

Kastrasyona Dirençli Metastatik Prostat Kanserinde Sistemik Tedavi

Tuğçe Kübra GÜNEŞ¹

GİRİŞ

Kastrasyon dirençli prostat kanseri erkeklerde en yaygın görülen kanserlerden biridir ve yüksek morbidite ve mortalite ile dünyada milyonlarca erkeği etkilemektedir (1). Testosteron seviyeleri düşük iken (testosteron <50 ng/dl) artan prostat spesifik antijen (PSA) değeri kastrasyon dirençli prostat kanseri (KDPK) olarak tanımlanır. PSA değeri kontrollü olsa bile hasta, yeni gelişen semptomaya yönelik görüntüleme yöntemleri ile değerlendirilmelidir. PSA değeri düşük iken radyolojik olarak tespit edilen progresse hastalık da metastatik KDPK olarak değerlendirilir. mKDPK'ı progrosyonu sıklıkla kemik metastazı, pelvik veya retoroperitonel lenf nodları ve viseral metastaz (karaciğer veya akciğer metastazı) ile tespit edilir (2). Viseral hastalık, birinci basamak endokrin tedavi altında da gelişebilmektedir ve kötü prognozla ilişkilidir (3, 4). Eğer hastalık prosresyonu beklenenden hızlı veya PSA düşüklüğüyle beraber yeni gelişen viseral metastaz varlığı mevcutsa hasta küçük hücreli ve nöroendokrin diferansiyasyon açısından yeniden biyopsi planı ile değerlendirilmelidir. mKDPK tedavisi kemoterapi, androjen deprivasyon tedavisi, androjen sentez inhibitörü ve androjen reseptör sinyal inhibitörleri (ASRİ), hedefe yönelik ilaçlar (PARP inhibitörleri), immünoterapi ve kemik hedefli tedaviler olmak üzere çeşitlidir. Metastatik hormon duyarlı prostat kanserinde (mHDPK) seçilebilecek daha fazla ilaç seçeneğiyle, mKDPK'de tedavi seçimi ve tedavilerin optimal sıralaması klinik pratiği zorlamaktadır. mKDPK takibinde PSA hastalık progresyonunda yüksek ise PSA duyarlı hastalık kabul edilip, PSA takibi ve aralıklı prostat spesifik membran antijen-pozitron emisyon tomografi-

¹ Uzm. Dr., Sağlık Bilimleri Üniversitesi Ümraniye Eğitim ve Araştırma Hastanesi, Tıbbi Onkoloji Kliniği, drtugcekuhragunes@gmail.com, ORCID iD: 0000-0002-7917-2459

SONUÇ

mKDPK'i tedavisinde kullanılan ADT, ASRI ve kemoterapilere ek radyonüklid tedaviler, immünoterapi ve hedefe yönelik diğer ajanların (PARP inhibitörleri) kullanımını hedefleyen çalışmalar yapılmıştır. Bu ilaçların prostat kanseri tedavisinde etkinliği ve kullanımı gelecek bölümlerde daha detaylı olarak incelenecektir.

KAYNAKLAR

1. Siegel RL, Miller KD, Fuchs HE, Jemal A. Cancer statistics, 2022. *CA Cancer J Clin.* 2022;72(1):7-33.
2. Beer TM, Armstrong AJ, Rathkopf DE, Loriot Y, Sternberg CN, Higano CS, et al. Enzalutamide in metastatic prostate cancer before chemotherapy. *N Engl J Med.* 2014;371(5):424-33.
3. Teply BA, Qiu F, Antonarakis ES, Carducci MA, Denmeade SR. Risk of development of visceral metastases subsequent to abiraterone vs placebo: An analysis of mode of radiographic progression in COU-AA-302. *Prostate.* 2019;79(8):929-33.
4. Pond GR, Sonpavde G, de Wit R, Eisenberger MA, Tannock IF, Armstrong AJ. The prognostic importance of metastatic site in men with metastatic castration-resistant prostate cancer. *Eur Urol.* 2014;65(1):3-6.
5. Bryce AH, Alumkal JJ, Armstrong A, Higano CS, Iversen P, Sternberg CN, et al. Radiographic progression with nonrising PSA in metastatic castration-resistant prostate cancer: post hoc analysis of PREVAAL. *Prostate Cancer Prostatic Dis.* 2017;20(2):221-7.
6. Hussain M, Wolf M, Marshall E, Crawford ED, Eisenberger M. Effects of continued androgen-deprivation therapy and other prognostic factors on response and survival in phase II chemotherapy trials for hormone-refractory prostate cancer: a Southwest Oncology Group report. *J Clin Oncol.* 1994;12(9):1868-75.
7. Taylor CD, Elson P, Trump DL. Importance of continued testicular suppression in hormone-refractory prostate cancer. *J Clin Oncol.* 1993;11(11):2167-72.
8. Freedland SJ, Aronson WJ. Commentary on "Integrative clinical genomics of advanced prostate cancer". Robinson D, Van Allen EM, Wu YM, Schultz N, Lonigro RJ, Mosquera JM, Montgomery B, Taplin ME, Pritchard CC, Attard G, Beltran H, Abida W, Bradley RK, Vinson J, Cao X, Vats P, Kunju LP, Hussain M, Feng FY, Tomlins SA, Cooney KA, Smith DC, Brennan C, Siddiqui J, Mehra R, Chen Y, Rathkopf DE, Morris MJ, Solomon SB, Durack JC, Reuter VE, Gopalan A, Gao J, Loda M, Lis RT, Bowden M, Balk SP, Gaviola G, Sougnez C, Gupta M, Yu EY, Mostaghel EA, Cheng HH, Mulcahy H, True LD, Plymate SR, Dvinge H, Ferraldeschi R, Flohr P, Miranda S, Zafeiriou Z, Tunariu N, Mateo J, Perez-Lopez R, Demichelis F, Robinson BD, Schiffman M, Nanus DM, Tagawa ST, Sigaras A, Eng KW, Elemento O, Sboner A, Heath EI, Scher HI, Pienta KJ, Kantoff P, de Bono JS, Rubin MA, Nelson PS, Garraway LA, Sawyers CL, Chinnaiyan AM. *Cell.* 21 May 2015;161(5):1215-1228. *Urol Oncol.* 2017;35(8):535.
9. Montgomery RB, Mostaghel EA, Vessella R, Hess DL, Kalthorn TF, Higano CS, et al. Maintenance of intratumoral androgens in metastatic prostate cancer: a mechanism for castration-resistant tumor growth. *Cancer Res.* 2008;68(11):4447-54.
10. Gillessen S, Bossi A, Davis ID, de Bono J, Fizazi K, James ND, et al. Management of patients with advanced prostate cancer-metastatic and/or castration-resistant prostate cancer: Report of the Advanced Prostate Cancer Consensus Conference (APCCC) 2022. *Eur J Cancer.* 2023;185:178-215.

11. Gafita A, Rauscher I, Weber M, Hadaschik B, Wang H, Armstrong WR, et al. Novel Framework for Treatment Response Evaluation Using PSMA PET/CT in Patients with Metastatic Castration-Resistant Prostate Cancer (RECIP 1.0): An International Multicenter Study. *J Nucl Med.* 2022;63(11):1651-8.
12. Wang Y, Galante JR, Haroon A, Wan S, Afaq A, Payne H, et al. The future of PSMA PET and WB MRI as next-generation imaging tools in prostate cancer. *Nat Rev Urol.* 2022;19(8):475-93.
13. Maluf FC, Schutz FA, Cronemberger EH, Luz MA, Martins SPS, Muniz DQB, et al. A phase 2 randomized clinical trial of abiraterone plus ADT, apalutamide, or abiraterone and apalutamide in patients with advanced prostate cancer with non-castrate testosterone levels (LA-COG 0415). *Eur J Cancer.* 2021;158:63-71.
14. Barrie SE, Potter GA, Goddard PM, Haynes BP, Dowsett M, Jarman M. Pharmacology of novel steroidal inhibitors of cytochrome P450(17) alpha (17 alpha-hydroxylase/C17-20 lyase). *J Steroid Biochem Mol Biol.* 1994;50(5-6):267-73.
15. O'Donnell A, Judson I, Dowsett M, Raynaud F, Dearnaley D, Mason M, et al. Hormonal impact of the 17alpha-hydroxylase/C(17,20)-lyase inhibitor abiraterone acetate (CB7630) in patients with prostate cancer. *Br J Cancer.* 2004;90(12):2317-25.
16. Reid AH, Attard G, Danila DC, Oommen NB, Olmos D, Fong PC, et al. Significant and sustained antitumor activity in post-docetaxel, castration-resistant prostate cancer with the CYP17 inhibitor abiraterone acetate. *J Clin Oncol.* 2010;28(9):1489-95.
17. Danila DC, Morris MJ, de Bono JS, Ryan CJ, Denmeade SR, Smith MR, et al. Phase II multicenter study of abiraterone acetate plus prednisone therapy in patients with docetaxel-treated castration-resistant prostate cancer. *J Clin Oncol.* 2010;28(9):1496-501.
18. de Bono JS, Logothetis CJ, Molina A, Fizazi K, North S, Chu L, et al. Abiraterone and increased survival in metastatic prostate cancer. *N Engl J Med.* 2011;364(21):1995-2005.
19. Fizazi K, Scher HI, Molina A, Logothetis CJ, Chi KN, Jones RJ, 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. *Lancet Oncol.* 2012;13(10):983-92.
20. Ryan CJ, Smith MR, Fizazi K, Saad F, Mulders PF, Sternberg CN, et al. Abiraterone acetate plus prednisone versus placebo plus prednisone in chemotherapy-naive men with metastatic castration-resistant prostate cancer (COU-AA-302): final overall survival analysis of a randomised, double-blind, placebo-controlled phase 3 study. *Lancet Oncol.* 2015;16(2):152-60.
21. Scher HI, Beer TM, Higano CS, Anand A, Taplin ME, Efstathiou E, et al. Antitumour activity of MDV3100 in castration-resistant prostate cancer: a phase 1-2 study. *Lancet.* 2010;375(9724):1437-46.
22. Scher HI, Fizazi K, Saad F, Taplin ME, Sternberg CN, Miller K, et al. Increased survival with enzalutamide in prostate cancer after chemotherapy. *N Engl J Med.* 2012;367(13):1187-97.
23. Beer TM, Armstrong AJ, Rathkopf D, Loriot Y, Sternberg CN, Higano CS, et al. Enzalutamide in Men with Chemotherapy-naïve Metastatic Castration-resistant Prostate Cancer: Extended Analysis of the Phase 3 PREVAIL Study. *Eur Urol.* 2017;71(2):151-4.
24. Tannock IF, Osoba D, Stockler MR, Ernst DS, Neville AJ, Moore MJ, et al. Chemotherapy with mitoxantrone plus prednisone or prednisone alone for symptomatic hormone-resistant prostate cancer: a Canadian randomized trial with palliative end points. *J Clin Oncol.* 1996;14(6):1756-64.
25. Tannock IF, de Wit R, Berry WR, Horti J, Pluzanska A, Chi KN, et al. Docetaxel plus prednisone or mitoxantrone plus prednisone for advanced prostate cancer. *N Engl J Med.* 2004;351(15):1502-12.

26. de Bono JS, Oudard S, Ozguroglu M, Hansen S, Machiels JP, Kocak I, et al. Prednisone plus cabazitaxel or mitoxantrone for metastatic castration-resistant prostate cancer progressing after docetaxel treatment: a randomised open-label trial. *Lancet*. 2010;376(9747):1147-54.
27. Eisenberger M, Hardy-Bessard AC, Kim CS, Géczi L, Ford D, Mourey L, et al. Phase III Study Comparing a Reduced Dose of Cabazitaxel (20 mg/m²) and the Currently Approved Dose (25 mg/m²) in Postdocetaxel Patients With Metastatic Castration-Resistant Prostate Cancer-PROSELICA. *J Clin Oncol*. 2017;35(28):3198-206.
28. Oudard S, Fizazi K, Sengeløv L, Daugaard G, Saad F, Hansen S, et al. Cabazitaxel Versus Docetaxel As First-Line Therapy for Patients With Metastatic Castration-Resistant Prostate Cancer: A Randomized Phase III Trial-FIRSTANA. *J Clin Oncol*. 2017;35(28):3189-97.