

Geriatrik Prostat Kanseri Hastalarına Yaklaşım

Hasan Hüseyin TAVUKÇU¹

Saadettin ESKİÇORAPÇI²

GİRİŞ

Dünyada ve ülkemizde genel yaşam yılı artmakta olup dolayısıyla prostat kanseri ile karşılaşan hastaların da büyük çoğunluğunu daha yaşlı hastalar oluşturmaktadır. Prostat kanseri tanısı alan hastaların yaş ortancası dünyada 66'dır ve çoğunlukla metastatik prostat kanseri tanısı daha geç yaşta konacaktır, ortanca ölüm yaşı ise 80 olarak bildirilmektedir. 2030 yılında Amerika Birleşik Devletleri'nde 65 yaş üzeri prostat kanseri tanısı alacak hastaların oranı %70 olarak tahmin edilmektedir (1). Yaşlı hastalarda erken ve geç prostat kanseri tedavisi önümüzdeki dekatlarda giderek artacak ve yaygın bir halk sağlığı sorunu haline gelecektir (2).

Amerika Birleşik Devletleri'nde 75 yaş üzeri erkeklerde orta ve ileri risk grubundaki hastaların yalnızca %41'ine küratif tedavi uygulanırken 65-74 yaş arası hastaların %88'ine küratif tedavi uygulanmaktadır (3). Lokalize prostat kanseri tedavisinde 10 yıl üzeri yaşam yılı beklentisi, lokal tedaviden fayda görülmesi için temel bir klinik faktördür. Bunun nedeni mevcut komorbiditelerin yaşam yılına olan etkisidir. Yapılan çalışmalar komorbidite varlığının lokalize prostat kanserinden ölümü ön görmede yaştan daha önemli bir faktör olduğunu rapor etmektedir (4). On yıl sonunda Charlson komorbidite indeksi >2 hastaların çoğu yaş veya kanser agresifliğine bakılmaksızın eşlik eden komorbid hastalıklarına bağlı ölmektedirler.

Bu bölümde prostat kanserli yaşlı hastalara tedavi yaklaşımında *komorbidite ağırlıklı* olarak öneriler ve tedavi yaklaşımları gözden geçirilecektir.

¹ Doç. Dr., İstanbul Medipol Üniversitesi, Üroloji Bölümü, hhtavukcu@yahoo.com, ORCID iD: 0000-0003-0956-7460

² Prof. Dr., Acıbadem Üniversitesi, Üroloji Bölümü, eskicorapci@gmail.com, ORCID iD: 0000-0003-1169-870X

KAYNAKLAR

1. Institute NC. SEERCancer Stat Facts: prostate cancer. 2018.
2. Arnold M, Karim-Kos HE, Coebergh JW, et al. Recent trends in incidence of five common cancers in 26 European countries since 1988: Analysis of the European Cancer Observatory. *European journal of cancer*. 2015;51(9):1164-1187.
3. Boyle HJ, Alibhai S, Decoster L, et al. Updated recommendations of the International Society of Geriatric Oncology on prostate cancer management in older patients. *European journal of cancer*. 2019;116:116-136.
4. Hamilton AS, Albertsen PC, Johnson TK, et al. Trends in the treatment of localized prostate cancer using supplemented cancer registry data. *BJU International*. 2011;107(4):576-584.
5. Droz JP, Balducci L, Bolla M, et al. Background for the proposal of SIOG guidelines for the management of prostate cancer in senior adults. *Critical reviews in oncology/hematology*. 2010;73(1):68-91.
6. Droz JP, Balducci L, Bolla M, et al. Management of prostate cancer in older men: recommendations of a working group of the International Society of Geriatric Oncology. *BJU International*. 2010;106(4):462-469.
7. Droz JP, Aapro M, Balducci L, et al. Management of prostate cancer in older patients: updated recommendations of a working group of the International Society of Geriatric Oncology. *Lancet Oncology*. 2014;15(9):e404-414.
8. Soubeyran P, Bellera C, Goyard J, et al. Screening for vulnerability in older cancer patients: the ONCODAGE Prospective Multicenter Cohort Study. *Public Library of Science one*. 2014;9(12):e1150-1160.
9. Droz JP, Albrand G, Gillissen S, et al. Management of Prostate Cancer in Elderly Patients: Recommendations of a Task Force of the International Society of Geriatric Oncology. *European Urology*. 2017;72(4):521-531.
10. Droz JP, Boyle H, Albrand G, et al. Role of Geriatric Oncologists in Optimizing Care of Urological Oncology Patients. *European Urology Focus*. 2017;3(4-5):385-394.
11. Oken MM, Creech RH, Tormey DC, et al. Toxicity and response criteria of the Eastern Cooperative Oncology Group. *American journal of clinical oncology*. 1982;5(6):649-655.
12. Wedding U, Ködding D, Pientka L, et al. Physicians' judgement and comprehensive geriatric assessment (CGA) select different patients as fit for chemotherapy. *Critical reviews in oncology/hematology*. 2007;64(1):1-9.
13. Wildiers H, Heeren P, Puts M, et al. International Society of Geriatric Oncology consensus on geriatric assessment in older patients with cancer. *Journal of clinical oncology*. 2014;32(24):2595-2603.
14. Decoster L, Van Puvelde K, Mohile S, et al. Screening tools for multidimensional health problems warranting a geriatric assessment in older cancer patients: an update on SIOG recommendationsdagger. *Annals of oncology*. 2015;26(2):288-300.
15. Conford P. TD, van der Bergh R.C.N., Eberli D., et al. EAU Guidelines. Edn. presented at the EAU Annual Congress Madrid 2025. 2025. Available from: <http://uroweb.org/guidelines/compilations-of-all-guidelines/>.
16. Şen V, Yıldız A, Bozkurt O, et al. Turkish Linguistic Validation of the Geriatric 8 Screening Tool. *Bulletin of Urooncology*. 2021;20(3):133-137.
17. Tsoi KK, Chan JY, Hirai HW, et al. Cognitive Tests to Detect Dementia: A Systematic Review and Meta-analysis. *JAMA internal medicine*. 2015;175(9):1450-1458.
18. Borson S, Scanlan JM, Chen P, et al. The Mini-Cog as a screen for dementia: validation in a population-based sample. *Journal of the American Geriatrics Society*. 2003;51(10):1451-1454.
19. Solomon DH. Geriatric assessment: methods for clinical decision making. *Journal of the American Medical Association*. 1988;259(16):2450-2452.
20. Reuben DB, Fishman LK, McNabney M, et al. Looking inside the black box of comprehensive geriatric assessment: a classification system for problems, recommendations, and implementation strategies. *Journal of the American Geriatrics Society*. 1996;44(7):835-838.
21. Ellis G, Gardner M, Tsiachristas A, et al. Comprehensive geriatric assessment for older adults admitted to hospital. *The Cochrane database of systematic reviews*. 2017;9(9):CD006211.
22. Puts MTE, Sattar S, Kulik M, et al. A randomized phase II trial of geriatric assessment and management for older cancer patients. *Supportive care in cancer*. 2018;26(1):109-117.
23. Schmidt H, Boese S, Lampe K, et al. Trans sectoral care of geriatric cancer patients based on comprehensive geriatric assessment and patient-reported quality of life - Results of a multicenter study to develop and pilot test a patient-centered interdisciplinary care concept for geriatric oncology patients (PIVOG). *Journal of geriatric oncology*. 2017;8(4):262-270.
24. Magnuson A, Lemelman T, Pandya C, et al. Geriatric assessment with management intervention in older adults with cancer: a randomized pilot study. *Supportive care in cancer*. 2018;26(2):605-613.

25. Kalsi T, Babic-Illman G, Ross P, et al. The impact of comprehensive geriatric assessment interventions on tolerance to chemotherapy in older people. *British journal of cancer*. 2015;112(9):1435-1444.
26. McCleary NJ, Wigler D, Berry D, et al. Feasibility of computer-based self-administered cancer-specific geriatric assessment in older patients with gastrointestinal malignancy. *Oncologist*. 2013;18(1):64-72.
27. Hurria A, Akiba C, Kim J, et al. Reliability, Validity, and Feasibility of a Computer-Based Geriatric Assessment for Older Adults With Cancer. *Journal of oncology practice*. 2016;12(12):e1025-e34.
28. Shahrokhni A, Tin A, Downey RJ, et al. Electronic Rapid Fitness Assessment: A Novel Tool for Preoperative Evaluation of the Geriatric Oncology Patient. *Journal of the National Comprehensive Cancer Network*. 2017;15(2):172-179.
29. Mohile SG, Dale W, Somerfield MR, et al. Practical Assessment and Management of Vulnerabilities in Older Patients Receiving Chemotherapy: ASCO Guideline for Geriatric Oncology Summary. *Journal of oncology practice*. 2018;14(7):442-446.
30. FRancisco UoCS. ePrognosis 2018 [<https://eprognosis.ucsf.edu/index.php>]. Available from: <https://eprognosis.ucsf.edu/index.php>.
31. Liu D, Lehmann HP, Frick KD, et al. Active surveillance versus surgery for low risk prostate cancer: a clinical decision analysis. *Journal of Urology*. 2012;187(4):1241-1246.
32. Albertsen PC, Hanley JA, Fine J. 20-year outcomes following conservative management of clinically localized prostate cancer. *Journal of the American Medical Association*. 2005;293(17):2095-2101.
33. Hamdy FC, Donovan JL, Lane JA, et al. 10-Year Outcomes after Monitoring, Surgery, or Radiotherapy for Localized Prostate Cancer. *The New England journal of medicine*. 2016;375(15):1415-1424.
34. Scosyrev E, Messing EM, Mohile S, et al. Prostate cancer in the elderly: frequency of advanced disease at presentation and disease-specific mortality. *Cancer*. 2012;118(12):3062-3070.
35. Briganti A, Spahn M, Joniau S, et al. Impact of age and comorbidities on long-term survival of patients with high-risk prostate cancer treated with radical prostatectomy: a multi-institutional competing-risks analysis. *European Urology*. 2013;63(4):693-701.
36. Bill-Axelsson A, Holmberg L, Garmo H, et al. Radical prostatectomy or watchful waiting in early prostate cancer. *The New England journal of medicine*. 2014;370(10):932-942.
37. Joniau S, Gontero P, Briganti A, et al. 363 Stratification of high-risk prostate cancer into prognostic categories; a European multi-institutional study. *The Journal of Urology*. 2012;187(4S):e148-e149.
38. Begg CB, Riedel ER, Bach PB, et al. Variations in morbidity after radical prostatectomy. *The New England journal of medicine*. 2002;346(15):1138-1144.
39. Stanford JL, Feng Z, Hamilton AS, et al. Urinary and sexual function after radical prostatectomy for clinically localized prostate cancer: the Prostate Cancer Outcomes Study. *Journal of the American Medical Association*. 2000;283(3):354-360.
40. Kundu SD, Roehl KA, Eggener SE, et al. Potency, continence and complications in 3,477 consecutive radical retropubic prostatectomies. *The Journal of urology*. 2004;172(6 Part 1):2227-2231.
41. Traboulsi SL, Nguyen DD, Zakaria AS, et al. Functional and perioperative outcomes in elderly men after robotic-assisted radical prostatectomy for prostate cancer. *World journal of urology*. 2020;38(11):2791-2798.
42. Islamoglu E, Aksaray EE, Tas S, et al. Elderly Patients' Outcomes After Robot-Assisted Radical Prostatectomy: A Single Center Experience. *Journal of laparoendoscopic & advanced surgical techniques. Part A*. 2023;33(11):1097-1101.
43. Haney CM, Kowalewski KF, Westhoff N, et al. Robot-assisted Versus Conventional Laparoscopic Radical Prostatectomy: A Systematic Review and Meta-analysis of Randomised Controlled Trials. *European Urology Focus*. 2023;9(6):930-937.
44. Kundu SD, Roehl KA, Eggener SE, et al. Potency, continence and complications in 3,477 consecutive radical retropubic prostatectomies. *The Journal of urology*. 2004;172(6 Pt 1):2227-2231.
45. Dearnaley D, Syndikus I, Mossop H, et al. Conventional versus hypofractionated high-dose intensity-modulated radiotherapy for prostate cancer: 5-year outcomes of the randomised, non-inferiority, phase 3 CHHiP trial. *Lancet Oncology*. 2016;17(8):1047-1060.
46. Incrocci L, Wortel RC, Aletayehu WG, et al. Hypofractionated versus conventionally fractionated radiotherapy for patients with localised prostate cancer (HYPRO): final efficacy results from a randomised, multicentre, open-label, phase 3 trial. *Lancet Oncology*. 2016;17(8):1061-1069.
47. Arcangeli G, Saracino B, Arcangeli S, et al. Moderate Hypofractionation in High-Risk, Organ-Confining Prostate Cancer: Final Results of a Phase III Randomized Trial. *Journal of clinical oncology*. 2017;35(17):1891-1897.
48. Catton CN, Lukka H, Gu CS, et al. Randomized Trial of a Hypofractionated Radiation Regimen for the Treatment of Localized Prostate Cancer. *Journal of clinical oncology*. 2017;35(17):1884-1890.

49. Lee WR, Dignam JJ, Amin MB, et al. Randomized Phase III Noninferiority Study Comparing Two Radiotherapy Fractionation Schedules in Patients With Low-Risk Prostate Cancer. *Journal of clinical oncology*. 2016;34(20):2325-2332.
50. Shahid N, Loblaw A, Chung HT, et al. Long-term Toxicity and Health-related Quality of Life after Single-fraction High Dose Rate Brachytherapy Boost and Hypofractionated External Beam Radiotherapy for Intermediate-risk Prostate Cancer. *Clinical oncology : a journal of the Royal College of Radiologists*. 2017;29(7):412-420.
51. Joseph N, Taylor C, O'Hara C, et al. A combined single high-dose rate brachytherapy boost with hypofractionated external beam radiotherapy results in a high rate of biochemical disease free survival in localised intermediate and high risk prostate cancer patients. *Radiotherapy and oncology*. 2016;121(2):299-303.
52. Morris WJ, Tyldesley S, Rodda S, et al. Androgen Suppression Combined with Elective Nodal and Dose Escalated Radiation Therapy (the ASCENDE-RT Trial): An Analysis of Survival Endpoints for a Randomized Trial Comparing a Low-Dose-Rate Brachytherapy Boost to a Dose-Escalated External Beam Boost for High- and Intermediate-risk Prostate Cancer. *International journal of radiation oncology, biology, physics*. 2017;98(2):275-285.
53. Rodda S, Tyldesley S, Morris WJ, et al. ASCENDE-RT: An Analysis of Treatment-Related Morbidity for a Randomized Trial Comparing a Low-Dose-Rate Brachytherapy Boost with a Dose-Escalated External Beam Boost for High- and Intermediate-Risk Prostate Cancer. *International journal of radiation oncology, biology, physics*. 2017;98(2):286-295.
54. Rodda S, Morris WJ, Hamm J, et al. ASCENDE-RT: An Analysis of Health-Related Quality of Life for a Randomized Trial Comparing Low-Dose-Rate Brachytherapy Boost With Dose-Escalated External Beam Boost for High- and Intermediate-Risk Prostate Cancer. *International journal of radiation oncology, biology, physics*. 2017;98(3):581-589.
55. Hoskin P, Rojas A, Ostler P, et al. Single-dose high-dose-rate brachytherapy compared to two and three fractions for locally advanced prostate cancer. *Radiotherapy and oncology*. 2017;124(1):56-60.
56. D'Amico AV, Chen MH, Renshaw AA, et al. Androgen suppression and radiation vs radiation alone for prostate cancer: a randomized trial. *Journal of the American Medical Association*. 2008;299(3):289-295.
57. Jones CU, Hunt D, McGowan DG, et al. Radiotherapy and short-term androgen deprivation for localized prostate cancer. *The New England journal of medicine*. 2011;365(2):107-118.
58. Studer UE, Collette L, Whelan P, et al. Using PSA to guide timing of androgen deprivation in patients with T0-4 N0-2 M0 prostate cancer not suitable for local curative treatment (EORTC 30891). *European Urology*. 2008;53(5):941-949.
59. Studer UE, Whelan P, Albrecht W, et al. Immediate or deferred androgen deprivation for patients with prostate cancer not suitable for local treatment with curative intent: European Organisation for Research and Treatment of Cancer (EORTC) Trial 30891. *J Clin Oncol*. 2006;24(12):1868-1876.
60. Sun M, Choueiri TK, Hamnvik OP, et al. Comparison of Gonadotropin-Releasing Hormone Agonists and Orchiectomy: Effects of Androgen-Deprivation Therapy. *JAMA Oncology*. 2016;2(4):500-507.
61. Klotz L, O'Callaghan C, Ding K, et al. Nadir testosterone within first year of androgen-deprivation therapy (ADT) predicts for time to castration-resistant progression: a secondary analysis of the PR-7 trial of intermittent versus continuous ADT. *Journal of clinical oncology*. 2015;33(10):1151-1156.
62. Limonta P, Montagnani Marelli M, Moretti RM. LHRH analogues as anticancer agents: pituitary and extrapituitary sites of action. *Expert opinion on investigational drugs*. 2001;10(4):709-720.
63. Hussain M, Tangen CM, Berry DL, et al. Intermittent versus continuous androgen deprivation in prostate cancer. *The New England journal of medicine*. 2013;368(14):1314-1325.
64. Magnan S, Zarychanski R, Pilote L, et al. Intermittent vs Continuous Androgen Deprivation Therapy for Prostate Cancer: A Systematic Review and Meta-analysis. *JAMA Oncology*. 2015;1(9):1261-1269.
65. 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. *Journal of clinical oncology*. 2018;36(11):1080-1087.
66. 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. *European Urology*. 2016;70(2):256-262.
67. Sweeney CJ, Chen YH, Carducci M, et al. Chemohormonal Therapy in Metastatic Hormone-Sensitive Prostate Cancer. *The New England journal of medicine*. 2015;373(8):737-746.
68. 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):1163-1177.

69. Fizazi K, Tran N, Fein L, et al. Abiraterone plus Prednisone in Metastatic, Castration-Sensitive Prostate Cancer. *The New England journal of medicine*. 2017;377(4):352-360.
70. Chi KN, Protheroe A, Rodriguez-Antolin A, et al. Patient-reported outcomes following abiraterone acetate plus prednisone added to androgen deprivation therapy in patients with newly diagnosed metastatic castration-naïve prostate cancer (LATITUDE): an international, randomised phase 3 trial. *Lancet Oncology*. 2018;19(2):194-206.
71. James ND, de Bono JS, Spears MR, et al. Abiraterone for Prostate Cancer Not Previously Treated with Hormone Therapy. *The New England journal of medicine*. 2017;377(4):338-351.
72. 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. *Annals of oncology*. 2018;29(5):1235-1248.
73. Wallis CJD, Klaassen Z, Bhindi B, et al. Comparison of Abiraterone Acetate and Docetaxel with Androgen Deprivation Therapy in High-risk and Metastatic Hormone-naïve Prostate Cancer: A Systematic Review and Network Meta-analysis. *European Urology*. 2018;73(6):834-844.
74. Parker CC, James ND, Brawley CD, et al. Radiotherapy to the primary tumour for newly diagnosed, metastatic prostate cancer (STAMPEDE): a randomised controlled phase 3 trial. *Lancet*. 2018;392(10162):2353-2366.
75. Italiano A, Ortholan C, Oudard S, et al. Docetaxel-based chemotherapy in elderly patients (age 75 and older) with castration-resistant prostate cancer. *European Urology*. 2009;55(6):1368-1375.
76. Parker C, Gillessen S, Heidenreich A, et al. Cancer of the prostate: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. *Annals of oncology*. 2015;26 Suppl 5:v69-77.
77. Davis ID, Martin AJ, Stockler MR, et al. Enzalutamide with Standard First-Line Therapy in Metastatic Prostate Cancer. *The New England journal of medicine*. 2019;381(2):121-131.
78. 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. *Journal of clinical oncology*. 2019;37(32):2974-2986.
79. Chi KN, Agarwal N, Bjartell A, et al. Apalutamide for Metastatic, Castration-Sensitive Prostate Cancer. *The New England journal of medicine*. 2019;381(1):13-24.
80. Aapro M, Saad F. Bone-modifying agents in the treatment of bone metastases in patients with advanced genitourinary malignancies: a focus on zoledronic acid. *Therapeutic advances in urology*. 2012;4(2):85-101.
81. 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 × 2 factorial design. *The Lancet*. 2022;399(10336):1695-1707.
82. Smith MR, Hussain M, Saad F, et al. Darolutamide and survival in metastatic, hormone-sensitive prostate cancer: a patient and caregiver perspective and plain language summary of the ARASENS trial. *Future oncology*. 2022;18(21):2585-2597.
83. Sternberg CN, Fizazi K, Saad F, et al. Enzalutamide and Survival in Nonmetastatic, Castration-Resistant Prostate Cancer. *N Engl J Med*. 2020;382(23):2197-2206.
84. Smith MR, Saad F, Chowdhury S, et al. Apalutamide Treatment and Metastasis-free Survival in Prostate Cancer. *The New England journal of medicine*. 2018;378(15):1408-1418.
85. Fizazi K, Shore N, Tammela TL, et al. Nonmetastatic, Castration-Resistant Prostate Cancer and Survival with Darolutamide. *The New England journal of medicine*. 2020;383(11):1040-1049.
86. Saad F, Bogemann M, Suzuki K, et al. Treatment of nonmetastatic castration-resistant prostate cancer: focus on second-generation androgen receptor inhibitors. *Prostate cancer and prostatic diseases*. 2021;24(2):323-334.
87. Berthold DR, Pond GR, Soban F, et al. Docetaxel plus prednisone or mitoxantrone plus prednisone for advanced prostate cancer: updated survival in the TAX 327 study. *Journal of clinical oncology*. 2008;26(2):242-245.
88. Kellokumpu-Lehtinen PL, Harmenberg U, Joensuu T, et al. 2-Weekly versus 3-weekly docetaxel to treat castration-resistant advanced prostate cancer: a randomised, phase 3 trial. *Lancet Oncology*. 2013;14(2):117-124.
89. Oudard S, Fizazi K, Sengelov L, et al. Cabazitaxel Versus Docetaxel As First-Line Therapy for Patients With Metastatic Castration-Resistant Prostate Cancer: A Randomized Phase III Trial-FIRSTANA. *Journal of clinical oncology*. 2017;35(28):3189-3497.
90. de Bono JS, Oudard S, Ozguroglu M, 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):1147-1154.

91. Eisenberger M, Hardy-Bessard AC, Kim CS, 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. *Journal of clinical oncology*. 2017;35(28):3198-3206.
92. Climent MÁ, Pérez-Valderrama B, Mellado B, et al. Weekly cabazitaxel plus prednisone is effective and less toxic for 'unfit' metastatic castration-resistant prostate cancer: Phase II Spanish Oncology Genitourinary Group (SOGUG) trial. *European Journal of Cancer*. 2017;87:30-7.
93. 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. *Lancet Oncology*. 2012;13(10):983-992.
94. 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. *Lancet Oncology*. 2015;16(2):152-160.
95. Scher HI, Fizazi K, Saad F, et al. Increased survival with enzalutamide in prostate cancer after chemotherapy. *The New England journal of medicine*. 2012;367(13):1187-1197.
96. Beer TM, Armstrong AJ, Rathkopf D, et al. Enzalutamide in Men with Chemotherapy-naïve Metastatic Castration-resistant Prostate Cancer: Extended Analysis of the Phase 3 PREVAIL Study. *European Urology*. 2017;71(2):151-154.
97. 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. *Lancet Oncology*. 2016;17(2):153-163.
98. Penson DF, Armstrong AJ, Concepcion R, et al. Enzalutamide Versus Bicalutamide in Castration-Resistant Prostate Cancer: The STRIVE Trial. *Journal of clinical oncology*. 2016;34(18):2098-2106.
99. de Bono J, Mateo J, Fizazi K, et al. Olaparib for Metastatic Castration-Resistant Prostate Cancer. *The New England journal of medicine*. 2020;382(22):2091-2102.
100. Hussain M, Mateo J, Fizazi K, et al. Survival with Olaparib in Metastatic Castration-Resistant Prostate Cancer. *The New England journal of medicine*. 2020;383(24):2345-2357.
101. Abida W, Patnaik A, Campbell D, et al. Rucaparib in Men With Metastatic Castration-Resistant Prostate Cancer Harboring a BRCA1 or BRCA2 Gene Alteration. *Journal of clinical oncology*. 2020;38(32):3763-3772.
102. Kantoff PW, Higano CS, Shore ND, et al. Sipuleucel-T immunotherapy for castration-resistant prostate cancer. *The New England journal of medicine*. 2010;363(5):411-422.
103. Marabelle A, Le DT, Ascierto PA, et al. Efficacy of Pembrolizumab in Patients With Noncolorectal High Microsatellite Instability/Mismatch Repair-Deficient Cancer: Results From the Phase II KEYNOTE-158 Study. *Journal of clinical oncology*. 2020;38(1):1-10.
104. Abida W, Cheng ML, Armenia J, et al. Analysis of the Prevalence of Microsatellite Instability in Prostate Cancer and Response to Immune Checkpoint Blockade. *JAMA Oncology*. 2019;5(4):471-478.
105. Prior JO, Gillesen S, Wirth M, et al. Radiopharmaceuticals in the elderly cancer patient: Practical considerations, with a focus on prostate cancer therapy: A position paper from the International Society of Geriatric Oncology Task Force. *European journal of cancer*. 2017;77:127-139.
106. Parker C, Zhan L, Cislo P, et al. Effect of radium-223 dichloride (Ra-223) on hospitalisation: An analysis from the phase 3 randomised Alpharadin in Symptomatic Prostate Cancer Patients (ALSYMPCA) trial. *European journal of cancer*. 2017;71:1-6.
107. Hofman MS, Emmett L, Sandhu S, et al. [(177)Lu]Lu-PSMA-617 versus cabazitaxel in patients with metastatic castration-resistant prostate cancer (TheraP): a randomised, open-label, phase 2 trial. *Lancet*. 2021;397(10276):797-804.
108. Sun M, Cole AP, Hanna N, et al. Cognitive Impairment in Men with Prostate Cancer Treated with Androgen Deprivation Therapy: A Systematic Review and Meta-Analysis. *The Journal of Urology*. 2018;199(6):1417-1425.
109. Ahmadi H, Daneshmand S. Androgen deprivation therapy: evidence-based management of side effects. *BJU International*. 2013;111(4):543-548.