
Erleada® (apalutamide) 60 mg tablets

# **PSA kinetics** as promising **prognostic markers** of survival in advanced prostate cancer[1-3]


**PSA kinetics**, including PSA decline, early PSA response and undetectable PSA rate, are **early indications of therapeutic efficacy in** patients with **advanced prostate cancer**[1,2]

Among advanced prostate cancer patients, having **detectable PSA** at 12 months is associated with:[1]

**3x**

Increase in the hazard of metastasis (p = 0.013)

**4.5x**

Increase in the hazard of prostate cancer-specific death (p = 0.042)

**2.5x**

Increase in the hazard death from any cause (p = 0.042)

For healthcare professionals only.

## Impact of **rapid, deep** and **durable PSA response**

- Improved overall survival[1-5]
- Lower risk of rPFS and MFS[1,3-5]
- Delayed time to castration resistance[6]
- Improved time to PSA progression[5]
- Favourable HRQoL improvement[7]
- Longer time to HRQoL deterioration[8]
- Reduced anxiety and distress[9,10]
- Increased physical and emotional well-being[7,8]
- Lower risk of having worst pain and fatigue intensity[8]
- Correlation with no AE bother[5]
- High treatment adherence[11]
- Delayed time to next treatment[6]

## NCCN Clinical Practice Guidelines in Oncology (NCCN Guideline®) recommendations for PSA monitoring in mHSPC management[12]

**Physical exam + PSA every 3-6 months[12]**

**Imaging for symptoms or increasing PSA[12]**

**Consider periodic imaging to monitor treatment response*[12]**

*Frequency of imaging should be based on individual risk, age, PSADT, Gleason score and overall health. Bone scans should be performed as often as 6 to 12 months.
PSA: prostate-specific antigen; rPFS: radiographic progression-free survival; MFS: metastasis-free survival; HRQoL: health-related quality of life; AE: adverse events; NCCN: National Comprehensive Cancer Network; mHSPC: metastatic hormone-sensitive prostate cancer; PSADT: PSA doubling time.

# A randomised controlled trial analysis (AUA 2021)

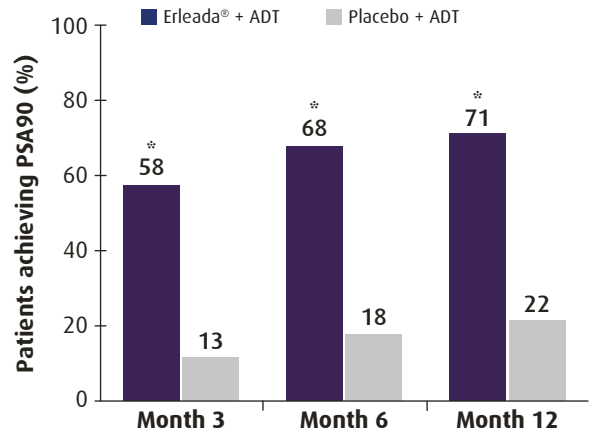
PSA kinetics in patients with advanced prostate cancer treated with apalutamide in TITAN study[3]

Erleada® (apalutamide) 60 mg tablets

## Erleada® demonstrates a **rapid, deep** and **durable PSA decline**[3]

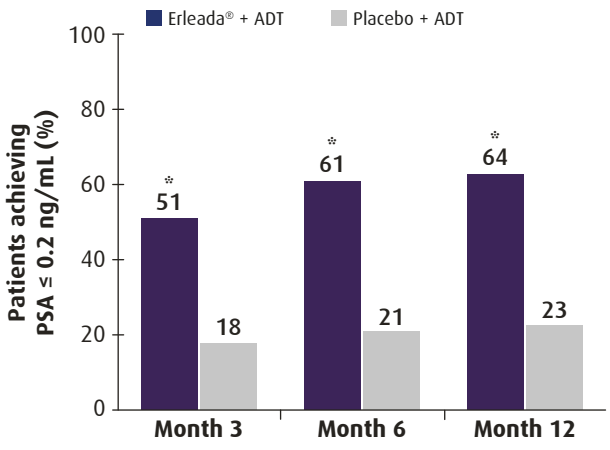
- Nearly **3 times** more patients receiving **apalutamide + ADT** achieved deeper PSA decline (PSA90 & ≤ 0.2 ng/mL response) vs. ADT alone

### PSA90 response rates, ITT




*Adapted from Chi KN, et al. The Journal of Urology 2021.*

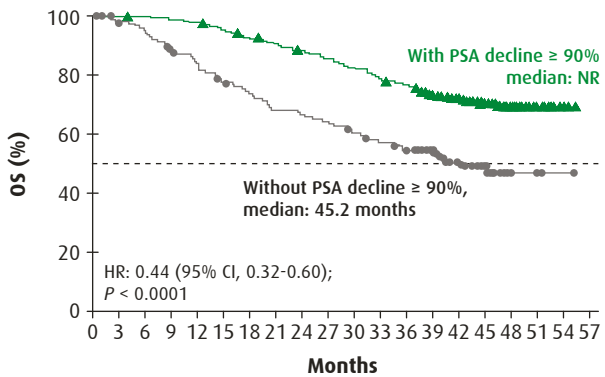
### PSA ≤ 0.2 ng/mL response rates, ITT




*Adapted from Chi KN, et al. The Journal of Urology 2021.*

## A **deeper PSA decline** is associated with **significant improvement in OS** in mHSPC patients treated with Erleada®[3]

### OS by PSA90 response, ITT

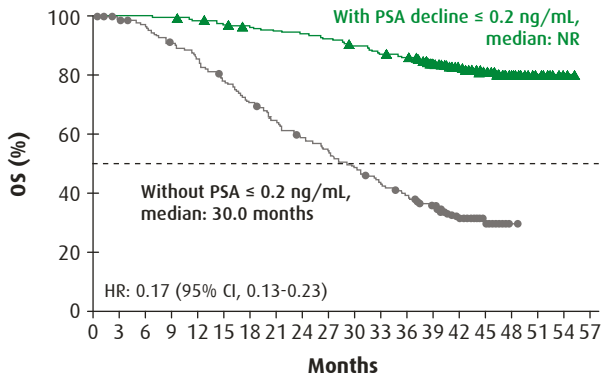



**Patients at risk with/without PSA ≥ 90% ↓**

| | | | | | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| With | 385 | 385 | 384 | 381 | 377 | 366 | 355 | 348 | 337 | 327 | 315 | 302 | 293 | 264 | 185 | 115 | 49 | 13 | 2 | 0 |
| Without | 140 | 134 | 129 | 119 | 112 | 103 | 97 | 90 | 88 | 85 | 79 | 74 | 69 | 57 | 42 | 24 | 3 | 2 | 1 | 0 |

*Adapted from Chi KN, et al. The Journal of Urology 2021.*

### OS by PSA ≤ 0.2 ng/mL response, ITT




**Patients at risk with/without PSA ≤ 0.2 ng/mL**

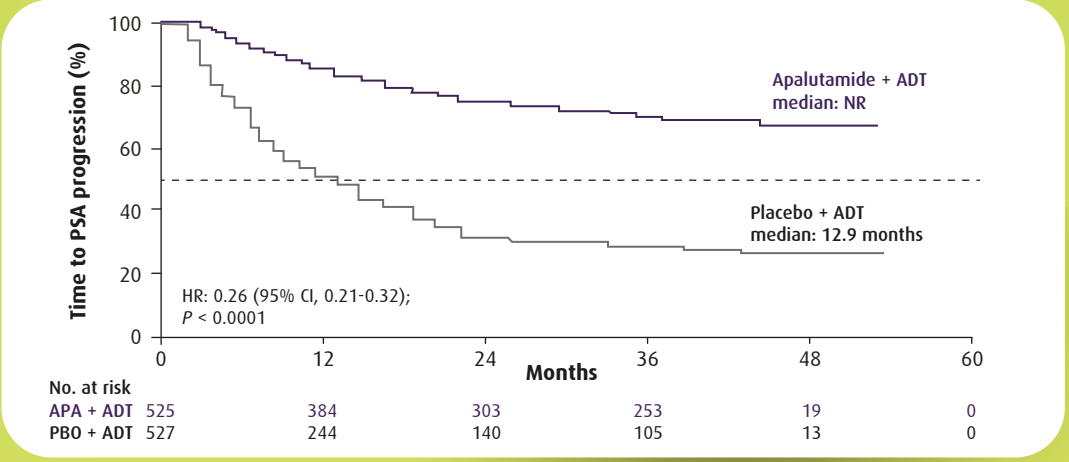
| | | | | | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| With | 356 | 356 | 356 | 353 | 350 | 343 | 338 | 334 | 331 | 325 | 316 | 306 | 300 | 270 | 194 | 121 | 51 | 15 | 3 | 0 |
| Without | 169 | 163 | 157 | 147 | 139 | 126 | 114 | 104 | 94 | 87 | 78 | 70 | 62 | 51 | 33 | 18 | 1 | 0 | 0 | 0 |

*Adapted from Chi KN, et al. The Journal of Urology 2021.*

AUA: American Urological Association; PSA: prostate-specific antigen; ADT: androgen deprivation therapy; ITT: intention to treat; OS: overall survival; mHSPC: metastatic hormone-sensitive prostate cancer; NR: not reached; HR: hazard ratio; CI: confidence interval.

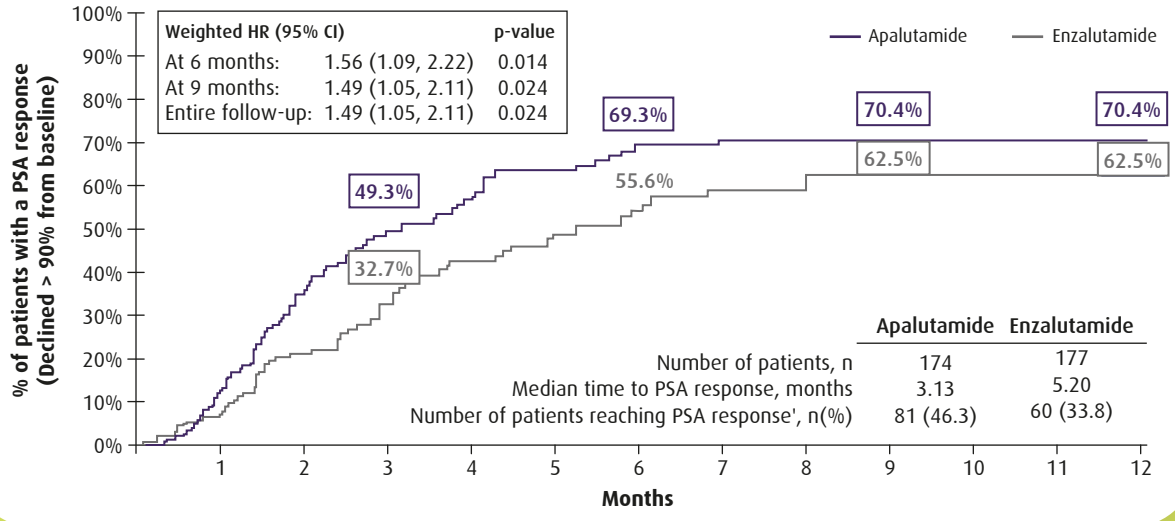
Erleada® (apalutamide) 60 mg tablets

## Erleada® significantly **improves time to PSA progression** in mHSPC patients (p < 0.0001)[6,13]




*Adapted from Chi KN, et al. J Clin Oncol. 2021; Chowdhury S, et al. 2021.*

## **ASCO-GU 2022 update:** In a real-world study of individuals with **mHSPC, significantly more** individuals attained an **early and deep PSA90 response** with **Erleada®** vs. enzalutamide*[14]




*Adapted from Lowentritt B, et al. Journal of Clinical Oncology 2022.*

- By 6 months and beyond, **significantly more** patients on **Erleada® attained PSA90 response** vs. enzalutamide (p ≤ 0.024)[14]
- **PSA90 response** was attained **significantly earlier** with **Erleada®** vs. enzalutamide (p ≤ 0.024; median time to PSA90: 3.1 vs. 5.2 months)[14]

***Disclaimer:** Enzalutamide is not approved for mHSPC indication in Malaysia.
mHSPC: metastatic hormone-sensitive prostate cancer; ADT: androgen deprivation therapy; PSA: prostate-specific antigen; OS: overall survival; APA: apalutamide; PBO: placebo; NR: not reached; HR: hazard ratio; CI: confidence interval; ASCO-GU: American Society of Clinical Oncology-Genitourinary.

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Janssen Oncology
PHARMACEUTICAL COMPANIES OF Johnson & Johnson

# Rapid, deep and durable PSA response improves lives.[3,6,13,14]

## Prescribe **Erleada**® for your prostate cancer patients today.

**ERLEADA® (Apalutamide) Film-Coated Tablets**

**Active Ingredient:** Apalutamide. **Indication:** In adult men for the treatment of non-metastatic castration-resistant prostate cancer (nmCRPC) who are at high risk of developing metastatic disease; in adult men for the treatment of metastatic hormone-sensitive prostate cancer (mHSPC) in combination with androgen deprivation therapy (ADT). **Posology:** The recommended dose is 240 mg (four 60 mg tablets) as an oral single daily dose. It should be swallowed whole and can be taken with or without food. Medical castration with gonadotropin releasing hormone analogue (GnRHa) should be continued during treatment in patients not surgically castrated. If a ≥ Grade 3 toxicity or an intolerable adverse reaction is experienced by the patient, dosing should be held rather than permanently discontinuing treatment until symptoms improve to ≤ Grade 1 or original grade, then should be resumed at the same dose or a reduced dose (180 mg or 120 mg), if warranted. If the toxicity recurs at Grade 3 or higher, then the dose of apalutamide should be reduced to the next lower dose level (from 240 mg to 180 mg, and from 180 mg to 120 mg). A maximum of 2 dose level reductions (to 120 mg) is allowed. If further dose reductions are needed, apalutamide should be discontinued. Permanently discontinue ERLEADA® in patients who develop a seizure during treatment. **Contraindications:** Hypersensitivity to the active substance or to any of the excipients listed; women who are or may become pregnant. **Warnings and Precautions:** ERLEADA® is not recommended in patients with a history of seizures or other predisposing factors e.g. underlying brain injury, recent stroke (within one year), primary brain tumours or brain metastases. If a seizure develops during treatment with ERLEADA®, treatment should be discontinued permanently. Patients should be evaluated for fracture and fall risk before starting ERLEADA®, monitored and managed according to established treatment guidelines and use of bone-targeted agents should be considered. Monitor for signs and symptoms of ischemic heart disease and ischaemic cerebrovascular disorders, and management of risk factors should be optimised. Co-administration with warfarin and coumarin-like anticoagulants should be avoided. If co-administered, additional International Normalised Ratio (INR) monitoring should be conducted. Monitor for risk factors e.g. hypercholesterolaemia, hypertriglyceridaemia, or other cardio-metabolic disorders since the safety has not been established in patients with clinically significant recent cardiovascular disease. Consider discontinuation of ERLEADA® for Grade 3 and 4 events. In patients with a history of or risk factors for QT prolongation, physicians should assess the benefit-risk ratio including the potential for Torsade de pointes prior to initiating ERLEADA®. **Interactions:** No initial dose adjustment is necessary when ERLEADA® is co-administered with a strong inhibitor of CYP2C8 (e.g. gemfibrozil, clopidogrel) and CYP3A4 (e.g. ketoconazole, ritonavir, clarithromycin). However, a reduction of the ERLEADA® dose based on tolerability should be considered. CYP2C8 and CYP3A4 inducers are not expected to have clinically relevant effects. Concomitant use of ERLEADA® with medicinal products that are primarily metabolised by CYP3A4 (e.g. darunavir, felodipine, midazolam, simvastatin), CYP2C19 (e.g. diazepam, omeprazole), CYP2C9 (e.g. warfarin, phenytoin), substrates of P-gp (e.g. colchicine, dabigatran etexilate, digoxin), BCRP or OATP1B1 (e.g. lapatinib, methotrexate, rosuvastatin, repaglinide) can result in lower exposure of these medicinal products. Caution is advised when prescribing ERLEADA® with medicinal products known to prolong QT interval or able to induce Torsade de pointes e.g. class IA (quinidine, disopyramide) or class III (amiodarone, sotalol, dofetilide, ibutilide) antiarrhythmic medicinal products, methadone, moxifloxacin, antipyschotics (e.g. haloperidol). **Adverse Reactions:** Decreased appetite, hot flush, hypertension, diarrhoea, skin rash, fracture, arthralgia, fatigue, decreased weight and fall. **Pharmaceutical Form:** Film-coated tablet. **Pack Size:** Bottle of 120's.
Please refer to the full prescribing information before prescribing. Full prescribing information is available upon request. [EU SmPC vJun2021].

**References**


**1.** Lim DM, Gulati R, Aleshin-Guendel S, *et al.* Undetectable prostate-specific antigen after short-course androgen deprivation therapy for biochemically recurrent patients correlates with metastasis-free survival and prostate cancer-specific survival. *Prostate.* 2018;10.1002/pros.23666. **2.** España S, Ochoa de Olza M, Sala N, *et al.* PSA kinetics as prognostic markers of overall survival in patients with metastatic castration-resistant prostate cancer treated with abiraterone acetate. *Cancer Manag Res.* 2020;12:10251-60. **3.** Chi KN, Saad F, Chowdhury S, *et al.* Prostate-specific antigen (PSA) kinetics in patients (pts) with advanced prostate cancer treated with apalutamide: Results from the TITAN and SPARTAN studies. Presentation PD34. *The Journal of Urology* 2021;206(3S):e587. **4.** Hussain MHA, Sternberg CN, Efstathiou E, *et al.* Overall survival (OS) and metastasis-free survival (MFS) by depth of prostate-specific antigen (PSA) decline in the phase III PROSPER trial of men with nonmetastatic castration-resistant prostate cancer (nmCRPC) treated with enzalutamide (ENZA). *Journal of Clinical Oncology* 2021;39(6_suppl):94. **5.** Saad F, Small EJ, Feng FY, *et al.* Deep prostate-specific antigen response following addition of apalutamide to ongoing androgen deprivation therapy and long-term clinical benefit in SPARTAN. *Eur Urol.* 2022;81(2):184-92. **6.** 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. *J Clin Oncol.* 2021;39(20):2294-303. **7.** Thiery-Vuillemin A, Fizazi K, Sartor O, *et al.* Post hoc health-related quality of life analysis according to response among patients with prostate cancer in the PROSELICA and FIRSTANA studies. *Oncologist.* 2021;26(7):e1179-88. **8.** Small E, Chi K, Chowdhury S, *et al.* Association between patient-reported outcomes (PROs) and changes in prostate-specific antigen (PSA) in patients (pts) with advanced prostate cancer treated with apalutamide (APA) in the SPARTAN and TITAN studies. *Journal of Clinical Oncology* 2022;40:73-73. **9.** Lofters A, Juffs HG, Pond GR, Tannock IF. "PSA-itis": knowledge of serum prostate specific antigen and other causes of anxiety in men with metaststic prostate cancer. *J Urol.* 2002;168(6):2516-20. **10.** Rönningås U, Fransson P, Holm M, Wennman-Larsen A. Prostate-specific antigen (PSA) and distress: a cross-sectional nationwide survey in men with prostate cancer in Sweden. *BMC Urol.* 2019;19(1):66. **11.** Lowentritt B, Brown G, Kernen K, *et al.* Real-world effectiveness and treatment adherence of apalutamide in non-metastatic castration-resistance prostate cancer patients. *J Urol.* 2021;206(suppl 1):e58. **12.** National Comprehensive Cancer Network (NCCN) Clinical Practice Guidelines in Oncology for Prostate Cancer V.3.2022. Available at https://www.nccn.org/guidelines/guidelines-detail?category=1&id=1459. Accessed on 4 April 2022. **13.** Chowdhury S, Bjartell A, Merseburger AS, *et al.* P0845: Apalutamide for metastatic castration-sensitive prostate cancer: outcomes in high-volume and low-volume disease from the TITAN final analysis. Presented at EAU21 Virtual, 8-12 July 2021. **14.** Lowentritt B, Pilon D, Khilfeh I, *et al.* Attainment of early, deep prostate-specific antigen response in metastatic castration-sensitive prostate cancer: A comparison of patients initiated on apalutamide or enzalutamide. *Journal of Clinical Oncology* 2022;40(6_suppl):43-43.