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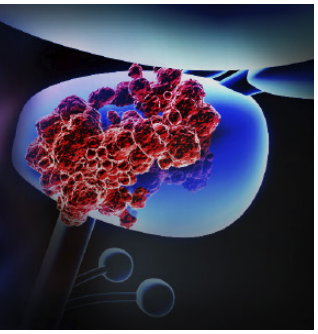
STUDY REVIEW

Apalutamide plus ADT to treat patients with mCSPC: TITAN study update and subgroup analysis



Making Education Easy 2023

Independent expert commentary by Dr. Laurence Krieger
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He is an active member of the bladder, testicular, renal and prostate cancer subcommittees for the ANZUP trials group and a member of the EVIQ urogenital committee. Dr. Krieger serves on multiple national and international advisory boards.

This publication summarises the treatment effect of apalutamide (ERLYAND®) plus androgen-deprivation therapy (ADT) in patients with metastatic castration-sensitive prostate cancer (mCSPC). Clinical subgroups of patients enrolled in the TITAN study were stratified according to disease volume, metastasis number and timing of metastasis presentation and a detailed assessment of patient outcomes was carried out using final cutoff data. Apalutamide is an antiandrogen therapy that acts by blocking the effects of testosterone to slow the growth and progress of prostate cancer.

Introduction

Prostate cancer is one of the leading causes of cancer among men worldwide. In 2021, 1 in 4 cancer diagnoses were attributable to the disease in the US.[1] Of the more than 300,000 estimated cancer-related deaths in the same year, prostate cancer accounted for 11%, the second-highest rate after lung cancer.[1] In general, the prognosis for prostate cancer is excellent, with a 5-year survival rate of 100% for localised cancer.[2] Once metastatic, however, 5-year survival drops to approximately 30%.[2]

In patients with mCSPC, high metastatic burden at diagnosis (synchronous disease) has been associated with less favourable prognosis, while a more favourable prognosis has been attributed to low metastatic burden occurring after primary treatment for localised prostate cancer (metachronous disease).[3]

For decades, standard treatment for patients with mCSPC has been ADT with either medical or surgical castration.[4] A key regulator of prostate growth, the androgen receptor (AR) is a ligand-activated transcription factor and is the primary therapeutic target in prostate cancer.[5] In the past 10 years, mCSPC management has undergone a revolution, with treatment intensification – the upfront addition of docetaxel or an AR inhibitor to ADT – now considered the pillar of therapeutic management.[6]

The phase 3 TITAN trial randomised patients with mCSPC to receive apalutamide or placebo added to ADT, and the positive treatment benefits have been previously reported in a broad population of patients and in patients with synchronous/metachronous or high-/low-volume disease, or in those with different metastatic burdens, using early data cutoffs.[7–11]

The objective of this study is to provide an update of the treatment effect and safety profile of apalutamide in patients with mCSPC enrolled in the TITAN study according to subgroups characterised by disease volume, number of metastases, and synchronous/metachronous presentation using final data cutoff.[12]

AR signalling axis

The main pathway involved in prostate cancer growth and disease progression is the AR signalling axis.[13–15] Androgens such as testosterone, the primary circulating form of androgen, and its most common active metabolite dihydrotestosterone (DHT), bind to the AR in the prostate epithelial cell cytoplasm, eliciting its translocation into the nucleus.[15] Ligand-bound AR molecules bind to specific DNA sequences, referred to as AR response elements (AREs), and act as transcription factors signalling downstream targets.[15,16] Second-generation AR inhibitors such as apalutamide act by disrupting this pathway, preventing AR translocation to the nucleus.[16]

Expert comment

Early escalation of treatment with the addition of a second therapy to androgen deprivation therapy (ADT) for men with metastatic disease is now the standard of care for most. Recently, a variety of novel androgen receptor inhibitor (ARI) therapies have become available and not just limited to docetaxel chemotherapy. Consideration of triplet therapy (ADT + ARI + chemotherapy) for fit patients with aggressive disease characteristics or a high metastatic burden is also warranted. As a result, a significant improvement in disease control and overall survival can be achieved whilst maintaining quality of life. Apalutamide has demonstrated this benefit with a once-daily dosing regimen coupled with a predictable and manageable side effect profile.

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Apalutamide for the treatment of mCSPC

A second-generation AR inhibitor, apalutamide (ERLYAND®) is indicated for the treatment of patients with mCSPC or non-metastatic castration-resistant disease.[17] Apalutamide is available as a tablet administered as 240 mg once daily,[17] and as of mid-2023, is available via the PBS for patients with mCSPC.[18]

Second-generation AR inhibitors not only act at a higher affinity than their first-generation predecessors, these agents have increased specificity to the AR compared with other steroidal receptors, and are exclusively antagonistic to AR without causing androgen withdrawal syndrome.[16] The benefits of treatment with second-generation AR inhibitors are considerable and include increased patient life span, extended metastases-free overall survival, and a decrease in circulating and intratumoral androgens and serum PSA (prostate specific antigen).[16]

In the phase 3, randomised, double-blind, placebo-controlled multinational TITAN trial, patients with mCSPC received either apalutamide or placebo in addition to ADT.[7,8] The coprimary endpoints of radiographic progression-free survival (rPFS) and overall survival (OS) significantly favoured apalutamide over placebo.[7,8] Secondary and other clinically relevant endpoints also favoured apalutamide treatment, including longer time to cytotoxic chemotherapy, delayed time to second progression-free survival (PFS2) and PSA progression and onset of castration resistance, compared with placebo.[7,8] Patient quality of life (QOL) was maintained during apalutamide treatment and there was no notable difference in safety profile between the two treatment groups.[7,8]

However, the TITAN investigators acknowledged that further study to determine whether apalutamide plus ADT affords a differential benefit between clinical subgroups was warranted.[12]

Apalutamide plus ADT in TITAN clinical subgroups

Patients enrolled in the TITAN trial (n=1052) had mCSPC with ≥1 distant metastases on conventional imaging and Eastern Cooperative Oncology Group (ECOG) performance status 0 or 1.[12] Patients' baseline demographics and disease characteristics are presented in **Table 1**.[12]

Table 1. Baseline demographics and disease characteristics (intent-to-treat population). All data are reported as n (%) unless otherwise stated.[12]

	Apalutamide + ADT (n=525)	Placebo + ADT (n=527)
Median age in years (range)	69 (45–94)	68 (43–90)
Race		
White	354 (67%)	365 (69%)
Asian	119 (23%)	110 (21%)
Black or African American	10 (1.9%)	9 (1.7%)
American Indian or Alaska native	6 (1.1%)	13 (2.5%)
Not reported	11 (2.1%)	8 (1.5%)
Other	24 (4.6%)	22 (4.2%)
Multiple	1 (0.2%)	0
Gleason score at initial diagnosis		
≤7	174 (33%)	169 (32%)
>7	351 (67%)	358 (68%)
ECOG PS		
0	328 (63%)	348 (66%)
1	197 (38%)	178 (34%)
2	0	1 (0.2%)
Disease volume		
High	325 (62%)	335 (64%)
Low	200 (38%)	192 (36%)
Previous docetaxel treatment	58 (11%)	55 (10%)
Median PSA, ng/mL (range)	5.97 (0–2682)	4.02 (0–2229)
Metastatic presentation at initial diagnosis		
Synchronous	411 (78%)	441 (84%)
Synchronous/high volume	273 (52%)	294 (56%)
Synchronous/low volume	138 (26%)	147 (28%)
Metachronous	85 (16%)	59 (11%)
Metachronous/high volume	32 (6.1%)	28 (5.3%)
Metachronous/low volume	53 (10%)	31 (5.9%)
MX	29 (5.5%)	27 (5.1%)
Most common (≥5%) mutually exclusive anatomical locations of metastases at study entry		
Bone-only	289 (55%)	269 (51%)
Bone-only ≤5 lesions	150 (29%)	136 (26%)
Bone-only >5 lesions	139 (27%)	133 (25%)
Bone ≤5 lesions + other locations	89 (17%)	109 (21%)
Bone >5 lesions + other locations	147 (28%)	149 (28%)
Bone + lymph node	163 (31%)	166 (32%)
Bone + viscera	24 (4.6%)	30 (5.7%)
Bone + lymph node + viscera	27 (5.1%)	35 (6.6%)
Bone + viscera + other locations (soft tissue or lymph node)	5 (1.0%)	7 (1.3%)
Bone + other locations*	180 (34%)	186 (35%)
Mean baseline BPI-SF pain score		
0: no pain	198 (38%)	200 (38%)
1–3: mild pain	195 (37%)	207 (39%)
4–7: moderate pain	98 (19%)	95 (18%)
8–10: severe pain	12 (2.3%)	11 (2.1%)
Missing data	22 (4.2%)	14 (2.7%)

*includes bone + lymph node, bone + soft tissue and bone + lymph node + soft tissue

ADT = androgen deprivation therapy; **BPI-SF** = Brief Pain Inventory-Short Form; **ECOG PS** = Eastern Cooperative Oncology Group performance status; **MX** = metastasis cannot be measured; **PSA** = prostate specific antigen.

The effect of apalutamide was assessed in the intent-to-treat population according to disease volume, synchronous/metachronous metastases, or both.[12] The modified CHAARTED[19] criteria were used to define high-volume disease as either visceral metastases with ≥1 bone lesion or ≥4 bone lesions including one outside of the vertebral column or pelvis; patients were considered to have low-volume disease if they did not meet the high-volume disease criteria.[12] Synchronous and metachronous disease were defined as metastases at initial diagnosis or developing after localised disease, respectively.[12] The number of metastatic lesions and their effect on apalutamide-treated patients with oligometastases (≤5 in bone only) versus polymetastases (>5 in bone with/without other locations or ≤5 in bone and other locations) was assessed using conventional imaging.[12] Subgroup analyses by disease volume and timing of metastasis presentation were defined in the TITAN protocol,[20] while other subgroup analyses were post hoc.[12]

Between December 2015 and July 2017, eligible participants with mCSPC received either apalutamide 240 mg once daily, or placebo, plus ongoing ADT; the prespecified first interim analysis and final analysis occurred within 22.7 months and 44.0 months of follow up, respectively.[12]

Coprimary TITAN trial endpoints were rPFS and OS.[12] Secondary endpoints included time to PFS2, confirmed PSA decline, time to PSA progression, and time to castration resistance.[12,21]

Apalutamide treatment effect in patient subgroups

Overall, coprimary endpoints improved across all patient subgroups following treatment with apalutamide, compared with ADT alone.[12] In patients with synchronous/high-volume disease and in those with metachronous/low-volume disease, OS improved with nominal p values <0.05 in apalutamide versus placebo recipients.[12] Although OS also improved with apalutamide in patients with synchronous/low-volume disease and in patients with metachronous/high-volume disease, nominal p values were >0.05.[12] A summary of patient outcomes across subgroups is shown in **Figure 1**.[12]

Apalutamide treatment improved rPFS compared with placebo in the synchronous/high-volume, synchronous/low-volume and metachronous/low-volume subgroups with nominal p values <0.05.[12] Although rPFS improvement favoured apalutamide in patients with metachronous/high-volume disease, nominal p value was >0.05 (see **Figure 1**).[12]

Except for the metachronous/high-volume subgroup, the addition of apalutamide to ADT improved PFS2 in all subgroups with nominal p values <0.05 (**Figure 1**).[12] Consistent with results for the coprimary endpoints, apalutamide plus ADT prolonged time to castration resistance (**Figure 1**) and PSA progression in all subgroups, compared with ADT alone.[12] In addition, the proportion of patients with confirmed best ≥50% PSA decline or deep PSA decline ≥90% or to ≤0.2 ng/mL at any time during the study increased following apalutamide plus ADT therapy, regardless of stratification.[12]

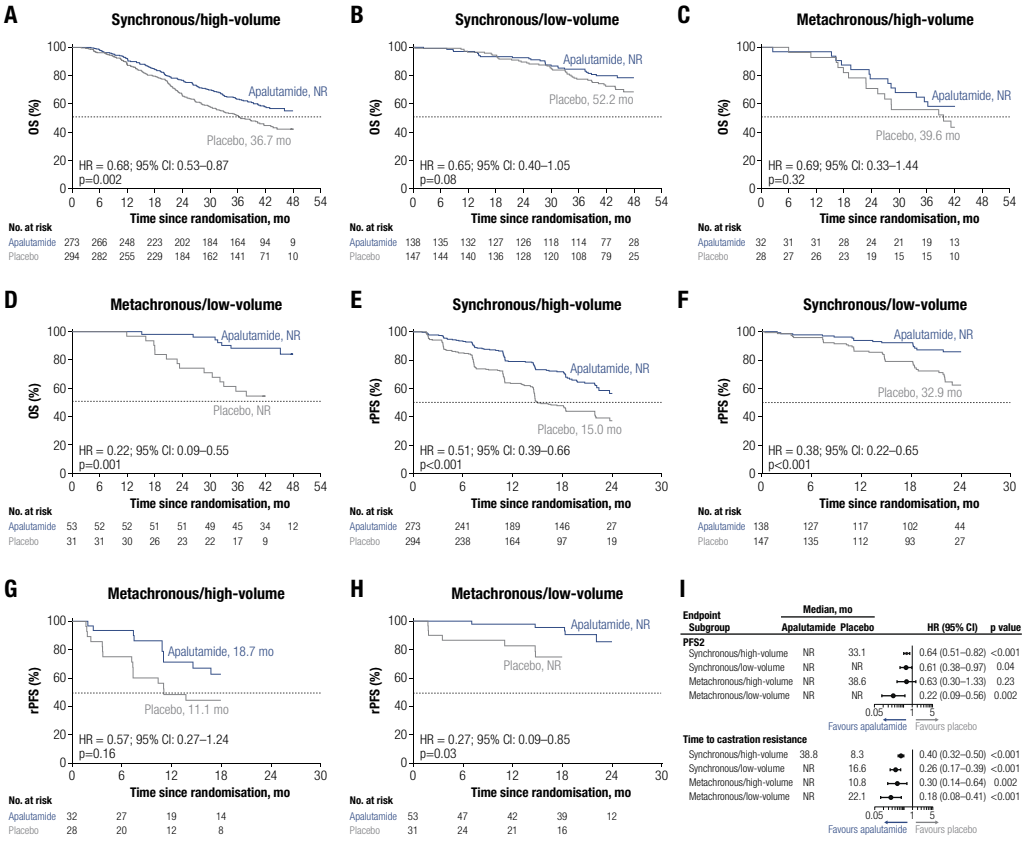

Figure 1. Apalutamide treatment effect grouped by disease volume or timing of metastasis occurrence.[12]

Kaplan-Meier plots for OS (A–D) and rPFS (E–H) and forest plots for PFS2 and time to castration resistance (I) were analysed in patients with synchronous/high-volume, synchronous/low-volume, metachronous/high-volume and metachronous/low-volume disease. Kaplan-Meier curves are truncated for instances in which the number at risk in a group was <5.

NR = not reached.

All outcomes improved following treatment with apalutamide plus ADT versus ADT alone with nominal p values <0.05 in synchronous/metachronous and high-/low-volume subgroups when the outcomes were assessed in subgroups stratified by one factor to increase the number of events.[12] Patients in the metachronous subgroup or in the low-volume subgroup who received apalutamide plus ADT experienced improved OS compared with apalutamide recipients in the synchronous or high-volume subgroups (p=0.046 and p<0.001, respectively).[12] Homogenous treatment effect was observed for OS and rPFS among apalutamide versus placebo recipients across the high- and low-volume subgroups (interaction effect p=0.262 and p=0.194 for OS and rPFS, respectively) and across the metachronous and synchronous subgroups (interaction effect p=0.075 and p=0.526, respectively).[12]

Expert comment

Apalutamide demonstrates significant clinical benefit in all men with metastatic prostate cancer. Meaningful endpoints such as overall survival, radiographic progression-free survival, depth of PSA response, delaying cytotoxic therapy and maintaining quality of life are clearly improved. Statistical significance associated with improving rPFS / rPFS2 as well as OS in subgroups that are likely to do very well, or very poorly, is tricky. One would argue that there are clinically relevant improvements in all groups. Ten percent of men in the TITAN study received docetaxel for hormone-sensitive prostate cancer (HSPC). Post progression therapy (including the use of abiraterone) will influence statistical interpretation too. In short, whether high- or low-volume disease, synchronous or metachronous metastases, intensification of therapy through the addition of apalutamide is an important consideration for all patients.

Number and location of metastases and patient outcomes following apalutamide

The most favourable OS and other clinical outcomes were observed in apalutamide recipients with oligometastatic disease with ≤5 bone-only metastases versus patients with polymetastatic disease with either >5 bone-only metastases, >5 bone metastases plus metastases in other organs or ≤5 bone metastases plus additional metastases in other organs (**Figure 2**).[12] Patients with polymetastatic disease with >5 bone metastases plus metastases in other locations experienced the poorest clinical outcomes (**Figure 2**).[12] Apalutamide recipients with metastases in bone plus viscera plus other locations (n=56) or those with bone plus metastases in other locations (n=180) had shorter OS (HR = 2.63 [95% CI: 1.68–4.10] and 190 [1.37–2.63]) and rPFS (HR = 3.42 [95% CI: 2.10–5.55] and 2.22 [1.52–3.25]; p<0.001 for all) versus patients with bone-only disease (n = 289).[12]

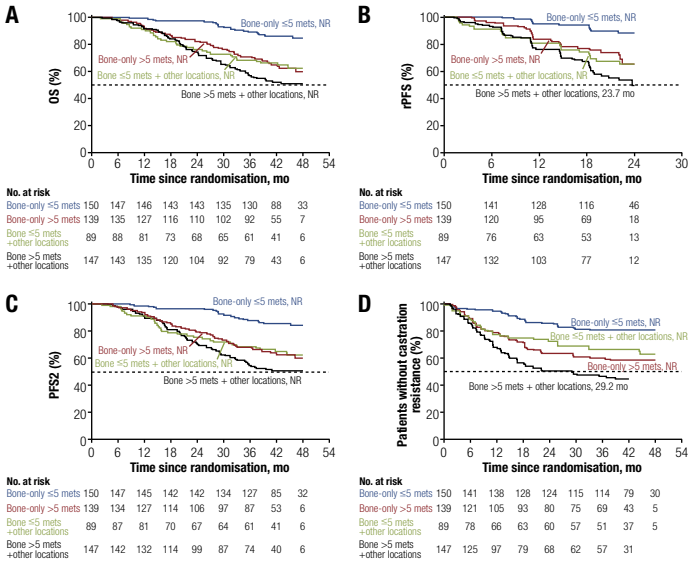

Figure 2. Effect of oligo- and polymetastatic disease on outcomes following apalutamide + ADT.[12]

OS (A), rPFS (B), PFS2 (C), and time to castration resistance (D).

Curves are truncated for instances in which the number at risk in a group was <5 metastases.

Mets = metastases; **NR** = not reached.

Safety data

Regardless of disease volume or metastatic presentation at diagnosis, the cumulative incidence of grade 3–4 treatment-emergent adverse events (TEAEs) was similar across treatment groups, as is shown in **Figure 3**.[12]

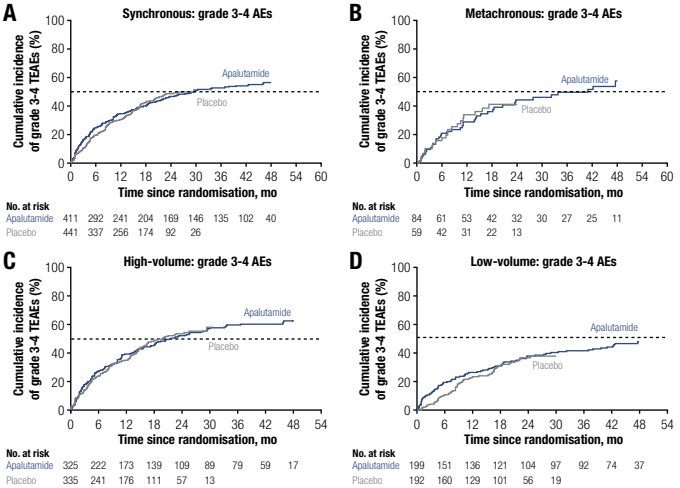

Figure 3. Cumulative incidence of grade 3–4 treatment-emergent adverse events (TEAEs)* in TITAN subgroups.[12]

Synchronous (A), metachronous (B), high-volume (C), and low-volume (D).

*defined as AEs occurring on or after the first dose of study drug through 30 days after last study treatment and graded according to National Cancer Institution Common Terminology Criteria for Adverse Events version 4.0.3. Grade 3 or severe (extreme distress, causing significant impairment of functioning or incapacitation; prevents normal everyday activities), grade 4 or life-threatening (urgent intervention indicated).

AE = adverse event.

TEAEs, grade 3–4 TEAEs and serious AEs in the high-volume subgroup occurred in a similar proportion of patients in the apalutamide plus ADT and ADT alone treatment groups (96%, 54% and 29% versus 97%, 47% and 22%).[12] Likewise, there was no substantial difference in the proportion of apalutamide recipients who reported TEAEs, grade 3–4 TEAEs and serious AEs in the low-volume subgroup, compared with placebo recipients (99%, 43% and 30% versus 96%, 33% and 21%).[12]

The rate of TEAEs, grade 3–4 TEAEs, serious AEs and TEAEs of interest was similar across treatment groups in both metachronous and synchronous subgroups; the exception was a higher rate of falls and fractures reported in patients in the metachronous than in the synchronous subgroup.[12]

Expert comment

Predictable and manageable side effects are an important consideration when discussing treatment with patients, particularly those at both ends of the disease or co-morbidity spectrum. Whilst the intention of improving the depth and duration of cancer control is often the primary consideration, the risk of toxicity influences clinician and patient decision making. For example, those with low-volume disease may have very few symptoms where immediately unnecessary side effects may not be acceptable, versus those experiencing significant disease or co-morbid related issues in whom added toxicity may be intolerable or unacceptable. It is not particularly surprising that the side effect profile was similar for all patient disease characteristics but what is more relevant is the low risk of significant treatment-specific adverse events and the ability to manage these easily and early, should they occur.

Conclusions

Regardless of stratification by disease volume, timing of metastatic presentation at diagnosis and number of metastases, patients with mCSPC who were treated with apalutamide plus ADT experienced a substantial and long-term benefit in clinical outcomes versus those who received ADT alone. Despite clinical benefit in terms of estimated hazard ratios (HRs) favouring apalutamide across all subgroups, nominal p values were >0.05 for OS, rPFS and PFS2 in the metachronous/high-volume disease subgroup or for OS in the synchronous/low-volume disease subgroup. The authors note that the statistical power decreased due to the small number of patients and events in these subgroups, thus studies with larger numbers of patients and longer follow ups should be conducted to confirm the conclusions for these subgroups. Nevertheless, the consistency of benefit was supported by the similarity of HR values for OS in the metachronous/high-volume and synchronous/low-volume versus synchronous/high-volume subgroups. The consistent treatment effect of apalutamide plus ADT is further supported by the lack of interaction with high-/low-volume or synchronous/metachronous disease presentation.

Take-home messages

- ERLYAND® plus ADT provided TITAN participants with mCSPC a robust, long-term benefit regardless of stratification by disease volume and timing of metastasis presentation.
- Patients with low-volume or metachronous disease benefited the most from ERLYAND® plus ADT.
- The TITAN subgroup comprising patients with synchronous/high-volume disease, a subgroup that has poor survival prognosis with ADT alone, also derived significantly improved survival and other clinical outcomes following treatment with ERLYAND® plus ADT.
- There was no substantial difference in the rate of high-grade or serious adverse events between ERLYAND® plus ADT and placebo plus ADT treatment groups.
- Data supports early intensification with ERLYAND® in patients with mCSPC.

Expert concluding remarks

Early intensification of therapy has significantly improved the prognosis for most men with advanced prostate cancer over recent years. Not only does this improve the depth of disease response and associated symptoms, but delaying the onset of castrate resistance improves long term survival, regardless of subsequent treatment. Patients with metachronous or low volume disease generally have a better prognosis due to their disease phenotype compared with those with the opposite presentation. But regardless of these factors, the addition of apalutamide to androgen deprivation has proven to be an important standard of care for all men with incurable prostate cancer.

References

1. Siegel RL, Miller KD, Fuchs HE, et al. Cancer Statistics, 2021. CA Cancer J Clin 2021;71:7–33. doi: 10.3322/caac.21654.
2. National Cancer Institute. Surveillance, Epidemiology and End Results Program. Cancer Stat Facts. Prostate Cancer. https://seer.cancer.gov/statfacts/html/prost.html. Accessed September 18, 2023.
3. E. Francini, K.P. Gray, W. Xie, G.K. Shaw, L. Valenca, B. Bernard, et al. Time of metastatic disease presentation and volume of disease are prognostic for metastatic hormone sensitive prostate cancer (mHSPC). Prostate, 78 (12) (2018), pp. 889-895, 10.1002/pros.23645
4. Harada K, Shiota M, Minato A, et al. Treatment strategies for Metastatic Castration-Sensitive Prostate Cancer: From "All-Comers" to "Personalized" Approach. Onco Targets Ther 2021;14:2967–74. doi: 10.2147/OTT.S306345.
5. Massie CE, Lunch A, Ramos-Montoya A, et al. The androgen receptor fuels prostate cancer by regulating central metabolism and biosynthesis. EMBO J 2011;30:2719–33. https://doi.org/10.1038/emboj.2011.158.
6. Gebrael G, Thomas VM, Swami U, et al. The Management of Metastatic Castrate-Sensitive Prostate Cancer: From Guidelines to Real-World Practice. Oncologist 2023;28:746–49. https://doi.org/10.1093/oncolo/oyad047.
7. Chi KN, Agarwal N, Bjartell A, Chung BH, Pereira de Santana Gomes AJ, Given R, et al. Apalutamide for metastatic, castration-sensitive prostate cancer. N Engl J Med 2019;381(1):13–24. https://doi.org/10.1056/NEJMoa1903307.
8. Chi KN, Chowdhury S, Bjartell A, Chung BH, Pereira de Santana Gomes AJ, Given R, 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):2294–303. https://doi.org/10.1200/JCO.20.03488.
9. Bjartell A, Agarwal N, Karsh L, Merseburger AS, Pereira de Santana Gomes AJ, Juárez Soto A, et al. Relationships of sites and burden of metastases with long-term outcomes and molecular subtypes in TITAN. Abstr MP24-08. J Urol 2021;206(Suppl.3):e414–5. https://doi.org/10.1097/JU.0000000000002015.08.
10. Bjartell A, Ye D, Agarwal N, Chung BH, Given R, Merseburger A, et al. Apalutamide (APA) for metastatic castration-sensitive prostate cancer (mCSPC) in TITAN: outcomes in patients (pts) with de novo (D1) mCSPC vs. progression to mCSPC after localized disease (D0) at diagnosis. Eur Urol Open Sci 2020;19(Suppl.2):e863. https://doi.org/10.1016/S2666-1683(20)33159-1.
11. Chowdhury S, Bjartell A, Merseburger AS, Chung BH, Uemura H, Ye D, et al. Apalutamide (APA) for metastatic castration- sensitive prostate cancer (mCSPC): outcomes in high-volume (HV) and low-volume (LV) disease from the titan final analysis (FA). Eur Urol 2021;79(Suppl.1):S1180–1. https://doi.org/10.1016/S0302-2838(21)01220-3.
12. Merseburger AS, Agarwal N, Bhaumik A, et al. Apalutamide plus androgen deprivation therapy in clinical subgroups of patients with metastatic castration-sensitive prostate cancer: A subgroup analysis of the randomised clinical TITAN study. Eur J Cancer Nov 2023;193:113290. https://doi.org/10.1016/j.ejca.2023.113290.
13. Aurilio G, Cimadamore A, Mazzucchelli R, et al. Androgen receptor signaling pathway in Prostate Cancer: From Genetics to Clinical Applications. Cells Dec 2020;9(12):2653. doi: 10.3390/cells912253.
14. Basu S and Tindall DJ. Androgen Action in Prostate Cancer. Horm Canc 2010;1:223–228. https://doi.org/10.1007/s12672-010-0044-4.
15. Fernandes RC, Hickey TE, Tilley WD, et al. Interplay between the androgen receptor signaling axis and microRNAs in prostate cancer. Endocr Relat Cancer 2019;26(5):R237–57. https://doi.org/10.1530/ERC-18-0571.
16. Rice MA, Malhotra SV, Stoyanova T. Second-Generation Antiandrogens: From Discovery to Standard of Care in Castration Resistant Prostate Cancer. Front Oncol 2019;9:801. doi: 10.3389/fonc.2019.00801.
17. Therapeutic Goods Administration. Australian Product Information. ERLYAND® (apalutamide). [updated 19 May 2023]. Available from: https://www.ebs.tga.gov.au/ebs/picmi/picmirepository.nsf/pdf?OpenAgent=&id=CP-2018-PI-02045-1&d=20230920172310101
18. Australian Government Department of Health and Aged Care. Australians battling with prostate cancer to benefit from new PBS listing. Available from: https://www.health.gov.au/ministers/the-hon-mark-butler-mp/media/australians-battling-with-prostate-cancer-to-benefit-from-new-pbs-listing#:~:text=From%201%20June%202023%2C%20Australians,are%20diagnosed%20with%20prostate%20cancer. Accessed September 26, 2023.
19. Kyriakopoulos CE, Chen Y-H, Carducci MA, et al. Chemohormonal Therapy in Metastatic Hormone-Sensitive Prostate Cancer: Long-Term Survival Analysis of the Randomized Phase III E3805 CHAARTED Trial. J Clin Oncol Apr 2018;36(11):1080–87. doi: 10.1200/JCO.2017.75.3657.
20. Chi KN, Agarwal N, Bjartell A, et al. Protocol for: Apalutamide for metastatic, castration-sensitive prostate cancer. N Engl J Med 2019;381:13–24. DOI: 10.1056/EJMoa1903307. Available from: https://www.nejm.org/doi/suppl/10.1056/NEJMoa1903307/suppl_file/nejmoa1903307_protocol.pdf
21. Chi KN, Agarwal N, Bjartell A, et al. Supplementary Appendix to: Apalutamide for metastatic, castration-sensitive prostate cancer. N Engl J Med 2019;381:13-24. DOI: 10.1056/NEJMoa1903307. Available from: https://www.nejm.org/doi/suppl/10.1056/NEJMoa1903307/suppl_file/nejmoa1903307_appendix.pdf

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