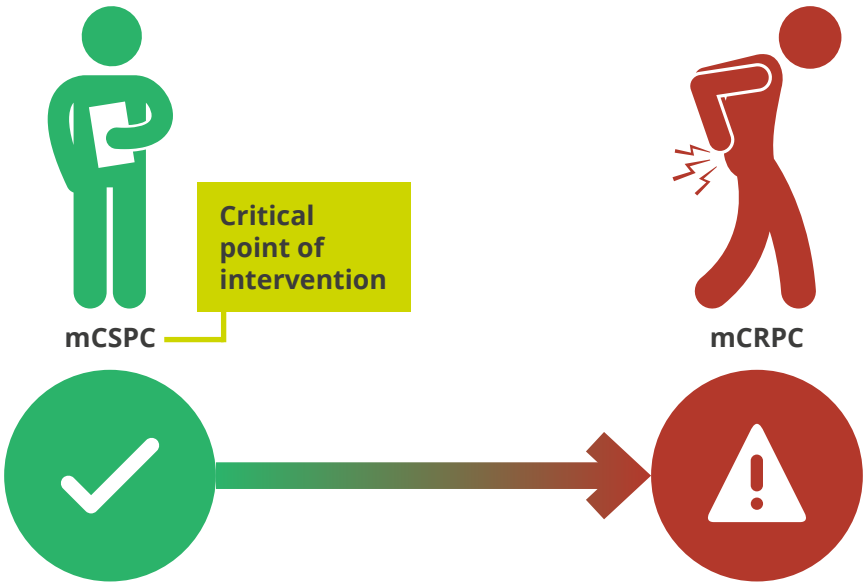
PATIENT VALUE MESSAGES AND KEY SUPPORTING EVIDENCE FOR APALUTAMIDE

UNMET NEED

Metastatic Castration-Sensitive Prostate Cancer (mCSPC) is a critical intervention point and represents the final opportunity to delay late-stage disease. It's critical to use the best treatment now to delay progression, symptoms and death



Low symptom burden in most patients; 4% to 26% of patients experience fatigue, urinary symptoms and bone pain[2-7]

Health Related Quality of LIfe (HRQoL) similar to the general population as most patients are not impacted by symptoms[3,8]

Severe symptom burden, including severe bone pain, skeletal related events and a considerable emotional burden[2,9-10]

Substantial negative impact on HRQoL due to severe symptoms[9]

ADT = androgen deprivation therapy; HCPs = healthcare practioners; HRQoL = health-related quality of life; mCRPC = metastatic castration-resistant prostate cancer; mCSPC = metastatic castration-sensitive prostate cancer

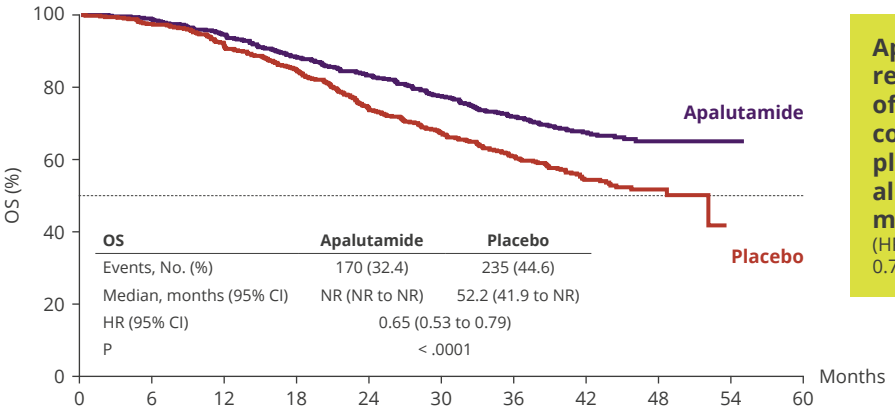
1. Janssen. mHSPC Patient & HCP Experiences - Final Report. (data on file). 2020.
2. European Association of Urology. EAU - EANM - ESTRO - ESUR - SIOG Guidelines on Prostate Cancer. 2020.
3. Brucker PS, Yost K, Cashy J, Webster K, Cella D. General Population and Cancer Patient Norms for the Functional Assessment of Cancer Therapy-General (FACT-G). Evaluation & the Health Professions. 2016;28(2):192-211.
4. Macmillan Cancer Support. Understanding advanced (metastatic) prostate cancer: Risk factors and symptoms of advanced (metastatic) prostate cancer. 2015.
5. de Freitas HM, Ito T, Hadi M, et al. Patient Preferences for Metastatic Hormone-Sensitive Prostate Cancer Treatments: A Discrete Choice Experiment Among Men in Three European Countries. Advances in therapy. 2019;36(2):318-332.
6. Hall F, de Freitas HM, Kerr C, et al. Estimating utilities/disutilities for high-risk metastatic hormone-sensitive prostate cancer (mHSPC) and treatment-related adverse events. Qual Life Res. 2019.
7. National Institute of Health and Care Excellence. Abiraterone (Zytiga) for hormone-naïve metastatic prostate cancer – first line. Horizon Scanning Report. September 2015 2015.
8. Janssen. TITAN Review of PRO Results and Messages (data on file). 2019.
9. Albertsen PC, Aaronson NK, Muller MJ, Keller SD, Ware JE, Jr. Health-related quality of life among patients with metastatic prostate cancer. Urology. 1997;49(2):207-216; discussion 216-207.
10. Burbridge C, Randall JA, Symonds T, et al. Qualitative study to understand the emotional response to a metastatic diagnosis in castration-resistant prostate cancer. Journal of Clinical Oncology. 2018;36(30_suppl):201-201.

EFFICACY

Apalutamide can help you live for longer compared to other therapy options

Treatment with apalutamide can delay progression of your prostate cancer

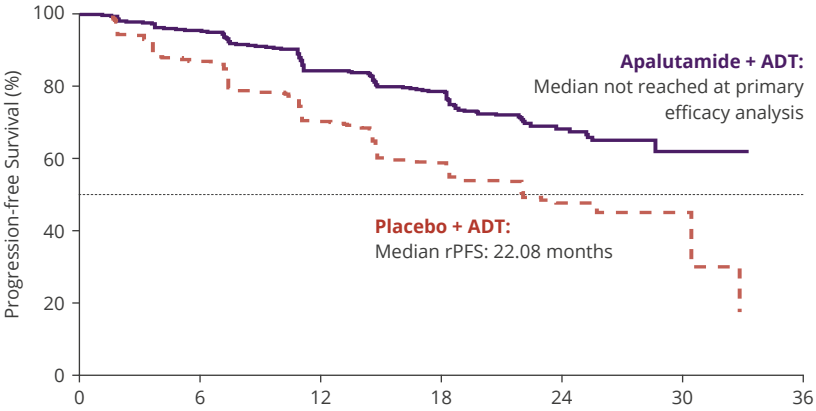
Overall survival in the TITAN trial (final analysis)



OS	Apalutamide	Placebo
Events, No. (%)	170 (32.4)	235 (44.6)
Median, months (95% CI)	NR (NR to NR)	52.2 (41.9 to NR)
HR (95% CI)	0.65 (0.53 to 0.79)	
P	< .0001	

Apalutamide + ADT reduced the risk of death by 35% compared with placebo + ADT in all patients with mCSPC
(HR: 0.65; 95% CI: 0.53, 0.79; nominal p<0.0001)[1]

Radiographic progression-free survival in the TITAN trial



Apalutamide + ADT reduced the risk of progression by 52% compared with placebo + ADT in all patients with mCSPC
(HR: 0.48; 95% CI: 0.39, 0.60; p<0.001)[2]

A period with no signs of disease development on a CT scan images after starting a new treatment is known as radiographic progression-free survival period.

ADT = androgen deprivation therapy; CAB = complete androgen blockade; CI = confidence interval; HR = hazard ratio; mCSPC = metastatic castration sensitive prostate cancer; OS = overall survival

1. Chi KN, Chowdhury S, Bjartell A, et al. Apalutamide in Patients With Metastatic Castration-Sensitive Prostate Cancer: Final Survival Analysis of the Randomized, Double-Blind, Phase III TITAN Study. Journal of Clinical Oncology. 2021:JCO. 20.03488.
2. Chi KN, Agarwal N, Bjartell A, et al. Apalutamide for Metastatic, Castration-Sensitive Prostate Cancer. New England Journal of Medicine. 2019;4(381(1)):13-24.

EFFICACY

Treatment with apalutamide will allow patients with mCSPC, like yourself, to live longer than treatment with enzalutamide

Overall survival (OS)

Based on the updated Janssen NMA using data-cuts closest to the TITAN final analysis (scenario 2)

Comparator	Median HR [95%CrI]	P(best)
Apalutamide + ADT	**--**	**44.83%**
AA+P+ADT	0.992 [0.755; 1.303]	40.12%
D+ADT	0.882 [0.695; 1.119]	2.929%
ENZA+ADT	0.803 [0.502; 1.287]	12.11%
ADT alone	0.651 [0.534; 0,793]	0.000%
NSAA+ADT	0.539 [0.315; 0.917]	0.018%

Apalutamide + ADT has the highest probability of providing a greater OS benefit than CAB, D+ADT, ADT alone, AA+P+ADT and ENZA+ADT in patients with mCSPC[1]

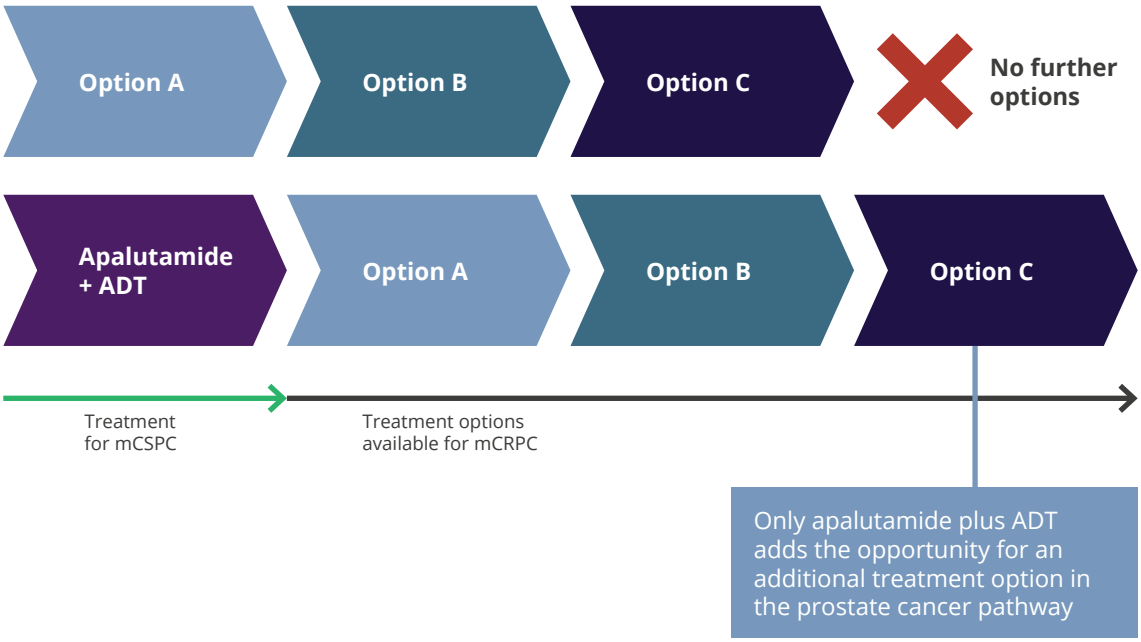
AA = abiraterone acetate; ADT = androgen deprivation therapy; CAB = complete androgen blockade; CI = confidence interval; D = docetaxel; ENZA = enzalutamide; HR = hazard ratio; mCSPC = metastatic castration sensitive prostate cancer; NMA = network meta-analysis; NSAA= Nonsteroidal antiandrogen; OS = overall survival; P = prednisone

1. Janssen. Network meta-analysis of apalutamide in the treatment of patients with Metastatic Hormone Sensitive Prostate Cancer (mHSPC) - Summary of Results TITAN FA update. (data on file). 2021.

EFFICACY

Using apalutamide now will maximise the number of treatment options available to you later on, if your prostate cancer progresses

Prescribing apalutamide to patients with mCSPC allows AA+P and enzalutamide to be **preserved for the later stages** of prostate cancer, in order to **maximise treatment options across the course of the disease**



In a large trial with 1052 number of patients (called TITAN trial), treatment with apalutamide + ADT significantly reduced the risk of subsequent systemic therapy for prostate cancer by 61% compared with placebo + ADT in patients with mCSPC (HR: 0.390; 95% CI: 0.302, 0.503; p<0.0001)[1]

mCRPC = metastatic castration-resistant prostate cancer; mCSPC = metastatic castration sensitive prostate cancer

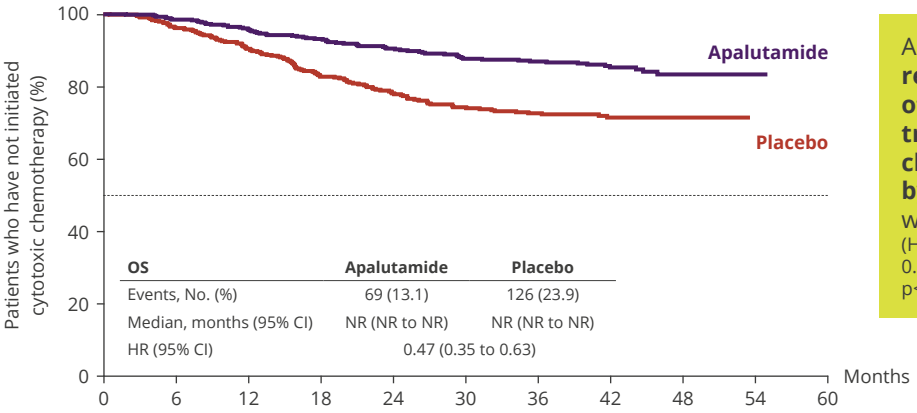
1. Janssen. Time to First Subsequent Systemic Therapy for Prostate Cancer - Stratified Analysis; Intent-to-treat Population (Study 56021927PCR3002). (data on file). 2019.

EFFICACY

Apalutamide delays the need for chemotherapy

Apalutamide can help keep your prostate-specific antigen (PSA) level low

Time to chemotherapy (TITAN final analysis)



OS	Apalutamide	Placebo
Events, No. (%)	69 (13.1)	126 (23.9)
Median, months (95% CI)	NR (NR to NR)	NR (NR to NR)
HR (95% CI)	0.47 (0.35 to 0.63)	

Apalutamide + ADT **reduced the risk of subsequent treatment with chemotherapy by 53%** compared with placebo + ADT (HR: 0.47; 95% CI: 0.35, 0.63; nominal p<0.0001)[1]

ADT = androgen deprivation therapy; CAB = complete androgen blockade; CI = confidence interval; HR = hazard ratio; mCSPC = metastatic castration sensitive prostate cancer; OS = overall survival

1. Chi KN, Chowdhury S, Bjartell A, et al. Apalutamide in Patients With Metastatic Castration-Sensitive Prostate Cancer: Final Survival Analysis of the Randomized, Double-Blind, Phase III TITAN Study. Journal of Clinical Oncology. 2021:JCO. 20.03488.
2. Chi KN, Agarwal N, Bjartell A, et al. Apalutamide for Metastatic, Castration-Sensitive Prostate Cancer. New England Journal of Medicine. 2019;4(381(1)):13-24.

DOSING

Apalutamide is an oral treatment that is taken once-daily at home at your convenience

It is not necessary to take steroids or restrict food intake with apalutamide

Treatment with apalutamide is simple for the patient: the oral tablet can be taken at home without food restrictions and only requires once-daily administration[1-3]

Unlike AA+P, apalutamide does not require co-administration of corticosteroids which require monitoring for mineralocorticoid excess, adrenocortical insufficiency and hepatotoxicity, and are associated with additional adverse events[1-3]

Apalutamide can be prescribed for all patients with mCSPC. In contrast, AA+P is only indicated for the treatment of patients with newly diagnosed high risk mCSPC[1-3]

AA = abiraterone acetate; mCSPC = metastatic castration-sensitive prostate cancer; P = prednisone

1. Food and Drug Administration (FDA). ERLEADA (apalutamide) tablets, for oral use. Prescribing Information. November 2020.
2. Janssen. Erleada Summary of Product Characteristics. December 2020.
3. Janssen. Prescribing Information (Zytiga). 2020; http://www.janssenlabels.com/package-insert/product-monograph/prescribing-information/ZYTIGA-pi.pdf. Accessed January 2021.

HRQoL

Apalutamide reduces your risk of experiencing the symptoms of late-stage prostate cancer, including bone fractures, pain and fatigue

Most men who have been treated with apalutamide have not reported any impact on HRQoL compared with how they felt before starting treatment. This means you can continue your normal daily activities

Patients treated with apalutamide + ADT were able to **maintain their functional, social and emotional well-being**[2]

At the final analysis of the phase III TITAN trial, apalutamide + ADT **reduced the risk of pain progression by 13%** (HR: 0.87; 95% CI: 0.70, 1.08; nominal p=0.1966) and **reduced the risk of chronic opioid use by 21%** compared with placebo + ADT (HR: 0.79; 95% CI: 0.58, 1.09; nominal p=0.1563)[1]

Patients treated with apalutamide + ADT in the phase III TITAN trial reported being **able to work and being able to continue their normal activities**[3,4]

ADT = androgen deprivation therapy; CI = confidence interval; ECOG PS = Eastern Cooperative Oncology Group Performance Status; HR = hazard ratio; HRQoL = health-related quality of life; mCSPC = metastatic castration sensitive prostate cancer;

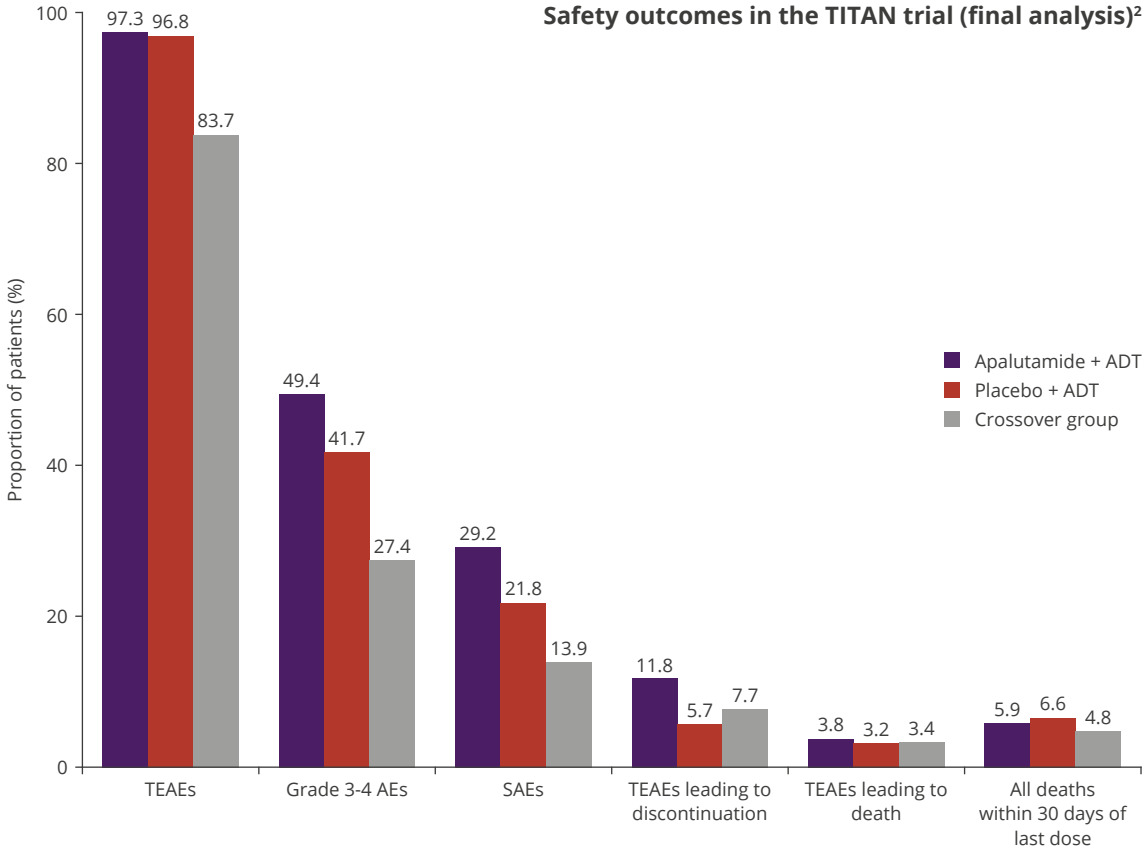
1. Agarwal N, McQuarrie K, Bjartell A, et al. Health-related quality of life after apalutamide treatment in patients with metastatic castration-sensitive prostate cancer (TITAN): a randomised, placebo-controlled, phase 3 study. The Lancet Oncology. 2019;20(11):1518-1530.
2. Janssen. TITAN Interim Clinical Study Report (CSR). 10 April 2019.
3. Janssen. Data on file. Topline results: A phase 3 randomized, placebo-controlled, double-blind study of apalutamide plus androgen deprivation therapy (ADT) versus ADT in subjects with metastatic hormone-sensitive prostate cancer (mHSPC). 15 October 2020.

SAFETY

Apalutamide is well-tolerated and does not cause additional bothersome side effects compared with ADT

In the phase III TITAN trial, **similar rates of treatment-related AEs and SAEs were observed with apalutamide + ADT and placebo + ADT** in patients with mCSPC at both the initial analysis and final analysis, despite a longer median treatment duration on apalutamide than placebo (Initial analysis: 20.5 months vs 18.3 months; final analysis: 39.3 months vs 20.2 months)[1,2]

Safety outcomes in the TITAN trial (final analysis)[2]



Patients' responses to the 'I am bothered by the side effects of treatment' item in the TITAN trial indicated that the tolerability of treatment was similar in the apalutamide + ADT and placebo + ADT treatment arms and that apalutamide did not cause any additional bothersome side effects[3]

Note: After the interim analysis, the TITAN trial was unblinded and patients in the placebo + ADT arm were allowed to crossover to the apalutamide + ADT arm; this group is referred to as the crossover group. In total, 208 patients (39.5%) crossed over into the apalutamide + ADT arm.[2]

ADT = androgen-deprivation therapy; AE = adverse event; mCSPC = metastatic castration-sensitive prostate cancer; SAE = serious adverse event; TEAE = treatment-emergent adverse event

1. Chi KN, Agarwal N, Bjartell A, et al. Apalutamide for Metastatic, Castration-Sensitive Prostate Cancer. New England Journal of Medicine. 2019;4(381(1)):13-24.
2. Chi KN, Chowdhury S, Bjartell A, et al. Supplementary Materials: Apalutamide in Patients With Metastatic Castration-Sensitive Prostate Cancer: Final Survival Analysis of the Randomized, Double-Blind, Phase III TITAN Study. Journal of Clinical Oncology. 2021:JCO. 20.03488.
3. Agarwal N, McQuarrie K, Bjartell A, 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. The Lancet Oncology. 2019;20(11):1518-1530.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