Informed Prostate Cancer Support Group Inc.
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APRIL 2024 NEWSLETTER

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Wednesday, April 10, 2024

Volume 17 Issue 04

Next Meeting *moved to* 4th Saturday,

April 27, 2024 IPCSG— 10:00am—Noon PDT.

- Dr. Kipper - Personal Experiences of Prostate Cancer Patients— Back by popular demand! Dr. Kipper, renowned for his expertise in PET/CT imaging technology for the diagnosis of prostate cancer, is set to offer a compelling presentation on the Personal Experiences of Prostate Cancer Patients.
- 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 to 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**

IPCSG Meeting Summary, March 16, 2024

Today's talk was an expert presentation on PET CT Imaging technology by Dr. Michael Kipper. The upcoming meeting will feature an annual update on the latest prostate cancer trials, testing, and treatments by Dr. Lam from Prostate Oncology Specialists. *The meeting is held on the third Saturday of every month, with the exception of April, when we will meet on the fourth Saturday (April 27) due to scheduling changes.*

Talk by Dr. Michael S Kipper, "PET/CT imaging technology"

Dr. Kipper in this segment discusses the significance and latest developments in imaging techniques for prostate cancer. He highlights his institution's role in staying at the forefront of these advancements and their commitment to sharing this knowledge with other institutions to benefit patient care. They specifically mention the combination of imaging and treatment, known as theranostics, and its promising future.

The session then shifts towards providing an overview of prostate anatomy, prevalence, and the importance of early detection using methods such as PSA tests and digital rectal exams. Dr. Kipper then elaborates on the role of ultrasound and MRI in prostate cancer diagnosis and how these tools are used to detect and biopsy suspicious lesions. He finishes by mentioning the importance of bone scans and DEXA studies to assess bone health during prostate cancer treatment. The overall message emphasizes the importance and progress of imaging techniques in

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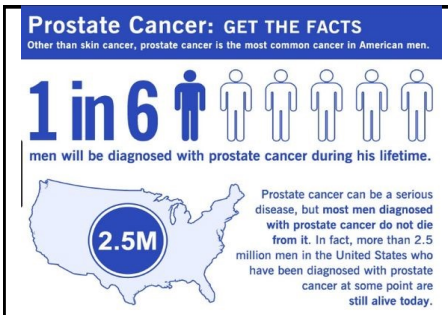

Organization

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

From the Editor (SLP)

In this issue:

For original articles see the blog at https://ipcsg.blogspot.com/ . First we have a claude.AI generated summary of last months very enlightening talk by Dr. Kipper. This month, we're trying a new format using AI to summarize each article in layman's terms so you can hopefully understand it, and then describe impact on clinical practice and questions to ask you physician. Links are still provided to original articles. Some important items of interest this month:

1. Real-world overall survival with abiraterone acetate versus enzalutamide in chemotherapy-naïve patients with metastatic castration-resistant prostate cancer | Prostate Cancer and Prostatic Diseases— *Zytiga less effective than Ztandi for Advanced PCa*
2. Is extended pelvic lymph node dissection REALLY required for staging of prostate cancer in the PSMA-PET era? | Prostate Cancer and Prostatic Diseases— *Ask your surgeon if you get a radical. The optimal approach going forward may be to use PSMA-PET imaging along with clinical prediction tools to guide which patients truly need an ePLND, rather than doing it routinely for everyone. This could minimize unnecessary ePLND procedures while still allowing radiation treatment of areas at risk based on imaging.*
3. Prostate Cancer-specific mortality twice as high in patients with specific genotype for HSD3B1 allele -Mutation Linked to Increased Risk of Prostate Cancer Mortality | MedPage Today— *Gene controls alternative sources of Androgen. Get your genetic information.*

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prostate cancer diagnosis and treatment.

Key Points From The Presentation:

Prostate Cancer Staging and Risk Stratification:

Staging prostate cancer accurately upfront is critical for guiding optimal treatment approach

Key factors include PSA level, Gleason score, evidence of extracapsular extension or seminal vesicle invasion on imaging, and presence of lymph node or distant metastases

This allows stratifying patients into low, intermediate, or high-risk groups

Imaging Modalities:

Conventional imaging has included bone scan, CT scan, ultrasound +/- biopsy

Limitations include bone scan remaining positive long after treatment, CT poor for visualizing the prostate itself

MRI emerged as excellent for assessing extracapsular extension, seminal vesicle invasion

MRI can be fused with ultrasound to guide targeted biopsies

PET/CT Imaging Agents:

Fluciclovine (Axumin) was first approved in 2013 but only for biochemical recurrence setting

PSMA-targeted radiotracers like Ga-68 PSMA and F-18 PSMA agents (e.g. Pylarify) can detect metastases much earlier, even at low PSAs

High specificity (95%) for prostate cancer outside the prostate bed

Can identify metastatic lesions in bone and soft tissue missed on conventional imaging

Advantages of PSMA PET/CT:

Significant impact - avoids additional conventional imaging in over 50% of cases

Detects metastases in 28% of patients read as M0 on conventional imaging

Allows radiation targeting of oligometastatic disease to sustain curative intent

Guides systemic treatment selection for polymetastatic disease

Theranostics:

Theranostics refers to the use of the same or closely related molecules/agents for both diagnostic imaging and therapeutic delivery. Dr. Kipper highlighted several theranostic pairs:

•Iodine radionuclides - Radioiodine has been used for decades for imaging and treating thyroid cancer/hyperthyroidism - one of the earliest theranostic approaches

•Radium-223 dichloride (Xofigo) - Diagnosis with fluciclovine (Axumin) PET to identify bone-predominant metastatic prostate cancer. Followed by treatment with the alpha-emitting radium-223 which targets areas of increased bone metabolism

PSMA-targeted agents - Currently the most promising theranostic approach in prostate cancer. Diagnosis with Ga-68 PSMA PET or F-18 PSMA (e.g. Pylarify) PET. Followed by treatment with Lu-177 PSMA radioligand therapy or other PSMA-targeted radionuclide therapies

Dr. Kipper showed examples of excellent responses being achieved with Lu-177 PSMA in patients with widespread metastatic disease visualized on the diagnostic PSMA PET scan.

Advantages of theranostics:

•Better stratification of patients most likely to benefit from targeted radiotherapy

•Ability to estimate radiation dosimetry to tumors and normal tissues

Potential for patient-specific dosing optimization

Dr. Kipper noted ongoing trials evaluating PSMA radioligand therapy earlier in the disease course, such as at initial biochemical recurrence, when lower tumor burden may improve outcomes.

Other theranostic approaches in development include FAPI tracers targeting fibroblast activation protein in multiple cancer types. FAPI (Fibroblast Activation Protein Inhibitor) tracers are a new class of imaging agents and potential therapeutics that target fibroblast activation protein (FAP).

Fibroblast Activation Protein:

•FAP is a protein that is overexpressed in the tumor microenvironment, especially on cancer-associated fibro-

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blasts.

•Cancer-associated fibroblasts play an important role in tumor growth, angiogenesis, metastasis, and resistance to therapy.

FAP expression is low in normal tissues, making it an attractive target for cancer imaging and therapy.

FAPI Tracers:

•FAPI tracers are low-molecular weight inhibitors that bind with high affinity to FAP.

•They can be radiolabeled with various PET isotopes (e.g. 68Ga, 18F) for diagnostic PET imaging.

The same FAPI molecules can potentially be radiolabeled with therapeutic isotopes (e.g. 177Lu, 225Ac) for targeted radionuclide therapy - the theranostic concept.

Potential Advantages:

•FAPI PET may be able to detect many solid tumor types based on FAP expression in the tumor stroma.

•Early studies show promising tumor visualization across cancers like breast, lung, colorectal, pancreatic, etc.

•As a theranostic pair, FAPI PET could guide patient selection for targeted radionuclide therapy with the therapeutic FAPI compound.

May help overcome resistance by targeting the tumor microenvironment.

Current Status:

•Clinical FAPI PET imaging trials are underway evaluating diagnostic performance across cancers.

•Preclinical studies evaluating therapeutic FAPI radiotracers are ongoing.

FAPI theranostics represent a promising tumor-type insensitive, stroma-targeting approach still in early development.

FAPI tracers target a validated tumor microenvironment protein FAP and have the potential to be a broad pan-cancer theranostic platform in the future.

So in summary, advanced PSMA PET imaging is transforming the initial staging and subsequent treatment paradigms in prostate cancer by more accurately delineating the burden and distribution of disease.

Q&A portion:

- There were several questions about when to order a PSMA PET scan versus conventional imaging like bone scans or CT scans. Dr. Kipper advised that for high-risk or biochemical recurrence cases, the PSMA PET provides much more accurate staging and can detect metastases missed by conventional imaging.
- A patient scheduled for proton therapy asked about getting a PSMA PET first. Dr. Kipper supported this, as it could reveal metastases that may change the treatment approach or allow targeting of multiple lesions with radiation.
- There were questions about calculating PSA doubling time, which Dr. Kipper noted is an important factor in assessing aggressiveness and can guide treatment decisions.
- A patient whose PSA jumped from 0.5 to 200 in weeks asked about that unusually rapid progression. Dr. Kipper explained it likely represented transformation to a more aggressive neuroendocrine subtype, occurring in around 10% of cases.
- There was discussion about whether the prostate still needs removal if imaging shows spread outside the prostate. Dr. Kipper said it depends on the extent and location of spread.
- A patient asked about trials investigating PSMA radioligand therapy earlier, like at biochemical recurrence. Dr. Kipper confirmed this is a major area of ongoing research.
- Dr. Kipper addressed accuracy rates of around 90% for PSMA PET/CT in detecting metastases.

For a high Gleason 9 case, Dr. Kipper noted an FDG PET may be reasonable as an initial scan for very aggressive tumors before considering PSMA PET.

So in summary, much of the Q&A involved clarifying appropriate use cases for ordering advanced PSMA PET imaging over conventional scans, especially in high-risk and biochemical recurrence settings.

Video of the meeting is viewable on youtube at https://youtu.be/xqhSMprhQ4A

Items of Interest

Real-world overall survival with abiraterone acetate versus enzalutamide in chemotherapy-naïve patients with metastatic castration-resistant prostate cancer | Prostate Cancer and Prostatic Diseases

nature.com

Daniel J. George, Krishnan Ramaswamy, Hongbo Yang, Qing Liu, Adina Zhang, Alexandra Greatsinger, Jasmina Ivanova, Betty Thompson, Birol Emir, Agnes Hong & Stephen J. Freedland

Prostate Cancer and Prostatic Diseases (2024)Cite this article

Summary

Here is a summary in layman's terms:

This study compared survival outcomes in men with metastatic castration-resistant prostate cancer who received either abiraterone or enzalutamide as their first treatment. The researchers looked at Medicare claims data from 2009-2020 for over 5,500 patients.

The key findings were:

- Patients who started on abiraterone (Zytiga) had worse overall survival compared to those who started on enzalutamide (Xtandi). The median survival was about 2 months shorter for abiraterone patients.
- Survival was significantly worse with abiraterone versus enzalutamide in certain subgroups, including older patients (age 75+), white patients, those with diabetes, cardiovascular disease, or kidney disease, and across all socioeconomic levels.
- About 40% of patients only received one line of treatment. In this group, abiraterone patients had much worse survival compared to enzalutamide (median 10.6 vs 13.6 months).

The survival detriment with abiraterone was consistently seen across previous real-world studies as well.

In summary, for men with advanced prostate cancer starting their first treatment, enzalutamide was associated with better overall survival compared to abiraterone, especially in certain higher-risk subgroups. This suggests enzalutamide may be a more effective initial treatment option for many patients.

Impact on Prostate Cancer Clinical Practice

This study's findings of worse overall survival with abiraterone compared to enzalutamide as initial treatment for metastatic castration-resistant prostate cancer could have significant impacts on clinical practice:

1. Treatment selection: The results suggest that enzalutamide may be a more appropriate first-line treatment choice over abiraterone for many patients, especially older men and those with comorbidities like cardiovascular disease or diabetes. Clinicians may favor starting with enzalutamide over abiraterone for its survival benefit.
2. Patient counseling: When discussing initial treatment options, clinicians can use these real-world data to inform patients about the potential survival differences between abiraterone and enzalutamide. Patients may opt for enzalutamide if survival is their top priority.
3. Guidelines and pathways: Medical societies and institutional treatment pathways may need to re-evaluate their recommendations for first-line therapy in this setting. The cumulative evidence from multiple real-world analyses favoring enzalutamide could lead to changes in clinical practice guidelines.
4. Managed care policies: Payers and health plans may use this data to guide their coverage policies, prior authorization criteria, and step-therapy approach for these two drugs as first-line treatment.

Future research: The consistent survival detriment with abiraterone raises questions about potential differences in efficacy, tolerability, or other factors that need further investigation in prospective studies.

In summary, these real-world findings suggesting improved overall survival with enzalutamide challenge the current equal first-line positioning of abiraterone and enzalutamide, which could prompt shifts in clinical

decision-making, guidelines, payer policies, and the design of future research studies.

What questions should I as an advanced prostate cancer patient ask my oncologist about these results

As an advanced prostate cancer patient, here are some important questions you could ask your oncologist regarding these study results comparing abiraterone and enzalutamide as initial treatments:

1. Based on my specific age, race, comorbidities (e.g. heart disease, diabetes), and overall health status, would you recommend starting with enzalutamide or abiraterone for my initial treatment? Why?
2. How concerning are the observed survival differences between these two drugs in the study populations relevant to my situation?
3. What are the potential side effects and risks I should be aware of with each of these medication options?
4. For patients who only receive one line of therapy, the survival detriment with abiraterone seemed more pronounced. Does my cancer's aggressiveness and prognosis suggest I may only tolerate or respond to one treatment?
5. Do you foresee any changes to the clinical practice guidelines recommending one drug over the other based on these real-world results?
6. Are there any biomarker or genomic tests that could help determine if I may respond better to one of these drugs?
7. What is your experience with prescribing these two medications in patients similar to me? Have you observed a difference in efficacy or tolerability?
8. If I start on one drug and it stops working, is it common to switch to the other medication as a next line of therapy?

Is extended pelvic lymph node dissection REALLY required for staging of prostate cancer in the PSMA-PET era? | Prostate Cancer and Prostatic Diseases

nature.com

Tilki, Derya

Summary

Here is a summary in layman's terms:

This article discusses whether an extended pelvic lymph node dissection (ePLND), which is the surgical removal of lymph nodes in the pelvic area, is really necessary for staging prostate cancer now that PSMA-PET imaging is available.

The key points are:

- ePLND has been the standard approach to check if prostate cancer has spread to pelvic lymph nodes. However, it carries risks like complications, longer surgery time, and side effects like lymphedema (swelling).
- PSMA-PET scans can now detect lymph node metastases with high accuracy, challenging the need for routine ePLND.
- If the PSMA-PET is positive (shows lymph node spread), radiation to the pelvic nodes after surgery may be more effective than ePLND at treating the cancer spread while avoiding surgical side effects.
- If the PSMA-PET is negative, an ePLND may be avoided, especially in intermediate-risk patients, since the chance of missing significant lymph node spread is very low based on study results. Clinical factors like risk calculators and MRI findings can provide additional guidance on whether to perform ePLND when the PSMA-PET is negative.

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The article proposes that PSMA-PET imaging, combined with risk calculations, could allow avoiding ePLND in many cases, reducing surgical risks and costs, while still effectively managing the cancer spread when present. Large studies are still needed to confirm this approach.

Potential Impact on Prostate Cancer Surgical Practice

The increasing use of PSMA-PET imaging for lymph node staging of prostate cancer could have a significant potential impact on surgical practice:

Reduced need for extended pelvic lymph node dissection (ePLND):

- With the high accuracy of PSMA-PET in detecting lymph node metastases, there may be less need to routinely perform an ePLND, which is an invasive procedure with risks of complications and side effects.
- For patients with negative PSMA-PET findings, especially those at intermediate risk, forgoing ePLND could become more accepted to avoid associated morbidities.

Change in lymph node dissection approach:

- If PSMA-PET shows positive lymph nodes, surgeons may opt for more targeted/radioguided lymph node dissection of only the involved areas rather than an extended template dissection.
- This could allow for lymph node removal with less extensive dissection and reduced operative times.

Rise of surgery plus adjuvant radiation paradigm:

- For PSMA-PET positive cases, definitive prostate surgery may be combined with adjuvant pelvic radiation to the positive nodes identified on imaging.
- This could replace or reduce the need for ePLND as the radiation would cover areas outside the typical surgical template.

Adoption of risk-stratified approach:

- Clinical practice may move towards an individualized, risk-stratified approach using PSMA-PET findings along with nomograms and risk calculators to determine which patients truly need ePLND versus avoiding it.

Training implications:

- Surgeons may need updated training on interpreting PSMA-PET imaging and selective/targeted lymph node dissection techniques if ePLND becomes less common.

Overall, increased reliance on PSMA-PET staging could reduce the frequency of routine extended lymph node dissection at surgery, impacting the complication rates, operative times, and surgical decision-making process for prostate cancer patients based on personalized risk assessment.

Questions to Ask

If you are a newly diagnosed prostate cancer patient considering surgery, here are some important questions you should ask your urologist or surgeon regarding the use of PSMA-PET imaging and lymph node dissection:

1. Will I be getting a PSMA-PET scan as part of my staging workup? If not, why not?
2. How will the results of my PSMA-PET scan factor into the decision of whether I need to undergo an extended pelvic lymph node dissection (ePLND) during my prostatectomy?
3. What is your approach or criteria for omitting ePLND if my PSMA-PET is negative for lymph node metastases? Do you use risk calculators/nomograms along with the imaging?
4. If my PSMA-PET shows potential lymph node involvement, will you do a more targeted lymph node dissection based on the imaging findings rather than a full ePLND?
5. In the case of positive lymph nodes on PSMA-PET, would you recommend adjuvant/additional

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radiation therapy after surgery instead of or in addition to lymph node dissection?

6. What are the potential risks and complications associated with ePLND, such as lymphedema, blood clots, and others? How does omitting ePLND reduce these risks?
7. For my specific case and risk profile, what are the chances that significant lymph node metastases could be missed if ePLND is omitted after a negative PSMA-PET?
8. How experienced is the surgical team in interpreting PSMA-PET for lymph node dissection guidance and performing more selective lymph node removals?
   Are there any clinical trials I could consider that are evaluating new approaches using PSMA-PET for lymph node staging and management?

Mutation Linked to Increased Risk of Prostate Cancer Mortality | Prostate Cancer-specific mortality twice as high in patients with specific genotype for HSD3B1 allele

MedPage Today

medpagetoday.com

Oncology/Hematology > Prostate Cancer

by Charles Bankhead, Senior Editor, MedPage Today March 20, 2024

Summary

Here is a summary in layman's terms:

The study found that men with a specific genetic mutation called HSD3B1(1245C) had double the risk of dying from prostate cancer compared to men without this mutation.

Some key points:

- The HSD3B1 gene is involved in producing testosterone from sources outside the testicles. The 1245C mutation makes this gene more active.
- Among all prostate cancer patients, those with two copies of the 1245C mutation (called the CC genotype) had a 4% risk of dying from prostate cancer within 5 years, compared to only 1.7% for men without this mutation.
- In the subgroup with metastatic prostate cancer, the 5-year death risk was 36% for men with the CC genotype versus only around 18% for others.
- This mutation seemed to make prostate cancers more resistant to hormone therapies like androgen deprivation therapy (ADT).

The mutation was less common in Black men compared to white men in this study.

The researchers suggest that testing for this HSD3B1 mutation could help identify prostate cancer patients at higher risk of dying from their disease. These higher-risk men may benefit from more aggressive treatment approaches that target the excess testosterone production caused by the mutation.

Overall, this genetic biomarker could allow for better personalizing of prostate cancer treatments in the future based on each patient's underlying biology.

Clinical Impacts

The findings regarding the HSD3B1(1245C) mutation and its association with increased prostate cancer mortality could potentially have several impacts on clinical practice:

Genetic testing and risk stratification

Testing for the HSD3B1 genotype, especially the high-risk CC genotype, may become more routine in prostate cancer patients.

Knowing a patient's HSD3B1 status could help better stratify their risk and personalize treatment intensity upfront.

Those with the CC genotype may be classified as higher-risk from the start, even with localized disease.

Treatment selection

ForCC genotype patients, clinicians may favor more aggressive upfront treatments like radical prostatectomy or radiation over active surveillance.

These patients may benefit from addition of hormone therapies that block extragonadal testosterone production driven by the HSD3B1 mutation.

Disease monitoring

More intensive monitoring with imaging and biomarkers may be warranted in CC genotype patients given their higher risk of metastases and shorter survival.

PSA levels and progression may need to be interpreted differently based on HSD3B1 status when deciding to change therapies.

Genetic counseling may also become important to discuss heritability and family implications.

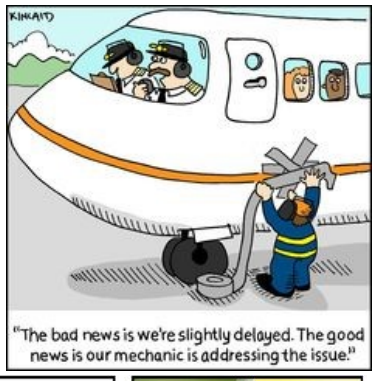
In summary, if validated in further studies, incorporating HSD3B1 genetic testing could enable more personalized and genotype-driven approaches to more accurately determine prostate cancer risk and appropriately intensify systemic treatments for patients found to have the high-risk CC mutation.

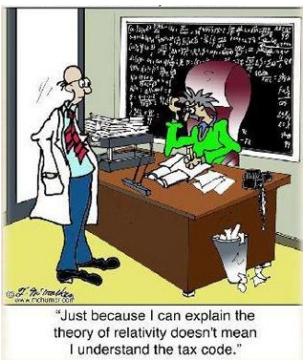
Questions

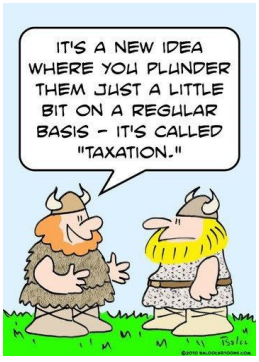
If you are a newly diagnosed prostate cancer patient, here are some important questions you could ask your physician regarding the potential impacts of HSD3B1 genetic testing:

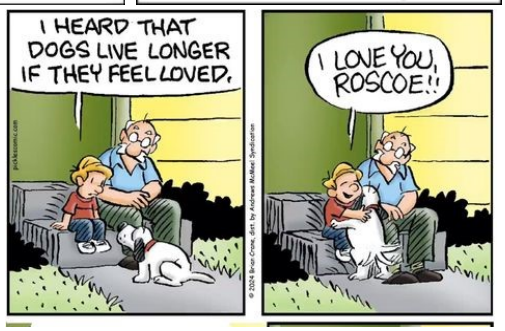
1. Will you be testing for the HSD3B1 gene mutation as part of my initial workup and staging? If not, why?
2. How might my treatment plan differ if I have the high-risk CC genotype for HSD3B1 compared to other genotypes?
3. For my specific clinical situation (e.g. localized vs. advanced disease), how much more aggressive would you recommend my treatment to be if the CC genotype is present?
4. Are there any specific medication options that target the pathway affected by the HSD3B1 mutation that you would consider?

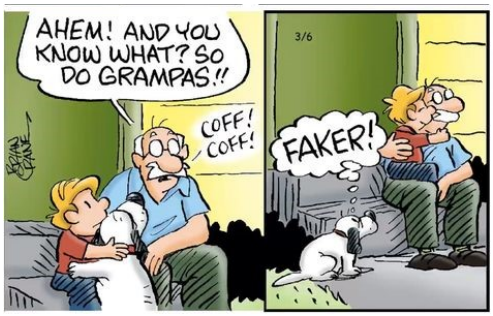
On the Lighter Side











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@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

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.