

# **BÖLÜM 30**

## **YENİ NESİL ANTIANDROJENLER**

Ahmet Kürşad DİŞLİ<sup>1</sup>

### **GİRİŞ**

Prostat kanseri, erkeklerde en sık görülen kanser olup her yıl ABD ve Avrupada yaklaşık 100.000 ölüme sebep olmaktadır<sup>1</sup>. Prostat kanseri gelişimi ve ilerlemesi androjen bağımlıdır ve bu nedenle androjen baskılayıcı tedaviler prostat kanseri tedavisinin temelini oluşturmaktadır. Prostat kanseri tedavisinde; kemoterapi, ADT, radyonüklid tedaviler ve hormonoterapi gibi tedavi seçenekleri bulunmaktadır. Bu bölümde prostat kanseri tedavisinde yeni nesil antiandrojen tedavilerden bahsedilecektir.

### **ABİRATERON ASETAT**

Abirateron asetat, testiküler, adrenal ve prostatik tümör dokularında eksprese olan 17 alfa-hidroksilaz/C17,20-liyaz (CYP17) enzimini inhibe ederek in vivo olarak androjen biyosentez inhibitörü olan abiraterona dönüşür<sup>2</sup>. CYP-17 inhibisyonu aynı zamanda adrenal bezler tarafından mineralokortikoid üretimini de arttırmaktadır<sup>3</sup>.

Androjene duyarlı prostat kanser tedavisi için androjen düzeylerinin azaltılması gerekmektedir. LHRH analogları, orşiektomi gibi tedaviler testislerde üretilen androjeni azaltmalarına rağmen adrenal bezler ve tümör dokusundaki androjen üretimini etkilememektedir. Bu nedenle bu tedavilerle birlikte abirateron asetat tedavisinin uygulanması serum testesteron düzeylerini düşürmektedir<sup>4</sup>.

Metastatik kastrasyon duyarlı prostat kanserinde (mKDPK) yeni tanı almış yüksek riskli hastalarda abirateron asetat+prednizonun, plasebo ile karşılaştırıldığı randomize çift kör faz 3 LATITUDE çalışmasına 34 ülkeden 235 merkez

<sup>1</sup> Uzm. Dr., Erciyes Üniversitesi Tıp Fakültesi Tıbbi Onkoloji BD ahmetkursad@erciyes.edu.tr

terapiye kadar geçen süre ve semptomatik iskelet olayına kadar geçen süre olmak üzere tüm sekonder sonlanım noktalarında fayda sağlanmışır<sup>20</sup>.

## KAYNAKLAR

1. Siegel RL, Miller KD, Fuchs HE, et al: Cancer statistics, 2022. 72:7-33, 2022
2. Tan G, Xuan Z, Li Z, et al: The efficacy and safety of abiraterone acetate in patients with high-risk prostate cancer: a meta-analysis based on six randomized control trials. 2020 9:1691-1699, 2020
3. Moreira RB, Debiasi M, Francini E, et al: Differential side effects profile in patients with mC-RPC treated with abiraterone or enzalutamide: a meta-analysis of randomized controlled trials. 8, 2017
4. Mottet N, van den Bergh RCN, Briers E, et al: EAU-EANM-ESTRO-ESUR-SIOG Guidelines on Prostate Cancer-2020 Update. Part 1: Screening, Diagnosis, and Local Treatment with Curative Intent. Eur Urol 79:243-262, 2021
5. Fizazi K, Tran N, Fein L, et al: Abiraterone acetate plus prednisone in patients with newly diagnosed high-risk metastatic castration-sensitive prostate cancer (LATITUDE): final overall survival analysis of a randomised, double-blind, phase 3 trial. Lancet Oncol 20:686-700, 2019
6. Clarke NW, Ali A, Ingleby FC, et al: Addition of docetaxel to hormonal therapy in low- and high-burden metastatic hormone sensitive prostate cancer: long-term survival results from the STAMPEDE trial. Ann Oncol 30:1992-2003, 2019
7. Fizazi K, Foulon S, Carles J, et al: Abiraterone plus prednisone added to androgen deprivation therapy and docetaxel in de novo metastatic castration-sensitive prostate cancer (PEACE-1): a multicentre, open-label, randomised, phase 3 study with a 2x2 factorial design. 399:1695-1707, 2022
8. Fizazi K, Scher HI, Molina A, et al: Abiraterone acetate for treatment of metastatic castration-resistant prostate cancer: final overall survival analysis of the COU-AA-301 randomised, double-blind, placebo-controlled phase 3 study. The Lancet Oncology 13:983-992, 2012
9. Ryan CJ, Smith MR, Fizazi K, et al: Abiraterone acetate plus prednisone versus placebo plus prednisone in chemotherapy-naïve men with metastatic castration-resistant prostate cancer (COU-AA-302): final overall survival analysis of a randomised, double-blind, placebo-controlled phase 3 study. The Lancet Oncology 16:152-160, 2015
10. Mostaghel EA: Abiraterone in the treatment of metastatic castration-resistant prostate cancer. Cancer Manag Res 6:39-51, 2014
11. Rice MA, Malhotra SV, Stoyanova T: Second-Generation Antiandrogens: From Discovery to Standard of Care in Castration Resistant Prostate Cancer. Front Oncol 9:801, 2019
12. Nadal R, Taplin ME, Bellmunt J: Enzalutamide for the treatment of prostate cancer: results and implications of the AFFIRM trial. Future Oncol 10:351-62, 2014
13. Beer TM, Armstrong AJ, Rathkopf DE, et al: Enzalutamide in metastatic prostate cancer before chemotherapy. N Engl J Med 371:424-33, 2014
14. Armstrong AJ, Lin P, Tombal B, et al: Five-year Survival Prediction and Safety Outcomes with Enzalutamide in Men with Chemotherapy-naïve Metastatic Castration-resistant Prostate Cancer from the PREVAIL Trial. Eur Urol 78:347-357, 2020
15. Tombal B, Saad F, Penson D, et al: Patient-reported outcomes following enzalutamide or placebo in men with non-metastatic, castration-resistant prostate cancer (PROSPER): a multicentre, randomised, double-blind, phase 3 trial. Lancet Oncol 20:556-569, 2019
16. Armstrong AJ, Szmulewitz RZ, Petrylak DP, et al: ARCHES: A Randomized, Phase III Study of Androgen Deprivation Therapy With Enzalutamide or Placebo in Men With Metastatic Hormone-Sensitive Prostate Cancer. J Clin Oncol 37:2974-2986, 2019
17. Shore ND, Chowdhury S, Villers A, et al: Efficacy and safety of enzalutamide versus bicalutamide for patients with metastatic prostate cancer (TERRAIN): a randomised, double-blind, phase

2 study. 17:153-163, 2016

18. Slovin S, Clark W, Carles J, et al: Seizure rates in enzalutamide-treated men with metastatic castration-resistant prostate cancer and risk of seizure: the UPWARD study. 4:702-706, 2018
19. Small EJ, Saad F, Chowdhury S, et al: SPARTAN, a phase 3 double-blind, randomized study of apalutamide (APA) versus placebo (PBO) in patients (pts) with nonmetastatic castration-resistant prostate cancer (nmCRPC), American Society of Clinical Oncology, 2018
20. Fizazi K, Shore ND, Tammela T, et al: Overall survival (OS) results of phase III ARAMIS study of darolutamide (DARO) added to androgen deprivation therapy (ADT) for nonmetastatic castration-resistant prostate cancer (nmCRPC), American Society of Clinical Oncology, 2020