

**Bölüm 3.7.1****HORMON DUYARLI METASTATİK PROSTAT KANSERİ TEDAVİSİ**Gökmen Umut ERDEM<sup>1</sup>**GİRİŞ**

Hormona duyarlı metastatik prostat kanserinde (HDMPK) bazı hastalar lokalize hastalığın definitif tedavisi sonrası metastaz ile başvururken, bazı hastalarda ise tanı anında metastatik hastalık bulunmaktadır. Hastaların serum testosteron seviyeleri tipik olarak >50 ng/dl'dir.

Androjenlerin prostat kanseri büyümesini uyarmadaki kritik rolü 1941 yılında Huggins ve Hodges (1) tarafından belirlenmiş ve ilerlemiş prostat kanserli hastalarda androjen yoksunluğu tedavisinin (ADT) geliştirilmesini sağlamıştır. Başlangıçta hastaların %90-95'inde ADT'ye yanıt alınsa da 24-36 ay içerisinde hastalık kastrasyon dirençli hale gelmektedir. Yeni tanı metastatik prostat kanserli hastaların yalnız ADT ile ortalama sağkalımı 42 aydır (2). Yeni çalışmalarla, ADT ile kombine tedavi yaklaşımlarının sağkalımı uzatma, komplikasyonları en aza indirme ve yaşam kalitesini korumada tek başına ADT'ye göre katkısı gösterilmiştir. Abirateron, dosetaksel, ve ikinci nesil antiandrojenler (enzalutamid ve apalutamid) ile birlikte ADT gibi kombine yaklaşımlar HDMPK'si olan erkekler için artık tercih edilen bir yaklaşım haline gelmiştir.

**PROGNOSTİK FAKTÖRLER**

Metastatik hastalığın heterojen olması nedeni ile sağkalım süreleri oldukça değişkenlik göstermektedir. Yapılan çalışmalarda tanı anında metastatik hastalı-

<sup>1</sup> Doç. Dr., Başakşehir Çam ve Sakura Şehir Hastanesi Tıbbi Onkoloji Kliniği, gokmenumut@hotmail.com

## KAYNAKLAR

1. Ch H, Hodges C. The effect of castration, of estrogen and of androgen injection on serum phosphatases in metastatic carcinoma of the prostate. *Cancer research*. 1941.
2. James ND, Spears MR, Clarke NW, et al. Survival with Newly Diagnosed Metastatic Prostate Cancer in the “Docetaxel Era”: Data from 917 Patients in the Control Arm of the STAMPEDE Trial (MRC PR08, CRUK/06/019). *Eur Urol*. 2015;67(6):1028-38.
3. Mottet N, Cornford P, van den Bergh RC, et al. EAU-EANM-ESTRO-ESUR-ISUP-SIOG guidelines on prostate cancer. *Arnhem: European Association of Urology*. 2022.
4. Kyriakopoulos CE, Chen YH, 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*. 2018;36(11):1080-7.
5. Fizazi K, Tran N, Fein L, et al. Abiraterone plus Prednisone in Metastatic, Castration-Sensitive Prostate Cancer. *N Engl J Med*. 2017;377(4):352-60.
6. Hussain M, Tangen CM, Higano C, et al. Absolute prostate-specific antigen value after androgen deprivation is a strong independent predictor of survival in new metastatic prostate cancer: data from Southwest Oncology Group Trial 9346 (INT-0162). *J Clin Oncol*. 2006;24(24):3984-90.
7. Harshman LC, Chen YH, Liu G, et al. Seven-Month Prostate-Specific Antigen Is Prognostic in Metastatic Hormone-Sensitive Prostate Cancer Treated With Androgen Deprivation With or Without Docetaxel. *J Clin Oncol*. 2018;36(4):376-82.
8. Hussain M, Tangen CM, Berry DL, et al. Intermittent versus continuous androgen deprivation in prostate cancer. *N Engl J Med*. 2013;368(14):1314-25.
9. James ND, Sydes MR, Clarke NW, et al. Addition of docetaxel, zoledronic acid, or both to first-line long-term hormone therapy in prostate cancer (STAMPEDE): survival results from an adaptive, multiarm, multistage, platform randomised controlled trial. *Lancet*. 2016;387(10024):1163-77.
10. Gravis G, Boher JM, Joly F, et al. Androgen Deprivation Therapy (ADT) Plus Docetaxel Versus ADT Alone in Metastatic Non castrate Prostate Cancer: Impact of Metastatic Burden and Long-term Survival Analysis of the Randomized Phase 3 GETUG-AFU15 Trial. *Eur Urol*. 2016;70(2):256-62.
11. 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*. 2019;30(12):1992-2003.
12. Sydes MR, Spears MR, Mason MD, et al. Adding abiraterone or docetaxel to long-term hormone therapy for prostate cancer: directly randomised data from the STAMPEDE multi-arm, multi-stage platform protocol. *Ann Oncol*. 2018;29(5):1235-48.
13. Sathianathan NJ, Philippou YA, Kuntz GM, et al. Taxane-based chemohormonal therapy for metastatic hormone-sensitive prostate cancer. *Cochrane Database Syst Rev*. 2018;10(10):CD012816.
14. Smith MR, Hussain M, Saad F, et al. Darolutamide and Survival in Metastatic, Hormone-Sensitive Prostate Cancer. *N Engl J Med*. 2022;386(12):1132-42.
15. 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 2 x 2 factorial design. *Lancet*. 2022;399(10336):1695-707.
16. 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*. 2019;20(5):686-700.

17. James ND, de Bono JS, Spears MR, et al. Abiraterone for Prostate Cancer Not Previously Treated with Hormone Therapy. *N Engl J Med.* 2017;377(4):338-51.
18. Chi KN, Agarwal N, Bjartell A, et al. Apalutamide for Metastatic, Castration-Sensitive Prostate Cancer. *N Engl J Med.* 2019;381(1):13-24.
19. 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.
20. 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. *Lancet Oncol.* 2019;20(11):1518-30.
21. Davis ID, Martin AJ, Zielinski RR, et al. Updated overall survival outcomes in ENZAMET (ANZUP 1304), an international, cooperative group trial of enzalutamide in metastatic hormone-sensitive prostate cancer (mHSPC). *American Society of Clinical Oncology*; 2022.
22. 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.* 2019;37(32):2974-86.
23. Armstrong AJ, Azad AA, Iguchi T, et al. Improved Survival With Enzalutamide in Patients With Metastatic Hormone-Sensitive Prostate Cancer. *J Clin Oncol.* 2022;40(15):1616-22.
24. Burdett S, Boeve LM, Ingleby FC, et al. Prostate Radiotherapy for Metastatic Hormone-sensitive Prostate Cancer: A STOPCAP Systematic Review and Meta-analysis. *Eur Urol.* 2019;76(1):115-24.
25. James ND, Clarke NW, Cook A, et al. Abiraterone acetate plus prednisolone for metastatic patients starting hormone therapy: 5-year follow-up results from the STAMPEDE randomised trial (NCT00268476). *Int J Cancer.* 2022;151(3):422-34.