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

JUNE 2022 NEWSLETTER

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Thursday, June 16, 2022

Volume 15 Issue 06

- **Next Meeting Saturday, June 18, 2022 IPCSG—Ga 68 PSMA and its use with a PET scan— Live-Stream Event, 10:00am PT**.
- ***Mary Hames PhD, EMBA - GA68 PSMA*** .

- Dr. Hames is the Medical Director at Telix Pharmaceuticals in Grand Rapids Michigan. She will be discussing Gallium Ga 68 PSMA and how it's used with a PET scan (positron emission tomography) of prostate-specific membrane antigen (PSMA) positive lesions in men with prostate cancer. Mary will also address Telix's commercially approved products as well as their pipeline diagnostics and therapeutics.
- 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
- **If you would like some copies of our new brochure by mail for distribution to your friends or physicians, please send email to bill@ipcsg.org or call Bill at (619) 591-8670**

May 2022 Informed Prostate Cancer Support Group Meeting

Summary by Bill Lewis

Immunotherapy Update

Dr. Tanya Dorff

Dr. Tanya Dorff is a medical oncologist who serves as associate professor of medicine in the Department of Medical Oncology and Experimental Therapeutics, and is the Head of the Genitourinary Cancers Program at City of Hope, a research and treatment center for cancer based in Duarte, CA. Dr. Dorff's research interests in prostate cancer range from clinical trials in PSA-recurrent prostate cancer, to the role of fasting in chemotherapy tolerability, to developing CAR T cells that are primed to target prostate cancer tissue.

"T-Cell therapy for MCRPC (metastatic castrate resistant prostate cancer) – Trials and Tribulations."

Why target T-cells for cancer therapy? They are the most active immune system cells, and can directly kill tumor cells. In contrast, Provenge (sipuleucel-T) looks for "things that shouldn't be there," and presents them to cytotoxic T cells for destruction.

CAR-T (chimeric antigen receptor) cells are made by extracting T cells from the patient (as for collecting platelets), and then activating by a virus (or another method) that changes the receptor that the T cells

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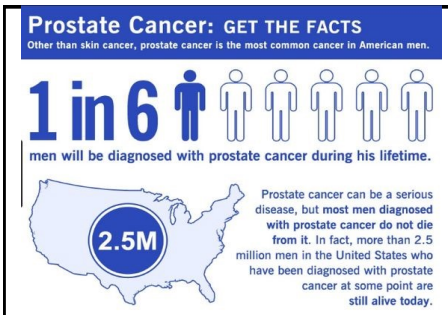

Organization

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.

Meeting Video DVD's

DVD's of our meetings are available for purchase on our website at https://ipcsg.org/purchase-dvds and are generally available by the next meeting date.

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 ; or **Director** Gene Van Vleet @ 619-890-8447.

From the Editor

Due to COVID-19, no in-person meetings will be held until further notice. We will continue to post and distribute the newsletter in the interim. Our speaker this month will be broadcast via the IPCSG website at https://ipcsg.org/live-stream and can be watched by scrolling down and clicking on the "WATCH THE PRESENTATION" button. The broadcast will begin approximately 10 minutes before to the listed start time.

In this issue:

Bill Lewis produced a summary of the last stream video, followed by a notice of the PCRI men's health fair.

Articles of Interest:

1. Article indicates patients taking enzalutamide and abiraterone may have significant health risks when used with ADT.
2. Article indicates Ivermectin may be valuable when used with chemo to suppress proliferation and metastases.
3. Article from Memorial Sloan Kettering describes how new imaging using PET/CT scan can help patients with metastatic disease to locate and eliminate Mets.

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will look for. Hundreds of millions of these modified cells are then created, and infused in a hospital, or sometimes now in outpatient settings. CAR-T cells are being studied for prostate cancer because of the great success that has been achieved in curing leukemia and lymphoma, after many other treatments have failed.

CAR-T cells are powerful medicine, but come with side effects, including cytokine release syndrome (inflammation leading to fever, fatigue, hypotension/tachycardia, nausea, capillary leak, or cardiac/hepatic dysfunction) and a few weeks later, neurological toxicity (confusion, delirium, aphasia [communication difficulties] or seizures). There is also potential for "on-target, off-tumor" toxicity – when the CAR-T cells find a binding site in some other tissue in the body.

At City of Hope, they are targeting PSCA (prostate stem cell antigen), found in 80% of prostate primary tumors, and 90% of metastases. There is some occurrence of this target in gastric and bladder tissue, which means that there "may be" side effects. They test prostate biopsy tissue for the presence of the protein, harvest T cells, manufacture the modified cells over two weeks, do CT, bone and MRI scans, infuse cytoreductive chemo for three consecutive days, and several days later, infuse the CAR-T cells at days 0, 1, 7, 14, 21, and 28, do a CT and a bone scan, then continue monthly injections for a year. There has been some temporary positive response in the 12 patients treated so far, but cystitis (bladder inflammation) has prevented the planned dose escalation. It is expected that multiple doses or additional treatment with radiation or a separate immune booster will be needed to improve the results. They are working on ways to reduce the side effects.

Dr. Dorff noted that they have found that MRI scans give a more accurate picture of bone metastases, than either CT or Tc-99 bone scans.

She discussed modestly encouraging results with a Poseida company's P-PSMA-101 CAR-T cells – see the video. Also, she outlined the perceived challenges for immunotherapy in prostate cancer, including the evolving of the cancer over time resulting in heterogeneity of tumor cells, including "antigen escape" where the tumor no longer expresses the original targeted protein. In another cancer (mesothelioma) where CAR-T cells became "exhausted" (ineffective), addition of a checkpoint inhibitor (pembrolizumab) resulted in a complete response, and she and other researchers have found this very encouraging.

Neuroendocrine prostate cancer (rare at initial PCa diagnosis, but occurs in some castrate-resistant patients as the cancer tries to survive despite anti-androgen therapy) is known to be difficult to treat, and Dr. Dorff showed how neither PSMA nor PSCA is significantly expressed in these tumors. However, a couple of other proteins are expressed more strongly, and might be targets for future therapies.

Another way of targeting prostate cancer is to use "BiTE" (bispecific T cell engaging antibodies), some of which are already approved for leukemia and some solid tumors. At City of Hope, they are studying two BiTE drugs from Amgen, one targeted to PSMA, and the other targeting a new target protein called STEAP-1. Results/details are in the video, including mention of severe but treatable cytokine release (especially fevers, chills and sometimes vomiting and diarrhea, requiring hospitalization) through the first few doses.

Other ways to leverage the immune system to target prostate cancer include the aforementioned immune checkpoint inhibitors and Provenge (sipuleucel-T, which activates dendritic cells against tumors). Interestingly, using both Provenge and Xofigo (radium-223) gave a surprising benefit – tripling the time to detectable progression of the disease (9 vs. 3 months), vs Provenge alone (C.H. Marshall, et al, GU ASCO abstract 2020). Dr. Dorff may try Xofigo in combination with her CAR-T cells.

Whereas pembrolizumab gave very poor effectiveness in metastatic castrate-resistant prostate cancer generally, for those 3% of men with microsatellite instability (detected by genetic testing), about 50% of

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them responded well. A study using two different checkpoint inhibitors gave unpromising results, and resulted in great toxicity in most patients.

At City of Hope, a combination of cabozantinib (an oral angiogenesis blocker – to prevent new blood vessel growth that would feed growing tumors) and atezolizumab (a checkpoint inhibitor) is giving very encouraging results. However, only men with soft tissue metastases are currently eligible for the phase 3 clinical trial.

Conclusion: "We believe we will achieve durable remissions!"

Questions:

What kinds of patients are being treated in the trials? Some have had chemo, others not. They prefer patients who are relatively healthy apart from the prostate cancer, so they can withstand the side effects.

What kinds of oncologists are aware of the upcoming availability of immune therapies and clinical trials? It varies a lot. BiTE therapy might become widely available to doctors' offices.

Other approaches? Therapies involving bacteria and viruses and metabolic factors are being studied by others at City of Hope. One promising approach, at least in mice, has been shown to confirm the role of the microbiome in immunotherapy. Mice failing immunotherapy immediately responded to the therapy after having microbiome transplanted in from a mouse that was responsive to the therapy. There have been reports of Opdivo, Yervoy and Keytruda (pembrolizumab) effectiveness being affected by the patient's microbiome.

See the video online for the talk and slides: https://www.youtube.com/watch?v=JVoCxkfRpho

A dvd of Dr. Dorff's talk will be available for purchase from the IPCSG by the time of next month's meeting. Order online from the IPCSG.org website.

On the Lighter Side

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Notice

The PCRI presents our 1st **Virtual Men's Health Fair!** On June 25th, 2022, we will host a one-day online educational event for men and their caregivers **via** Www.pcri.org. Expert physicians will present each topic, followed by in-depth Q&A sessions. Topics will include:

- Overall Men's Health
- Annual Lab Tests
- Cardiovascular Health
- Osteoporosis
- Erectile Dysfunction
- Diet
- Exercise
- and more

The event will be moderated by Mark Moyad, MD, MPH, and will conclude with an extended Q+A session with Dr. Moyad and our Executive Director, Mark Scholz, MD.

JUNE 2022

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Sign up today, this event is 100% free!

GO TO EVENT PAGE

https://pcri.org/pcriorg/2022-mens-health-fair

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Articles of Interest

Common Prostate Cancer Medications May be Less Safe Than Previously Thought

cookwithkathy.wordpress.com

Posted on May 28, 2022 by cookwithkathy

Men taking either of the two most common oral medications for advanced prostate cancer who had also undergone hormone therapy to treat their disease were at higher risk of serious metabolic or cardiovascular issues than patients who were only receiving hormone therapy, Michigan Medicine researchers found.

Patients taking abiraterone had 1.77 times the risk of being admitted to the emergency room or the hospital due to diabetes, hypertension or heart disease compared to those who were only on hormone therapy. Those receiving enzalutamide were at 1.22 times the risk of these issues.

Compared to patients not receiving abiraterone, those taking abiraterone were also more likely to need an outpatient visit with their physician related to at least one of these health conditions. That was not the case if the man was taking enzalutamide.

Abiraterone and enzalutamide were both found to be relatively safe in clinical trials, but concerns that the population of patients who participated in the trials was different than those in real-life settings prompted the researchers to take another look at the effects of the drugs.

For instance, this research exclusively analyzed patients with Medicare health insurance, and the majority of men studied were significantly older than those in the drugs' clinical trials.

"Patients enrolled in clinical trials tend to be highly selected and often times do not reflect the patient population in day-to-day practice," said Lillian Y. Lai, M.D., M.S., a National Institutes of Health T32 Urologic Oncology Research Fellow at Michigan Medicine and the first author of the study. "Trial participants also undergo stringent safety evaluations that some of our patients do not have access to. By studying adverse events in real-life settings, we can better understand the risks of these life-prolonging cancer treatments and help clinicians and patients make informed decisions regarding treatment."

Since metabolic and cardiovascular conditions tend to be under the purview of primary care providers, Lai and her fellow authors recommend team-based care that involves PCPs for patients with advanced prostate cancer as a way to manage these higher risks.

"With continued expansion of the indications for abiraterone and enzalutamide to earlier stages of the disease, increasing numbers of men will be receiving these therapies for longer periods of time," Lai said. "This will potentially amplify the scope of men affected and increase the magnitude of the risks of adverse events, making careful attention to management of these issues crucial."

Source: University of Michigan

Filed under: Health, Medicine, News and Articles, Study | Tagged: Prostate Cancer |

Ivermectin, a potential anticancer drug derived from an antiparasitic drug

sciencedirect.com

Highlights

•Ivermectin effectively suppresses the proliferation and metastasis of cancer cells and promotes cancer cell death at doses that are nontoxic to normal cells.

•Ivermectin shows excellent efficacy against conventional chemotherapy drug-resistant cancer cells and revers-

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es multidrug resistance.

•Ivermectin combined with other chemotherapy drugs or targeted drugs has powerful effects on cancer.

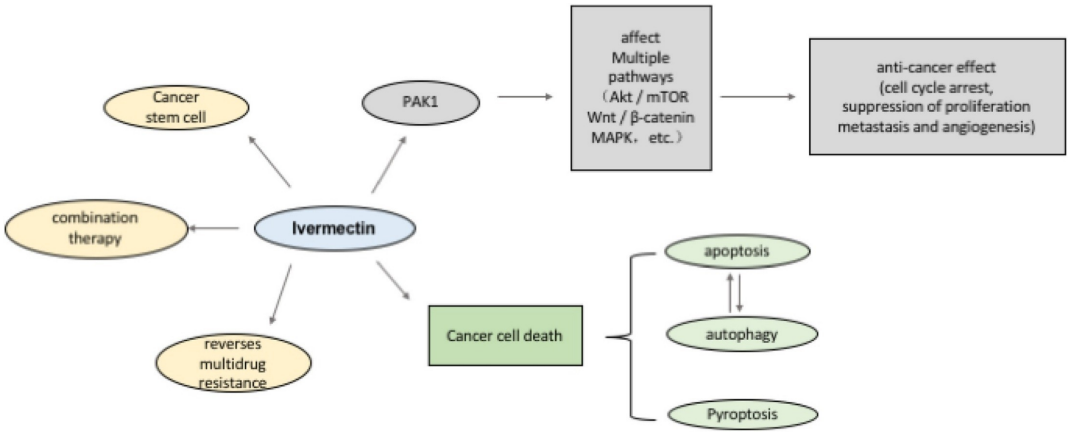
•The structure of crosstalk centered on PAK1 kinase reveals the mechanism by which ivermectin regulates multiple signaling pathways.

•Ivermectin has been used to treat parasitic diseases in humans for many years and can quickly enter clinical trials for the treatment of tumors.

Abstract

Ivermectin is a macrolide antiparasitic drug with a 16-membered ring that is widely used for the treatment of many parasitic diseases such as river blindness, elephantiasis and scabies. Satoshi ōmura and William C. Campbell won the 2015 Nobel Prize in Physiology or Medicine for the discovery of the excellent efficacy of ivermectin against parasitic diseases. Recently, ivermectin has been reported to inhibit the proliferation of several tumor cells by regulating multiple signaling pathways. This suggests that ivermectin may be an anticancer drug with great potential. Here, we reviewed the related mechanisms by which ivermectin inhibited the development of different cancers and promoted programmed cell death and discussed the prospects for the clinical application of ivermectin as an anticancer drug for neoplasm therapy.

Graphical abstract



Ivermectin has powerful antitumor effects, including the inhibition of proliferation, metastasis, and angiogenic activity, in a variety of cancer cells. This may be related to the regulation of multiple signaling pathways by ivermectin through PAK1 kinase. On the other hand, ivermectin promotes programmed cancer cell death, including apoptosis, autophagy and pyroptosis. Ivermectin induces apoptosis and autophagy is mutually regulated. Interestingly, ivermectin can also inhibit tumor stem cells and reverse multidrug resistance and exerts the optimal effect when used in combination with other chemotherapy drugs.

Finding Hidden Cancer Cells: FDA Approval of New Imaging Tool Could Transform Treatment Decisions for Advanced Prostate Cancer

mskcc.org

Thursday, May 27, 2021

Prostate cancer diagnosis and treatment took a major step forward today as the US Food and Drug Administration approved an imaging technology that enables doctors to pinpoint the location of prostate cancer cells that would otherwise be hidden in the body. This new technology is especially helpful to track and treat prostate cancer that has spread.

"This is the biggest diagnostic advance for prostate cancer since the 1980s, when the PSA [prostate-specific antigen] test was introduced," says Memorial Sloan Kettering medical oncologist Michael Morris. Prostate cancer is the second leading cause of cancer death in men and kills 34,000 Americans every year.

The new technology (called piflufolastat F 18 or PYLARIFY®) consists of a radioactive targeting molecule which, upon injection, selectively seeks out and attaches to a protein on the cancer cells' surface. The protein, called prostate-specific membrane antigen (PSMA), is not found on most normal cells. When the radioactive tracer binds to the prostate cancer cells, they show up as bright spots on a PET scanner.

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Dr. Morris played a leading role in two phase III clinical trials testing a particular imaging tracer that is easy to manufacture and can be used at all institutions. MSK radiologist Hebert Alberto Vargas and interventional radiologist Jeremy Durack were key collaborators in the development and testing of the tracer. Today's approval is the first for a tracer that can have national, widespread use.

A similar tracer was fully FDA-approved in December 2020, but only for use at two institutions. Similarly, the Molecular Imaging and Therapy Service at MSK has been offering PSMA imaging with a slightly different tracer for the past three years under an FDA-approved investigational new drug (IND) application, benefiting more than a thousand patients thus far.

"Imaging has been the Achilles heel of prostate cancer because the disease is hard to detect after it has spread," Dr. Morris says. "Now we can be much more confident that we are correctly identifying the location of the disease to make an accurate treatment plan."

The benefits this advance will bring to men with this common disease cannot be overstated.

Michael J. Morris medical oncologist

Pinpointing Cancer's Return

Kevin Taylor has benefited greatly from the new imaging. A 65-year-old textile designer living in New York City's Financial District with his wife and two teenage boys, he has been under the care of Dr. Morris for a decade. After being diagnosed with prostate cancer in 2010, he had his prostate removed at another New York City hospital and came to MSK in the spring of 2011 when his disease relapsed.

Over the next eight years, his cancer came back twice. It was temporarily held at bay with different treatments — including radiation and a clinical trial testing an experimental vaccine — only to rear its head again.

After conventional imaging scans had shown that Kevin had no disease, Dr. Morris asked if he was willing to enroll in a clinical trial, called OSPREY, which was testing PSMA PET imaging. Participation held virtually no risk and might benefit him.

"I had already been in one trial and was glad to try another," Kevin says. "I thought even if it didn't help me, it might help somebody else down the road."

Several weeks after the conventional imaging found no disease, he had a PSMA PET scan that produced a worrisome result: Prostate cancer was detected in lymph nodes in Kevin's pelvis. But the precision of the imaging –- showing that the cancer had spread to the nodes but nowhere else –- allowed Dr. Morris to concentrate treatment on those specific sites.

Kevin received radiation targeted to those nodes along with hormone therapy, completing his treatment in late April 2020. As a result of the radiation and hormone therapy, Kevin's PSA dropped to zero and has remained so for more than a year. He has needed no further therapy.

"We were able to take a family trip to India ten days after I received my last radiation treatment," Kevin says. "My two boys were very young when I was diagnosed, and it has been very gratifying for me to be around for them."

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A Clearer Picture

Kevin's experience illustrates the striking advantages of the new imaging technology. Traditionally, doctors knew prostate cancer had returned after initial therapy if a patient's PSA levels began to rise. Knowing where the disease was located was usually not feasible, especially when the PSA levels were low. And if the cancer had spread to the lymph nodes, the only way to tell was when the nodes swelled up, after the cancer had already been there a while.

The OSPREY trial proved the imaging method to be very accurate. It identified the location of cells that were highly likely to be prostate cancer –- more than 80% in some cases and more than 90% in others. Results of the trial, published in the *Journal of Urology*, were partly responsible for the FDA approval.

"With PSMA PET, we can now detect the cancer cells directly and much earlier than we could with standard

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CT or PET scans," Dr. Morris says. "For newly diagnosed men with high-risk disease who were preparing to undergo surgery or radiation, we had to wonder whether there was disease outside of the prostate that we couldn't identify. For men like Kevin whose prostate cancer relapsed, we often did not know where the cancer was and had to decide on a treatment plan without this knowledge."

Today, Kevin remains active with his family –- shepherding his younger son to soccer games six times a week. He enjoys cooking, listening to music and is looking forward to resuming travel for leisure. After 40 years in New York, he and his wife are even contemplating moving the family back to his native England.

"My main fear is not being able to access MSK for my checkups and treatments," he says. "I have 100% trust in Dr. Morris and wouldn't go to anyone else –- my only regret about this whole experience is that I didn't go to him first when I was diagnosed."

For Dr. Morris, knowing the FDA approval will benefit people across the entire spectrum of this stubborn disease is especially gratifying.

"I have been involved in the PSMA research since the end of my fellowship at MSK in the late 1990s, and it's amazing to see it all come to fruition this year," Dr. Morris says. "The benefit this advance will bring to men with this common disease cannot be overstated."

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On the Lighter Side

"If we can break up the kidney stones, we don't have to operate."

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NETWORKING

Please help us in our outreach efforts. Our speakers bureau consisting of Gene Van Vleet 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@ipcsg.org) to coordinate.

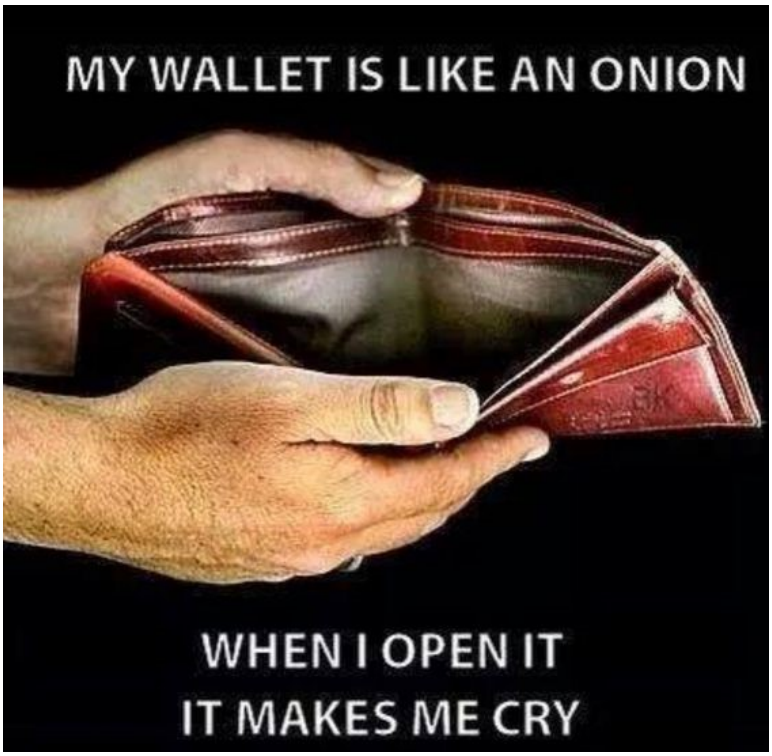
Member John Tassi is the webmaster of our website and welcomes any suggestions to make our website simple and easy to navigate. Check out the Personal Experiences page and send us your story. Go to: https://ipcsg.org/personal-experience

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.

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

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