Prostate Cancer Academy 2016: Presentation Summaries

[Rev Urol. 2016;18(4):205-213 doi:10.3909/riuPCA2016]

© 2016 MedReviews®, LLC

KEY WORDS

Prostate cancer • Screening • Biomarkers • Robotic prostatectomy • Androgen deprivation therapy • Immunotherapy • Intensity-modulated radiation therapy

Prostate Cancer Academy convened September 16-18, 2016, in Denver, Colorado. The conference presented, discussed, and debated all available preventative, diagnostic, therapeutic, and management options for prostate cancer in a highly interactive format. This program included didactic lectures, case-based discussions, and faculty panels.

Prostate Cancer Screening: Biomarkers

Presented by E. David Crawford, MD

Many challenges exist for the clinician to detect prostate cancer. How can we improve the interpretation of prostate-specific antigen (PSA) levels and increase the likelihood of an initial positive biopsy result, thus allowing our primary care colleagues to enhance referral efficiency for urology evaluation? Are tests available that will decrease unnecessary negative rebiopsies and enhance prostate cancer detection? Are tests available that will enhance risk stratification of patients with newly diagnosed prostate cancer? A first PSA threshold of 1.5 to 4.0 ng/mL represents the early warning PSA zone. Patients with a PSA level $>$ 1.5 ng/mL have an increased risk of developing prostate cancer and/or prostate enlargement. Using this cutoff, 70% of men require no discussion regarding prostate cancer when seen by their primary care physician or urologist.

Several tests were discussed that help identify which patients should be biopsied. These are shown in Table 1.

The goal of these biomarkers is to help improve the diagnosis of prostate cancer. Clinicians can start screening earlier and screen less frequently in patients who have low PSA levels. In doing so, they can focus on specific higher-risk populations. The urologist's goal should be to screen for high-risk prostate cancer and not overtreat low-risk disease. As such, we should embrace active surveillance and encourage our primary care physicians to refer early and wisely. An algorithm for the urologist and family practitioner is shown in Figure 1.

Molecular Markers: Repeat Biopsy and Risk Stratification

Presented David M. Albala, MD

Biomarkers have been used to assess risk in patients with newly diagnosed and recently surgically treated prostate cancer. Digital rectal examination,

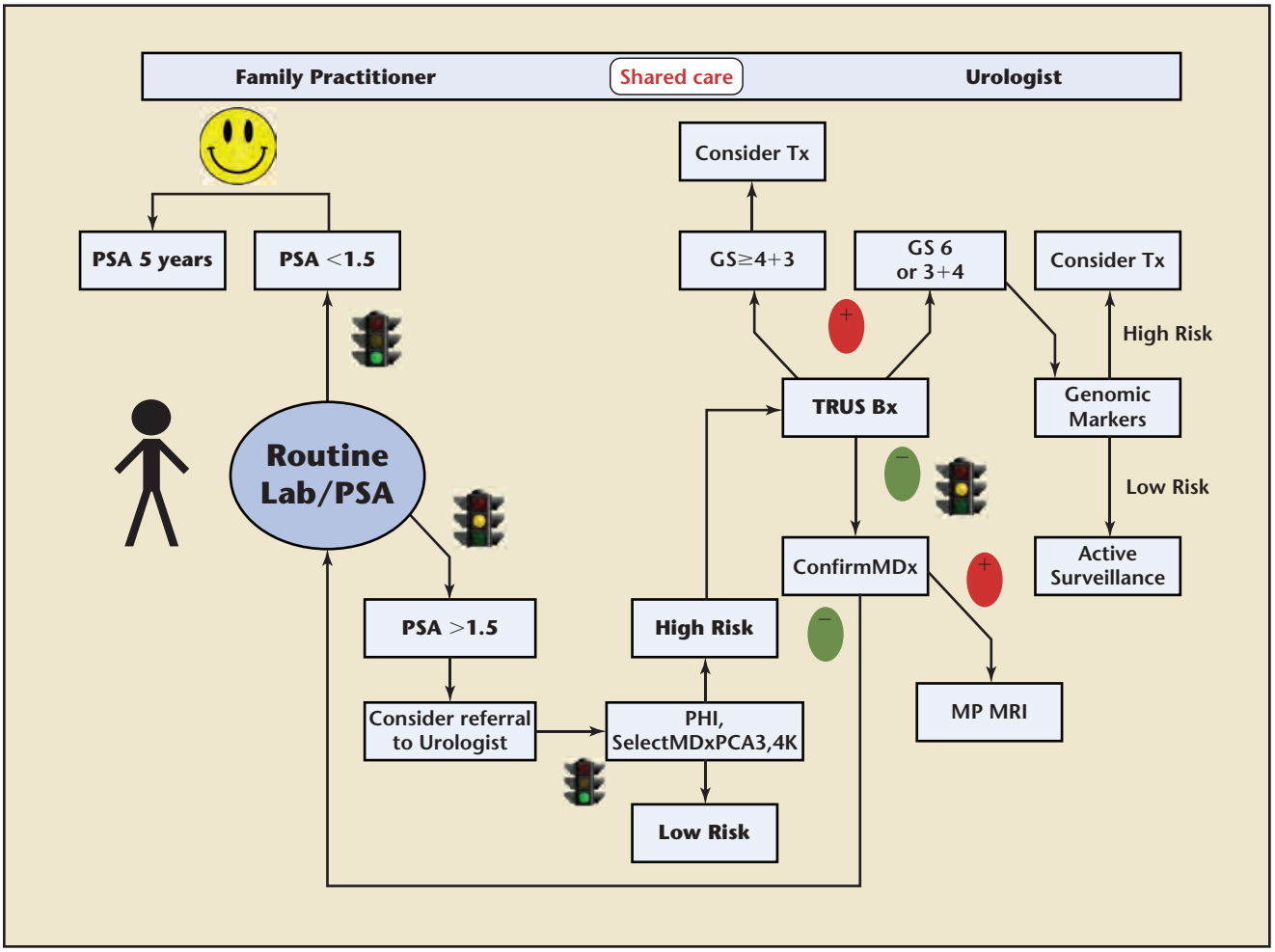


Figure 1. A referral algorithm for the urologist and family practitioner. PSA, prostate-specific antigen; GS, Gleason score; mpMRI, multiparametric magnetic resonance imaging; TRUS, transrectal ultrasonography.

TABLE 1

Identification of Patients to Biopsy

Assay Characteristics	phi	4Kscore	PROGENSA PCA3	SelectMDx for Prostate Cancer
Company	Beckman Coulter	Opko	Hologic	MDxHealth
Specimen	Blood	Blood	Urine	Urine
Methodology	Immuno assay	Immuno assay	qPCR	qPCR
	3 protein biomarkers	4 kallikriens biomarkers	mRNA test, 1 biomarker	2 mRNA biomarkers
	tPSA and fPSA, proPSA	PSA, fPSA, Intact PSA, HK-2	PCA3	DLX1, HOXC6
Regulatory	FDA/CE	LDT/CLIA/CE	FDA/CE	LDT/CLIA/CE
List price ($)	$499	$1900	$500	$500
Assay performance (AUC)	AUC 0.73	AUC 0.82	AUC 0.68	AUC 0.89
Comments	Requires phlebotomist	Requires phlebotomist & centrifuge	Urine sample—in-office procedure	Urine sample—in-office procedure

PSA measurement, Gleason score, and clinical stage have an 80% predictive diagnostic accuracy for prognosis. As such, this has led to a problem of overdiagnosis and overtreatment and the main reason the US Preventive Services Task Force recommended against prostate cancer screening. In 2016, biomarkers have begun to play a more critical role in better assessing tumor characteristics. This can be done initially after a positive biopsy result or after a prostatectomy. The currently available tests are shown in Table 2.

Oncotype Dx® (Genomic Health, Redwood City, CA) is a 17-gene assay that provides information on favorable and unfavorable pathology in men with clinically low-risk prostate cancer. Prolaris® (Myriad Genetics, Salt Lake City, UT), which assesses cell cycle progression with 46 genes, provides information on prostate cancer-specific mortality before prostatectomy and biochemical recurrence after prostatectomy. ProMark® (Metamark Genetics, Waltham, MA) is an eight-protein signature that predicts prostate cancer aggressiveness. Decipher® (GenomeDx Biosciences, San Diego, CA) is a 22-gene assay that predicts high-grade disease, 5-year metastasis, and 10-year prostate cancer-specific mortality in both the pre- and postprostatectomy environments. Each of these tests has been validated and has also had clinical utility studies done showing their value in changing treatment decisions.

These risk stratification tests may determine if patients receive active surveillance or definitive treatment in the biopsy space, and whether they may benefit from radiotherapy or systemic therapy after prostatectomy. Disease management will become more precise and efficient, leading to more cost-effective treatment choices for patients and physicians alike. The ideal biomarker is easily obtained, accurately stratifies risk by meaningful endpoints, and provides independent and actionable information.

TABLE 2

New Ways to Assess Prostate Cancer

	Test	Company	Price	Available	Sample	Measures
Screening Reduce the number of unnecessary (negative) biopsies spurred by elevated PSA levels.	Prostate Health Index	Beckman Coulter (Danaher)	N/A	2013	Blood	Variants of PSA
	4Kscore	Opko Health	N/A	2013	Blood	Variants of PSA and a related compound
	Prostarix	Metabolon	N/A	2013	Urine[1]	Sarcosine and other chemicals associated with cancer
After a positive biopsy Distinguish aggressive cancers that need treatment from non-aggressive ones that do not.	Prolaris	Myriad Genetics	$3400	2012	Biopsy	Gene activity pattern
	Genomic Prostate Score	Genomic Health	N/A	2013	Biopsy	Gene activity pattern
	ProstaVysion	Bostwick Laboratories	$1100	2011	Biopsy	Two genetic markers associated with progression
	Metamark Biopsy Test	Metamark Genetics	N/A	2013	Biopsy	Marker proteins
After a negative biopsy If PSA levels stay high despite a negative biopsy, is a repeat biopsy needed?	Progensa PCA3	Gen-Probe (Hologic)	S440	2012	Urine	Expression of PCA3 gene
	Prostate Core Mitomic Test	Mitomics	N/A	2011	Biopsy	Deletions of mitochondrial DNA that would occur if a tumor is nearby
	ConfirmMDx	MDxHealth	$2500	2012	Biopsy	Methylation (silencing) of three genes that would occur if a tumor is nearby
After surgery Is additional treatment necessary if pathology shows risk after surgery?	Decipher	GenomeDx Biosciences	N/A	2013	Tissue removed	Gene activity pattern

The New York Times, March 26, 2013.
PSA, prostate-specific antigen.

The Role of Magnetic Resonance Imaging in Prostate Biopsy: Who and How to Biopsy?

Presented by
James S. Wysocki, MD

Multiparametric magnetic resonance imaging (mpMRI) is being used more frequently by urologists around the country to help identify patients with prostate cancer. Transrectal ultrasound-guided prostate biopsy is currently the standard of care in the United States, with a 37% detection rate when 10 to 12 cores are taken, and a 41% detection rate when 18 to 24 cores are taken. Nearly 30% of clinically significant tumors are missed on the first biopsy and 40% of core specimens underestimate the true Gleason score. mpMRI has emerged as an important risk stratification tool in detecting prostate cancer, with a specificity and sensitivity of 0.88 and 0.74, respectively. Magnetic resonance imaging (MRI) of the prostate will increase the detection of clinically significant disease and decrease the incidental detection of insignificant/indolent disease. MRI of the prostate is indicated in patients with a negative biopsy result, as it assesses regions often missed on systemic biopsy, including the anterior/transition zone, the anterior lateral horn of the peripheral zone, the extreme apex, and the midline. In addition, it can improve risk stratification for active surveillance by improving disease characterization and decreasing undergrading. The European Society of Urogenital Radiology recommends the following MRI guidelines:

1. Anatomic T2-weighted images
2. Plus two functional techniques
   a. Diffusion-weighted imaging
   b. Dynamic contrast enhanced imaging
   c. Optional MRI spectroscopy

Targeted biopsies diagnosed 30% more Gleason ≥ 4+3 cancers than standard biopsies and 17% fewer low-risk (Gleason 3+3) cancers. Men on active surveillance had an 8% increase in their detection rate with targeted biopsies in those with Gleason ≥ 4+3 scores and a 3% increase in those with Gleason 3+3 scores. The negative predictive value of mpMRI is 89% (83%-94%), and getting an mpMRI prior to biopsy would have avoided biopsy in 27% of men and failed to diagnose 2% of clinically significant prostate cancers. The American Urological Association Consensus White Paper recommendations are listed in Table 3.

mpMRI is an increasingly useful instrument for diagnosing prostate cancer. More experience with this technology will lead to improved patient outcomes.

Surgical Pearls: Robotic Prostatectomy

Presented by
Herbert Lepor, MD

Robotic surgery has quickly made its way into the mainstream of urologic surgery in the United States, spanning from hospital systems to universities, and even some private institutions. It has proven itself to be a better successor—in some respects—to its older sibling, laparoscopy. There are several aspects of the da Vinci® (Intuitive Surgical, Sunnyvale, CA) surgical system that lend themselves to this.

Robotic-assisted laparoscopy has several key features that, when in the hands of an experienced and highly trained surgeon, can prove to be beneficial for patients and surgeons alike. It allows the surgeon to view his or her movements and surroundings on a full high-definition screen with three-dimensional visualization and zooming capabilities, correcting a major deficit of laparoscopic surgery (the loss of natural hand-eye coordination and intuitive movement experienced by the physician). The da Vinci software provides a solution to this issue by aligning the motion of the surgical tools with the physician's frame of reference and positioning the image of the surgical site atop the physician's hands, which provides both spatial and visual alignment.

The system also utilizes a motion-scaling technology that filters out small, unintentional, and uncontrollable movements in the surgeon's hand, providing a steadier, more deliberate approach

TABLE 3

American Urological Association White Paper on the Prevention and Treatment of the More Common Complications Related to Prostate Biopsy Update

Consensus Statement (not a guideline)

- Recommend mpMRI and targeted biopsy following prior negative biopsy and continued clinical suspicion for PI-RADS 3-5
- mpMRI must be of **"high quality"**
- PI-RADS™ v2 reporting criteria
- Consider additional biomarkers (PCA3,4Kscore)

mpMRI, multiparametric magnetic resonance imaging; PI-RADS, Prostate Imaging Reporting and Data System.

to surgical processes. This allows the surgeon to achieve a level of manual dexterity that would otherwise be unobtainable. Another potentially overlooked benefit is that the surgeon is able to sit at the surgical console controlling the robot in a more ergonomic position, leading to a lower incidence of fatigue during procedures.

The leading use of robotics in urologic surgery is for robotic-assisted laparoscopic prostatectomy (RALP); as such, there is a plethora of data surrounding oncologic, surgical, and functional outcomes from these procedures. The rate of biochemical reoccurrence following RALP is similar to both open and laparoscopic prostatectomy. Additionally, RALP is associated with similar rates of positive surgical margins when compared with both alternate modalities. Furthermore, data on functional outcomes and complication rates are similar among the three methods with RALP, having a positive impact on hospital stay, blood loss, and transfusion requirements. RALP has also been associated with better postsurgical continence rates and has been shown to have some advantages in recovery of potency.

The benefit of robotic surgery is clear; however, as with any new surgical technique, dedicated training and acquisition of a unique set of cognitive and technical skills are necessary to achieve competence. Robotic surgery has made a significant impact on urologic procedures throughout the world. However, there is still no uniformity with regard to how to train and credential surgeons using this technology. Training programs, simulation technology, and proctors/preceptors will help reduce this learning curve so robotics may be adapted into many urologic procedures.

Treatment of Locally Advanced Prostate Cancer

Presented by
Ashley E. Ross, MD, PhD

Locally advanced prostate cancer (T3b-T4) is considered too advanced to eradicate; although it may appear to be localized, it often has a micrometastatic component. The types of treatment available for locally advanced prostate cancer include systemic therapy, external beam radiation therapy (EBRT), and localized therapy. Patients most likely at risk for succumbing to prostate cancer are the best candidates for clinical trials. Most clinicians agree that < five lesions outside the prostate constitute oligometastatic cancer, which is another term for locally advanced disease. This category places patients between clinically localized disease and widespread metastatic disease. Diagnostic imaging, such as sodium fluoride positron emission tomography (PET) scanning, may detect metastatic disease earlier than traditional bone scanning.

The most effective means to treat locally advanced prostate cancer is to remove the primary tumor. Most very high-risk and locally advanced prostate cancer patients require additional local therapy. EBRT and brachytherapy combined with long-term androgen suppression may be required to reach the level of local control provided by radical prostatectomy and adjuvant radiation therapy or salvage radiation therapy. The method of prostatectomy (radical retropubic prostatectomy or robotic-assisted laparoscopic radical prostatectomy) is unlikely to be as important as surgeon experience.

In assessing the extent of locally advanced prostate cancer, several biomarkers have proven to be useful. These markers have been used to predict response rates to radiation therapy as well as predicting 5-year metastatic rates. Various new medications have been used for treatment of locally advanced prostate cancer. These include abiraterone, which inhibits adrenal hormones and intratumoral hormones, and enzalutamide, which blocks the signal pathway of the androgen receptors. The CHAARTED and STAMPEDE trials demonstrated a key role for docetaxel in treating locally advanced prostate cancer. The current clinical literature suggests that these and other therapies work best when administered when there is low-volume disease. Newer therapies such as immunotherapy and drugs that target DNA repair deficiencies show great future promise.

Intensity-modulated Radiation Therapy, Proton Beam, and Cyberknife: Pros and Cons

Presented by
Steven E. Finkelstein, MD

Radiation therapy works by damaging the DNA within the cancer cell and destroys their ability to reproduce. It can be used in two ways: (1) to cure cancer by destroying tumors that have not spread, and (2) to reduce symptoms and alleviate pain. The first report of using ionizing radiation to treat clinically localized prostate cancer occurred in 1910. Since then, a variety of types of radiation therapies have been developed. EBRT, utilizing a linear accelerator, has enjoyed the most widespread clinical use in recent years. Interstitial radiation therapy (or brachytherapy) uses a variety of radioactive substances that are implanted directly into the prostate. There have been no prospective randomized trials comparing surgery with radiation therapy (EBRT or brachytherapy) for prostate cancer; all

outcome comparisons have been retrospective.

D'Amico at Harvard University looked retrospectively at outcomes based on risk groups and treatments given. His findings suggested the following: (1) in low-risk patients, surgery, EBRT, and brachytherapy are equivalent; (2) in intermediate-risk patients, surgery, ERBT, and hormone suppression followed by brachytherapy are equivalent; and (3) in high-risk patients, surgery and ERBT are equivalent; brachytherapy with or without hormone suppression is inferior.

Complications associated with EBRT are most frequently related to the gastrointestinal tract or the lower urinary tract. Approximately 30% to 40% of patients will have gastrointestinal symptoms while undergoing treatment. The most common problems include diarrhea, mucosal ulcers, anorectal fistulas, and anal stenosis. Fewer side effects are seen in patients treated with brachytherapy.

Luteinizing Hormone-releasing Hormone Antagonists Versus Agonists

Presented by Thomas Keane, MD, MBBCh, FRCSI, FACS

Prostate carcinomas are heterogeneous tumors composed of hormone-sensitive and hormone-insensitive cells. Since Huggins first demonstrated the hormone dependency of prostate cancer, the introduction of various means of hormonal manipulation has resulted in significant achievements. Orchiectomy reduced testosterone but was irreversible and associated with a reduced quality of life. Diethylstilbestrol represented the first alternative to surgical castration. However, cardiovascular adverse events severely limited its use. The luteinizing hormone-releasing hormone (LHRH) agonists offered true medical castration but had problems with testosterone surge and tumor flare. Complete androgen blockade is better than monotherapy; however, there is only a small clinical benefit. Androgen deprivation therapy (ADT) has clear roles in the management of advanced prostate cancer and high-risk localized disease.

These medications, as part of ADT, can also pose significant risks for patients. The complications of androgen deprivation include osteoporosis, hot flushes, gastrointestinal side effects, anemia, gynecomastia, sarcopenia, cardiac disease, central nervous system effects, change in body weight, sexual dysfunction, loss of bone density, and increased risk of bone fracture and hot flushes. While receiving ADT, patients should be aware of factors that can reduce cardiac risk: aspirin consumption, blood pressure and cholesterol reduction, cigarette cessation, diabetes, diet, and exercise monitoring. Preliminary trials show a decreased cardiovascular disease event risk with degarelix (an LHRH antagonist).

Studies have compared agonists with orchiectomy and combined androgen blockade. These studies showed that patients with moderate or severe comorbidities had a greater risk of fatal myocardial infarction when receiving radiotherapy plus ADT than ADT alone. Results have shown an approximate 20% to 25% increase in cardiovascular disease in men treated with ADT via orchiectomy, estrogens, or gonadotropin-releasing hormone (GnRH) agonists. In comparison, LHRH antagonists have shown a relative risk reduction in cardiovascular disease. Regarding osteoporosis prevention, increased physical activity, moderation of alcohol and caffeine consumption, smoking cessation, and vitamin D and calcium replacement have all been shown to be effective.

LHRH agonists work by upregulation and receptor stimulation, leading to T-lymphocyte activation. This produces CD40 and interferon-γ. In comparison, the LHRH antagonist does not have T-cell stimulation. The antagonist causes cessation of activity and maintains suppression. Individuals should be treated with antagonists if the PSA level is $>$ 20 mg/dL, or with metastatic disease. Patients with a lower urinary tract symptoms score and an International Prostate Symptom Score score $>$ 12 should receive an antagonist. Patients with metastases should receive chemotherapy treatment and a rapid castration agent.

Managing Bone Health in Advanced Prostate Cancer: What Every Urologist Should Know

Presented by Stephen Freedland, MD

In patients receiving GnRH agonists, there is associated decrease in bone mineral density (BMD) in men with prostate cancer. BMD may decrease 4% to 13% per year with ADT use. Patients on hormonal therapy are at risk of ADT-induced bone loss, similar to osteoporosis, as seen in postmenopausal women. Skeletal-related events include pathologic fractures, spinal cord compression, bone surgery, or bone radiotherapy.

A detailed medical history and physical examination to assess preexisting risk factors is necessary. A dual-energy radiographic absorptiometry scan (DEXA; reported as a T-score) is a good baseline diagnostic tool to assess BMD. Ideally, this should be obtained before starting

hormonal therapy. The World Health Organization Fracture Risk Assessment Tool, developed in 2008, calculates the 10-year risk of any major osteoporotic fracture. It allows assessment of risk in populations without access to DEXA testing. Calcium (1200-1500 mg/d) and vitamin D (800 IU/d) supplementation is recommended. However, these dietary measures alone are not proven in the prevention or treatment of bone loss in men receiving ADT for prostate cancer.

Several studies suggest that skeletal related events (SREs) are linked with poor survival. Several pharmaceutical treatments are available to clinicians to prevent SREs. These include bisphosphonates, toremifene (an estrogen blocker, which is not United States Food and Drug Administration [FDA] approved), and denosumab. Bisphosphonates intercalate into the bone matrix and prevent osteoporosis in postmenopausal women. A meta-analysis suggests that bisphosphonates reduce facture risk in men on ADT with the greatest effects seen with zoledronic acid. Toremifene may improve bone health and possibly lower fracture risk. Denosumab (120 mg every 4 weeks) is a monoclonal antibody targeting RANK ligands. It stimulates maturity of osteoclasts and is given as a subcutaneous injection.

Radiotherapy to bones is the most common skeletal-related event resulting in bone loss. Patients with metastatic castrate-resistant disease are most vulnerable to bone loss. In those patients with significant bone loss, monitoring calcium and vitamin D levels is not enough to prevent bone loss. Bisphosphonates, toremifene, and denosumab all improve BMD; toremifene, and denosumab have been shown to prevent fractures. When metastatic disease is present and the risk is high for SREs, zoledronic acid and denosumab have been shown to be effective. Denosumab is more efficacious and easier to give with slightly more on-target side effects.

Advanced Prostate Cancer: Role of Oral Therapies

Presented by
Richard Harris, MD

The development and role of oral therapies in treating advanced prostate cancer has changed rapidly over the past several years. The roots of this treatment date back to the 1940s, when Charles Huggins showed the link between testosterone and prostate cancer. In the 1980s and 1990s, research on the first generation of androgen receptor inhibitors took place, resulting in the approval of flutamide (1989), bicalutamide (1995), and nilutamide (1996). The adverse effects of nilutamide and flutamide forced them from the market. Between 2012 and 2016, an explosion of new drugs developed in the castrate-resistant prostate cancer (CRPC) space.

During this time, a special focus was placed on developing oral agents that focused on the androgen pathway. Testosterone proliferation occurs when 5-α reductase is converted to dihydrotestosterone and goes into the cell nucleus. There are several sources of androgen production in the body: these include testes (~ 90%), adrenal glands (~ 10%), and the prostate. These medications work by regulating androgen receptors and interfering with testosterone production. These medications bind with testosterone and sex hormone-binding globulin, and pass into the cytoplasm. CRPC has a sensitivity to low levels of androgen (de novo and precursors).

Only two antiandrogens are approved by the FDA for treating CRPC. The first is bicalutamide, which starts as an antagonist and can develop into an agonist. It has recently been joined by enzalutamide, which has a high affinity and selectivity for the androgen receptor. Enzalutamide has been approved in the pre- and post-chemotherapy space. Another drug, abiraterone, is an androgen synthesis inhibitor. It inhibits testosterone production (through the CYP17 enzyme complex) in the testes, adrenal, and prostate tumor cells. Coadministration of a corticosteroid suppresses adrenocorticotropic hormone drive, reducing the incidence and severity of mineralocorticoid adverse reactions. This agent also has FDA approval in both the pre- and postchemotherapeutic space. A comparison of abiraterone and enzalutamide is shown in Table 4.

Advanced Prostate Cancer: Role of Infusion Therapies

Presented by
Neal D. Shore, MD, FACS

Infusion therapies have been used to treat advanced prostate cancer. The first treatment before 2010 was docetaxel. This agent was used with palliative therapy and prolongation agents to improve patient outcomes. Cabazitaxel, another taxane-based chemotherapy agent, followed. Sipuleucel-T was then approved as an autologous immunotherapy for the treatment of asymptomatic or minimally symptomatic CRPC. Radiopharmaceuticals (eg, radium Ra 223 dichloride) are now given as infusion therapy to alleviate advanced prostate cancer symptoms.

Immunotherapies are designed to redirect the patient's immune system to recognize and remove cancerous cells. Sipuleucel-T was the first autologous cellular immunotherapy to be approved by the

TABLE 4

Comparison of Abiraterone Acetate and Enzalutamide

	Abiraterone acetate	Enzalutamide
Mechanism of action	CYP17 inhibition	Antiandrogen
Efficacy after docetaxel	OS, PFS	OS, PFS
Efficacy before docetaxel	PFS, OS (NS)	PFS, OS
Major potential adverse effects	Hypertension Hypokalemia LFT abnormalities	Seizures Hypertension ALT elevation
Requires prednisone	Yes	No
Cost	$$$$	$$$$

ALT, alanine transaminase; LFT, liver function test; OS, overall survival; PFS, progression-free survival.

FDA. Sipuleucel-T is manufactured from the patient's own immune cells. These cells are removed by leukapheresis and sent to a processing facility, where they are enriched for peripheral blood mononuclear cells, which include antigen-presenting cells (APCs), T cells, B cells, and natural killer cells. The cells are then cultured with PA2024, a fusion protein combining granulocyte-macrophage colony-stimulating factor with prostatic acid phosphatase. This leads to activation of APCs. The resulting product is sipuleucel-T, which is returned to the clinic where it is administered to the patient by intravenous infusion. In a full course of therapy, this process is repeated twice at approximately 2-week intervals. Early screening and diagnosis are important to identify patients who may benefit most from sipuleucel-T treatment. Data from the Identification of Men with a Genetic Predisposition to Prostate Cancer study (IMPACT) have shown that the greatest magnitude of benefit occurs in patients with a lower disease burden.

Radium Ra 223 dichloride is an alpha particle emitting a radioactive therapeutic agent indicated for treatment of CRPC with symptomatic bone metastases and no known visceral metastatic disease. The agent is given in six injections at 4-week intervals. The most common side effects are nausea, diarrhea, vomiting, and peripheral edema.

Advanced Prostate Cancer: Role of Chemotherapy

Presented by
Charles J. Ryan, MD

Chemotherapy has had a significant role in prostate cancer management. The prognosis of patients with advanced prostate cancer has improved over the past several years. In addition to the new antihormonal treatment, chemotherapy with agents such as docetaxel and cabazitaxel has contributed to the improved prognosis. Taxanes are the only cytotoxic class of medications to have demonstrated an overall survival in CRPC. The drugs work by stabilizing microtubules and causing apoptosis of cancer cells, through binding of cell receptors. After the introduction of abiraterone and enzalutamide, conventional chemotherapy seemed to become less important, but the discussion about the use of chemotherapy for hormone-sensitive prostate cancer has gained attention again. Combining docetaxel with conventional ADT improves survival compared with ADT alone. In addition, docetaxel and cabazitaxel now represent the standard for first and second line therapy in patients with castration-resistant prostate cancer.

Several studies have addressed the outcomes from clinical trials such as the XRP6258 Plus Prednisone Compared to Mitoxantrone Plus Prednisone in Hormone Refractory Metastatic Prostate Cancer (TROPIC) study, the CHAARTED study, and the STAMPEDE study. The results gleaned from these clinical trials have focused on their efficacy in treating metastatic prostate cancer. The STAMPEDE study showed how docetaxel can be used in patients with de novo metastatic disease and improve overall survival.

Additional research has focused on poly(ADP-ribose) polymerase (PARP) inhibitors (eg, olaparib), which are used for treating prostate cancer by a DNA repair alteration with promising results. Many patients have genetic-based deficiencies, such as BRCA or DNA repair defects, that can be treated with PARP inhibitors. Chemotherapy has shown promising results in patients, and further studies will continue to evaluate these treatments.

Preliminary data have been encouraging for other types of treatments such as enzalutamide, abiraterone, and even radium and cabazitaxel. Platinum-based therapies have been used in germ cell tumors, bladder cancer, and a variety of other cancers. Several studies have addressed the outcomes from clinical trials such as the TROPIC study, the CHAARTED study, and

the STAMPEDE study. The results gleaned from these clinical trials have focused on their efficacy in treating metastatic prostate cancer. The STAMPEDE study showed how chemotherapy can be used in patients with de novo metastatic disease.

Paclitaxel and taxanes work by stabilizing microtubules and causing apoptosis of cancer cells, through binding of cell receptors. ■