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

Friday, April 14, 2023

APRIL 2023 NEWSLETTER

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Volume 16 Issue 04

Next Meeting Saturday, April15, 2023 IPCSG—10:00am PT.

"The Medical Journey of a Prostate Cancer Patient"

- Presentation by Dr. Richard Lam of Prostate Oncology Specialists in Marina del Rey, California. Dr. Lam is a double board-certified internist and oncologist, who has been specializing in the treatment of prostate cancer since 2001. The talk will include updates on the latest trials, testing and treatment options available for prostate cancer patients. As always, his presentations are very informative and presented in an easily understood format. He also brings a great wit with a touch of humor.
- As always, spouses/partners and caregivers are welcome and encouraged to attend!
- *After the meeting a light lunch will be served in the foyer outside the meeting room*
- **For links to further Reading: https://ipcsg.blogspot.com/ (includes member suggested links)**
- **If you have Comments, Ideas or Questions,** email Newsletter@ipcsg.org
- **For more information, please send email to bill@ipcsg.org or call Bill at (619) 591-8670 or Gene at (619) 890-8447**

March 2023 Informed Prostate Cancer Support Group Meeting

Summary by Bill Lewis

New Prostate Cancer Tests – and some Old Ones

Our speaker was Paul Dato, MD – Medical Director of the Prostate Cancer Center at Unio Health Partners. As requested, he covered a wide range of tests, with comments to help us sort out which are best at various stages of our prostate cancer (PCa) journeys. Those stages include initial screening to detect possible cancer and its likely aggressiveness, first and possibly second biopsies to confirm prostate cancer and its Gleason grade, what to do after negative biopsies, guidance for active surveillance, pre-treatment decisions, and post-treatment tests.

PSA testing has been validated across many studies, is relatively inexpensive (covered by insurance, or $22 via the discount available through ipcsg.org), and has strong negative predictive value if the value is low (indicating no meaningful cancer). PSA values vary by age, but not so much due to other factors such as race. However, PSA can be elevated due to inflammation or infection, so should be considered a "check engine" light. The traditional boundary between "low" and elevated was 4.0, but now we know that 1.0 is a better standard for middle-aged or elderly men, and even lower for young men. An early "baseline" value is helpful for initial screening, to compare

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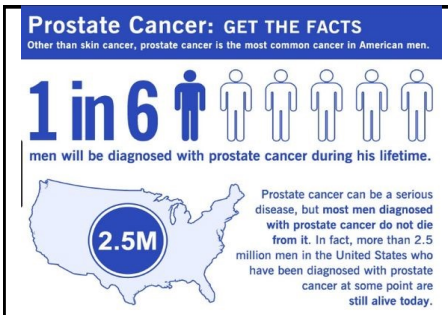

Organization

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

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NEWSLETTER

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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.

Join the IPCSG TEAM

If you consider the IPCSG to be valuable in your cancer journey, realize that we need people to step up and HELP. Call **President** Bill Lewis @ (619) 591-8670 "bill@prostatecancerhelp.info"; or **Director** Gene Van Vleet @ 619-890-8447.

From the Editor

In this issue:

Bill Lewis produced a summary of Dr. Dato's talk last meeting. There's also notice of the new social media account on instagram. Since the talk summary was full of useful detail, articles of interest are summarized only with links to source. See the blog at https://ipcsg.blogspot.com/

1. "MDxHealth: Who Doesn't Love A Good Prostate Exam?"
2. "ETV4 mediates dosage-dependent prostate tumor initiation and cooperates with p53 loss to generate prostate cancer"
3. "ENZAMET shows promise as prostate cancer treatment"
4. "Safety and Survival Outcomes of 177Lu-Prostate-Specific Membrane Antigen Therapy in Patients with Metastatic Castration-Resistant Prostate Cancer with Prior 223Ra treatment: The RALU Study"

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later values and the rate of rise.

Additional pre-biopsy testing includes "multivariable calculators," MRI, various biomarkers (to be discussed below) and **PSAD** (psa density; psa divided by prostate volume). But PSA remains important throughout the cancer journey. [I have bolded the more useful tests in this summary, for easy review and comparison.]

The multivariable calculators include **PCPT**, which has an attractive, easy-to-understand, graphical output. A more complex European ERSPC series of six different risk calculators is not commonly used. The **UCSF Primary Care Protocol** suggests time-to-recheck PSA, based on PSA for 45-60 year olds, or 61-75 year olds, that allows a five-year interval to the next test if PSA is <1, but recommends a referral to a urologist for immediate discussions if PSA is >2 or >3, respectively. Intermediate values would indicate rechecks at certain intervals – see the video.

The PRS (polygenic risk score) is based on SNPs (single nucleotide polymorphisms), the most common type of genetic variation among people. It represents a difference in a single nucleotide that makes up the cellular DNA, and can occur either within or in-between genes. The score represents the total number of risk-associated genetic variants that an individual has, which permits assessment of their heritable risk of developing a particular disease. Unfortunately, this is not yet available commercially for PCa screening. A version called the PROMPT test was temporarily available (until the company was sold and the new owners have not marketed it). Dr. Dato found it useful with several patients.

The PCA3 test is FDA approved for prior negative biopsy, giving improved specificity over PSA alone in some cases. It has good NPV (indicates no cancer) at/below low score (≤20), and good PPV (indicates PCa) at/above high score (≥60). It is less consistent as a predictor for high grade disease. It has been incorporated into newer tests.

The **4K score** analyzes total PSA, free PSA, intact PSA, and hK2 (human kallikrein 2 – see note below), and includes clinical factors: age, previous Bx (biopsy), and DRE (digital rectal exam). Contraindications: DRE w/in 96 hours, known history of PCa, use of 5-ARI (finasteride or dutasteride) within 6 months, or any prostate procedure within 6 months. It allows for individualized risk prediction based on the score found. Low risk: <7.5% -- Intermediate risk: 7.5% - 19.9% -- High risk: ≥20%. For Gleason Grade Group ≥2, the test has high sensitivity (94% ability to find PCa) as well as an NPV of 95% at the 7.5% cutoff.

The **ExoDx test** is relatively new and based on urine exosomes, which are lipid vesicles secreted by cells. They contain proteins, RNA, and other molecules which are closely representative of the content of their cellular origin. They also contain both PCA3 and TMPRSS2:ERG fusion mRNA. The test provides a molecular signature predictive of PCa, and a DRE is not required. An at-home test was available during the Covid lockdown years. The test was validated in over 1000 patients across two prospective validation trials to differentiate the risk of ≥GG2 from GG1 (GG is "Grade Group") cancer and benign disease. It is predictive of Gleason Score ≥ 7 PCa with NPV 91%, PPV 36%, Sensitivity 92%, Specificity 34%. Very commonly used in Dr. Dato's office. Notes: Sensitivity = (True Positives (A)) / (True Positives (A) + False Negatives (C))

Specificity = (True Negatives (D)) / (True Negatives (D) + False Positives (B))

Positive Predictive Value = (True Positives (A)) / (True Positives (A) + False Positives (B))

Negative Predictive Value = (True Negatives (D)) / (True Negatives (D) + False Negatives(C))

The Prostate Health Index ("phi") was FDA approved in 2012. It analyzes via p2PSA/fPSA x $\sqrt{}$ tPSA. [The p2PSA biomarker is an isoform of free PSA that was identified as the most prostate cancer-specific form found in tumor extracts. fPSA is free PSA. tPSA is total PSA.] It is indicated for age ≥ 50, non-suspicious DRE and PSA 4 – 10. Gives a "better" NPV; but relatively low specificity and PPV, so Dr. Dato doesn't use it.

The **Select MDx test** is a urine-based test detecting two mRNA's (HOXC6 and DLX1) and requires a DRE / prostate massage [not particularly fun]. Sensitivity 76.9%; specificity 49.6%; NPV 82.09%; PPV 41.67 for Gleason score ≥7. The NPV improved to 93% with Select MDX + MRI. It is intended through the NPV to provide guidance as to whether a biopsy can be avoided, when there is no indication of serious cancer.

MyProstate Score 2.0 is an updated test that combines PCA3 with 17 additional markers, and currently requires a DRE. Application prior to 2nd biopsy has been suggested. At a threshold of 15, it is 100% sensitive for GG≥2. There is a current clinical trial to determine whether the DRE is necessary. The "gas gauge" report format is helpful to patients and appreciated by doctors.

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The **Confirm MDx test** is used to determine if something was missed in an earlier negative biopsy. It is an epigenetic tissue test based upon methylation. Adding a chemical group (e.g., a methyl group) to DNA doesn't change the gene itself, but typically blocks the proteins that attach to DNA from "reading" the gene. This methylation is reversible and is one of the ways the cell controls itself. The test focuses on normal tissue adjacent to a tumor, which may harbor changes "induced" by the tumor cells. Analysis of these non-tumor cells can decrease the likelihood of a false-negative result from the biopsy.

The test determines the DNA methylation status of three known tumor suppressor genes: GSTP1, APC, and RASSF1. In two studies, Confirm MDx was associated with a very high NPV of 96%, and in methylation-positive men, the degree of methylation was significantly higher in those with Gleason ≥7 versus those with Gleason ≤6.

A note on Serum Kallikreins – there are 15 tissue kallikreins (enzymes able to break protein chains) in humans. Three (hK3, hK2, & hK4) are produced in the prostate and are androgen (i.e., testosterone) regulated. The **PSA test** is actually measuring the level of hK3, and is the only stand-alone kallikrein test. It and the others are incorporated into other tests. [As was explained in the October group meeting, the main function of hK3 (PSA) is to liquify semen.]

Other tests to be aware of – "**hits and misses**".

PAP (Prostatic Acid Phosphatase), no longer commonly used, because it was supplanted by PSA. For about forty years, it was used for screening and to monitor response to therapy. Recently, the PSA/PAP ratio has been suggested as a prognostic factor for intermediate and high-risk PCa.

EPCA (Early Prostate Cancer Antigen) and a second marker, EPCA-2 have not been confirmed as useful markers. They are proteins in the nuclear matrix.

GSTP1-methylation assay (incorporated in Confirm MDX test) – the glutathione S-transferase P1 gene codes for a protein involved in cell cycle regulation and detoxification of some toxins. The gene is highly expressed in cells of benign glands; but is zero in malignant glands due to methylation. As previously noted, methylation is frequently associated with tumor development and poor prognosis. No current practical application for the stand-alone test or as a stain for biopsy tissue.

AMACR Antibody is alpha-methylacyl-CoA racemase – a class of enzymes within peroxisomes and mitochondria, responsible for breakdown of various substances: e.g., fatty acids & toxins. It is overexpressed in prostate cancer, with low expression in normal tissues. Current usage is in immunohistochemical analysis (staining) of pathology samples.

Sarcosine (N-methylglycine) is an amino acid not used in making proteins. It was proposed as a urinary marker for PCa, but testing was problematic: expensive equipment and high analytical demands to detect low concentrations. Not currently of practical value.

IGFBP-3 (Insulin-like growth factor binding protein) is a metastasis suppression gene, with proapoptotic (promoting cell death) and anti-angiogenic (preventing new blood vessel growth) effects. Studies suggest low levels are associated with greater risk of aggressive metastatic disease. Current usage is only in assessing adequate growth hormone production in children and adolescents.

PSP94 is a prostate-secreted protein of 94 amino acids. Loss of expression correlates with high Gleason grade, advanced stage, and nodal metastasis. PSAP94 loss + PTEN deletion gives additional prognostic information. Has potential use in clinical prognosis, and may be available in clinical trials. [Wikipedia notes: Urinary MSMB (another name for PSP94) has been found to be superior to urinary PSA at differentiating men with prostate cancer, at all Gleason grades. PMID 20967219]

IL-6 is a proinflammatory cytokine (one of many small proteins important in cell signaling. Cytokines include chemokines, interferons, interleukins, lymphokines, and tumour necrosis factors. They act through cell surface receptors and are especially important in the immune system.) IL-6 is expressed in prostate tumors, and regulates proliferation, apoptosis, angiogenesis and differentiation. It may be a growth factor for androgen-independent cells. It is found in elevated levels in untreated metastatic PCa (i.e., hormone sensitive), as well as in CRPC (castrate-resistant prostate cancer – which grows independently of the androgen/testosterone level).

Inhibition of IL-6 with an anti-IL-6 antibody sensitizes androgen-independent prostate cancer cells to chemotherapeutic agents, at least in vitro. There is evidence that IL-6 plays a major role in the transition from hormone sensitive. to CRPC, working through activation of the AR (androgen receptor). Efforts to find an MAB (monoclonal antibody) against the IL-6 signaling pathway are giving mixed results, so there is no commercial therapy yet.

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Serum antibodies have been proposed as a screening test, based upon identification of antibodies against cancer antigens, such as p53 and AMACR. Not proven successful. Has a possible role in clinical research, to study response to immunomodulating therapies.

Neuroendocrine markers are markers of neuroendocrine differentiation for histologic evaluation (in pathology). The most common are chromogranin A, CD56, synaptophysin, and neuron-specific enolase. There is a small subset of patients with AR-independent biology (Neuroendocrine or small-cell cancer, which grows despite lack of testosterone). Such biology has poor prognosis and is associated with early/extensive visceral metastases, low PSA production, and lytic (breaking down) bone lesions. These patients are not yet able to be diagnosed by markers, but only by clinical characteristics (PSA-independent tumor growth) and histology (pathology of tissue samples).

Utilization of the various tests before biopsy (pre-diagnosis):

Consider the conundrum (dilemma): Current screening using PSA alone has poor specificity (there can be various causes of an elevated PSA), and often leads to unnecessary biopsies and overdiagnosis of low-risk disease. It is associated with potential treatment related toxicity, expense, and anxiety for the patient. Such screening gives only a small overall improvement in PCa-specific survival. Yet a PSA level below median has strong negative predictive value for meaningful cancer. How can we build on early baseline PSA testing? We need a balance between identifying higher risk disease and limiting the number of biopsies, while determining those who need treatment and those who don't. We want to limit the risk, discomfort, inconvenience of biopsies. Hopefully, we can use biomarkers, MRI scans, or a combination.

NPV for GG≥2 with **MRI** is 76% (but based on template biopsy). There is interobserver variability – but Dr. Ross Schwartzberg at Imaging Healthcare Specialists is the best MRI interpreter in our area.

The various blood and urine tests discussed above do not of themselves have the desired combination of a high percentage of avoided biopsies with a low percentage of missing high-grade cancer. See the video for a table of these disappointing data.

So an algorithm is needed, to create the best combination of tests. Starting with an elevated PSA, should one do an MRI scan or a biomarker test alone before a proposed biopsy, do them in succession, or always do both? See the video for a very detailed set of bar graphs showing the various approaches' effectiveness in retrospective studies. There is no conclusive answer, but to this member, the most promising seem to be the 4K Score or ExoDx tests, followed by MRI and possibly a biopsy, if the score is not in the low range.

Post Diagnosis – Tissue and blood based genomic testing

Prolaris is a gene expression assay that measures the expression of 31 cell cycle progression (CCP) genes, compared to 15 "housekeeping" genes. It has been validated for DSM (disease-specific mortality), distant metastases (10-year risk), and in its ability to help predict which men with high-risk disease will benefit from ADT and which patients with lower-risk prostate cancer can safely avoid such treatments. It utilizes clinical features through the CAPRA (cancer of the prostate risk assessment) calculator.

Oncotype Dx GPS – based on the levels of expression of 17 genes in tissue. The expression levels are related to four pathways known to be involved in PCa progression: stromal expression, cellular organization, androgen pathway, and proliferation. It has been validated as a strong prognostic indicator of adverse pathology, biochemical recurrence, distant metastases and PCa-related related death in men with localized PCa after RP (radical prostatectomy).

The GPS assay is also a strong, independent prognostic indicator of time to BCR (biochemical recurrence), DM (distant metastases) and PCD (PCa related death) in men with localized PCa undergoing EBRT (external beam radiation therapy).

Decipher is a 22-gene genomic classifier panel and prediction model for metastasis. It includes both protein coding and non-coding RNAs with roles in cell proliferation, cell-cycle progression, immune response, cell structure, cell adhesion, and motility. It has been validated on biopsy cores as a predictor of metastasis and prostate cancer specific mortality within 10 years of RP or RT (radiation therapy). Also useful to decide if RT post-prostatectomy is advisable.

The Decipher "grid" is an artificial intelligence platform and database. It accumulates genomic data and aids the development of new products / collaborating to accelerate drug development and clinical trials.

The individual's genomic signature derived from the database is useful in determining dosing for salvage radio-

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therapy (SRT) using the Post-Operative Radiation Therapy Outcomes Score (PORTOS). The data also can predict response to treatment: moving from who will / who will not do well, to what treatment to use.

Canary PASS (Canary Prostate Active Surveillance Study) is a multi-center research calculator (not a biomarker) for active surveillance. Active surveillance in PASS means closely monitoring men with prostate cancer and offering treatment if test results show the cancer is getting worse. You can go to the website and plug your numbers in, to get a risk prediction of taking action(s) or not. Great for being your own advocate.

Circulating Tumor DNA (ctDNA) and Tumor Cells (CTC). ctDNA uses small segments of DNA from tumors, and through analysis of mutations and of DNA methylation changes, provides prognosis and treatment-response predictions. Quantity of ctDNA available to detect is based upon tumor type and stage.

Circulating Tumor Cell (CTC) analysis is being considered for early diagnosis, prognosis assessment, prediction of treatment efficacy, and early detection of relapse. Both tests are often referred to as "Liquid Biopsy." Advantages include avoidance of biopsy -- especially if tissue is scarce or inaccessible, e.g., bone metastases; ease of use; larger sample size; and co-morbidities are irrelevant. Disadvantages include current detection limitations with low tumor volume, cost and insurance coverage, and varying levels of detection.

Current thinking is that the cancer genomics don't change very much over time, so a test soon after diagnosis could have long-term relevance. But insurance coverage is easier to get for advanced cancer. The tests are currently done either/or, but as costs come down, they may be combined.

Currently available genetic tests

Germline (heritable) and Somatic Mutations -- Ambry: Cancer Next®, Prostate Next® for germline testing; Myriad's MyRisk®; Invitae; **Guardant 360® CDx; Foundation One® CDx; Tempus xT, xF** (with the latter three the leaders for liquid and tissue biopsies).

TriNetra™ - a very new test that utilizes CTC (circulating tumor cells -- instead of circulating tumor dna). Claims to detect early-stage PCa at >99% accuracy with no false positives. Currently indicated for men 55-69 years with a PSA ≥3. The FDA has given this test a "Breakthrough Device Designation," which speeds up development, assessment, and review, while preserving the statutory standards for premarket approval.

Up-and-coming tests

Initial diagnosis: the "**EpiSwitch(PSE)**" test combines PSA with an epigenetic "EpiSwitch" test, and claims to be 94% accurate for detection.

Northstar "**Select and Response**" looks at mutation profiling, but also gives therapy response monitoring via tumor methylation changes. They have improved identification of single nucleotide variants (SNV's) and insertions/deletions (Indels). They claim an LOD (limit of detection) 2x lower than other tests.

Multi-cancer early detection tests involve ctDNA based screening. Several are in development – the best known is GRAIL Galleri®, which screens for 50+ tumor types. They say it is "...not a diagnostic test and is intended to be used as a complement to existing cancer screenings." It predicts where the cancer is coming from "with high accuracy" … but the average sensitivity is 51.5% and varies based on the cancer type and stage. The false positive rate is <1%, but it is relatively poor for detecting very early cancers – on average only 16.8% of stage I cancers were detected.

Issues remain: Failure to detect following a positive MCED (Multi-cancer early detection) test, potential for unnecessary invasive tests to find a cancer, premature discontinuation of proven screening, potential overdiagnosis of indolent/slow-growing cancers, and uncertain impact on cancer-specific survival.

Unmet Needs

Validated biomarkers for active surveillance beyond PSA to avoid unnecessary biopsies, reduce the frequency of follow up biopsies and reduce serial repeated MRIs.

Imaging modality better than MRI (less expensive, more available, easier interpretation, lower false negative rate – currently 20-25%). Micro-ultrasound can be extremely helpful, as Dr. Dato's office has found.

Minimal residual disease detection/confirmation. Currently limited to assessing effectiveness in hematologic cancers: CLL (chronic lymphocytic leukemia), multiple myeloma, or B-ALL (B-cell acute lymphoblastic leukemia).

Ways to better determine the cancer treatment effectiveness and to guide further treatment plans.

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Questions:

Has Covid caused rises in PSA? Dr. Dato does suspect so, due to an inflammatory response. If the PSA goes back down later, that would seem to confirm the effect.

What about the rumored shortage of Pluvicto? It has just become generally known. Gene noted that his immediate past treatment was delayed, but he is about to get another infusion, without a delay. So apparently the situation is already improving. Current patients will likely not be delayed, but new patients may be waiting longer to begin treatment.

Is a biopsy clear-cut to interpret? Mostly clear, but a small percentage of equivocal samples. [It's a good practice to request one's biopsy cores be sent to Dr. Epstein's group at Johns Hopkins for a second opinion – just look them up on the internet and ask your doctor to arrange.] Regarding scans to guide biopsies, MRI fusion (overlaying a prior MRI with the ultrasound used to guide needle placement) has been a great boon to locate any tumors. Since MRI has a false negative rate of about 20% (missing some tumors), use of biomarkers can help decide to look more closely, such as with a micro-ultrasound scan or even a "saturation" (very many cores taken) biopsy. If the location of the tumor is identified, it may then be possible to use a focal therapy, rather than treating or removing the whole prostate gland.

Would you prefer that all MRI's now be done with the rsi-MRI technology (see Dr. Seibert's talk in January), or are there cases where an "ordinary" MRI would satisfy you? He would prefer that everyone get an rsi-MRI, and get it at IHS (Imaging Healthcare Specialists), where he trusts the interpretations of the scans, and can directly access them himself (vs. merely getting a cd of a scan from other health systems).

What about making PSMA the standard scan? The cash price is $4,500, so insurance companies only approve in cases of high risk PCa with rising PSA. Also, about 10% of prostate cancer cases do not produce the PSMA protein, so the scan would fail. But "a great approach" otherwise!

What about rsi-MRI for metastatic disease? Dr. Dato does not know how helpful it would be. For instance, it is known that radiation causes significant morphological changes within the prostate, making MRI scan interpretations more difficult.

For patients on ADT after surgery and radiation, what active surveillance regimen would you follow? Typically, on a three-month schedule he would check PSA, testosterone (to ensure it stays low, especially if gnrh agonists like Lupron are being used), and a complete metabolic panel. The panel helps assess general health, including liver & renal function and glucose (since ADT can lead to diabetes). He will occasionally add CBC (complete blood count, which can be affected by ADT) and lipid tests (if covered by the patient's insurance). If intermittent ADT, he likewise follows the testosterone recovery and whether PSA stays low.

What's a center of excellence? In contrast with a general urology office, a center of excellence focuses on prostate cancer and has specialized expertise and equipment such as fusion biopsy, micro-ultrasound etc. As an example of greater care, Dr. Dato's office does a rectal swab to verify that the bacteria there will be susceptible to the selected antibiotics (multiple, not just a single) that are used prior to / during the biopsy to avoid sepsis. They have staff who are able to maximize insurance authorizations for the very expensive medications not used for PCa. New patient appointments are allocated an hour, not just a brief consultation.

See the video online for the entire meeting: https://www.youtube.com/watch?v=nf2AH-CsIGo

Note that you can skip directly to the talk (at 6:42) using a link in the information section under the video.

DVD's of IPCSG meetings are no longer being made. See the talk online on your own device, or on that of a friend or relative, or elsewhere.

Notice

Please go to https://www.instagram.com/ipcsg3/ and observe our post images. We have prepared and begun posting on the Instagram platform, posts that encourage regular PSA testing. Many of the posts are aimed at the "younger generation," who are more likely than their elders to use Instagram. We hope to get some of them to encourage their elders to take care of their health -- in particular, by PSA testing..

Summaries of Articles of Interest

"MDxHealth: Who Doesn't Love A Good Prostate Exam?" https://seekingalpha.com/article/4592144-mdxhealth-who-doesnt-love-a-good-prostate-exam

The article is about MDxHealth, a company that specializes in developing and commercializing molecular diagnostic tests for cancer. The author focuses on the company's prostate cancer test, which is designed to help physicians determine whether a patient's prostate cancer is aggressive or indolent. The test, called ConfirmMDx, has been shown to be highly accurate in clinical studies and has the potential to reduce unnecessary biopsies and treatments for low-risk prostate cancer.

"ETV4 mediates dosage-dependent prostate tumor initiation and cooperates with p53 loss to generate prostate cancer" https://www.science.org/doi/10.1126/sciadv.adc9446

The article reports on a study that investigated the role of a gene called ETV4 in prostate cancer initiation and progression. The researchers found that ETV4 plays a crucial role in driving prostate cancer development in a dose-dependent manner. They also discovered that ETV4 cooperates with loss of the tumor suppressor gene p53 to accelerate tumor growth and metastasis. The study was conducted in mice and human prostate cancer cells, and the findings suggest that targeting ETV4 could be a promising strategy for the treatment of prostate cancer, especially in patients with p53 mutations. The study sheds light on the molecular mechanisms underlying prostate cancer development and provides potential targets for future therapeutic interventions.

"ENZAMET shows promise as prostate cancer treatment" https://medicalxpress.com/news/2023-03-enzamet-prostate-cancer-treatment.html-

The article reports on a clinical trial called ENZAMET, which evaluated the efficacy of two different treatments for metastatic hormone-sensitive prostate cancer. The trial found that the addition of the drug enzalutamide to standard hormone therapy improved overall survival compared to standard hormone therapy alone. The results were particularly significant in patients who had not received prior chemotherapy. The trial also showed that the combination therapy was generally well-tolerated by patients. The findings suggest that enzalutamide could be an effective treatment option for patients with metastatic hormone-sensitive prostate cancer and could improve overall survival outcomes.

"Safety and Survival Outcomes of 177Lu-Prostate-Specific Membrane Antigen Therapy in Patients with Metastatic Castration-Resistant Prostate Cancer with Prior 223Ra treatment: The RALU Study" https://jnm.snmjournals.org/content/64/4/574?rss=1

The study investigated the safety and efficacy of a treatment called 177Lu-prostate-specific membrane antigen (PSMA) therapy in patients with metastatic castration-resistant prostate cancer (mCRPC) who had previously received 223Ra treatment. The study found that the treatment was well-tolerated by patients and resulted in a median overall survival of 12.7 months. The study also showed that the treatment was effective in controlling disease progression, with 49% of patients experiencing a decrease in their prostate-specific antigen (PSA) levels. The findings suggest that 177Lu-PSMA therapy could be a promising treatment option for patients with mCRPC who have previously received 223Ra treatment and could improve overall survival outcomes.

On the Lighter Side

NETWORKING

Please help us in our outreach efforts. Our speakers bureau consisting of Gene Van Vleet and Bill Lewis is available to speak to organizations of which you might be a member. Contact Gene 619-890-8447 or gene@ipcsg.org or Bill 619-591-8670 (bill@prostatecancerhelp.info) to coordinate.

Member 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

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!

DIRECTIONS TO MEETINGS

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.