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PROSTATE CANCER: INSIGHTS IN PATHOGENESIS, MOLECULAR DIAGNOSTICS, AND EMERGING THERAPEUTIC STRATEGIES-A COMPREHENSIVE REVIEW

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ABSTRACT

Prostate cancer (pca) is one of the common cancers occurring in the male population, with the second-highest occurrence, with more than 1.4 million new cases and 375,000 deaths annually. Thought there Have been improvement in the early diagnosis of cancer using the prostate-specific antigen test, there are still cases of castration-resistant prostate cancer, which have a poor prognosis. The current review article is an attempt to compile the knowledge available on the development of prostate cancers, especially with regard to the role of the androgen receptor, genetic factors, and the role of the tumor microenvironment.in addition the current review article is an attempt to offer insights into the recent developments in the field of liquid biopsy, multiparametric MRI- guided biopsy, and role of PSMA, ctDNA exosomal microRNA, which have shown promising results in the early diagnosis of prostate cancers. We also cover emerging therapies in prostate cancer, such as PARP inhibitors in BRCA mutated tumors, PSMA radioligand therapy with 177Lu-PSMA-617, immunotherapy checkpoints, as well as emerging AR signaling pathway inhibitors such as enzalutamide and apalutamide. We also cover emerging trends in prostate cancer treatment, such as the emerging role of artificial intelligence and machine learning in grading pathology and making treatment decisions in prostate cancer. We also cover challenges in the field as well as future directions in this emerging field of precision medicine in prostate cancer treatment.

KEYWORDS: *Prostate Cancer; Androgen receptor; CRPC; PSMA; PARP Inhibitors; liquid biopsy; immunotherapy; precision oncology; AI in oncology*.

1. INTRODUCTION

Prostate cancer is the most common cancer in men, excluding skin cancers, in developed countries. It is a major health problem worldwide. The American cancer society estimates that there will be over 300,000 new cases and 35,000 deaths from prostate cancer in the us in 2025[1].prostate cancer is diverse and ranges from slow-growing cancers that my not require treatment to aggressive cancers that spread and have a poor prognosis.[8]

The prostate is a part of the male reproductive system. The normal function of the prostate is dependent on androgen hormones. Thus, hormonal therapy has played an important role in the treatment of prostate cancer since the discovery of the role of androgens in the growth and function of the prostate by Huggins and hodges in 1941.[9] although androgen deprivation therapy is the main treatment of advanced prostate cancer, resistance to therapy is common in most patients, highlighting the need for new treatment options.[10]

Over the last 10 years, there has been unprecedented there has been a tremendous increase in our understanding of the molecular basis of prostate cancer, which has led to many new drugs being approved to help patients live longer. There have also been many advances in how doctors use imaging, genomics, and artificial intelligence to diagnose and treat patients with prostate cancer. This review aims to provide a general overview of the biology, diagnosis, and treatment of prostate cancer, a s well as a glimpse into the future of precision medicine.[11]

2. EPIDEMIOLOGY

Prostate cancer shows differences in the incidence rate depending on various ethnic populations. Countries with high incidence rates of prostate cancer are found in north America, Australia, and northern Europe. Countries with low incidence rates of prostate cancer are found in Asia. This could be due to differences in the use of the psa test for early detection of cancer. African-American men have the highest incidence rate of prostate cancer compared to European-American men. This could be due to genetic factors, socioeconomic status, and availability of health care.[13]

Prostate cancer risk factors that have been established include age, where men older than 65 years have a high risk of getting prostate cancer. Having a close family member with prostate cancer doubles the risk of getting the disease. Men with brca1/2 gene mutation or lynch syndrome have a high risk of getting prostate cancer include obesity, high-fat-diet, lack of exercise, and inflammation. However, there is not enough evidence showing how these factors increase risk. There is emerging evidence showing that there is a link-between the microbine and prostate cancer, specifically through its role in metabolism.

Stage	5 Yr Survival	% Of Cases	Defining Feature
Localized	99%	79%	Confined To Prostate
Regional	99%	12%	Adjacent Lymph Nodes
Distant	32%	6%	Distant Metastasis

3. RISK FACTORS AND ETIOLOGY

3.1. Age

Age is considered the main risk factor for prostate cancer. Prostate cancer is rarely found in men under 40, but the risk is high shortly thereafter. More than 60% of men with prostate cancer are 65-year-old or older, and autopsy studies show that up to 80% of men in their eighties have evidence of prostate cancer under the microscope.[13] as men age, cancer develops because of accumulated genetic mutations, changes in how genes function and changes in their environment.[3]

3.2. Genetic Factors

About 5-10% of all prostate cancers result from strong inherited genetic mutations, meaning that if men have a close relative who had prostate cancer, their risk is about twice that of others.[9,14]

Some of these risk genes include:

- Brca2: men with this gene have a 5 to 8 times increased risk of getting prostate cancer, and their cancers cell to be more aggressive, high grade, and have a worse outcome.[10]
- Brca1: men with this gene have their risk of getting prostate cancer increased about three times, but their cancers cell to be less aggressive than those related to brca2.[10]

Hoxb13(g84e variant): this rare but important variation is strongly associated with hereditary and early-onset prostate cancer cases.[12]

Lynch syndrome (mlh1, msh2, msh6, pms2): moderately increases the risk for developing prostate cancer and may also help predict the response of patients to immune checkpoint inhibitors.[37] today, more clinicians are employing the use of multigene panel testing for patients with high-risk or metastatic prostate cancer. this also helps in the testing of other members of the patient's family.[30,34]

3.3. Diet, Lifestyle, and Environmental Factors

Diets consuming a diet with a high amount of red and processed meats and saturated fats increases the risk for developing prostate cancer. On the other hand, a diet with a high amount of lycopene, cruciferous vegetables, and omega-3 fatty acids may reduce the risk for developing the disease.[13] Obesity has also been linked with an increased risk for developing aggressive forms of the cancer.[13] Lack of physical activity, smoking and excessive alcohol consumption are also other factors that may contribute to the development of the cancer.[13] Military veterans exposed to agent orange are also at an increased risk for developing the cancer.[6,13]

4. MOLECULAR PATHOGENESIS

4.1. Androgen Receptor Signaling

The androgen receptor plays a central role in regulating gene expression in prostate cancer cells. When it binds to testosterone or dihydrotestosterone, it enters the cell nucleus and binds to androgen response elements that regulate cell growth and differentiation genes and survival genes.[17] in castration-resistant prostate cancer, the androgen receptor is active in the presence of low levels of androgens. This may be due to androgen receptor gene amplification, activating point mutations such as l702h, w742c, and h875y, or the presence of a constantly active androgen receptor splice variant such as ar-v7, or the tumor cells producing their own androgens.ar-v7 lacking ligand-binding domain, is particularly relevant to clinical practice. If ar-v7 is present in ctcs, the tumor is likely to be resistant to enzalutamide and abiraterone, but may still benefit from taxane chemotherapy.[20] new therapies targeting AR coactivators, the AR-N terminus, and AR splicing are currently being researched.[21]

4.2. Genomic Landscape

The Genomic Landscape of Pca Has Been Extensively Studied Through The Genomic Characterization of Primary Pca By The Cancer Genome Atlas (TCGA) Project. The Most Common Genomic Alterations In Primary Pca Include ETS Gene Fusions, PTEN Deletions, TP53 Mutations, RB1 Deletions, CDK12 Alterations, And Epigenetic Regulator Mutations In KDM6A And KMT2D.[22,23]

The Genomic Alterations in mCRPC are Even More Complex. The Alterations Include a Higher Frequency of AR Alterations, TP53 And RB1 Co-Deletions Associated With Neurodecrine Features, And Significant Mutations In Homologous Recombination Repair (HRR) Genes. The Most Common Mutations in The HRR Genes In mCRPC INCLUDE Brca2 (13%), BRCA1(3%), ATM(7%), and CDK12 (7%).[24] These Mutations In The HRR Genes Play A Critical Role in The Prediction of Response to PARP Inhibitors And Have Significant Implications in Genetic Counseling Since These Mutations are Imherited.[25]

4.3. Tumor Microenvironment

The tumor microenvironment in prostate cancer is composed of cancer-associated fibroblasts, tumor-associated macrophages, myeloid-derived suppressor cells, and cytotoxic T cells in a complex extra cellular environment. prostate cancer is classified as an immunologically “cold” tumor type due to the low number of mutations, low number of infiltrating immune cells, and immunosuppressive tumor microenvironment. This is the reason for the failure of immunotherapy using immune checkpoint inhibitors in prostate cancer patients. New approaches include combining PARP inhibitors with PD-1 or PD-L1 inhibitors to exploit the potential immunogenicity of tumors with BRCA mutations, targeting tumor-associated myeloid cells, and using specific T cells engagers targeting PSMA. Tumors with CDK12 mutations have a unique genomic instability pattern characterized by tandem duplications and may be responsive to immunotherapy.[27,30]

5. Novel Diagnostic Approaches

5.1 PSA and Beyond

Despite the efficacy of PSA testing in reducing deaths form prostate cancer, there have been concerns about overdiagnosis and overtreatment of insignificant cancers. In this respect various researchers have proposed alternative types of PSA testing, such as the free-to-total PSA ratio, prostate health index, and 4K score, which have shown potential in making PSA testing more specific [31]. In addition, there is a FDA-approved prostate cancer prevention trial Risk Calculator that uses aPSA test result, a digital rectal exam result, age, race and a family history to provide a more individualized risk assessment tool.[32]

5.2. Multiparametric MRI and PSMA PET

It utilizes T2-weighted imaging, diffusion-weighted imaging, and dynamic contrast-enhanced imaging. This has improved the diagnostic capabilities for prostate cancer. PI-RADS v2.1 is a system that allows for a standard reporting system to guide targeted transperineal biopsies. This is useful in identifying significant cancers while avoiding unnecessary biosies. PRECISION and MRI-FIRST studies have shown that shown that mpMRI biopsies have increased the rate of identifying significant cancers, whereas fewer insignificant cancers have been identified compared to systematic biopsies.[33,34]

PSMA is present in larger amounts in cancer cells compared to normal cells. PET/CT scans that utilize PSMA have increased sensitivity and specificity in identifying recurrent and metastatic cancer compared to traditional imaging studies. This is due to the use of 68Ga-PSMA-11 or 18F-DCFPyl (piflufolastat F-18). This imaging modality is approved for use in identifying recurrent and metastatic cancer. The proPSMA and CONDOR studies have shown that PSMA PET is useful in identifying biochemical recurrence as well as in metastatic castration -sensitive prostate cancer.[36,37]

5.3. Liquid Biopsy

Liquid biopsy techniques involve various blood-based markers, such as circulating tumor cells(CTCs), ctDNA and exosomes. Liquid biopsy is less invasive foe tumor profiling, disease monitoring, and therapy selection.[38] Detection of CTCs, AR-V7, using Veridex Cell search, epic sciences, etc., is highly prognostic and guides therpy decisions in mCRPC[20]. ctDNA profiling can detect alterations in HRR genes, dMMR and AR copy number variations.[39] New microRNA signatures found in exosomes have the potential to act as future diagnostic and predictive biomarkers.[40]

6. Emerging and novel therapeutic strategies

6.1. Next-Generation Androgen Pathway Inhibitors

The Current Status of AR-Targeted Therapy Has Been Revolutionized By Second-Generation Agents. Enzalutamide A Patent AR Antagonist Devoid of Agonist Effects, and Abiraterone Acetate, A CYP17A1 Inhibitor With Activity Against Extra Steroid Synthesis, Have Proven a Survival Advantages In mCRPC, Followed By mCSPC and nmCRPC in Pivotal Phase Iii Trials (AFFIRM,COU-AA-302,ARCHES,TITAN,SPARTAN,Andprosper).[41,42] Apalutamide, A Novel AR Antagonist With Excellent Central Nervous System Penetration, is also Approved For nmCRPC, The Novel Therapeutic Strategy Based On AR-Targeted Therapy in Combination With ADT,I.E., Intensification of Systemic Therapy. Represents A Novel Paradigm In The Management Of High- Volume mCSPC And Has Been Validated By Recent Phase III Trails(CHAARTED,LATITUDE, And ENZAMET).The Efficacy of Darolutamide in Combination With Docetaxel And ADT In mCSPC Has Been Validated by The ARASENS Study, Thereby Establishing A Novel Paradigm In Pca Thereby, I,E., Intensified Initial Therapy.[45]

6.2. PARP Inhibitors

The Discovery That About 25% Of mCRPC Patients Have Pathogenic Alterations In HRR Genes Provided A Rationale For The Use of These Agents In This Context. FDA Approval In 2020 For Use In mCRPC Patients With BRCA1/2 And ATM Mutations After Progression On AR- Targeted Therapy Based On The PRO Found Study. Which Was The First Biomarker-Selected Phase III Study In Pca That Showed Improved OS in This Patient Group.[46] Rucaparib Gained Approval Based on The Results From The TRITON2/3 Trails In BRCA Mutant mCRPC.

Combos Using API Have Shown Promising Synergistic Effects In Preclinical Models. The Propel And TALAPRO-2 Trials Have Shown Improved Radiographic Progression-Free Survival in The Overall mCRPC Patient Group Regardless Of HRR Status in Combination With Abiraterone And Enzalutamide, Respectively. These Have Gained Approval and Rise Important Questions About Patient Selection in This Context.[48,49]

6.3. PSMA-targeted radio ligand therapy

One of The Most Important Therapeutic Development In Pca In Recent Years Is The Radioligand Therapy 1778Lu-PSMA-617(Lutetium Vipivotide Tetraxetan), Marketed As Pluvicto. This Targeted Therapy Delivers Beta-Particle Radiation To PSMA-Positive Tumour Cells And tumour Microenvironment. The VISION Trial Is A Phase III Randomized Controlled Trial That Confirmed The Efficacy And Safety of Radio ligand Therapy In Conjunction With Standard Care in mCRPC Patients With PSMA-Positive Disease. The Trial Showed That Radio ligand Therapy Significantly Improved OS And Radiographic Progression-Free Survival in Heavily Pre-treated mCRPC Patients With PSMA-Positive Disease Compared To Standard Care Alone(OS:15.3 Vs 11.3 Months; Hazard Ratio,0.62).[5] This Therapeutic Agent Received FDA Approval In March 2022.Further Studies are in Progress to Evaluate The Efficacy of This Drug Early-Stage Disease States In Conjunction With AR Pathway Inhibitors, PARP Inhibitors, And

Immunotherapy To Explore Synergistic Benefits in mCRPC PATIENTS. Another Radioligand Therapy, The Alpha-Particle Emitting Actinium 225 Labelled PSMA.[51]

7. Artificial intelligence in prostate cancer

The Use of Artificial Intelligence (AI) And Machine Learning (ML) Technology Has Greatly affected The Way In Which Doctors Approach The Treatment of Patients With Prostate Cancer. In Pathology, Deep Learning Algorithms Have The Capability of Analyzing Images of Sections of The Tumor That Are Stained With The Most Commonly Used Stain, Hematoxylin And Eosin With Equal If Not Batter, Precision Than A Human Pathologist, Paige Prostate And Ibex Galen Are Examples of AI Technology That Have Been Approved. On The Other Hand, In Radiology, AI Helps In The Interpretation of Results From An mpMRI Scan Using Computer-Aided Detection (CAD) Software. This Helps In Attaining Better PI-RADS Scores, Minimizes Variability And Helps Non-Expert Radiologists Achieve Expert Results. Machine Learning Algorithms Can Also Be Used For The Integration of Genomic And Clinical Data, Thus Providing Tools That Can Be Used For Forecasting Risks, Recurrence, Metastasis And Survival. Furthermore, AI Technology Helps in The Integration Of Natural Language Processing, Whereby Data Is Extracted From Electronic Health Recorders, Thus Aiding In Conducting Research.[63]

8. Current Challenges and Future Directions

Despite All These Developments, There Are Many Challenges That Need To Be Overcome If One Is To Effectively Manage Prostate Cancer. Among these Challenges Is Determining The Sequence of Therapy, Overcoming Resistance, Such As AR-V7, CDK 12, And Neuroendocrine Prostate Cancer, As Well As Creating Predictive Biomarkers For New Drugs.[64] Another Challenges Is Considering The Side Effects Of These Combination Therapies, Especially Because Most Patients With Prostate Cancer Are Older.[65] In The Future, There Are Many Issues That Need To Be Considered, Such As Using Both Germline And Somatic Genomic Testing To Determine The Best Course of Therapy, Informing Families About Inherited Risk, Using Ctdna And Liquid Biopsy As Part of Routine Monitoring, Creating CAR-T Cell Immunotherapies, Specific Antibody Immunotherapies, Which Take Advantage of The Unique Immune Landscape of Prostate Cancer, Combining PSMA-PET Scans With Targeted Radioligand Therapies, Using AI To Create Personalized Therapy Plans, Matching Patients With Trials, And Targeting Epigenetic Weaknesses, Such As EZH2 And Lsd1, Found In Neuroendocrine Prostate Cancer, Which Often Develops During Therapy.[66,67]

9. CONCLUSION

Prostate Cancer Research Is Making Rapid Progress With Emerging Discoveries And Increasing Treatment Options. New Technologies In Precision Genomics, Imaging Biomarkers, And AI Technologies Are Revolutionizing The Way Doctors Treat Prostate Cancer. New PARP Inhibitors, PSMA Targeted Radioligand Therapies, And Next-Generation AR Targeted Therapies Have Improved The Prognosis For Men With Advanced Prostate Cancer. However, for All Patients to Benefit From Emerging Research And Innovations In Prostate Cancer. However, For All Patients To Benefit From Emerging Research And Innovations In Prostate Cancer Treatment, It Is Essential To Continue Supporting Research And Providing Equal Opportunities For Healthcare.

REFERENCES

1. Sung H, Ferlay J, Siegel RL, et al. Global Cancer Statistics 2020: GLOBOCAN Estimates of Incidence and Mortality Worldwide for 36 Cancers in 185 Countries. CA Cancer J Clin, 2021; 71(3): 209-249.
2. Sweeney CJ, Chen YH, Carducci M, et al. Chemohormonal Therapy in Metastatic Hormone-Sensitive Prostate Cancer. N Engl J Med, 2015; 373(8): 737-746.
3. Haffner MC, Zwart W, Roudier MP, et al. Genomic and phenotypic heterogeneity in prostate cancer. Nat Rev Urol, 2021; 18(2): 79-92.
4. Corcoran RB, Chabner BA. Application of Cell-free DNA Analysis to Cancer Treatment. N Engl J Med, 2018; 379(18): 1754-1765.
5. Sartor O, de Bono J, Chi KN, et al. Lutetium-177-PSMA-617 for Metastatic Castration-Resistant Prostate Cancer. N Engl J Med, 2021; 385(12): 1091-1103.
6. de Bono JS, Oudard S, Ozguroglu M, et al. Prednisone plus cabazitaxel or mitoxantrone for metastatic castration-resistant prostate cancer progressing after docetaxel treatment. Lancet, 2010; 376(9747): 1147- 1154.
7. Mateo J, Chakravarty D, Dienstmann R, et al. A framework to rank genomic alterations as targets for cancer precision medicine: the ESMO Scale for Clinical Actionability of molecular Targets (ESCAT). Ann Oncol, 2018; 29(9): 1895-1902.
8. Loeb S, Bjurlin MA, Nicholson J, et al. Overdiagnosis and Overtreatment of Prostate Cancer. Eur Urol, 2014; 65(6): 1046-1055.
9. Huggins C, Hodges CV. Studies on Prostatic Cancer: I. The Effect of Castration, of Estrogen and of Androgen Injection on Serum Phosphatases in Metastatic Carcinoma of the Prostate. Cancer Res, 1941; 1: 293-297.
10. Ryan CJ, Smith MR, de Bono JS, et al. Abiraterone in Metastatic Prostate Cancer without Previous Chemotherapy. N Engl J Med, 2013; 368(2): 138-148.
11. Litwin MS, Tan H. The Diagnosis and Treatment of Prostate Cancer: A Review. JAMA, 2017; 317(24): 2532-2542.
12. Center MM, Jemal A, Lortet-Tieulent J, et al. International variation in prostate cancer incidence and mortality rates. Eur Urol, 2012; 61(6): 1079-1092.
13. Rebbeck TR. Prostate Cancer Genetics: Variation by Race, Ethnicity, and Geography. Semin Radiat Oncol, 2017; 27(1): 3-10.
14. Castro E, Goh C, Olmos D, et al. Germline BRCA Mutations Are Associated With Higher Risk of Nodal Involvement, Distant Metastasis, and Poor Survival Outcomes in Prostate Cancer. J Clin Oncol, 2013; 31(14): 1748-1757.
15. Discacciati A, Wolk A. Lifestyle and Dietary Factors in Prostate Cancer Prevention. Recent Results Cancer Res, 2014; 202: 27-37.
16. Sfanos KS, Isaacs WB, De Marzo AM. Infections and inflammation in prostate cancer. Am J Clin Exp Urol, 2013; 1(1): 3-11.
17. Knudsen KE, Scher HI. Starving the addiction: new opportunities for durable suppression of AR signaling in prostate cancer. Clin Cancer Res, 2009; 15(15): 4792-4798.
18. Watson PA, Arora VK, Sawyers CL. Emerging mechanisms of resistance to androgen receptor inhibitors in prostate cancer. Nat Rev Cancer, 2015; 15(12): 701-711.
19. Dehm SM, Tindall DJ. Alternatively spliced androgen receptor variants. Endocr Relat Cancer, 2011; 18(5): R183-

R196.

20. Antonarakis ES, Lu C, Wang H, et al. AR-V7 and Resistance to Enzalutamide and Abiraterone in Prostate Cancer. N Engl J Med, 2014; 371(11): 1028-1038.
21. Xie N, Cheng H, Lin D, et al. The expression of glucocorticoid receptor is negatively regulated by active androgen receptor signaling in prostate tumors. Int J Cancer, 2015; 136(4): E27-38.
22. Cancer Genome Atlas Research Network. The Molecular Taxonomy of Primary Prostate Cancer. Cell, 2015; 163(4): 1011-1025.
23. Tomlins SA, Rhodes DR, Perner S, et al. Recurrent fusion of TMPRSS2 and ETS transcription factor genes in prostate cancer. Science, 2005; 310(5748): 644-648.
24. Robinson D, Van Allen EM, Wu YM, et al. Integrative Clinical Genomics of Advanced Prostate Cancer. Cell, 2015; 161(5): 1215-1228.
25. Pritchard CC, Mateo J, Walsh MF, et al. Inherited DNA-Repair Gene Mutations in Men with Metastatic Prostate Cancer. N Engl J Med, 2016; 375(5): 443-453.
26. Sfanos KS, De Marzo AM. Prostate cancer and inflammation: the evidence. Histopathology, 2012; 60(1): 199- 215.
27. Boudadi K, Antonarakis ES. Resistance to Novel Antiandrogen Therapies. Clin Med Insights Oncol, 2016; 10(S1): 1-9.
28. Jiao S, Xia W, Yamaguchi H, et al. PARP Inhibitor Upregulates PD-L1 Expression and Enhances Cancer-Associated Immunosuppression. Clin Cancer Res, 2017; 23(14): 3711-3720.
29. Tran B, Horvath L, Dorff TB, et al. Bispecific T-cell engager targeting PSMA for the treatment of metastatic castration-resistant prostate cancer. Expert Opin Investig Drugs, 2021; 30(4): 295-307.
30. Schweizer MT, Ha G, Gulati R, et al. CDK12-Mutated Prostate Cancer: Clinical Outcomes With Standard Therapies and Immune Checkpoint Blockade. JCO Precis Oncol, 2020; 4: PP.382-392.
31. Catalona WJ, Partin AW, Sanda MG, et al. A multicenter study of [-2]pro-prostate specific antigen combined with prostate specific antigen and free prostate specific antigen for prostate cancer detection in the 2.0 to 10.0 ng/ml prostate specific antigen range. J Urol, 2011; 185(5): 1650-1655.
32. Thompson IM, Ankerst DP, Chi C, et al. Assessing prostate cancer risk: results from the Prostate Cancer Prevention Trial. J Natl Cancer Inst, 2006; 98(8): 529-534.
33. Turkbey B, Rosenkrantz AB, Haider MA, et al. Prostate Imaging Reporting and Data System Version 2.1: 2019 Update of Prostate Imaging Reporting and Data System Version 2. Eur Urol, 2019; 76(3): 340-351.
34. Kasivisvanathan V, Rannikko AS, Borghi M, et al. MRI-Targeted or Standard Biopsy for Prostate-Cancer Diagnosis. N Engl J Med, 2018; 378(19): 1767-1777.
35. Hofman MS, Lawrentschuk N, Francis RJ, et al. Prostate-specific membrane antigen PET-CT in patients with high-risk prostate cancer before curative-intent surgery or radiotherapy (proPSMA): a prospective, randomised, multicentre study. Lancet, 2020; 395(10231): 1208-1216.
36. Morris MJ, Rowe SP, Gorin MA, et al. Diagnostic Performance of 18F-DCFPyL-PET/CT in Men with Biochemically Recurrent Prostate Cancer: Results from the CONDOR Phase III, Multicenter Study. Clin Cancer Res, 2021; 27(13): 3674-3682.
37. Fendler WP, Calais J, Eiber M, et al. Assessment of 68Ga-PSMA-11 PET Accuracy in Localizing Recurrent Prostate Cancer: A Prospective Single-Arm Clinical Trial. JAMA Oncol, 2019; 5(6): 856-863.
38. Pantel K, Alix-Panabières C. Liquid biopsy and minimal residual disease — latest advances and implications for

cure. Nat Rev Clin Oncol, 2019; 16(7): 409-424.

39. Annala M, Vandekerkhove G, Khalaf D, et al. Circulating Tumor DNA Genomics Correlate with Resistance to Abiraterone and Enzalutamide in Prostate Cancer. Cancer Discov, 2018; 8(4): 444-457.
40. Shi M, Jiang Y, Yang L, et al. Decreased levels of serum exosomal miR-638 predict poor prognosis in prostate cancer. Cancer Biomark, 2019; 26(4): 397-403.
41. Beer TM, Armstrong AJ, Rathkopf DE, et al. Enzalutamide in Metastatic Prostate Cancer before Chemotherapy. N Engl J Med, 2014; 371(5): 424-433.
42. Fizazi K, Tran N, Fein L, et al. Abiraterone plus Prednisone in Metastatic, Castration-Sensitive Prostate Cancer. N Engl J Med, 2017; 377(4): 352-360.
43. Smith MR, Saad F, Chowdhury S, et al. Apalutamide Treatment and Metastasis-free Survival in Prostate Cancer. N Engl J Med, 2018; 378(15): 1408-1418.
44. 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): 338-351.
45. Smith MR, Hussain M, Saad F, et al. Darolutamide and Survival in Metastatic, Hormone-Sensitive Prostate Cancer. N Engl J Med, 2022; 386(12): 1132-1142.
46. de Bono J, Mateo J, Fizazi K, et al. Olaparib for Metastatic Castration-Resistant Prostate Cancer. N Engl J Med, 2020; 382(22): 2091-2102.
47. Abida W, Patnaik A, Campbell D, et al. Rucaparib in Men With Metastatic Castration-Resistant Prostate Cancer Harboring a BRCA1 or BRCA2 Gene Alteration. J Clin Oncol, 2020; 38(32): 3763-3772.
48. Clarke NW, Armstrong AJ, Thiery-Vuillemin A, et al. Abiraterone and Olaparib for Metastatic Castration-Resistant Prostate Cancer. NEJM Evid, 2022; 1(9):EVIDoa2200043.
49. Agarwal N, Azad AA, Carles J, et al. Talazoparib plus enzalutamide in men with first-line metastatic castration-resistant prostate cancer (TALAPRO-2): a randomised, placebo-controlled, phase 3 trial. Lancet, 2023; 402(10398): 291-303.
50. Hofman MS, Emmett L, Sandhu S, et al. [177Lu]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.
51. Sathekge M, Bruchertseifer F, Knoesen O, et al. 225Ac-PSMA-617 in chemotherapy-naive patients with advanced prostate cancer: a pilot study. Eur J Nucl Med Mol Imaging, 2019; 46(1): 129-138.
52. Le DT, Durham JN, Smith KN, et al. Mismatch repair deficiency predicts response of solid tumors to PD-1 blockade. Science, 2017; 357(6349): 409-413.
53. Antonarakis ES, Piulats JM, Gross-Goupil M, et al. Pembrolizumab for Treatment-Refractory Metastatic Castration-Resistant Prostate Cancer: Multicohort, Open-Label Phase II KEYNOTE-199 Study. J Clin Oncol, 2020; 38(5): 395-405.
54. Kantoff PW, Higano CS, Shore ND, et al. Sipuleucel-T Immunotherapy for Castration-Resistant Prostate Cancer. N Engl J Med, 2010; 363(5): 411-422.
55. Humeau L, Bhatt DL, Bhutani M, et al. Preclinical efficacy of the auristatin-based antibody-drug conjugate (ADC) PSMA-ADC in patient-derived prostate cancer xenografts. Mol Cancer Ther, 2021; 20(11): 2042- 2052.
56. Zhong S, Cui L, Zhang L, et al. Efficacy of CAR T-cell therapy targeting prostate-specific membrane antigen for prostate cancer. Transl Oncol, 2021; 14(1): 100905.

57. Parker C, Nilsson S, Heinrich D, et al. Alpha Emitter Radium-223 and Survival in Metastatic Prostate Cancer. N Engl J Med, 2013; 369(3): 213-223.
58. Smith M, Parker C, Saad F, et al. Addition of radium-223 to abiraterone acetate and prednisone or prednisolone in patients with castration-resistant prostate cancer and bone metastases (ERA 223): a randomised, double-blind, placebo-controlled, phase 3 trial. Lancet Oncol, 2019; 20(3): 408-419.
59. Bulten W, Kartasalo K, Chen PC, et al. Artificial intelligence assistance significantly improves Gleason grading of prostate biopsies by pathologists. Mod Pathol, 2021; 34(3): 660-671.
60. Raciti P, Sue J, Ceballos R, et al. Novel artificial intelligence system increases the detection of prostate cancer in whole slide images of core needle biopsies. Mod Pathol, 2020; 33(10): 2058-2066.
61. Schelb P, Kohl S, Radtke JP, et al. Classification of Cancer at Prostate MRI: Deep Learning versus Clinical PI-RADS Assessment. Radiology, 2019; 293(3): 607-617.
62. Spratt DE, Tang Z, Sun Y, et al. Artificial intelligence (AI) predictive models for overall survival and metastasis in prostate cancer. JCO Clin Cancer Inform, 2021; 5: 568-578.
63. Park JJH, Detry MA, Murthy S, et al. Use of Machine Learning to Analyze Administrative Claims Data to Predict Outcomes in Patients With Prostate Cancer. JCO Clin Cancer Inform, 2021; 5: 297-306.
64. Vlachostergios PJ, Puca L, Beltran H. Emerging Variants of Castration-Resistant Prostate Cancer. Curr Oncol Rep, 2017; 19(5): 32.
65. Cornford P, van den Bergh RCN, Briers E, et al. EAU-EANM-ESTRO-ESUR-SIOG Guidelines on Prostate Cancer. Part II—2020 Update: Treatment of Relapsing and Metastatic Prostate Cancer. Eur Urol, 2021; 79(2): 263-282.
66. Xu K, Wu ZJ, Groner AC, et al. EZH2 oncogenic activity in castration-resistant prostate cancer cells is Polycomb-independent. Science, 2012; 338(6113): 1465-1469.
67. Beltran H, Rickman DS, Park K, et al. Molecular Characterization of Neuroendocrine Prostate Cancer and Identification of New Drug Targets. Cancer Discov, 2011; 1(6): 487-495.