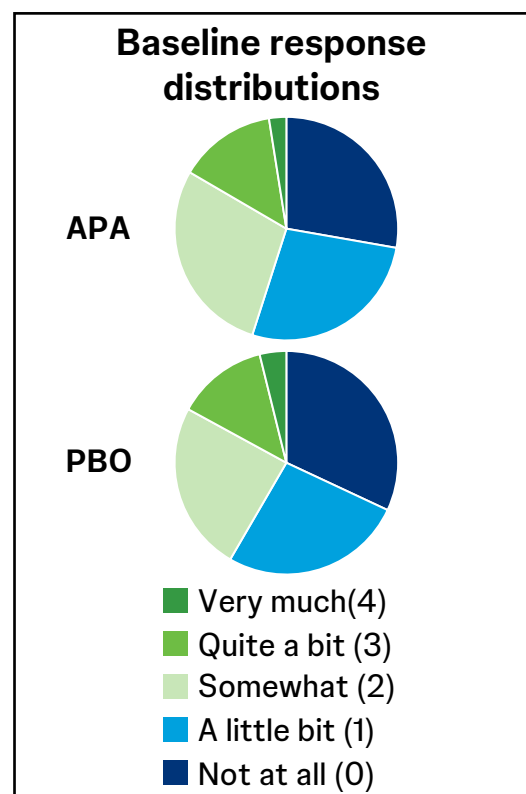
APA, apalutamide; FACT-P, Functional Assessment of Cancer Therapy-Prostate; PBO, placebo.
Saad F, et al. SUO 2021; Abstract 1455 (poster presentation).



Urinary frequency was comparable between apalutamide and placebo groups and stable over time

TITAN: Urinary frequency

FACT-P item BL2: "I urinate more frequently than usual"



APA, apalutamide; FACT-P, Functional Assessment of Cancer Therapy-Prostate; PBO, placebo.
Saad F, et al. SUO 2021; Abstract 1455 (poster presentation).

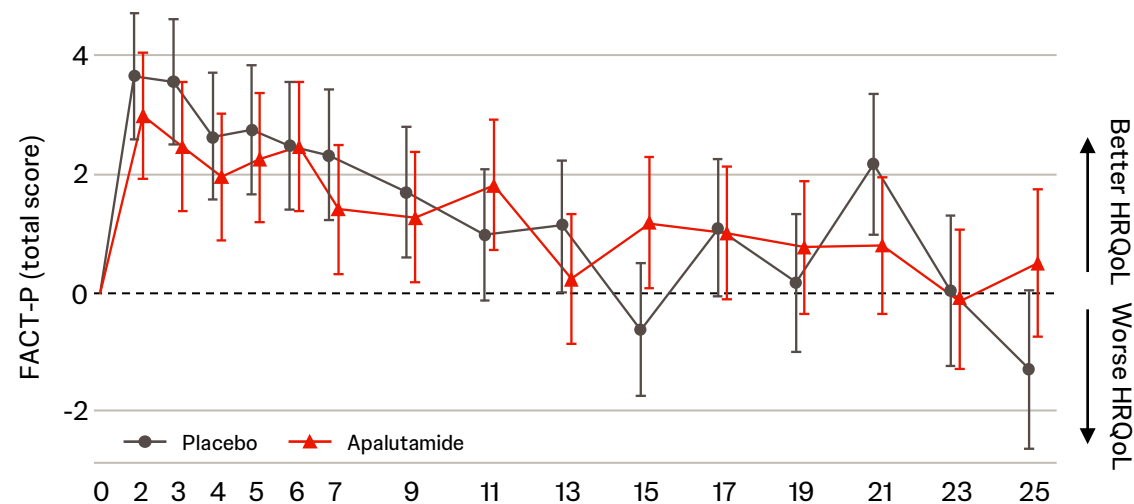


Changes in patient-reported QoL were similar between apalutamide and placebo groups

TITAN: Patient-reported changes in FACT-P and FACT-G

Patient-reported changes for mean change from baseline using repeated-measures mixed-effect analyses

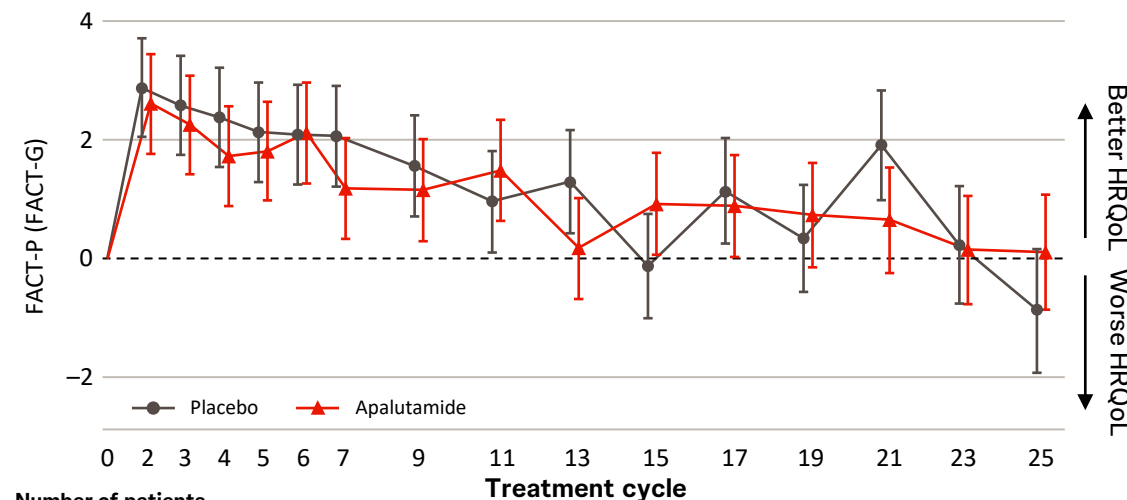
A) FACT-P



Number of patients

Placebo	366	359	355	348	334	300	310	286	262	245	214	193	171	130	103
Apalutamide	358	350	349	342	333	315	306	302	298	278	265	252	225	188	147

B) FACT-G



Number of patients

Placebo	366	359	355	348	334	300	310	286	262	245	214	193	171	130	103
Apalutamide	358	350	349	342	333	315	306	302	298	278	265	252	225	188	147

Error bars are the standard error of the mean.

FACT-G, Functional Assessment of Cancer Therapy-General; FACT-P, Functional Assessment of Cancer Therapy-Prostate. HRQoL, health-related quality of life.

Reprinted from The Lancet Oncology, 20(11). Agarwal N, et al. Health-related quality of life after apalutamide treatment in patients with metastatic castration-sensitive prostate cancer (TITAN): a randomised, placebo-controlled, phase 3 study. 1518–1530, 2019, with permission from Elsevier.

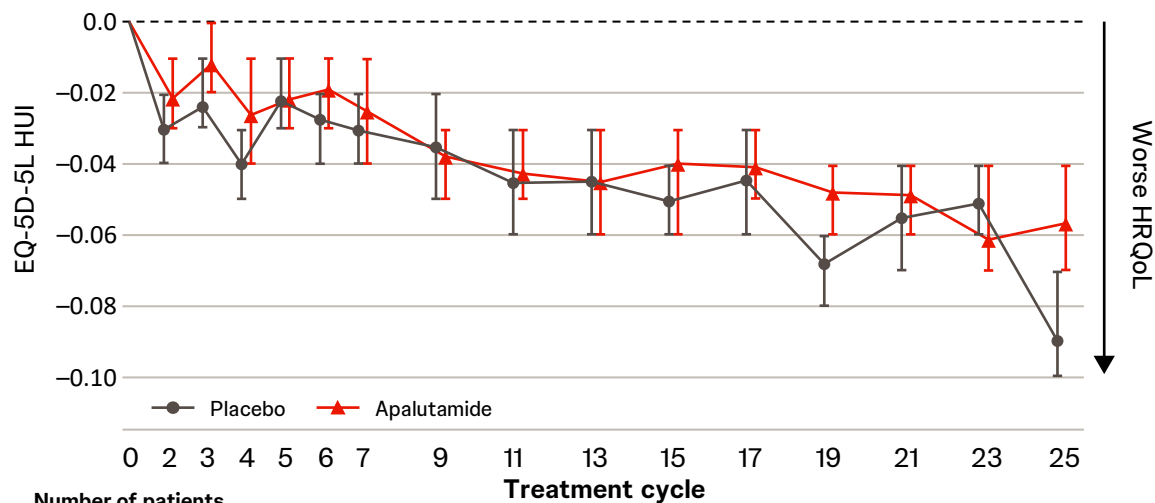


Changes in patient-reported QoL were similar between apalutamide and placebo groups

TITAN: Patient-reported changes in EQ-5D-5L HUI and VAS

Patient-reported changes for mean change from baseline using repeated-measures mixed-effect analyses

A) EQ-5D-5L HUI



Number of patients

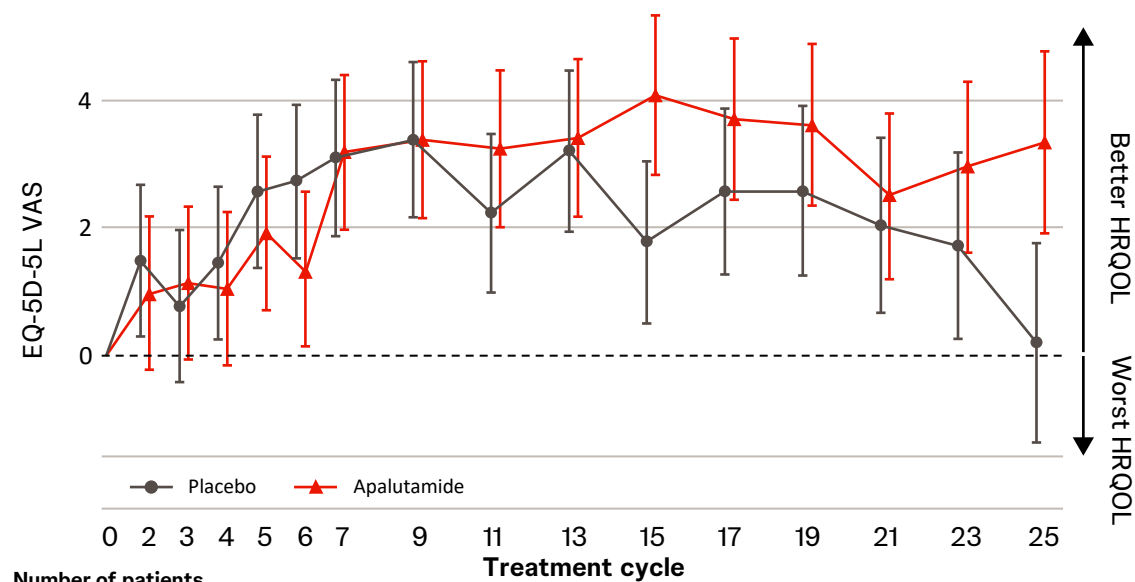
Placebo	366	359	355	348	334	300	310	286	262	245	214	194	171	130	103
Apalutamide	358	350	349	342	333	315	306	303	298	278	265	252	225	188	147

Error bars are the standard error of the mean.

EQ-5D-5L, EuroQoL 5D questionnaire 5 level; HUI, health utility index; HRQoL, health-related quality of life; VAS, visual analogue scale.

Reprinted from The Lancet Oncology, 20(11). Agarwal N, et al. Health-related quality of life after apalutamide treatment in patients with metastatic castration-sensitive prostate cancer (TITAN): a randomised, placebo-controlled, phase 3 study. 1518–1530, 2019, with permission from Elsevier.

B) EQ-5D-5L VAS



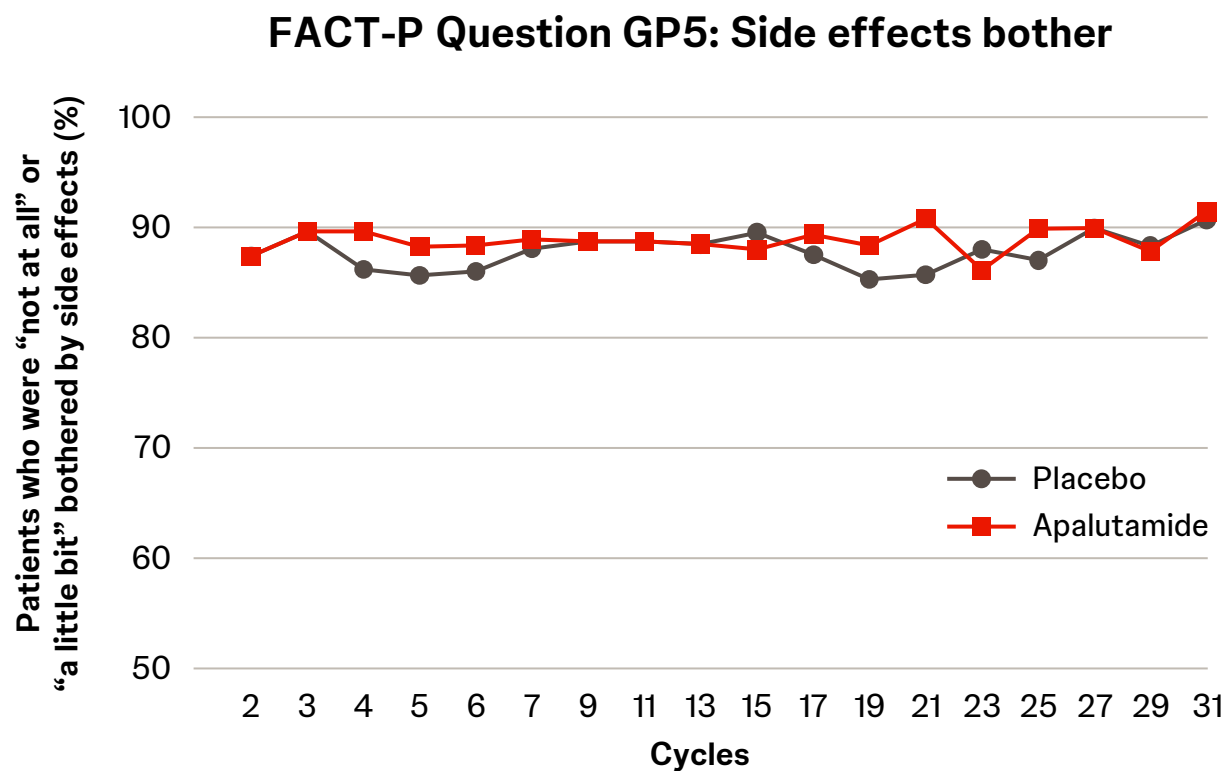
Number of patients

Placebo	366	359	355	348	334	300	310	286	262	245	214	194	171	130	103
Apalutamide	358	350	349	342	333	315	306	303	298	278	265	252	225	188	147



No difference in reported side effect bother with apalutamide versus placebo

TITAN: FACT-P treatment bother



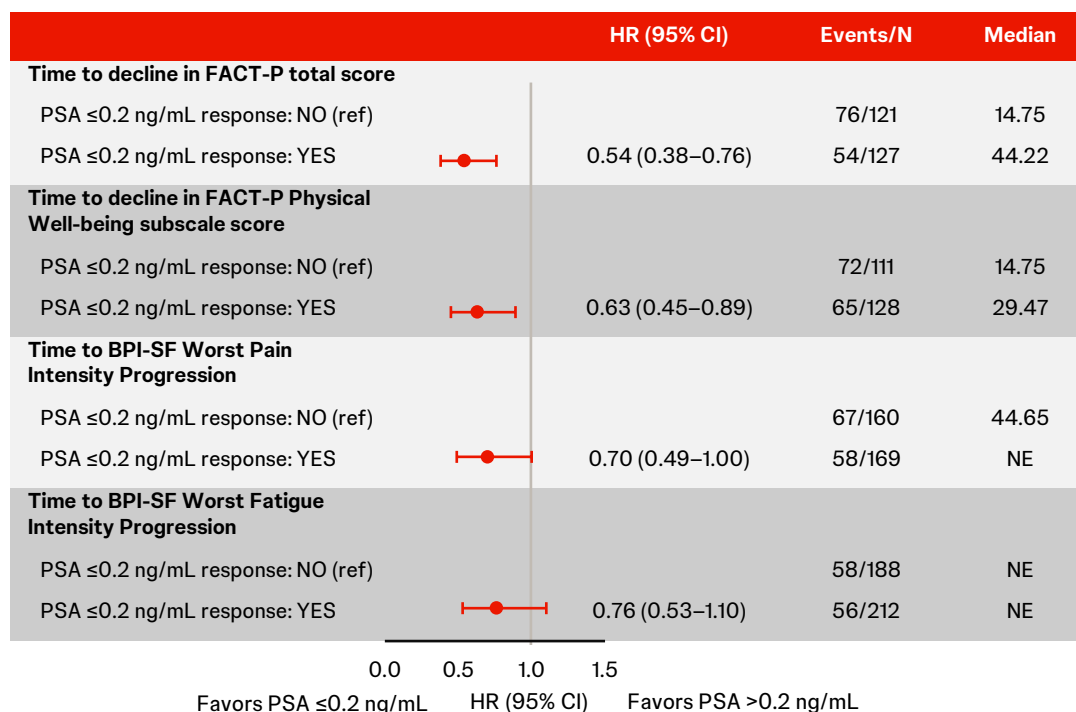
APA, apalutamide; FACT-P, Functional Assessment of Cancer Therapy-Prostate; PBO, placebo.
Agarwal N, et al. ASCO 2021; Abstract 5068 (poster presentation).



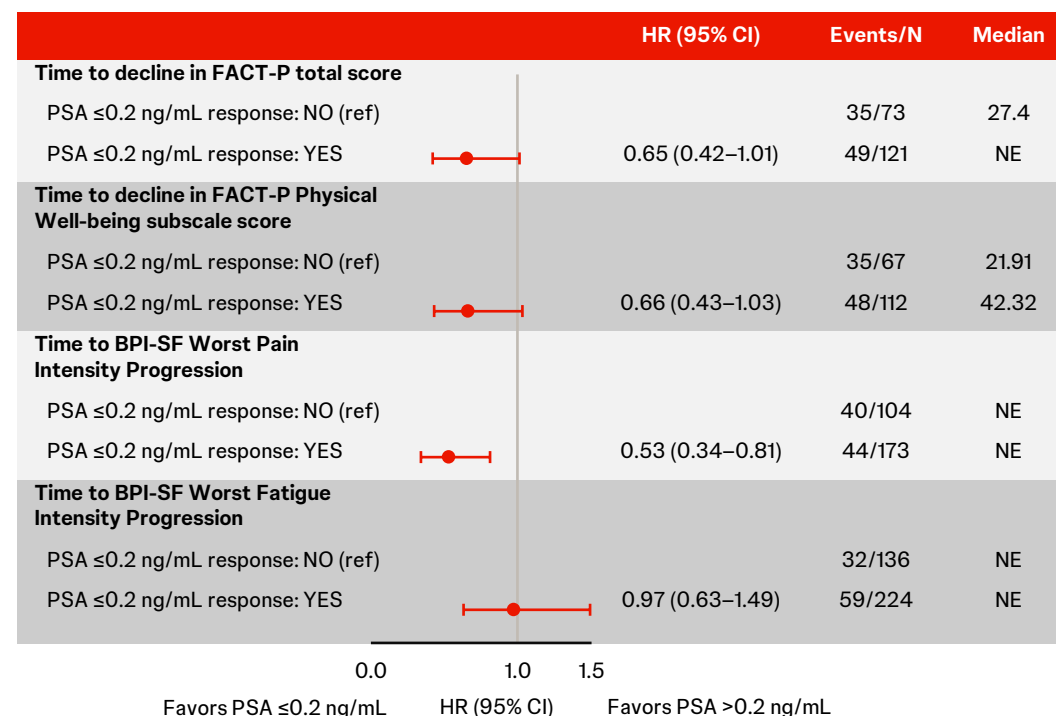
Achieving PSA ≤ 0.2 ng/mL was associated with longer time to decline in physical well-being and pain

TITAN: Post hoc exploratory analysis on PSA and PROs

At Month 3, HRQoL measures based on PSA response



At Month 6, HRQoL measures based on PSA response



NOTE: These data are currently not found in the apalutamide Prescribing Information.

BPI-SF, Brief Pain Inventory-Short Form; CI, confidence interval; FACT-P, Functional Assessment of Cancer Therapy-Prostate; HR, hazard ratio; HRQoL, health-related quality of life; NE, not estimable; PRO, patient-reported outcome; PSA, prostate-specific antigen; ref, reference.

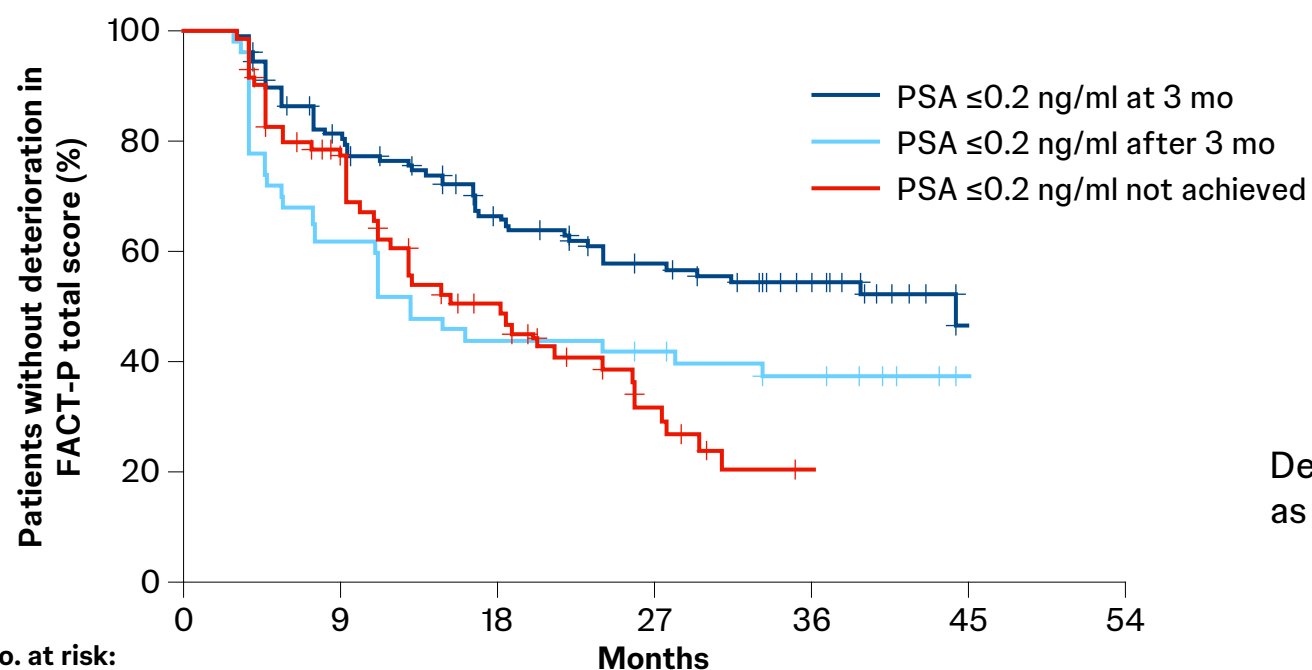
Small EJ, et al. ASCO GU 2022; Poster #D1 (poster presentation).



Deep PSA declines within 3 months of apalutamide treatment prolonged TTD in overall HRQoL

TITAN: Post hoc analysis of deep PSA decline and HRQoL

TTD in overall HRQoL by achievement of a deep PSA decline



NOTE: These data are currently not found in the apalutamide Prescribing Information.

FACT-P, Functional Assessment of Cancer Therapy-Prostate; HRQoL, health-related quality of life; PSA, prostate-specific antigen; TTD, time to deterioration.

Reprinted from European Urology Oncology, 7(4). Small EJ, et al. Post hoc analysis of rapid and deep prostate-specific antigen decline and patient-reported health-related quality of life in SPARTAN and TITAN patients with advanced prostate cancer. 844–852, 2024, with permission from Elsevier.