Informed Prostate Cancer Support Group Inc.
"A 501 C 3 CORPORATION ID # 54-2141691"

July 2019 NEWSLETTER

P.O. Box 420142 San Diego, CA 92142
Phone: 619-890-8447 Web: http://ipcsg.org
We Meet The Third Saturday of Each Month
(except December)

Monday, July 15, 2019

Volume 12 Issue 7

Next Meeting— July 20, 2019-10:00 AM to Noon

Location: SBP Auditorium, 10905 Road to the Cure, San Diego, CA 92121

Next **IPCSG** Member Panel Round Table

A panel of members will discuss their experiences, what treatments they choose, how they are doing today, and pass along their lessons learned. Then the group will break-out into sessions by treatment type (Active Surveillance, Surgery, ADT, Radiation, Chemo) for networking. This is when you can get all your questions answered by other members who are currently going through treatment, or have had treatment. All areas related to prostate cancer will also be discussed.

- **For further Reading: https://spendergast.blogspot.com/2019/03/prostate-cancer-news-of-interest-for.html**
- **For Comments, Ideas and Questions,** email to Newsletter@ipcsg.org

June 2019 Informed Prostate Cancer Support Group Meeting:

Diagnosing and Managing Prostate Cancer: A Paradigm Shift

Summary by Bill Lewis

Dr. Franklin Gaylis, Chief Scientific Officer – Genesis Healthcare Partners;
Voluntary Professor, Urology – UCSD

US health care is too expensive! We now spend 18% of GDP on health care, with about 70% of that on chronic care management, and the percentage is rising. Compared to ten other first-world countries, we rank last on the combination of quality, access, efficiency, and equity, along with indicators of healthy lives such as infant mortality. There is a chasm between the health care that we now have, and what we could have with appropriate changes.

Prostate cancer (PCa) is the most common visceral cancer in men, occurring in 14% of US men. It is the second or third-leading cause of cancer death in men. Current methods cannot accurately distinguish between indolent and aggressive tumors. PSA testing has been helpful in reducing overall death rates by 50%, but there has been a dilemma of over-diagnosis and over-treatment of low-risk PCa. Active surveillance has become one route to resolving this dilemma. Genetics appears to be a way to further help.

Dr. Gaylis noted that the "standard" of considering PSA values up to 4.0 to be normal (i.e., safe) has been shown to be inaccurate. He has personally treated a man with PCa whose PSA was only 0.7.

Last year, there were about 240.000 new cases of PCa diagnosed in the US. This year, it appears that

(Continued on page 3)

Organization

a 501c3 non-profit organization - all positions are performed gratis

IPCSG

Officers

Lyle LaRosh President

Additional Directors

Gene Van Vleet
George Johnson
John Tassi
Bill Manning

Honorary Directors

Dr. Dick Gilbert
Judge Robert Coates

George Johnson, ... Facilitator
Bill Manning, ...Videographer
John Tassi, ...Webmaster
Bill Bailey, ...Librarian
Jim Kilduff, ...Greeter
Chuck Grim, ...Meeting Set-up
Stephen Pendergast ..... Editor

NEWSLETTER
Table of Contents

PROSTATE CANCER—*2 WORDS, NOT A SENTENCE*

What We Are About

Our Group offers the complete spectrum of information on prevention and treatment. We provide a forum where you can get all your questions answered in one place by men that have lived through the experience. Prostate cancer is very personal. Our goal is to make you more aware of your options before you begin a treatment that has serious side effects that were not properly explained. Impotence, incontinence, and a high rate of recurrence are very common side effects and may be for life. Men who are newly diagnosed with PCa are often overwhelmed by the frightening magnitude of their condition. Networking with our members will help identify what options are best suited for your life style.

Be your own health manager!!

Meeting Video DVD's

DVD's of our meetings are available in our library for $10ea. Refer to the index available in the library. They can also be purchased through our website: http://ipcsg.org Click on the 'Purchase DVDs" tab.

The DVD of each meeting is available by the next meeting date.

From the Editor

WE ARE SEEKING REPLACEMENT FOR SOME OF OUR IPCSG TEAM

If you consider the IPCSG to be valuable in your cancer journey, realize that we need people to step up. ***The current staff are aging, and without new men to share the work, someday the 3rd Saturday may see no meeting of the group.*** Serving in this team can be rewarding and is a way to pay it forward to the group. To offer your services and/or ask questions about functions, contact any of the individuals at their listed phone number.

FUNCTIONS NEEDED:

1. **President**: IPCSG public relations, research and advice. Lyle LaRosh has performed for 18 years. 619-892-3888
2. **Vice President**: Support all team members, assist in monthly planning and speaker acquisition. *currently vacant* Gene Van Vleet has performed Functions 2, 4, 5 for 11 years. 619-890-8447.
3. **Meeting facilitator**: Monthly planning and speaker acquisition. George Johnson has performed for 8 years. 858-456-2492
4. **Treasurer/Secretary**: Handle banking, accounting, government reporting (see 2)
5. **Hot Line**: Communicate directly with newcomers and handle phone inquiries. (see 2)

.

(Continued from page 1)

only about 180,000 new cases will be found. This means that about 60,000 men very likely have prostate cancer, but just don't know about it. Typically, about 1/3 of cases diagnosed are of indolent / low risk PCa, but the other 2/3 are "clinically significant" (Gleason 7 or above). So there are probably about 40,000 men who should know that they have significant PCa, but won't learn about it this year.

Prostate cancer screening is intended to find clinically significant PCa early, when it can still be cured (i.e., by surgery or radiation), recognizing that often, patients are asymptomatic until the disease is incurable.

In 2012, The US Preventative Services Task Force (USPSTF) decided that the harms of over-diagnosis and over-treatment from PSA-based early detection outweighed the benefits, and recommended against PSA screening. But in 2018, they reversed themselves, because the increased use of active surveillance has greatly reduced the rate of over-treatment. They now recommend "shared decision making" between doctor and patient, recognizing that patients are much more informed than in the past, and less likely to accept a doctor's opinion (i.e., bias toward active treatment) without question.

Active surveillance (AS) is for apparently-indolent disease (Dr. Gaylis noted that doctors are wrong in this assessment about 30-50% of the time!), to monitor it and treat it if/when disease progression is detected. The concept of standardized, multi-parameter risk stratification for prostate cancer was introduced way back in 1998, and low-risk PCa was defined (PSA < 10 ng/ml, Gleason = 6, Clinical stage T2a [small lump] or less). The safety and feasibility of AS was demonstrated in academic centers ten to twenty years ago, and immediate treatment of low-risk prostate cancer was declared to be overtreatment. However, rates of AS in "real-world," community-based practices remained low and actually fell through the 1990s and into the 2000s. At the end of the last decade**,** AS rates for low-risk disease remained under 10% nationally**.** But now in the present decade**,** AS rates have dramatically improved (already 40-49% by 2015). It has been argued that the rate should be 80%, which would mean that an additional 60,000 men would be put on active surveillance, at a significant cost saving, and with avoidance of treatment side effects.

How well is active surveillance being done? NCCN guidelines recommend a biopsy every two years, and a PSA test every six months. In Michigan (probably typical of the US), 70% of active surveillance patients did not meet these guidelines. Dr. Gaylis noted that many patients would rather avoid biopsies because they are uncomfortable and have side effects and risks, and said that patients with a particularly low burden of disease might not need such frequent biopsies.

This year, active surveillance has become the recommended standard of care for low-risk PCa. (Men with low risk PCa and less than ten years life expectancy due to age and/or other illnesses may undergo "Watchful Wait," which basically means no biopsies unless symptoms appear.) It was determined in a large study in the UK, that about 55% of men randomized to active surveillance needed to "cross over" into active treatment within ten years. This points up the need for improved selection criteria for deciding which patients should go on active surveillance. It's complicated. Early treatment may improve chances of cure, but delaying treatment puts off the side effects of treatment. There is a broadly collaborative effort called the Prostate Cancer Active Surveillance Project (PCASP) almost ready to start. The effort has taken two years to set up, and funding is hoped for in the next two months.

There are three project areas/goals of the PCASP: 1) Implementation of specific interventions to promote active surveillance adoption, 2) improve guideline adherence and 3) decrease conversion to active treatment by pre-screening out or clarifying the options and risks for those who would likely need conversion (to active treatment while still in the "window of curability"). It will use "dashboards" and genomic testing using the Decipher genomic classifier (which predicts high, medium or low PCa aggressiveness based on a panel of genetic markers).

As an example of a dashboard, the experience of

(Continued on page 4)

(Continued from page 3)

Genesis working with 23 doctors in their system was that the overall adoption of AS only rose from 30 to 39% after two years of education efforts, but jumped to 58% in a single year when the doctors were shown their "performance" relative to the other doctors in the group. (The group is now up to 77%.) This performance chart (percentage of each doctor's low-risk PCa patients that are on AS) is the "dashboard." It works on the natural competitiveness of the doctors, to encourage them to adopt active surveillance for their low-risk patients.

Why genetics? A major drawback of AS as a management strategy for favorable-risk prostate cancer is that it is not currently possible to identify accurately patients with seemingly favorable risk disease that harbor an occult life-threatening tumor. 30-40% of such men initially managed with AS later are found to have more aggressive disease features, and up to 50% whose treatment was delayed by a period of AS have been reported to miss the "window of curability."

Genetics studies can reveal important components of inherited risk for PCa, which is one of the most heritable of cancers. Genetic markers of "germline" (i.e., inherited) mutations studied include about 160 commonly occurring single nucleotide polymorphisms (SNPs; substitution of one nucleic acid by another one in the DNA, which can affect the occurrence and are believed to affect the aggressiveness of PCa) and rare but high-risk "high penetrance genes" (HPGs), such as the BRCA2, ATM and MMR genes. The BRCA gene is a DNA repair mutation (i.e., a defect -- poor repair leads to cancer), but PCa patients who are carriers of this gene do respond to the new PARP inhibitors and to platinum-based chemotherapy. (See the April 2019 IPCSG newsletter or the March dvd for more detailed info on genetics, from a talk by Dr. Rana McKay.) Men who have metastatic PCa have been found to more often have an inherited DNA repair mutation (11.8% of them) vs. men with localized PCa (4.6%). There are dozens of different possible repair mutations being investigated.

A large prospective study is needed to find genetic markers predicting failure of active surveillance, to learn which men with seemingly low-risk PCa will progress on AS and therefore should receive early treatment.

Somatic mutations of genes occur after conception, whether in the embryo/fetus or in the child/adult body, and affect only some cells/tissues (whereas germline mutations are carried in every cell). In PCa, tumors may undergo (somatic) mutations, so metastatic tumors may differ in their genetics from the tumor(s) in the prostate, and from each other.

A 2019 American Urological Association meeting presentation taught that 5-10% of cancers are hereditary, usually due to a single inherited genetic mutation that greatly increases lifetime risk. Examples of such mutations are BRCA1, BRCA2, Lynch syndrome, and HOXB13. Familial cancers comprise 15-20% of cases, but no specific mutation can be identified. Possibly these are due to unidentified genetic mutations, plus environmental effects. Close family members have increased risks. So-called sporadic cancers (70-80% of cases) comprise those with no known exact cause, no features of hereditary or familial cancers, and no increased risk for close family members.

New guidelines from the National Comprehensive Cancer Network (NCCN) suggest that patients with a) regional or metastatic PCa or b) localized PCa but a suspicious family history should undergo germline testing for the following genes associated with an increased incidence and/or aggressiveness of prostate cancer: MLH1; MSH2; MSH6; PMS2 (for Lynch syndrome); and the homology-directed repair genes BRCA1, BRCA2, ATM, PALB2, and CHEK2.

SNPs (single nucleotide polymorphisms) have been found useful for predicting PCa risk. The Prompt Test looks for 33 of these markers. Most of these SNPs are not in known genes.

In the recent ASCO 2019 meeting, based on prolonged survival of patients with androgen sensitive / castrate sensitive metastatic disease taking Xtandi or Erleada, it was stated that "It is clear that almost every patient [with metastatic hormone-sensitive prostate cancer] needs ADT plus an additional therapy — a next androgen-targeted therapy. There are evolving data that may provide insight on

(Continued on page 5)

one or the other choice."

Dr. Gaylis also presented information about Micro-Ultrasound. This is ultrasound using 29MHz energy, versus 6-9MHz used in traditional ultrasound scans, and gives 300% higher resolution. The PRI-MUS protocol is used to identify and target areas that are suspicious for PCa. Lots of early data is showing equivalence to MRI scans. This is exciting because the equipment is much cheaper than for MRI, so can be made more widely available. Genesis Healthcare just received the first unit to be installed in the San Diego area, the week of this talk.

Questions:

If prostate cancer comes back after surgery, where is it likely to be? Usually it would be in the prostate bed, but can occur elsewhere. An Axumin or PSMA scan may be needed to be sure that it is only in the local area, where radiation can readily target and destroy it.

If imaging doesn't show where the recurrent cancer is, what then? Dr. Dato at Genesis Healthcare is an expert in this area. It may be necessary to go on ADT treatment. Every patient is different.

Does the Gleason score ever change? Prostate cancer, even within the prostate, usually has multiple spots of cancer. A biopsy samples less than 1% of the prostate tissue. After radical prostatectomies, the tissue is examined and about 30% of the time, higher-grade lesions are found. In connection with going on active surveillance, it is protocol to have a confirmatory biopsy 6-12 months after the first one, to confirm that the Gleason score is really a 6. Sometimes, years later Gleason = 7 may be found, and we don't know if it was missed earlier, or if the biology of a tumor has changed.

How soon after a first Lupron shot, would side effects be expected? For the first 3 weeks, testosterone production is stimulated. After that, it is shut down, and that is when side effects may begin.

What affects PSA variation? Most often it's due to a medication being taken, but we don't always know why a PSA value may go down.

A member, Chuck Grim, noted that PSMA testing is available at UCLA for $2700, and is no longer available at UCSF (which only charged $700), apparently because their funding ran out.

How high can the PSA get, with the cancer confined to the prostate? Hard to say.

Can MRI or a micro-ultrasound substitute for a biopsy? We don't know yet, but both can provide help in targeting a biopsy to suspicious areas. We don't know which is most sensitive for small, low-grade lesions, but one advantage (besides lower cost of the equipment) is that micro-ultrasound does not require the gadolinium contrast agent used with MRI, about which there are some health concerns.

More details are given in the video of this presentation, including the PowerPoint slides, which will be available for purchase via the website shortly before the next meeting, or at the July meeting on the 20th.

On the Lighter Side

"You fell off the operating table."

"I hate giving these injections. Look at my hands shaking."

Hormone Therapy for Prostate Cancer Tied to Dementia

Androgen deprivation therapy for prostate cancer is associated with an increased risk of Alzheimer's disease and other forms of dementia.

https://www.nytimes.com/2019/07/03/well/live/hormone-therapy-for-prostate-cancer-tied-to-dementia.html

By Nicholas Bakalar July 3, 2019

Hormone therapy for prostate cancer is associated with an increased risk for dementia, a new study has found.

Androgen deprivation therapy, or A.D.T., is used to treat prostate cancer of varying degrees of severity. It can significantly reduce the risk for cancer progression and death.

The study, in JAMA Network Open, included 154,089 men whose average age was 74 and who had diagnoses of prostate cancer. Of these, 62,330 received A.D.T. and the rest did not.

In an average follow-up of eight years, the scientists found that compared with men who had no hormone therapy, one to four doses of A.D.T. was associated with a 19 percent increased risk for both Alzheimer's disease and other forms of dementia, and the risk increased with the number of doses. At five to eight doses the increased risk was 28 percent for Alzheimer's and 24 percent for other dementias.

The study adjusted for socioeconomic status, age, race, severity of prostate cancer and other factors.

The lead author, Ravishankar Jayadevappa, an associate professor at the University of Pennsylvania Perelman School of Medicine, said that for advanced cancer, A.D.T. can be a lifesaving treatment and should not be avoided because of any increased risk for dementia. But, he said, "Patients with localized cancer should be looking at the risks of dementia, and possibly avoiding A.D.T."

Association Between Androgen Deprivation Therapy Use and Diagnosis of Dementia in Men With Prostate Cancer | Dementia and Cognitive Impairment | JAMA Network Open | JAMA Network: This cohort study uses data from the Surveillance, Epidemiology, and End Results (SEER)–Medicare database to investigate the association between androgen deprivation therapy and diagnosis of Alzheimer disease or dementia among elderly men with prostate cancer.

Early Treatment of Advanced Prostate Cancer with PSMA-Targeted Radioligand Therapy Prolongs Life

June 26, 2018

PHILADELPHIA (Embargoed until 12 p.m. EDT, Tuesday, June 26, 2018) – Research presented at the 2018 Annual Meeting of the Society of Nuclear Medicine and Molecular Imaging (SNMMI) demonstrates for the first time the benefit of providing earlier lutetium-177 (^{177}Lu) prostate-specific membrane antigen (PSMA) radioligand therapy to patients with metastatic prostate cancer. Until now, this therapy has only been used in patients with end-stage disease.

The study included 224 patients with metastatic prostate cancer, who were restaged following diagnosis with gallium-68 (^{68}Ga)-PSMA positron emission tomography/computed tomography (PET/CT)—the diagnostic partner of ^{177}Lu-PSMA radioligand therapy (PRLT); the two form a theranostic nuclear medicine pairing. *Theranostics* refers to the combination of a predictive biomarker, in this case PSMA, identified through diagnostic imaging using radiolabeled ligands (which lock onto the specific cancer cell receptor/biomarker), with precise therapy targeted on the now-identified cancer cells. The cancer cells are destroyed, while healthy cells are unharmed—minimizing side effects and improving quality of life for patients.

The patients were grouped according to previous therapies, which included surgery, chemotherapy and external beam radiation therapy. Serum prostate specific antigen (PSA) levels were monitored before and after therapy with ^{177}Lu PRLT.

Study results showed a reduction in PSA level in 70 percent of the patients treated with ^{177}Lu PRLT, and 54 percent had their PSA decline by more than 50 percent. The median overall survival in all patients was 27 months. First-line PRLT was associated with the longest survival (all 18 patients alive at 55 months). Patients previously treated with chemotherapy had a significantly shorter survival (median of 19 months). Survival was also shorter in patients with previous radium-223 (^{223}Ra) treatment (17 months). On the other hand, prior surgical or radiation treatment of the primary tumor had no significant

(Continued on page 7)

(Continued from page 6)

effect on overall survival. Patients demonstrating a PSA decline of more than 50 percent after at least two PRLT cycles, lived significantly longer (38 months). Additional treatment with newer antiandrogen agents Abiraterone or Enzalutamide in combination with ^{177}Lu PRLT also prolonged survival.

"Our study demonstrates a potential survival benefit and superior response after early initiation of ^{177}Lu-PSMA radioligand therapy," explains Harshad R. Kulkarni, MD, of the THERANOSTICS Center for Molecular Radiotherapy and Molecular Imaging, Zentralklinik Bad Berka in Bad Berka Germany. "PRLT was safe with no or minimal side effects. These results are, therefore, likely to have a significant impact on patients' lives—maintaining their quality of life for longer."

He points out, "This approach of precision oncology uses the concept of theranostics—i.e., we see what we treat, and we treat what we see. ^{177}Lu-PRLT patients were selected and followed-up with ^{68}Ga-PSMA PET/CT, using the same ligand for molecular imaging and molecular radiotherapy."

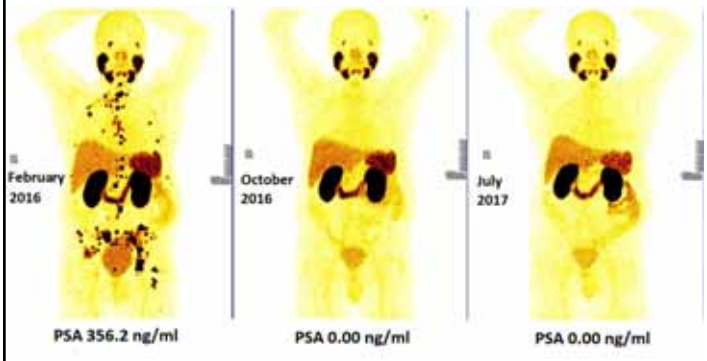


FIGURE: Persistent complete remission on long-term follow-up after early Lu-177 PSMA radioligand therapy.

Kulkarni adds, "These findings will help to determine the right place of ^{177}Lu-PSMA radioligand therapy in the treatment of metastatic prostate cancer—for example before chemotherapy—and serve as a starting point for a prospective randomized controlled clinical trial."

Lymph node and osseous metastatic, castration-resistant, and chemotherapy-naive prostate cancer (status post androgen-deprivation therapy using LHRH analogs and Bicalutamide) in a 62-year-old patient demonstrated no evidence of disease on Ga-68 PSMA PET/CT 8 months (center) and 17 months (right) after first PRLT. *Credit: HR Kulkarni et al., THERANOSTICS Center for Molecular Radiotherapy and Molecular Imaging, Zentralklinik Bad Berka, Germany*

Abstract 529: "Early initiation of Lu-177 PSMA radioligand therapy prolongs overall survival in metastatic prostate cancer," Harshad R. Kulkarni, MD; Christiane Schuchardt; Aviral Singh, MD, MSc; Thomas Langbein; and Richard P. Baum, MD, PhD, THERANOSTICS Center for Molecular Radiotherapy and Molecular Imaging, Zentralklinik Bad Berka, Bad Berka, Germany. SNMMI's 65th Annual Meeting, June 23-26, Philadelphia.

Link to Abstract

Prostate Cancer Research Results

Diagnosing Prostate Cancer

Improving Biopsies

Traditionally, prostate cancer has been diagnosed using a biopsy: needles are inserted into the prostate gland in several places under the guidance of transrectal ultrasound (TRUS) imaging to collect samples of tissue.

However, ultrasound does not generally show the location of cancer within the prostate. It is mainly used to make sure the biopsy needles go into the gland safely. Therefore, biopsy samples using ultrasound guidance can miss cancer altogether, or identify low-grade cancer while missing areas of high-grade, potentially more aggressive cancers.

Some doctors, concerned that a TRUS biopsy showing only low-grade cancer could have missed a high-grade cancer, may suggest surgery or radiation. However these treatments are for a cancer that may have never caused a problem, which is considered overtreatment.

Using MRI and ultrasound. Scientists at NCI have developed a procedure that combines magnetic resonance imaging (MRI) with TRUS for more accurate prostate biopsies. MRI can locate potential areas of cancer within the gland but is not practical for real-time imaging to guide a prostate biopsy. The new procedure, known as a fusion biopsy, uses computers to fuse an MRI image with an ultrasound image. This lets doctors use ultrasound guidance to biopsy areas of possible cancer seen on MRI.

In a recent clinical trial, the PRostate Evaluation for Clinically Important Disease (PRECISION) trial, an MRI-targeted biopsy approach was more successful in detecting higher-grade cancers that were likely to require treatment than biopsies guided by ultrasound alone. Fusion biopsy was also better at identifying low-grade cancers that were *not* likely to require treatment.

Testing machine learning. Researchers are testing the use of machine learning, also called artificial intelligence (AI), to better recog-

(Continued from page 7)

nize suspicious areas in a prostate MRI that should be biopsied. AI is also being tested to improve the analysis of biopsy samples to more accurately determine which cancers need to be treated and which could be managed using active surveillance.

Pinpointing Recurrent Prostate Cancer

NCI-supported researchers are developing new imaging techniques to improve the diagnosis of recurrent prostate cancer. A protein called prostate-specific membrane antigen (PSMA) is found in large amounts—and almost exclusively—on prostate cells. By fusing a molecule that binds to PSMA to a compound used in PET scan imaging, scientists have been able to see tiny deposits of prostate cancer that are too small to be detected by regular imaging.

The ability to detect very small amounts of metastatic prostate cancer could help doctors and patients make better-informed treatment decisions. For example, if small amounts of metastatic cancer are found when a man is first diagnosed, he may choose hormone therapy instead of surgery, since the cancer has already spread. Or doctors may be able to treat cancer recurrence—either in the prostate or metastatic disease—earlier, which may lead to better survival.

Prostate Cancer Treatment

Treatments for prostate cancer that has not spread elsewhere in the body are surgery or radiation therapy (RT), with or without hormone therapy. Active surveillance is also an option for men who have a low risk of their cancer spreading.

Hormone Therapy

Over the last few years, several new approaches to hormone therapy for advanced or metastatic prostate cancer have been approved for clinical use.

Many prostate cancers that originally respond to treatment with standard hormone therapy become resistant over time, resulting in castrate-resistant prostate cancer (CRPC). Two new drugs have been shown to extend survival in men with CRPC:

Enzalutamide (Xtandi) blocks the action of hormones that drive CRPC.

Abiraterone (Zytiga) inhibits the synthesis of hormones that drive CRPC.

The survival benefit for these drugs has been seen regardless of whether men have previously received chemotherapy.

In addition, both enzalutamide and the drug, apalutamide (Erleada), have been shown to decrease the risk of metastases in men with CRPC that has not yet spread to other parts of the body.

Both abiraterone and apalutamide have also been shown to increase the survival of men with metastatic castrate-sensitive prostate cancer when added to standard hormone therapy.

Scientists are continuing to study novel treatments and drugs, along with new combinations of existing treatments, in men with metastatic CRPC.

Immunotherapy: Vaccines

Immunotherapies are treatments that harness the power of the immune system to fight cancer. These treatments can either help the immune system attack the cancer directly or stimulate the immune system in a more general way.

Vaccines and checkpoint inhibitors are two types of immunotherapy being tested in prostate cancer. Treatment vaccines are injections that stimulate the immune system to recognize and attack a tumor.

One type of treatment vaccine called sipuleucel-T (Provenge) is approved for men with few or no symptoms from metastatic CRPC.

Another prostate cancer treatment vaccine, rilimogene-galvacirepvec (PROSTVAC), was developed at NCI and is being tested in clinical trials. PROSTVAC has not been shown to improve the survival of men with metastatic disease. However, other trials are evaluating the effects of this vaccine in earlier stages of prostate cancer.

For example, PROSTVAC is being studied in men with localized prostate cancer who have chosen active surveillance. The goal of the trial is to see if the vaccine can cause immune cells to recognize and attack early prostate tumors. If it does, PROSTVAC may be tested for secondary prevention: preventing early cancer from progressing to more aggressive disease.

Studies are also testing PROSTVAC in combination with other immunotherapies or chemotherapy for metastatic cancer.

Immunotherapy: Checkpoint Inhibitors

An immune checkpoint inhibitor is a type of drug that blocks proteins on the immune cells, making the immune system more effective at killing cancer cells.

A checkpoint inhibitor called pembrolizumab (Keytruda) has been approved for the treatment of tumors, including prostate cancers, that have specific genetic features. But few prostate cancers have these genetic features, and prostate cancer in general has largely been resistant to treatment with checkpoint inhibitors and other immunotherapies, such as CAR T-cell therapy.

Research is ongoing to find ways to help the immune system recognize prostate tumors and help immune cells penetrate prostate tumor tissue. Studies are looking at whether combinations of immunotherapy drugs, or immunotherapy drugs given with other types of treatment, may be more effective in treating prostate cancer than single immunotherapies alone.

PARP Inhibitors

Some prostate tumors have genetic defects that limit their ability to repair DNA damage. Such tumors may be sensitive to a class of drugs called PARP inhibitors, which also block DNA repair. An ongoing randomized clinical trial is testing a PARP inhibitor in men whose tumors are deficient in DNA repair. Future trials may test PARP inhibitors in combination with hormone therapy or other treatments.

(Continued from page 8)

Targeted Radiation Therapy

Scientists are also developing targeted therapies based on PSMA, the same protein that is being tested for imaging prostate cancer. For treatment, the molecule that targets PSMA is chemically linked to a radioactive compound. This new compound can potentially find, bind to, and kill prostate cancer cells throughout the body. Early clinical trials of this method of targeting PSMA are under way.

Personalized Clinical Trial Enrollment

Research is uncovering more information about the genetic changes that happen as prostate cancers develop and progress. Although early-stage prostate cancer has relatively few genetic changes compared with other types of cancer, researchers have learned that metastatic prostate cancers usually accumulate more mutations as they spread through the body.

These mutations may make men with metastatic prostate cancers candidates for what are called "basket" clinical trials of new drugs. Such trials enroll participants based on the mutations found in their cancer, not where in the body the cancer arose. In the NCI-MATCH trial, a high percentage of enrolled men with advanced prostate cancer had mutations that could potentially be targeted with investigational drugs.

NCI-Supported Research Programs

See a full list of prostate cancer research projects that NCI funded in FY 2017.

Diagnostic accuracy of ^{68}Ga-prostate-specific membrane antigen (PSMA) positron-emission tomography (PET) and multiparametric (mp)MRI ...

Matthijs J. Scheltema, John I. Chang, Phillip D. Stricker, et al. — First published: 09 July 2019

https://doi.org/10.1111/bju.14794

Abstract

Objective: To evaluate the ability of prostate-specific membrane antigen (PSMA)-positron-emission tomography (PET)/computed tomography (CT) to detect intermediate-grade intra-prostatic prostate cancer (PCa), and to determine if PSMA-PET improves the diagnostic accuracy of multiparametric magnetic resonance imaging (mpMRI).

Patients and Methods: A total of 56 consecutive patients with International Society of Urological Pathology (ISUP) grade 2–3 PCa after radical prostatectomy, who underwent both mpMRI and PSMA-PET CT (hereafter PSMA-PET) preoperatively, were enrolled in this study. The accuracy of PSMA-PET, mpMRI alone, and the two procedures in combination was analysed for identifying ISUP grades 1–3 within a 12-segment model. The accuracy of a combined predictive model (PSMA-PET and mpMRI) was determined. Receiver-operating characteristic curve analysis to determine the optimal standardized uptake value (SUVmax) for PSMA-PET in discriminating between ISUP grades 1 and ≥2 was performed.

Results: On a per-patient basis, the sensitivities for PSMA-PET and mpMRI in identifying ISUP grades 2–3 PCa were 100% and 97%, respectively. Assessing ISUP grade ≥2 PCa using a 12-segment analysis, PSMA-PET demonstrated greater diagnostic accuracy (area under the curve), sensitivity, specificity, negative predictive value (NPV) and positive predictive value (PPV), with values of 0.91, 88%, 93%, 95% and 85%, respectively, than did mpMRI (Prostate Imaging Reporting and Data System [PI-RADS] 3–5), at 0.79, 68%, 91%, 87%, and 75%, respectively. When used in combination (PSMA-PET and mpMRI PIRADS 4–5), sensitivity, specificity, NPV and PPV were 92%, 90%, 96% and 81%, respectively. The sensitivity for both techniques reduced markedly when assessing ISUP grade 1 PCa (18% for PSMA-PET, 10% for mpMRI). An SUVmax value of 3.95 resulted in 94% sensitivity and 100% specificity.

Conclusion: PSMA-PET is accurate in detecting segments containing intermediate-grade intra-prostatic PCa (ISUP grade ≥ 2), compared with and complementary to mpMRI. By contrast the detection rate for ISUP grade 1 disease for both PSMA-PET and mpMRI was low.

*What is an ISUP Grade Group?

In 2014, the International Society of Urological Pathologists released supplementary guidance and a revised prostate cancer grading system, called the ISUP Grade Groups.

The ISUP Grade Group system is simpler than the Gleason, with just five grade groups, 1 through 5:

1. Low (Gleason ~6 or less
2. Intermediate favorable (~Gleason 3+4)
3. Intermediate unfavorable (~Gleason 4+3)
4. High (~Gleason 8)
5. High (~Gleason 9-10)

NETWORKING

Please help us in our outreach efforts. Our speakers bureau consisting of Lyle LaRosh, Gene Van Vleet and George Johnson are available to speak to organizations of which you might be a member. Contact Gene 619-890-8447 or gene@ipcsg.org to coordinate.

Member and Director, John Tassi is the webmaster of our website and welcomes any suggestions to make our website simple and easy to navigate. Check out the Personal Experiences page and send us your story. Go to: https://ipcsg.org/personal-experience

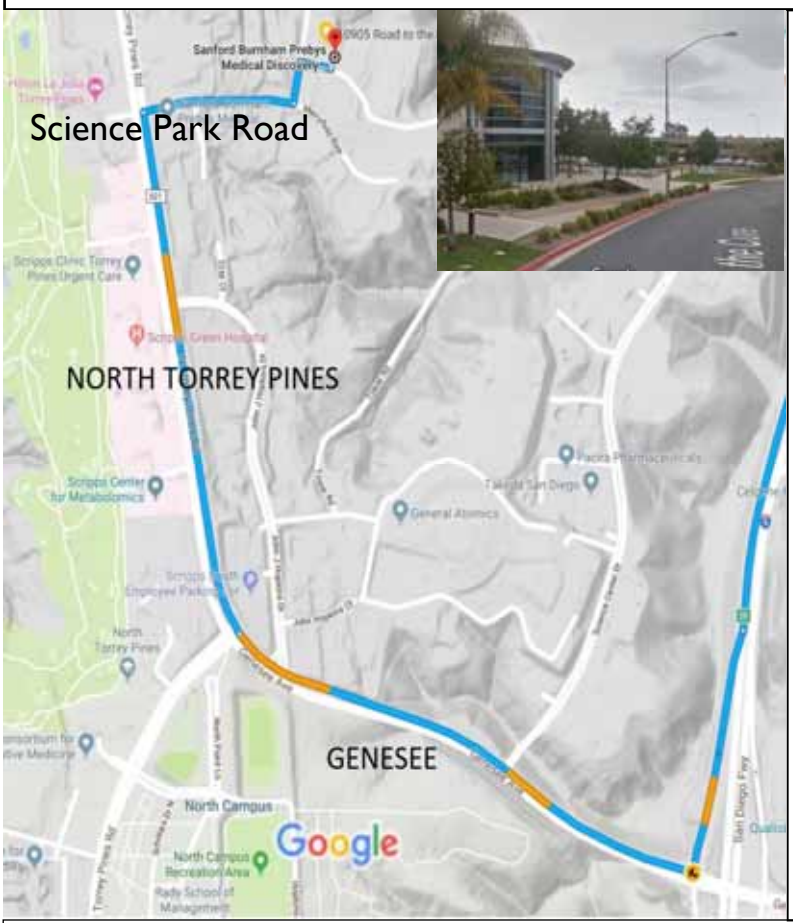
Our brochure provides the group philosophy and explains our goals. Copies may be obtained at our meetings. Please pass them along to friends and contacts.

FINANCES

We want to thank those of you who have made special donations to IPCSG. Remember that your gifts are tax deductible because we are a 501(c)(3) non-profit organization.

We again are reminding our members and friends to consider giving a large financial contribution to the IPCSG. This can include estate giving as well as giving in memory of a loved one. You can also have a distribution from your IRA made to our account. We need your support. We will, in turn, make contributions from our group to Prostate Cancer researchers and other groups as appropriate for a non-profit organization. Our group ID number is 54-2141691. Corporate donors are welcome!

If you have the internet you can contribute easily by going to our website, http://ipcsg.org and clicking on "Donate" Follow the instructions on that page. OR just mail a check to: IPCSG, P. O. Box 4201042, San Diego CA 92142



Directions to Sanford-Burnham-Prebys Auditorium
10905 Road to the Cure
San Diego, CA 92121

- Take I-5 (north or south) to the Genesee exit (west).
- Follow Genesee up the hill, staying right.
- Genesee rounds right onto North Torrey Pines Road.
- **Do not turn into the Sanford-Burnham-Prebys Medical Discovery Institute or Fishman Auditorium**
- Turn right on Science Park Road. Watch for our sign here.
- Turn Left on Torreyana Road. Watch for our sign here.
- Turn Right on Road to the Cure (formerly Altman Row). Watch for our sign here.