Informed Prostate Cancer Support Group Inc.
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July 2020 NEWSLETTER

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Friday, July 17, 2020

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Next Meeting: Saturday, July 18th, Live-Stream Event, 10:00am PDT (San Diego California Time)

Three of IPCS's members tell of their journey with Prostate Cancer.

- **Gene Van Vleet** – Welcome message and overview of IPCSG's mission. Gene will then discuss his personal journey with Prostate Cancer, how it was detected and his decisions about treatment.
- **Dick Howard** – He was under the care of an oncologist late last year. A biopsy was done, but complications occurred. A very scary time for Dick. He talks about his journey from the biopsy to how he found IPCSG, and how IPCSG helped him become his own case manager!
- **Ralph Hughes** - His journey started in May 2014 with a PSA of 3.95 and rising. Following a Biopsy, he had a prostatectomy, but as many of us have experienced, he had a Recurrence. Ralph shares several valuable lessons he learned along his journey.
- Visit https://ipcsg.org/live-stream to watch

Due to COVID-19, no in-person meetings at the Sanford Burnham Prebys Medical Discovery Institute will take place until further notice. This meeting will be live-streamed and will also be available on DVD.

- **For further Reading: https://ipcsg.blogspot.com/**
- **For Comments, Ideas and Questions,** email to Newsletter@ipcsg.org

June 2020 Informed Prostate Cancer Support Group Online Presentations

1. Prostate Cancer Basic Science
2. Sexual Side Effects of Treatments

Summary by Bill Lewis

Abstract:

Dr. Andrew Goldstein, PhD Professor-in-Residence of Urology, David Geffen School of Medicine at UCLA explained how healthy prostate cells develop into cancer, and how prostate cancer cells develop resistance to therapy, which is critical for improving disease diagnosis and identifying new treatment options. He presented some of his laboratory's basic science research that will enable us to better understand prostate cancer biology and may lead to new approaches for therapy in the future.

Dr. Irwin Goldstein, MD, Director of San Diego Sexual Medicine spoke about some of the negative side effects of prostate cancer treatment and their management, including urinary incontinence and erectile dysfunction. He also discussed contemporary research in these areas.

1. Basic Science Research of Prostate Cancer to Support Clinical Treatment

Understanding how cells survive androgen deprivation: Prostate cancer growth and proliferation depends on

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Organization

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

IPCSG

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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.

Be your own health manager!!

Meeting Video DVD's

DVD's of our meetings are available through our website: https://ipcsg.org/purchase-dvds

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

From the Editor

Because of COVID-19, our usual meeting place, the *Sanford Burnham Prebys Medical Discovery Institute* is not available. We will keep you updated as to when these facilities are once again open and our in-person meetings can resume. Until then, we will be live-streaming our monthly presentations on the third Saturday of each month, starting promptly at 10:00 PDT (San Diego California time).

We will continue to post and distribute the newsletter in the interim.

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** Lyle LaRosh @ 619-892-3888; or **Director** Gene Van Vleet @ 619-890-8447.

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dihydrotestosterone (DHT) binding to a receptor on the cell, which then gives a signal to make proteins that allow growth. Androgen deprivation therapy (ADT) with Lupron or Firmagon or the like targets the production of, and reduces the blood level of testosterone and dihydrotestosterone, which starves many cancer cells, and causes disease regression. Anti-androgens such as Casodex and Xtandi, by blocking the binding of DHT to the receptor, accomplish the same purpose. However, in either case, some cancer cells survive, and may lead to a resurgence and increased aggressiveness of the cancer. The goal of Dr. Andrew Goldstein's research is to understand how cells survive these treatments, and then to improve the efficacy of therapy in eliminating cancer cells.

Prostate cancer cells grown in petri dishes in the lab, and treated with Xtandi (enzalutamide) show a decrease in their growth rate at first – as expected – but then after 4 weeks of treatment begin to grow more rapidly again. Under the microscope, the cells that have become tolerant to the presence of Xtandi look very different from their appearance early in the experiment. Instead of a normal oval appearance, the cells have become elongated, with projections like neurons.

The research team was also able to use genetic analysis of the petri-dish cells, to evaluate changes in genes and groups of genes. The found up-regulation of groups of genes for "axonal guidance," which would normally only be active in brain cells. Individual genes associated with the androgen receptor were "down," and some genes that normally are only turned on in neurons were "up." Verification that this effect was not just something that happens in petri-dish grown cells, came from tissue samples that were analyzed similarly, from a 2014 study of biopsy samples from men (with locally advanced or metastatic prostate cancer) who were treated with Xtandi for 22 weeks. The very same trends were seen in those samples. So this suggests that petri-dish studies may be helpful for testing combinations of drugs, where a second drug is combined with Xtandi, and hopefully would be found to have more long-term effectiveness in controlling or eliminating the cancer.

The approach currently being considered is based on the hypothesis that as tumor cells adapt to the first drug (Xtandi in this case), their energy/food requirements change. So far, they have found that the amino acid serine, a so-called non-essential amino acid (because cells can make it themselves as needed), is not synthesized as effectively by Xtandi-tolerant cells (i.e., after they become tolerant to its presence), so they become more reliant on external sources (diet) for their need. Lab / dish studies are starting, to confirm whether "dietary reduction" of serine may help Xtandi therapy be more effective long-term.

On the subject of prostate cancer and the COVID-19 virus, it has been reported both from China and from Italy, that men more often are infected and more often die from the virus vs. women. A study of 4500 men in Italy reported that men on ADT were four times less likely to get the disease, and five times less likely to die, vs. men not on ADT. It was then hypothesized that ACE2 and TPRSS2, proteins ('receptors") that make it easier for SARS-CoV-2 to enter our cells, may be regulated (controlled) by androgens (testosterone, etc.). Some data for lung tissues seems to confirm this. Dr. Goldstein's group tested the hypothesis in nasal cells of mice – since inhalation may lead to infection via nasal tissues. A week of treatment with either Xtandi or Casodex (bicalutamide) did cause a large reduction in the number of TPRSS-2 receptors. Several clinical studies in the Veterans Administration system are testing the effect of an anti-androgen [I believe that Firmagon is being used] on infection and severity of COVID-19 disease. Nasal swabs are being taken in those studies, and may confirm what Dr. Goldstein has seen in mice nasal tissues and others have seen in lung.

Questions: How long would one need to be on ADT to see the effects described? In the human trial mentioned, the men were on ADT for 22 weeks. But really, we don't know the answer to this question yet.

What foods are rich in serine? Consult a nutritionist. A concept would be to make protein shakes that omit the particular amino acid being targeted. However, if this were the whole diet, it might not be popular.

How long to bring this research to practical application? Typically 5-10 years for new classes of therapies (i.e., drugs), but perhaps a dietary therapy could be introduced in a few years.

How do you pick patients for your research? He doesn't do research on human subjects. He is "modeling" prostate cancer, and gets his cells from UCLA with no info on who they came from. But if his research leads to clinical trials, they certainly will try to determine which patients would most likely benefit from it.

Would Lupron give a similar benefit for protection against COVID-19? Quite possibly, but that hasn't been published yet.

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2. Sexual Health Issues in Men with Prostate Cancer

Dr. Irwin Goldstein's practice is in sexual medicine, which is the study, diagnosis and treatment of sexual health concerns of men and women. His office contains specialists, including pelvic floor physical therapists, nurse practitioners for physiologic care, and a sex therapist trained at the McKinsey Institute, to address Sociocultural Influences, Interpersonal Relationship issues, and Psychological issues.

Erectile Dysfunction: The penis must have sufficient axial rigidity to penetrate the vagina, which requires a force of about 1 kilogram. There was a lot of hope that "nerve sparing" surgery on the prostate would preserve erectile function, but the reality is that most surgery patients (75% or more, based on study data) never achieve their former results, even with this surgical approach, and even with the assistance of Viagra or the like. Besides pills, other "symptomatic" treatments may involve vacuum devices, self-injections, pellets and even prostheses. Dr. Goldstein particularly likes and often prescribes a restriction device called "Giddy."

"Disease modification" strategies used in his office include sex therapy (usually in couples), physical therapy, endocrine [hormone] therapy, neurologic therapy, penile revascularization, drug eluting stents, regenerative stem cell treatment, platelet rich plasma and low-intensity shockwave therapy. In regard to the latter, a Dr. Hartmut Porst (in Germany) published a report on benefits of "low-intensity extracorporeal shockwave therapy" that have been confirmed in Dr. Goldstein's practice. It can improve/heal the scarred erectile tissue for better blood flow and retention for erections. But he warns that there are scams using underpowered devices that should be avoided.

Dr. Goldstein is beginning a clinical trial of shockwave therapy for men with erectile dysfunction, and the video shows the lists of inclusion and exclusion criteria. Contact his office if interested in participating.

Urinary incontinence is another issue that improved surgical techniques were supposed to avoid, but many post-surgery patients suffer from it.

The "BTL Emsella" chair is an FDA-approved device for improving urinary continence. It sends electromagnetic pulses that stimulate muscle contractions, equivalent to 11 thousand Kegel exercises ("supramaximal pelvic floor muscle contractions"), in a 28-minute session. The patient remains fully clothed during the procedure. Its effectiveness is based on focused electromagnetic energy with sufficient depth penetration to stimulate the entire pelvic floor area. (Note: Dr. Goldstein is a biomedical engineer from Brown University, and loves bioengineering devices!)

He is also starting a clinical trial for men with stress or urge urinary incontinence (or both). Again, inclusion /exclusion criteria are listed in the video, and you can contact his office to enroll in the trial.

Peyronies disease is common after radical prostatectomy, though the reasons for it are not known. The penis is shorter and has a curve in any direction. It can affect the man with a loss of sexual confidence, performance anxiety, mood disturbance, low self-esteem and self-image, and general emotional distress. Perhaps surprisingly, the psychosocial impairment does not appear to correlate with the degree of curvature deformity. The FDA has approved a treatment involving a series of injections into the plaque that causes the curvature, resulting in less deformation, and increased penis length. [The name of the medicine was not mentioned.]

Testosterone supplementation: In selected (low risk) prostate cancer survivors, who don't have significant PSA values, administering testosterone ameliorates the symptoms of hypogonadism (i.e., low testosterone), decreases the risks of long-term effects of hypogonadism, and can significantly improve quality of life. It has been reported in a variety of studies (listed in the video) that men who are diagnosed with prostate cancer, while also having low testosterone, tend to have a worse prognosis than men with a normal or high (natural; endogenous) testosterone level. It is recommended that individualized discussions be held to consider the risks and benefits of administering testosterone to candidate hypogonadal men.

Dr. Goldstein noted the many side effects of long-term ADT (androgen deprivation therapy): Metabolic syndrome (especially abdominal obesity), Elevated triglycerides, lowered HDL, elevated cholesterol, elevated LDL. Increased blood pressure. Insulin insensitivity, elevated glucose (including A1C), and increased insulin levels. Sexual dysfunction -- reduced erection, reduced libido, reduced orgasm, and Peyronies disease. Increased BPH (prostate enlargement) and lower urinary tract symptoms. Osteopenia and osteoporosis (weaker bones). Depressive and/or anxiety symptoms, cognitive and decision-making ability effects. Endothelial dysfunction (impairment of the inner lining of the small arteries), elevated C-reactive protein, and elevated cardiovascular mortality.

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Testosterone can be supplemented for hypogonadal men using gels, injections, patches or pellets. Dr. Goldstein is now giving his patients the "Jatenzo" oral formulation, approved a few months ago, which is a pre-drug (or prodrug, if you prefer), taken twice daily, that is coated with a lipoprotein that causes it to go into the intestinal lymphatic system (avoiding the liver, which would be damaged by ingested testosterone), and then eventually is converted by esterase enzymes in the systemic blood circulation to free testosterone.

Benefits documented for testosterone supplementation: bone health, improvement in lower urinary tract symptoms, blood pressure reduction, conversion of fat to muscle, better cholesterol/HDL, and lower A1C (blood sugar). May increase blood pressure a bit -- must monitor. No change in PSA in the vast majority of patients.

Other sexual dysfunctions: hypofunction or hyperfunction. He looks for blockages or reasons for too much signal. Some such dysfunctions are due to spinal cord problems, which may be treated with shockwave therapy or surgery.

Partner issues: A number of articles discuss this, and are available on request. His office has a sex counselor, and he feels this is an important area to address.

Questions:

Medicare coverage? His services are cash-only, because his visits are typically 2-3 hours, and Medicare only covers very short visits. However, both clinical trials he is starting are no-cost.

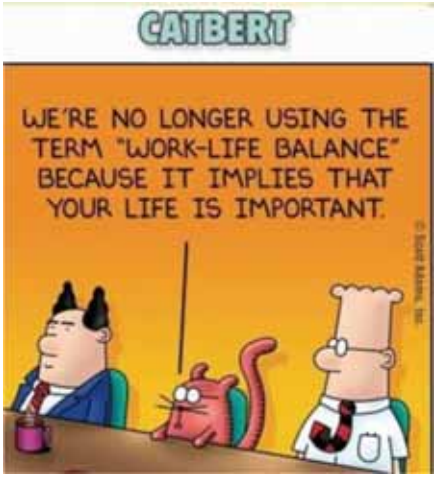
His email? dr.irwingoldstein@gmail.com (but you might have to wait for an answer because he works really long hours!)

Is Jatenzo compatible with taking antidiuretic hormone? No interference.

Approximate costs? $450 per shockwave therapy treatment. Emsella is $125 per treatment. The initial visit cost is $600.

Do ADT side effects reverse after treatment ends? Yes, to a large extent.

On the lighter side



"The small neat scar was from the surgery. The long jagged scar is where I sneezed."

Articles of Interest

Enzalutamide Improves Survival in Men With Metastatic Prostate Cancer

By Will Boggs MD

medscape.com

NEW YORK (Reuters Health) - Enzalutamide improves five-year survival in men with chemotherapy-naive metastatic castration-resistant prostate cancer (mCRPC), but increases the risk of fatal adverse events, according to final results from the PREVAIL trial.

"When docetaxel was FDA (Food and Drug Administration) approved as the first life-prolonging therapy for men with metastatic castration resistant disease back in 2004, the 5-year survival was less than 5% of these men," said Dr. Andrew J. Armstrong of Duke Cancer Institute, in Durham, North Carolina.

"The gratifying data from this PREVAIL trial of enzalutamide shows that many more men with mCRPC are living past 5 years, with 42% of lower-risk men and nearly a quarter of intermediate-risk men," he told Reuters Health by email.

PREVAIL was stopped after a preplanned interim analysis revealed enzalutamide superiority compared with placebo in terms of survival and radiographic progression-free survival. At that point, eligible placebo patients were invited to cross over to enzalutamide in an open-label extension.

In the current study, Dr. Armstrong and colleagues evaluated long-term safety and efficacy of enzalutamide and five-year survival estimates based on pretreatment prognostic factors and risk groups, as well as posttreatment declines in PSA.

Placebo patients who crossed over to enzalutamide in the extension study were included in the placebo group for the final analysis of overall survival.

At the five-year overall survival analysis, enzalutamide reduced the hazard of death by 17% compared with placebo (P<0.001). At a median follow-up of 69 months, median overall survival was 36 months in the enzalutamide group versus 31 months in the placebo group, the researchers report in European Urology.

Enzalutamide maintained a long-term survival advantage over placebo despite 68% of placebo-treated men receiving subsequent enzalutamide or abiraterone.

Only among men with baseline liver metastases did enzalutamide not appear to confer an overall survival advantage.

Based on an updated 11-factor prognostic model, five-year survival rates decreased with increasing risk group, from 42% for the low-risk group to 24% for the intermediate-risk group and 5% for the high-risk group.

Similarly, five-year survival rates increased with greater drops in prostate-specific antigen (PSA) after treatment (from 9% for men with no PSA decline to 67% for men whose PSA declined to undetectable levels).

Men treated with enzalutamide had higher rates of treatment-emergent adverse events leading to death (6.9% vs. 3.8% with placebo), fatal cardiovascular treatment-emergent adverse events (1.6% vs. 0.4%), and drug-related fatal cardiovascular events (two cases, or 0.2%, vs. none with placebo).

The prognostic model used to stratify patients in this study is available as an online calculator that can provide patient-specific information to guide communications and goals for care at https://www.mdcalc.com/prevail-model-prostate-cancer-survival.

"While no prognostic model is perfect, and treatment advances every year are pushing survival beyond current expectations, it is important to have the most up-to-date estimates of risk for patient communications," Dr. Armstrong said. "This calculator can also be invaluable for the design of new treatments which intend to beat these expectations, particularly in those men with higher risk metastatic prostate cancers."

"We still need better treatment for high-risk men in this setting, as these patients still have a less than 5% 5-year survival," he said.

Dr. Philip Kantoff of Memorial Sloan Kettering Cancer Center and Weill Cornell Medical School, in New York City, who studies advanced prostate cancer, told Reuters Health by email, "Enzalutamide has life-prolonging effect in men with metastatic castration-resistant prostate cancer but has toxicity including increased rates of non-cancer death. Risks and benefits need to be balanced and individualized."

He added that enzalutamide is "one of multiple options for men, including abiraterone, apalutamide, and darolutamide."

Pfizer Inc. funded the study and had financial ties to all of the authors.

SOURCE: https://bit.ly/37CGvWJ European Urology, online June 9, 202

Breakthrough discovery to transform prostate cancer treatment

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A novel formulation of the prostate cancer drug abiraterone acetate -- currently marketed as Zytiga -- will dramatically improve the quality of life for people suffering from prostate cancer, as pre-clinical trials by the University of South Australia show the new formulation improves the drug's effectiveness by 40 per cent.

Developed by Professor Clive Prestidge's Nanostructure and Drug Delivery research group at UniSA's Cancer Research Institute, the breakthrough discovery uses an oil-based oral formulation that not only enables a smaller dose of the drug to be effective, but also has the potential to dramatically reduce possible side effects, such as joint swelling and diarrhea.

Despite Zytiga being the leading formulation to treat prostate cancer, lead researcher, Dr Hayley Schultz says the new formulation will ultimately provide a better treatment for patients with prostate cancer.

Prostate cancer is the most commonly diagnosed cancer in men, with one in six at risk of diagnosis before the age of 85. In 2019, more than 19,500 cases of prostate cancer were diagnosed in Australia. Globally, prostate cancer cases reached 1.28 million in 2018.

"Many drugs are poorly water soluble, so when they're ingested, they enter the gut but don't dissolve, which means that their therapeutic effect is limited," Dr Schultz says.

"This is the case for Zytiga. Here, only 10 per cent of the dose is absorbed, leaving the other 90 per cent undissolved, where it simply passes through the body as waste.

"On top of this, patients taking Zytiga must fast for two hours prior to taking the drug, and another hour after taking the drug to achieve predictable absorption. And as you can imagine, this can be painstakingly inconvenient.

"Our new formulation changes this. By using oils to mimic pharmaceutical food effects, we're able to significantly increase the drug's solubilisation and absorption, making it more effective and a far less invasive treatment for patients."

The new formulation uses very high levels of abiraterone acetate dissolved within a specific oil and encapsulated within porous silica microparticles to form a powder that can be made into tablets or filled into capsules. Applied to human treatment, it could reduce the dose from 1000mg to 700mg per day, without the need for fasting.

Prof Prestidge says if the team can secure funding, clinical trials in humans could be just two years away.

"Based on our knowledge of this drug's pharmaceutical food effect, we hypothesise its absorption in humans will be extensively improved using this technology," Prof Prestidge says.

"Anything we can do to contribute to the development of a commercialised product to improve the lives of patients, is invaluable.

"This novel formulation is flexible enough to be adopted by thousands of different medicines; its potential to help patients of all kinds is exponential."

Story Source:

Materials provided by **University of South Australia**.

Note: Content may be edited for style and length

Does Radiotherapy Boost Prostate-Cancer Survival?

By Will Boggs MDmedscape.com

NEW YORK (Reuters Health) - Radiotherapy appears to provide better survival outcomes in men with low- and intermediate-risk localized prostate cancer, compared with focal laser ablation, according to a database study.

Active surveillance, radiotherapy and radical prostatectomy are all accepted treatments for men with low-risk or intermediate-risk localized prostate cancer, but focal laser ablation (FLA) is increasingly used to ablate tumors while sparing adjacent structures.

Trials of FLA have yielded encouraging short-term oncologic and functional outcomes, but information regarding long-term survival is lacking.

Dr. Qiang Wei and colleagues from West China Hospital of Sichuan University, in Chengdu, China, used 2004-2015 data from the Surveillance, Epidemiology, and End Results (SEER) database to evaluate overall survival and prostate-cancer-specific mortality at long-term follow-up in more than 93,000 men treated with radiotherapy and 428 men treated with FLA.

On multivariate regression analysis, the hazard ratio for overall survival was 91% higher following radiotherapy than following FLA ($P<0.001$). The benefit was somewhat diminished (hazard ratio, 1.49) but remained significant after adjusting for age, T stage, PSA level, and Gleason score.

In contrast, radiotherapy and FLA provided similar cancer-specific mortality rates, the researchers report in Scientific Reports.

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In a propensity score-matched subgroup of 2,568 radiotherapy-treated patients and 428 FLA-treated patients, radiotherapy was associated with a 50% better chance of overall survival, but cancer-specific mortality did not differ between the groups. Instrument variate adjusted analyses yielded similar results.

"In the future, if FLA can solve its current technical shortcomings, such as navigation, imaging, and precision, its therapeutic effect may be better with favorable survival benefits and functional protection at the same time," the authors conclude. "But at present, radiotherapy should have a priority over FLA in the management of low-risk and intermediate-risk prostate cancer."

Dr. Herbert Lepor of NYU School of Medicine and NYU Langone Health, in New York City, who has reviewed focal ablation of prostate cancer, told Reuters Health by email, "This paper is based on a statistical model and absolutely no long-term survival data available regarding focal laser ablation. I am surprised this article was published in the absence of any data to inform the model."

"Focal therapy is an emerging treatment options that avoids many of the side effects associated with whole gland treatments of radical prostatectomy and radiation therapy," he said. "Long-term survival data are lacking."

"I no longer offer focal laser ablation," Dr. Lepor said. "My energy preference for focal therapy is cryotherapy, since we achieve better energy confluence within the planned ablation zone."

"I would offer focal therapy over radiotherapy to an individual with a Gleason 7 (Gleason Grade Group 2 or 3) who has cancer confined to the side of the prostate with a unifocal MRI lesion shown to harbor prostate cancer whose priority is preservation of quality of life (potency, GI and bowel issues)," he said.

Dr. Lepor added, "Another advantage of focal therapy in these cases is avoidance of side effects of neoadjuvant androgen-deprivation therapy which is given to men undergoing radiotherapy. This represents a large proportion of cases. Our early data show 98% oncological control following extensive biopsy at 6 months with cryoablation."

The study had no commercial funding, and the authors report no conflicts of interest.

Dr. Wei and coauthor Dr. Lu Yang did not respond to a request for comments.

SOURCE: https://go.nature.com/2AxD9bg Scientific Reports, online June 4, 2020.

MRI Reliably Identifies Significant Prostate Cancer

Ingrid Hein—medscape.com

Prostate cancers that are missed on multiparametric (mp)MRI are small and "not life-threatening," according to an analysis of data from the Prostate MR Imaging Study (PROMIS).

"Our work suggests that MRI scans of the prostate appear to deliver crucial information about a man's risk of dying from prostate cancer, even before he has a biopsy," said Joseph Norris, BM BS, from University College London.

"This may mean that we can finally move prostate cancer to a position in which we can use imaging as the primary tool to direct further investigations, treatment, and prediction of risk," he told *Medscape Medical News.*

This is "a position that all other solid organ cancers have reached," said Norris, who will present the findings at the upcoming virtual European Association of Urology 2020 Congress.

All 576 PROMIS participants underwent an mpMRI scan, a transrectal ultrasonography (TRUS)-guided biopsy, and a template prostate mapping (TPM) biopsy taken at 5 mm intervals across the entire prostate.
PROMIS researchers previously showed that mpMRI had a 93% sensitivity for clinically significant cancer, whereas TRUS biopsy had only a 48% sensitivity, as reported by *Medscape Medical News*. And they concluded that the use of mpMRI as a first-line diagnostic tool could prevent 27% of all biopsies, which can have serious adverse effects, such as pain, urinary problems, infection, bleeding, and erectile dysfunction.

However, in their study looking at the accuracy of mpMRI and TRUS biopsy, the researchers did not investigate the severity of the 7% of cancers that mpMRI missed. "What if those missed cancers are, in fact, aggressive? That's what we set out to examine," Norris explained.

So he and his colleagues conducted a post ad hoc analysis of the PROMIS participants in whom clinically significant cancer had been detected with TPM biopsy to see which of those cancers had been detected with mpMRI. The findings were published online in *European Urology*.

Cancers met the strict definition of clinically significant if they had a Gleason score of at least 4+3 for a tumor of any length, or a maximum cancer core length (MCCL) greater than 6 mm for a cancer of any grade. They met the less-strict definition if they had a Gleason

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Clinically Significant Cancers Detected With TPM Biopsy But Missed With Other Diagnostic Tools

Diagnostic Tool	Strict Definition (n = 230) n	%	Less-Strict Definition (n = 331) n	%
mpMRI	17	7	44	13
TRUS-guided biopsy	119	52	132	40

score of at least 3+4 for a tumor of any length, or a MCCL greater than 4 mm for a cancer of any grade.

In PROMIS, TPM biopsy detected 230 cancers that met the strict definition of clinically significant and 331 that met the less-strict definition.

CTC Count Can Predict Outcome in Prostate Cancer

by Greg Laub, Director, Video, MedPage Today June 18, 2020

— Amir Goldkorn describes the valuable biomarker that will help guide treatment

medpagetoday.com

Baseline circulating tumor cell (CTC) count was found to be significantly predictive of clinical outcome in a phase III trial of metastatic castration-sensitive prostate cancer (mCSPC) presented at the 2020 American Society of Clinical Oncology virtual scientific meeting.

In this exclusive MedPage Today *video, lead researcher Amir Goldkorn, MD, of the Keck School of Medicine and Norris Comprehensive Cancer Center at the University of Southern California, explains that the results suggest that CTC count could be used as a noninvasive biomarker to help guide treatment decisions.*

Following is a transcript of his remarks:

Hi, my name is Amir Goldkorn. I'm a medical oncologist and an associate professor at University of Southern California Keck School of Medicine. I want to tell you briefly about the results of our study looking at circulating tumor cells, or CTCs, in metastatic castrate-sensitive prostate cancer that we just presented as an oral abstract at the ASCO 2020 meeting.

So currently in metastatic castrate-sensitive prostate cancer, the standard of care for therapy is combination of androgen deprivation therapy, or ADT, usually plus another drug, sometimes abiraterone or enzalutamide or chemotherapy. But we have very few biomarkers to guide the way that we treat patients to tell us who will respond and for how long. The FDA-cleared CELLSEARCH platform has been looked at extensively in metastatic castration-resistant prostate cancer, a more advanced disease state. So we asked them for this study whether we could also use it as a biomarker, the CTC counts, to tell us how patients will respond and for how long in metastatic castrate-sensitive prostate cancer.

We did this in a large phase III clinical trial, SWOG S1216, a study run by the NCI Southwest Oncology Group. The PI on the clinical trials is Neeraj Agarwal of the University of Utah. What we did in our CTC study was we obtained baseline CTC counts for men going on trial. These men, 1,200 men, were randomized to receive ADT with either bicalutamide or orteronel, which is a CYP17 inhibitor in a class like abiraterone. And what we looked at for readouts is a response to hormonal therapy, which we defined as the 7-month PSA. That means after the 6 months of treatment, at month seven, had the PSA fallen to less than 0.2, 0.2-4.0, or >4.0, which has been previously shown to be an intermediate endpoint actually for overall survival as well. And the other thing we looked at is progression, 2-year progression-free survival.

And what we found was actually pretty significant. There was a very big difference between men who had versus did not have CTCs. For example, comparing a man who had zero CTCs at baseline versus a man who had five or more CTCs, the man who had zero CTCs had more than a six-fold odds ratio of having a complete response in terms of a 7-month PSA on hormonal therapy, relative to the man who had five or more CTCs. And conversely, the man who had five or more CTCs had an almost four-fold odds ratio for progression 2 years on therapy relative to the man who had zero CTCs. And these sorts of relationships held across different cut points. We also looked at men with fewer than five versus greater than five, which is a cut point often used in castrate-resistant disease. We also looked at having any CTCs versus no CTCs, and all of these had statistically significant differences.

So, we conclude from this study that baseline CTC counts were indeed highly prognostic of PSA response and progression in this cohort of men with metastatic castrate-sensitive prostate cancer who were just starting their therapy with hormonal treatment. And the implications for this in the clinical setting is that, hopefully even at this stage, it might give us a little bit more information about our patients when they come through the door.

For example, if we have a gentleman coming in to begin therapy who is older or more frail, but has zero CTCs, we may feel that he would do quite well with standard hormonal therapies and feel comfortable knowing that he would have favorable outcomes. Versus another gentleman who comes in the door, but maybe has many more CTCs, we may consider him to have a less likely chance of having favorable outcomes with just hormonal therapies. And someone like that we may be more likely to try to use more intensified therapies or even trials of new combination therapies for more aggressive treatment. Ultimately we want to get the final overall survival data from this trial and all the data compiled. We would look at this also to look at CTC counts as a predictive factor, meaning can they help us select between different types of treatments, so we will do that analysis by treatment arm of this trial. And ultimately we may be able to build on this with new trials, where CTC counts could be taken into account to help us predict who will respond and who will not respond to particular treatments such as ADT plus chemo versus abiraterone or enzalutamide. So ultimately we hope that this will tell us not only how patients will do overall, but perhaps be useful to help guide specific choice of treatment.

NETWORKING

Please help us in our outreach efforts. Our speakers bureau consisting of Lyle LaRosh, and Gene Van Vleet 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 by mail or email on request. Please pass them along to friends and contacts.

Ads about our Group are in the Union Tribune the week prior to a meeting. Watch for them.

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!

While our monthly meetings are suspended, we still have continuing needs, but no monthly collection. 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 420142, San Diego CA 92142