CDMRP
DEPARTMENT OF WAR
CONGRESSIONALLY DIRECTED
MEDICAL RESEARCH PROGRAMS

Prostate Cancer Research Program

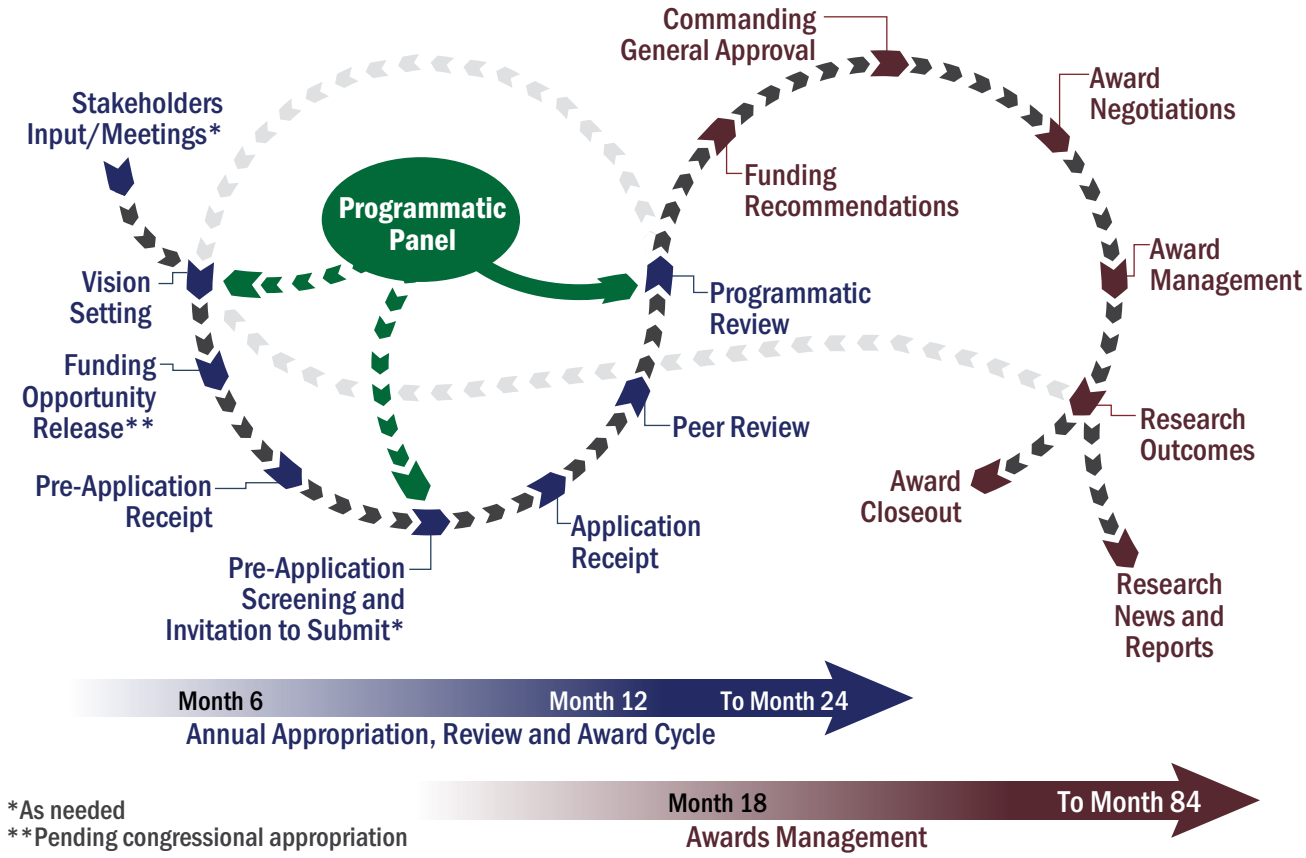
Advancing Innovative Research to Address Gaps and Impact Patients

For more information, please visit
cdmrp.health.mil/pcrp

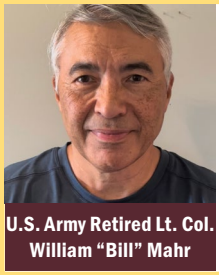
CONGRESSIONALLY DIRECTED MEDICAL RESEARCH PROGRAMS

Congress established the Congressionally Directed Medical Research Programs in response to a grassroots effort in 1992 led by the breast cancer advocacy community. That effort resulted in a congressional appropriation of funds for breast cancer research and initiated a unique partnership among the public, Congress and the military. Since then, Congress appropriated funding for additional targeted research programs. The CDMRP managed over $20.322 billion in congressional special interest funds from inception through fiscal year 2025. Congress provides general intent for each program and specifies funding as part of the annual Department of Defense appropriations bill.

The CDMRP uses a two-tier research application review process. This process involves dynamic interaction between scientists, clinicians, consumers from advocacy communities, members of the military and other specialists, as applicable. The first tier of evaluation is a scientific peer review of applications measured against established criteria determining scientific merit. The second tier is a programmatic review where applications with higher scientific or technical merit are evaluated for potential impact, adherence to the intent of the award mechanism, relevance to program goals and portfolio composition.



CDMRP Two-Tier Review Process



U.S. Army Retired Lt. Col. William "Bill" Mahr

ZERO Prostate Cancer, FY24-FY26 Programmatic Panel Member

"The PCRP provides much needed funds for innovative research not otherwise funded by the private sector. As a result, this has led to treatments that have extended and improved the quality of life of prostate cancer patients."

PROSTATE CANCER RESEARCH PROGRAM

SCOPE OF THE PROBLEM

Estimated **313,750** new diagnoses and **35,770** deaths from prostate cancer in 2025[1]

From 2017 to 2021, 70% of cases found localized; **22%** found **beyond the primary site**[2]

Available treatments can result in **urinary**, **bowel** and **sexual dysfunction**[3]

High-risk populations continue to show **increased incidence and mortality**[4]

VISION

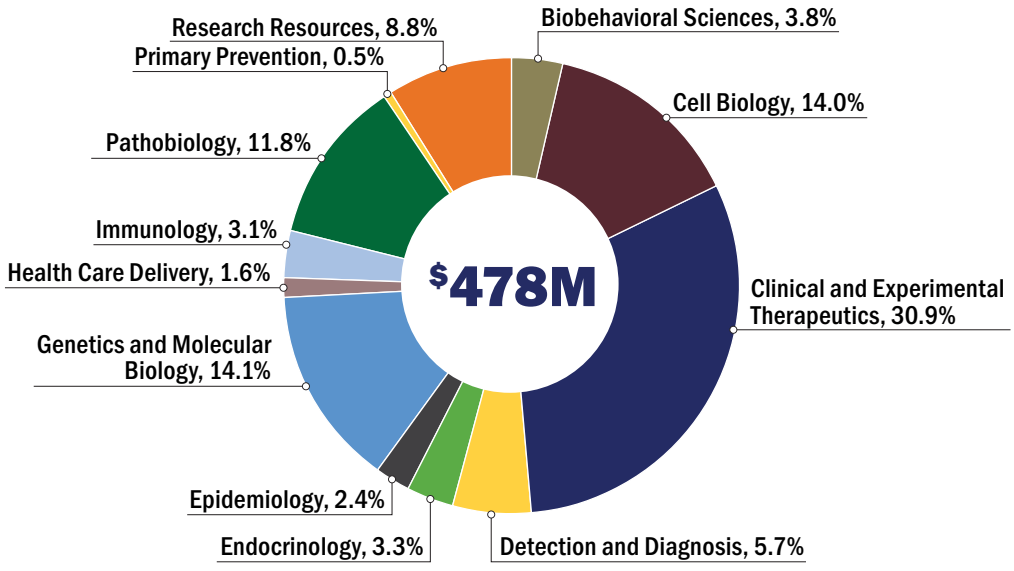
Conquer prostate cancer

MISSION

Fund research that will eliminate death and suffering from prostate cancer and enhance the well-being of Service Members and their Families, Veterans and all the patients and caregivers who are experiencing the impact of the disease

RELEVANCE TO MILITARY HEALTH

Military Health System Medical Encounters for Prostate Cancer 2014-2023[5]	Average Patients/Year	Out-Patient Encounters	Hospital Bed Days
Service Members	219	12,350	804
Other Beneficiaries	72,363	3.55M	103,358



Funding Portfolio by Scientific Classification System Code, FY20-FY24

[1] National Cancer Institute. https://seer.cancer.gov/statfacts/html/common.html.

[2] Hurwitz LM, et al. *J Natl Cancer Inst*, 113, no. 6, 2020:727-734.

[3] Al Hussein Al Awamlh B, et al. *JAMA*, 331, no. 4, 2024:302-317.

[4] Giaquinto AN, et al. *CA Cancer J Clin*, 72, no. 3, 2022:202-229.

[5] Military Health System data from the Defense Medical Surveillance System, Armed Forces Health Surveillance Division, Defense Health Agency, Silver Spring, Maryland, 2014-2023; October 2024.

OVERARCHING CHALLENGES

The PCRP defines specific overarching challenges critical to addressing the knowledge, research and clinical gaps that make prostate cancer a global health issue. To ensure that supported research will benefit patients diagnosed with lethal prostate cancer or improve quality of life for men diagnosed with this disease, all PCRP-funded projects must address at least one of the following overarching challenges listed to the right.

IMPROVE
overall health, wellness and survivorship for those impacted by prostate cancer

DEVELOP
new or improve upon existing therapies to improve outcomes for men with lethal prostate cancer

DEFINE
the biology of prostate cancer progression to lethal prostate cancer to reduce death

ENHANCE
clinical care for all patients with prostate cancer

INVESTMENT STRATEGY

The PCRP offers a variety of award mechanisms, all of which work together to address the overarching challenges and advance the mission of the PCRP. The PCRP supports research in the following areas:

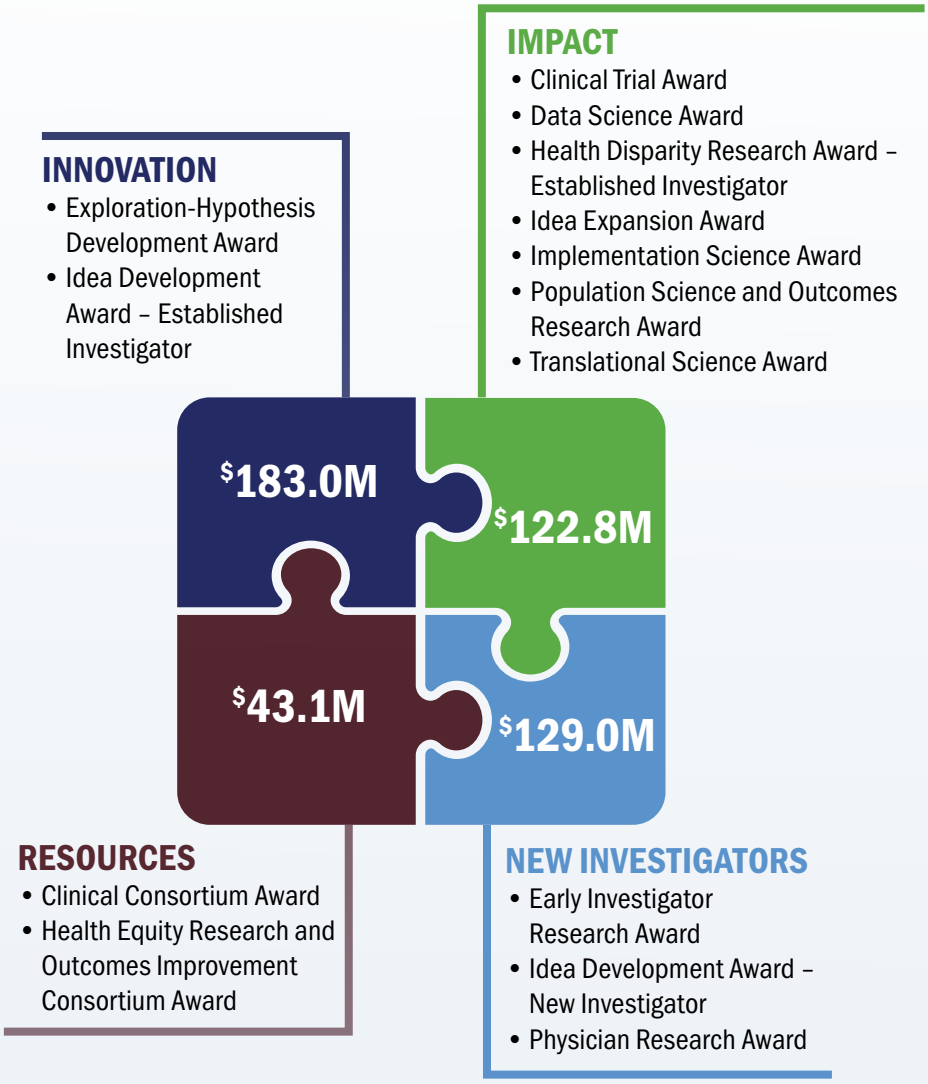
INNOVATION: Novel and potentially high-risk approaches to answer important research questions that could provide significant impact for the field and for patients

IMPACT: Research with a high potential to make a significant impact for prostate cancer patients in the near future

NEW INVESTIGATORS: Support for new prostate cancer research investigators who will become leaders in the field

RESOURCES: Infrastructure support that brings together renowned scientific, clinical and institutional resources to facilitate the translation of findings from bench to bedside

FY20-FY24 Investment



THE PROSTATE CANCER CLINICAL TRIALS CONSORTIUM

In fiscal year 2005, the PCRP funded the multi-institutional Prostate Cancer Clinical Trials Consortium to accelerate clinical testing of novel therapies that would lead to improved standards of care. The PCCTC facilitates rapid patient recruitment and trial completion and also fosters the co-development of new clinical trials and projects between investigators, research sites and industry partners, all of which contribute to impactful prostate cancer clinical research developments. To date, the PCCTC contributed to U.S. Food and Drug Administration approvals of 12 therapies for prostate cancer.

12 Therapies Approved by FDA		
177Lu-PSMA-617; Pluvicto®	Darolutamide; Nubeqa®	Olaparib; Lynparza®
Abiraterone acetate; Zytiga®, Yonsa®	Degarelix; Firmagon®	Rucaparib; Rubraca®
Apalutamide; Erleada®	Enzalutamide; Xtandi®	Sipuleucel-T; Provenge®
Cabazitaxel; Jevtana®	Niraparib; Zejula®	Talazoparib; Talzenna®

RESEARCH HIGHLIGHTS

Overarching Challenge

DEFINE BIOLOGY OF LETHAL DISEASE

Noah Warfel, Ph.D., The University of Arizona

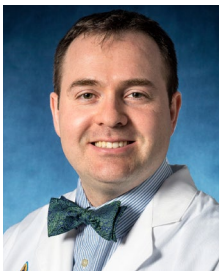
NEW INVESTIGATOR

Defining the Role of PIM Kinases in Hypoxia-Induced Invasion and Metastasis

To help develop therapeutic strategies for metastatic prostate cancer and particularly hard to treat bone-metastatic prostate cancer, this project aims to understand the role that hypoxia, or low oxygen concentration, plays in prostate cancer metastasis and developing resistance to chemotherapies. These studies identified a molecular pathway by which hypoxia enables the protein Proviral Integration site for Moloney murine leukemia virus 1 kinase, or PIM1, to regulate the cellular structure and promote cellular migration. Further, PIM1 activity promotes migration through a layer of smooth muscle tissue, a first step necessary before eventual metastasis to other organs, including bone. Future work investigates potential therapeutics targeting PIM kinases as a strategy to treat bone-metastatic prostate cancer.

Overarching Challenge

DEVELOP TREATMENTS FOR LETHAL DISEASE



Eugene Shenderov, M.D., D.Phil., Johns Hopkins University School of Medicine

NEW INVESTIGATOR

Understanding Antitumor T Cell Immunity in High-Risk Localized Prostate Cancer After Neoadjuvant Treatment With an Antibody Targeting B7-H3

Enoblituzumab is a therapeutic antibody candidate with antibody-dependent cellular cytotoxicity under investigation for treating high-risk localized prostate cancer. To better understand the mechanisms of action of the drug, this study examined prostate tissue samples, collected as part of a phase 2 clinical trial funded by other sources, from patients before and after treatment with enoblituzumab. Findings suggested that enoblituzumab treatment increases tumor-specific inflammation and promotes T cell recruitment, a promising result that shows a biological response to immunotherapy. Researchers also identified exploratory candidate biomarkers for treatment response and prognosis to assess in larger-scale clinical trials.

Utilizing B7-H3 Targeted Therapeutics to Prevent Lethal Prostate Cancer: The Help Elucidate & Attack Longitudinally, or HEAT, Prostate Cancer Trial Cohort

This randomized phase two study continues previous investigation of enoblituzumab for high risk localized prostate cancer, examining patient samples alongside a clinical trial. Based on previous results, investigators examined whether enoblituzumab treatment prevented recurrence following prostatectomy and whether the previously identified biomarkers differentiated responders from non-responders to treatment. This clinical trial is ongoing, with results pending trial completion. Parallel biological studies suggest enoblituzumab's target, B7-H3, remains broadly expressed by prostate cancer cells from initial diagnosis through metastasis, making B7-H3 a promising cell surface molecule for targeted prostate cancer treatment.

Sean Collins, M.D., Ph.D.

University of South Florida, FY19-FY26 Programmatic Panel Member, FY25-FY26 Chair

"For over twenty years, the PCRP has supported military Veterans and the general public with prostate cancer by creating a partnership between the government, scientific community, advocates and patients to address the most relevant and current unmet needs. The PCRP supports innovative, high-impact research with the potential for clinical translation that might not otherwise be addressed by alternative funding mechanisms. Finally, the PCRP has initiated funding mechanisms to develop new visionary prostate cancer investigators and reward multi-institution team science leading to rapid improvements in prostate cancer care for all."

DEVELOP TREATMENTS FOR LETHAL DISEASE cont.

Ana Aparicio, M.D., The University of Texas MD Anderson Cancer Center

Chemoimmunotherapy for Aggressive Variant Prostate Cancers, or AVPCs

Aggressive variant prostate cancers require more intense treatment strategies compared to other, more common prostate cancers that respond to hormone blocking therapies. This clinical trial evaluated the addition of cetrelimab to intravenous chemotherapy and post-chemotherapy maintenance with niraparib for AVPCs. Cetrelimab is a drug that activates T cells, the type of immune cells that attack cancer cells, and niraparib is an oral DNA damaging agent. The results of this trial showed that the addition of cetrelimab improved progression-free and overall survival compared to maintenance therapy with niraparib alone. Investigators continue to analyze patient samples for biomarkers that will help identify patients who may benefit most from this treatment strategy.

Robert Flavell, M.D., Ph.D., University of California, San Francisco

Development of Radiopharmaceutical Therapy Targeting CD46 for Treatment of Metastatic Prostate Cancer

To develop a combined therapeutic and imaging strategy targeting metastatic prostate cancer, this study combined an antibody targeting CD46, a cell surface protein expressed by advanced metastatic cancer cells, with zirconium-89 or actinium-225 for imaging or radiation therapy, respectively. Preclinical findings confirmed that the combinations targeted prostate tumor cells and allowed detection of the tumors via PET scanning. Additionally, radiation therapy demonstrated antitumor activity in both cellular and preclinical models of prostate cancer. Further, studies with a novel radioimmunoconjugate with improved chelator and linker chemistry suggest enhanced efficacy. Future studies will assess the safety profiles and dosing requirements for clinical translation of this targeted radiopharmaceutical therapy.

Saul Priceman, Ph.D., University of Southern California

Combining CAR-T Cells With Blockade of Tumor-Induced Immunosuppression to Target Metastatic Prostate Cancer

Advances in CAR-T cell therapies for other cancers prove limited in activity against prostate cancer. This study will assess a new CAR-T cell targeting prostate stem-cell antigen, a cellular target for both primary and metastatic prostate cancers, in a preclinical model that mimics the human immune response, including how immune cells interact, or fail to interact, in the local tumor environment. While preclinical studies continue and phase 1 trial data emerges, results found that improving the therapeutic potential of CAR-T cells requires manipulation of local immune cells, including blocking programmed death ligand-1 and/or elevating interferon gamma signaling. Findings in preclinical systems suggest effective antitumor activity through engineering CAR-T cells with molecules that dynamically remodel the local tumor environment.

RESEARCH HIGHLIGHTS cont.

Overarching Challenge

DEVELOP TREATMENTS FOR LETHAL DISEASE cont.

Zhenbang Chen, Ph.D., Meharry Medical College

Novel Mechanism and Targeting of Neuroendocrine Prostate Cancer

Following initial treatment with androgen deprivation therapy, many patients develop castration-resistant or therapy-induced neuroendocrine prostate cancer, which resists traditional therapeutics and presents with modified gene expression compared to localized prostate cancer. This study evaluated how a family of gene expression regulators, KDM5, contributes to initiation and progression of castration-resistant prostate cancer. Results in cell models demonstrated that inhibiting KDM5 stopped cancer cell growth. Additionally, combining KDM5 inhibition with another cell cycle regulation inhibitor prevented cells from activating an alternative pathway and further reduced cancer cell growth and migration, suggesting a potential new therapeutic strategy for castration-resistant or therapy-induced neuroendocrine prostate cancer.

Mengdie Wang, Ph.D., University of Massachusetts Chan Medical School

NEW INVESTIGATOR

Targeted Inhibition of Neuropilin-2 to Enhance Immunotherapy of Lethal Prostate Cancer

Neuroendocrine prostate cancer typically evolves after treatment of other, earlier forms of prostate cancer, during which the cancer cells undergo genetic changes that increase their ability to grow, spread and resist additional therapies. This project evaluated how one particular growth factor receptor, neuropilin-2, contributes to the aggressive characteristics of neuroendocrine prostate cancer. Findings in a preclinical model revealed that blocking NRP2 with a monoclonal antibody reduced tumor growth and the ability of tumor cells to evade immune cells, sensitizing the tumor cells to a natural antitumor immune response. These results set the stage for clinical translation of an anti-NRP2 antibody as a new immunotherapy for neuroendocrine prostate cancer.

RESEARCH RESOURCES

THE PROSTATE CANCER BIOREPOSITORY NETWORK

In fiscal year 2009, the PCRP launched the Prostate Cancer Biorepository Network to provide high-quality, well-annotated human prostate cancer biospecimens, including cancer tissue from primary tumors and metastatic sites as well as other patient samples such as blood, to the prostate cancer research community. The PCBN comprises a collaborative network of leading research institutions that develop optimized processes and policies to collect and distribute high-quality prostate cancer biospecimens in a systematic, reproducible fashion.

Overarching Challenge

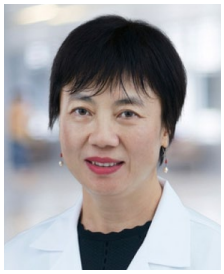
IMPROVE OVERALL HEALTH, WELLNESS AND SURVIVORSHIP

Zachary Klaassen, M.D., Augusta University

NEW INVESTIGATOR

Implications of Mental Health Illness on Outcomes of Prostate Cancer Patients in the Veterans Affairs Medical System

Many Veterans will seek care for both mental health illness and prostate cancer through the Veterans Health Administration. This project investigated the role that mental health illness plays, if any, in Veterans receiving care for prostate cancer. The investigators determined that Veterans with mental health illness are 20% less likely to receive a diagnosis of prostate cancer but twice as likely to have an aggressive form of prostate cancer compared to Veterans without a mental health illness. Further, Veterans with mental health illness initiated treatment more often but failed to adhere to follow-up appointments, and therefore maintained higher risk of recurrence, compared to Veterans without a mental health illness. These findings provide an opportunity for tailoring interventions and treatment plans to improve health care for Veterans with prostate cancer.



Lixin Song, Ph.D., R.N., F.A.A.N., The University of Texas Health Science Center at San Antonio

Developing and Pilot Testing the Support Communication and Information Program for Prostate Cancer – Interactive, or SCIPI

To better support patients throughout all stages of their health care experience for localized prostate cancer, including before, during and after treatment, researchers developed a comprehensive and personalized digital support program for patients, caregivers and providers. The SCIPI platform provides easy-to-understand educational content to help decision making regarding care, improves communication with providers, and offers professional and peer support via online communication and forums. Stakeholder feedback during development helps to improve how easy SCIPI is to use and access, which will improve quality of life for patients during its pilot evaluation.

THE NORTH CAROLINA-LOUISIANA PROSTATE CANCER PROJECT

In fiscal year 2002, the PCRP launched the North Carolina-Louisiana Prostate Cancer Project, or PCaP, led by James Mohler, M.D., at Roswell Park and Jeannette Bensen, Ph.D., at the University of North Carolina Chapel Hill. The PCaP represents the largest population-based study of newly diagnosed prostate cancer in African American and Caucasian American men ever conducted, with 2,258 participants. In men younger than 65 years of age, African Americans experience prostate cancer mortality at 3.1 times the rate of Caucasian Americans. In men older than 65 years of age, African Americans experience prostate cancer mortality at 2.3 times the rate of Caucasian Americans.

IN THE CLINICAL PIPELINE

Agent/Technique	Description
To Patients	
AR-V7 mRNA assay	A clinically validated noninvasive assay to detect AR-V7 mRNA in circulating tumor cells in the blood.
Oncotype DX® AR-V7 Nucleus Detect™ test	A liquid biopsy assay that measures AR-V7 levels in the nucleus of tumor cells circulating in the blood helps predict whether a patient's prostate cancer will respond to taxane-based chemotherapy or androgen receptor signaling inhibitors.
NuSAP1 marker, part of the Prolaris® and Decipher® assays	A prognostic marker for recurrent prostate cancer tumors, NuSAP1, is part of the Prolaris and Decipher gene expression tool validated in several clinical contexts.
MRI-based treatment planning for radiotherapy	An MRI-based treatment planning protocol for intensity-modulated radiation therapy, specifically targeting prostate tumor tissue and avoiding damaging normal tissues.
Quantitative Total Bone Imaging software, QTBI	QTBI software automatically identifies and contours tracer updates in bone for full or partial body imaging scans to evaluate changes in tumor metastases, including response to treatment.
Elekta Synergy®	A cone-beam computed tomography imaging system for delivering high doses of radiation to the tumor while minimizing damage to adjacent normal tissues.
Velcade®, bortezomib, PS-341	The PCRP supported preclinical studies on PS-341, a protein degradation inhibitor. The FDA approved bortezomib for the treatment of multiple myeloma and relapsed mantle cell lymphoma.
Erleada®, apalutamide	A next-generation androgen receptor signaling inhibitor for treating metastatic castration-sensitive prostate cancer and non-metastatic castration-resistant prostate cancer.
Zytiga®, abiraterone acetate	An anti-androgen treatment for metastatic castration-resistant prostate cancer expanded for treatment of metastatic castration-sensitive prostate cancer.
Xtandi®, enzalutamide	An anti-androgen treatment for metastatic castration-resistant prostate cancer expanded for treatment of non-metastatic castration-resistant prostate cancer and metastatic castration-sensitive prostate cancer.
Xgeva®, denosumab	An antibody treatment that prevents skeletal-related events in patients with bone metastases and slows disease progression.
Xofigo®, radium-223	Approved for treating castration-resistant prostate cancer with symptomatic bone metastases. A phase 3 study is evaluating radium-223 plus docetaxel chemotherapy.
Jevtana®, cabazitaxel	A chemotherapy treatment used in combination with prednisone for patients with metastatic castration-resistant prostate cancer previously treated with docetaxel.
18-Fluorine-DCFPyL and 68-Gallium PSMA-11	Two positron emission tomography imaging agents, initially developed as fluorine-18-DCFBC, targeting prostate-specific membrane antigen.
Phase 3	
Ipilimumab	A monoclonal antibody that enhances response to androgen deprivation therapy for treating metastatic prostate cancer in patients who did not receive chemotherapy.
Phase 2/3	
Gallium-68-RM2	A positron emission tomography imaging agent for detecting recurrent cancer lesions when used in combination with conventional MRI.
Phase 2	
Durvalumab plus olaparib	Combining a DNA damage repair inhibitor, olaparib, and an immunotherapy, durvalumab, for treating metastatic castration-resistant prostate cancer.
Phase 1/2	
Nivolumab and ipilimumab	Evaluation of biomarkers, dosing and side effects of combining immunotherapies nivolumab and ipilimumab followed by nivolumab monotherapy in patients with metastatic castration-resistant prostate cancer with CDK12 mutations.
Iodine-124-anti-PSCA A11 minibody	An antibody fragment, or minibody, targeting prostate stem cell antigen combined with iodine-124 for positron emission tomography imaging.
MRI-guided robotic needle placement device	An MRI-guided robotic device for improved biopsy needle and radiation therapy placement.

Agent/Technique	Description
Phase 1/2	
Fluorine-18-fluorocholine	A positron emission tomography imaging agent for combined PET and computed tomography imaging for localizing resistant tumors in advanced prostate cancer.
Restriction spectrum imaging-MRI	A noninvasive MRI technique for detecting and distinguishing aggressive from slow-growing prostate cancer as well as for measuring tumor response to radiotherapy, including metastases.
3βHSD1 mutation	A genetic mutation in the 3βHSD gene as a predictive biomarker of resistance to androgen deprivation therapy and response to other therapies, such as apalutamide.
Venclexta®, venetoclax plus enzalutamide	Combining venetoclax, a chemotherapeutic approved for treating certain types of leukemia and lymphoma, with enzalutamide to prevent enzalutamide resistance.
Indomethacin plus enzalutamide	Combining indomethacin and enzalutamide for patients with progressive castration-resistance prostate cancer following abiraterone treatment.
(R)-9bMS	An inhibitor of the androgen receptor pathway for patients with metastatic castration-resistant prostate cancer.
Bavdegalutamide, ARV-110	An androgen receptor-targeting protein degrader for patients with metastatic castration-resistant prostate cancer who previously received two therapies.
Mifepristone plus enzalutamide	Combining mifepristone, a glucocorticoid receptor, with enzalutamide to overcome androgen-deprivation therapy resistance in patients with castration-resistant prostate cancer.
3,3'-diindolylmethane	A compound found in cruciferous vegetables, such as broccoli and cabbage, that acts as an anti-androgen, suppresses AR-V7 expression and slows the growth of prostate cancer cells.
BP-GMAX-CD1	A vaccine that combines an immune-activating agent, AP1903, and the ARGENT™ cell-signaling regulation technology for patients with advanced, androgen-independent prostate cancer.
pTVG-HP	A vaccine against prostatic acid phosphatase, a protein specific to prostate cancer cells, for use in combination with immunotherapy for patients with either early- or late-stage prostate cancer.
MEDI6383	An engineered immunotherapy for patients with recurrent or metastatic prostate cancer.
Mipsagargin	An engineered chemotherapy targeting a plant-derived toxin to prostate-specific membrane antigen for patients with localized, high-risk prostate cancer prior to prostatectomy.
ZEN003694 and enzalutamide	Combining ZEN003694, which targets genetic activation of an androgen receptor mutation, and enzalutamide for patients with metastatic castration-resistant prostate cancer.
Gamitrinib	A first-in-class mitochondrial-targeted inhibitor for patients with advanced and metastatic prostate cancer.
Phenelzine sulfate	A neurotransmitter inhibitor, previously approved for the treatment of depression, for patients with biochemical recurrent castrate-sensitive prostate cancer.
Entinostat, MS-275, plus isotretinoin	Combining entinostat, a DNA modification inhibitor, with isotretinoin, previously approved for the treatment of severe acne, for prostate or other cancers.
JNJ-64041809, ADU-741	A listeria-based vaccine targeting three prostate cancer antigens for patients with advanced or metastatic castration-resistant prostate cancer.
SM7L adoptive cell therapy	A cell-based treatment using engineered T cells, a type of immune cell, expressing SM7L, a “cancer suicide” molecule based on an immune signaling protein, that specifically target prostate cancer tumor cells, accompanied by a bioengineered tracking system to monitor the T cells and therapeutic response.
Lutetium-177-J591 plus ketoconazole	An antibody-drug conjugate comprised of J591, an antibody targeting prostate membrane-specific antigen, and lutetium-177, which targets radiation to tumor cells, combined with ketoconazole, an approved antifungal treatment, in patients with high-risk castrate biochemically relapsed prostate cancer. The PCRP supported a phase 2 clinical trial, NCT00859781.
Adenoviral PSA Vaccine	A vaccine-based treatment using engineered adenovirus expressing prostate-specific antigen for patients with recurrent prostate cancer or prostate cancer that no longer responds to hormone therapy. The PCRP supported phase 2 clinical trials, NCT00583752 and NCT00583024.

For more information, please visit
https://cdmrp.health.mil
or contact us at:
dha.detrick.rd-mrdc-cdmrp.mbx.public-affairs@health.mil

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