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

January 2020 NEWSLETTER

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

Tuesday, January 07,

Volume 13 Issue 1

Next Meeting:

JANUARY 18, 2020 10:00am—12:00

Sanford Burnham Prebys Medical Discovery Institute Auditorium

Dr. A. J. Mundt is Professor & Chair of Radiation Medicine and Applied Sciences at UCSC, and now also Senior Deputy Director of Moores Comprehensive Cancer Center.

An internationally-recognized academic radiation oncologist whose career has focused on the development and implementation of novel radiation technologies in a wide number of malignancies, he is an author of over 200 journal articles and book chapters, predominantly focused on advanced radiation technologies, Dr. Mundt has edited 3 academic textbooks.

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

2019 Informed Prostate Cancer Support Group Meetings:

Much information has been conveyed to the group over the last year, and we provide a roadmap to it here. Summaries by Bill Lewis in the succeeding month's newsletter for free, and dvds containing videos of meeting and presentations are available for purchase via the web site: http://www.ipcsg.org

1) January 2019 Radiation Therapy and Prostate Cancer – 2019 Update & Perspectives Dr. Arno J. Mundt, Professor & Chair of the Dept. of Radiation Oncology, and Sr. Deputy Director, Moores Cancer Center at UCSD.
   There is a long history of the use of radiation therapy for prostate cancer, both as a definitive treatment (without surgery) and as an adjuvant treatment following surgery. Two main types of radiation are used: External beam radiation therapy (EBRT) using photons (X-rays) or protons (particles), normally delivered over several weeks; and Brachytherapy. The latter is internal radiation therapy, in which radioactive pellets are introduced into the prostate, either permanently (low dose rate) or temporarily (high dose rate). Deciding which approach to use depends on multiple factors, of which the most important is the risk group the patient is in. The risk group may be low, medium or high and depends on the PSA enzyme blood level (whether <10, moderate, or >20), the Gleason score (6, 7, or

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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.

Be your own health manager!!

Meeting Video DVD's

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

From the Editor

In the Newsletter this Month

We ended this year of meetings in November with an informative talk by Dr. Lam summarized last month. In this issue we give a roadmap to all our meetings last year. .Also in this issue, we have some articles of interest including::

- In our first paper, a Urologic Surgeon, Dr Sam S Chang, MD, shares insight into recent developments in treatment of PCa, including genetic testing, salvage therapy, oligometastatic disease, and surgical techniques.
- In the second paper, Dr. David F Penson looks at expanding combinations for ADT including PARP inhibitor immunotherapy.
- The 3rd paper covers Philip Owens and CU Cancer Researchers reporting on subclassification of bone mets into blastic and lytic types by gene activity for targeted therapies.
- In the 4th paper a new derivative of Saccharin is shown to kill prostate cancer cells without harming normal cells.

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; **Vice President** Gene Van Vleet @ 619-890-8447; or **Meeting facilitator** George Johnson @ 858-456-2492.

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≥ 8), and the "T Stage" (originally based on rectal exam results as to whether nodules are present, and now also whether the seminal vesicles are involved, or whether other organs have been invaded). The intermediate risk group is subdivided into "favorable" and "unfavorable" groups, mainly depending on how much higher-Gleason-grade disease is present.

2) February Member Panel: Tim D'Andrea; Elliot Shev and his wife, Dr. Wendi Maurer ; John Tassi
3) March— Dr. Rana McKay – Evolving Paradigms of High-Risk and Advanced Prostate Cancer: Novel Trials and Genomics. Deaths due to prostate cancer have been declining since their peak in the early 1990's, due to the many treatments now available and advances made in surgery, radiation and ADT (androgen deprivation therapy), including new drugs such as Abiraterone (Zytiga), Enzalutamide (Xtandi), Apalutamide (Erleada), and Radium-223 (Xofigo), complementing or as alternatives to chemo drugs such as Docetaxel (Taxotere) or Cabazitaxel (Jevtana).
4) April—Acoustic/Shock Wave Therapy for Erectile Dysfunction. Mitt Kocher, Charles Downing, Dr. Dan Keiller, Urologist – ARC Mens Health, in Mission Valley; arcmenshealth.com. At the ARC Mens Health clinic, about 400 men have been treated so far over the past year and a half, with 80% success rate.
5) May—Sexual Function Rehabilitation: Revolutionary Breakthroughs in Men's Health, Dr. T. Mike Hsieh, Urologist, UCSD Men's Health Center. Dr. Hsieh (pronounced "shay" noted that the principles of cancer treatment are safety, cancer control and minimizing side effects. With prostate cancer, cancer control is generally approached through surgery, radiation, or hormones (i.e., ADT). Beyond control, preserving urinary continence and sexual function are principal goals, and are referred to by urologists as the "Trifecta." Quality of life has become very important in patients' choices of treatments.
6) June—Diagnosing and Managing Prostate Cancer: A Paradigm Shift - Dr. Franklin Gaylis, Chief Scientific Officer – Genesis Healthcare Partners; Voluntary Professor, Urology – There is a broadly collaborative effort called the Prostate Cancer Active Surveillance Project (PCASP) There are three project areas/goals of the PCASP: 1) Implementation of specific interventions to promote active surveillance adoption, 2) improve guideline adherence and 3) decrease conversion to active treatment by pre-screening out or clarifying the options and risks for those who would likely need conversion (to active treatment while still in the "window of curability"). It will use "dashboards" and genomic testing using the Decipher genomic classifier (which predicts high, medium or low PCa aggressiveness based on a panel of genetic markers).
7) July— Member Stories: Aaron Lamb, Gene Van Vleet, Bob Keck, Jim Kilduff.
8) August—How to Manage Our Case – an interactive discussion with George Johnson and Gene Van Vleet: 1. Why and How We Should Manage Our Own Case: You are the most important person on your prostate cancer (PCa) health-care team. You are the expert on you! Your doctor has thousands of patients and only allots a few minutes for your visits. There are choices to be made. Take time to think about your personal goals and the therapy for your life style. Get a second (third?) opinion on diagnostics and treatment decisions. Get copies of all medical reports and tests, keep a file and track the changes over time. Take the file to your appointments for your questions, and write answers. Here are elements of PCa case management knowledge that are covered in IPCSG meetings, most of which you will not learn about from your doctor: PSA TESTING, BIOPSIES, GLEASON & STAGE, TREATMENT OPTIONS, PARTIN TABLE, DOUBLING TIME, ADT PRETREATMENT, ACTIVE SURVEILANCE, PSA SHIFT POST-TREATMENT, ADT SIDE EFFECTS, DIET – DAIRY PRODUCTS/ PROTEIN, PSA STANDING ORDER, TARGETED BIOPSY, DIHYDROTESTOSTERONE,

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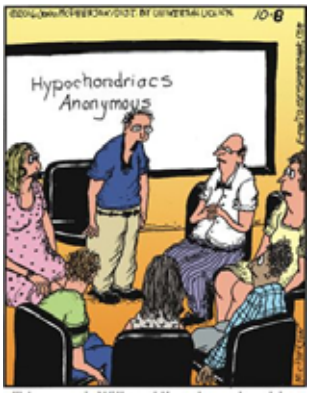
T & DHT TESTING, PSA TESTING FREQUENCY, CASODEX/AVODART, FEMARA, ADT INTERMITTENT, PSA 2X AVODART, PRIMARY PCa TUMOR, NEW TREATMENT OPTIONS, PARTICIPATION IN CLINICAL TRIALS

9) September— Member "Experts" Tell Their Stories: Bill Trepanier, Bill Pitts, Tom Selgas.
10) October— Dr. Phranq D. Tamburri Medical Director of Prostate Second Opinions, in Phoenix, Scottsdale and Seattle. The Prostate Cancer Management: When to Pull the Ripcord presentation was directed toward helping surgery- and radiation-averse men decide when conventional treatment options become necessary. A doctor-focused article on this issue is available online at https://ndnr.com/mens-health/cap-update-2018-when-to-pull-the-ripcord/
11) November—**Androgen Deprivation Therapy—** By Richard Lam, MD Prostate Oncology Specialists, Marina del Rey, CA. Testosterone is a hormone that stimulates development of male reproductive tissues, and is made throughout life, but gradually less with age. It is produced mainly in the testicles, but also (10%) in the adrenal glands. It stimulates secondary sexual characteristics such as increased muscle, bone integrity, and body hair. It can stimulate growth of both benign and cancerous prostate cells. **Androgen deprivation therapy (ADT)** deprives tumor (and normal) cells of testosterone.

On the Lighter Side



"My name is Will, and I'm a hypochondriac, and I'm TEN TIMES sicker than any of you will EVER be!"

Articles of Interest

Expert Shares Insight on Recent Prostate Cancer Developments

https://www.onclive.com/web-exclusives/expert-shares-insight-on-recent-prostate-cancer-developments?p=2

Ellie Leick

With research showing potential for PARP inhibitors for patients with prostate cancer with homologous recombination repair gene alterations, there needs to be wider implementation of genetic testing to determine who will best respond to this therapy, explained Sam S. Chang, MD.

"We have a better idea of the genetic profile of prostate cancer. Why is that important? Surgeons as a whole have avoided any genetic testing and any molecular classification of prostate cancer because it's a higher Gleason score," said Chang. "Five years ago, a urologist would have never thought about who is *BRCA1/2*-positive because that wasn't in our vocabulary. Truth be told, for most urologists, [molecular classification] is not even considered."

In findings from the phase III PROfound trial, for example, the median radiographic progression-free survival by blinded independent review for patients with heavily pretreated metastatic castration-resistant prostate cancer (mCRPC) with *BRCA1/2* or *ATM* alterations was 7.39 months with the PARP inhibitor olaparib (Lynparza) versus 3.55 months for those treated with abiraterone (Zytiga) or enzalutamide (Xtandi; HR, 0.34; 95% CI, 0.25-0.47; *P* <.0001).

Beyond genetic testing, other advances have moved through the paradigm, including FDA approvals in nonmetastatic CRPC and novel surgical techniques that could further transform clinical practice.

In an interview during the 2019 *OncLive*® State of the Science Summit™ on Genitourinary Cancers, Chang, the Patricia and Rodes Hart Endowed chair of Urologic Surgery, and professor in the Department of Urology at Vanderbilt University Medical Center, discussed the utility of genetic testing in prostate cancer and pivotal research efforts.

***OncLive*: What does the prostate cancer field currently look like?**

Chang: With prostate cancer, we're looking at moving all of these new advanced treatments that we have [been used in] mCRPC earlier in the treatment paradigm to nonmetastatic castration-resistant disease.

To me, the most exciting part, as a urologic surgeon, is looking at options for neoadjuvant therapy as well as adjuvant treatment. We don't yet have data on that, but as we see disease being treated at earlier stages, we have some [treatments that] are very exciting for us to actually utilize [in the nonmetastatic setting]. Unfortunately, despite all of our advances, we don't have a cure yet. The ability to prolong life and maintain quality of life (QoL) are very exciting.

How is genetic testing currently implemented in prostate cancer?

Now, we understand that a small subset [of patients] have characteristics that could help us successfully treat them with PARP inhibitors. We know most prostate cancers are [not] going to respond to PARP inhibitors. Understanding that a small subset [of patients], where we didn't have successful therapies before, could get benefit [from these agents] is very exciting. It will behoove urologic surgeons to have a better idea of what's going on in terms of systemic therapies that can be considered. We would have never even thought about PARP inhibitors.

What other genes, besides *BRCA*, are being explored in prostate cancer?

Nobody really knows yet. We have these genetic changes but a lot of them are not yet actionable; that is the disconnect. We're going to have a better idea of which genes may not be predominant but [are found] in a subset of patients that seem to play a role. If we have therapies that can correspond to success, that will be exciting.

What advice do you have for making genetic testing more widespread in practice?

Education is the first thing. Then, we must understand the different types of commercial genetic tests that are available to do simple germline testing for these patients. There are a variety of tests currently available. You start off with, "Which test do I order? How do I order the test? Once the results come back, what do I do with them?" It's a big educational barrier that we will have to overcome.

[Germline testing] continues to evolve and need updates. We need to understand that we must consider [genetic testing]. [Genetic testing] showed up in the National Comprehensive Cancer Network guidelines, and it will show up in upcoming American Urological Association guidelines regarding advanced prostate cancer. In high-risk, localized disease, we need to have a better understanding that genetic testing should be considered.

Are there any updates in the nonmetastatic prostate cancer space?

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From a surgical standpoint, we are learning. We struggle with adjuvant versus salvage radiation therapy for patients with high-risk disease. Early data suggest that early salvage therapy is better than late salvage therapy. We have known that salvage therapy given too late is worse than adjuvant therapy.

As we see more results with both adjutant and salvage trials, we have learned that these treatments come with a complication risk. Doing a better job of predicting who is going to recur will be important with genetic testing. Additionally, we need to understand when to initiate salvage therapy and whether adjuvant treatment is better than salvage therapy. We're starting to get more knowledge to answer those questions and combine radiation therapy with systemic therapy.

Everyone feels comfortable that a combination of therapies, including surgery, radiation, and systemic therapy would be most beneficial in these high-risk patients. We will get a better understanding as time goes, [especially] as we start looking at the oligometastatic population.

The emphasis for all academicians has been on clinical trials that are looking at combining not only localized therapy for oligometastatic disease, but treating the oligometastatic sites after local treatment. We're learning more and more right now. I hope we don't go too far to being overly aggressive. At the same time, we need to give opportunities to those patients to actually make a benefit, best served by clinical trials.

How would you describe the evolution of surgical techniques in prostate cancer?

For years, we talked about robotic versus open [surgery]; that ship has sailed. There are discussions regarding single-port prostatectomy, among other techniques. The real question is whether we should focus on focal therapy versus continued whole-gland treatment. Are the less-invasive focal therapies appropriate? Are they necessary? Are they effective? Those 3 questions are the key because if someone doesn't need therapy and I give them therapy, they're going to do great from an oncological standpoint. If you don't do much, they're going to do great from an adverse event (AE) standpoint.

For patients who have significant disease, can they be treated with less-invasive therapies and can they be treated successfully? The hope is that focal therapy will be effective as well as have fewer AEs of whole-gland radiation or radical prostatectomy. The area of focal therapy will continue to be studied very carefully. It is already getting a lot of momentum.

Surgical radical prostatectomy does not have a lot of changing techniques. There are subtle changes, such as using a single port. There is also a move toward retzius-sparing surgery, where the approach is done differently in an attempt to improve continence rates. Those who have adopted this technique have impressive results regarding early urinary control and early continence. [This technique] gives positive thought in terms of whether we should be adopting these therapies. Some of those subtle changes will improve QoL. Will they change the success of the surgery? If you define successes as cancer control and maintaining QoL, then yes, because they are important.

Hussain M, Mateo J, Fizazi K, et al. PROfound: phase III study of olaparib versus enzalutamide or abiraterone for metastatic castration-resistant prostate cancer (mCRPC) with homologous recombination repair (HRR) gene alterations. *Ann Oncol*. 2019;30(suppl 5): mdz394.039. doi: 10.1093/annonc/mdz394.039.

Prostate Cancer Treatment Options Expand With ADT Combinations

Ellie Leick
https://www.onclive.com/web-exclusives/prostate-cancer-treatment-options-expand-with-adt-combinations

David F. Penson, MD, MPH, MMHC

Treatment for prostate cancer has evolved over the past few years to include androgen receptor therapy (ADT) combined with other agents, such as next-generation androgen receptors, explained David F. Penson, MD, MPH, MMHC.

"There have been a lot of advances in metastatic hormone-sensitive prostate cancer in the last 5 years, even in the last year, regarding how to treat this disease. Specifically, people are realizing that [treatment requires] more than just ADT. It's ADT in combination with chemotherapy with abiraterone acetate (Zytiga) and with certain next-generation androgen receptors," said Penson.

The phase III ENZAMET trial examined the use of enzalutamide (Xtandi) in metastatic hormone-sensitive prostate cancer and showed improvement in overall sur-

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vival at 80% versus 72% in patients who received a different nonsteroidal antiandrogen (HR, 0.67; 95% CI, 0.52-0.86; *P* = .002).[1] Updated data from the ENZAMET trial presented at the 2019 ESMO Congress showed that adding enzalutamide to ADT was associated with modest impairments in fatigue, cognitive function, and physical function, but not general quality of life.[2]

A similar trial, the ARCHES study, looked at enzalutamide plus ADT in patients with metastatic hormone-sensitive prostate cancer. The ARCHES trial showed that at a median follow-up of 14.4 months, the median radiographic progression-free survival was not reached in those who received enzalutamide versus 19.45 months in patients who were given placebo, translating into a 61% reduction in the risk of radiographic progression or death with enzalutamide (HR, 0.39; 95% CI, 0.30-0.50; *P* <.0001).[3] Updated data presented at the 2019 ESMO Congress demonstrated enzalutamide provides clinical benefit in other areas, though overall survival data is still immature.

In the phase III TITAN trial, results showed that apalutamide (Erleada) plus ADT led to a 33% reduction in the risk of death compared with placebo/ADT in this patient population (HR, 0.67; 95% CI, 0.51-0.89; *P* = .0053).[4] These data led to the **FDA approval of apalutamide** in September 2019 for the treatment of patients with metastatic castration-sensitive prostate cancer. Updated data of the TITAN trial at the 2019 ESMO Congress showed that health-related quality of life was preserved with the addition of apalutamide, and pain and fatigue were improved.[5]

In an interview during the 2019 *OncLive*® State of the Science Summit™ on Genitourinary Cancer, Penson, the chair of the Department of Urology and the Paul V. Hamilton, MD and Virginia E. Howd Chair of Urologic Oncology at Vanderbilt University Medical Center, discussed the current armamentarium and ongoing research in prostate cancer.

OncLive: What next-generation inhibitors are available to treat metastatic prostate cancer?

Penson: There are 3 [next-generation inhibitors available], including enzalutamide, apalutamide, and darolutamide (Nubeqa), in metastatic hormone-sensitive prostate cancer. We don't have any information yet about darolutamide but we have a lot of information about enzalutamide and apalutamide. The 2 studies on enzalutamide, ENZAMET and ARCHES, plus the TITAN study looking at apalutamide show that both of these agents improve outcomes in men with hormone-sensitive metastatic disease.

How do you determine what agent to give patients?

If you look, it's not just those 2 agents. We also have now abiraterone (Zytiga). We have docetaxel based on STAMPEDE data and LATITUDE data. It comes down to the individual patients. Some patients, for example, have a seizure or epilepsy history, making them ineligible for enzalutamide. Some patients shouldn't be on prednisone because perhaps they're brittle diabetic.

Some people say higher-volume patients should get docetaxel and lower-volume patients should get the androgen receptor blockers. I don't necessarily subscribe to that theory, but others do. In the end, it becomes the patient's preference, and sometimes insurance coverage, as well. We want to make sure we do the best for our patients.

Are there differences in safety profile between the drugs?

That's a really important point and a research interest of mine is quality of life and the patient experience. The drugs are very comparable, tend to maintain quality of life, and help patients have a good experience.

There are some adverse events (AEs), however, that will affect patients. For example, enzalutamide is associated with a fair amount of fatigue and that can affect quality of life. Those patients often will switch agents. Apalutamide has a rash in some patients. You'll want to switch [agents]. [The process is] you try out the drug and if the drug has an AE, you switch to one of the other drugs. The great thing about all of these drugs is when you get the right one, the quality of life is maintained and, in the long run, it's probably better than if the patient was just on ADT alone.

What questions remain regarding next-generation agents?

It's not just the next-generation agents. There are a lot of questions out there that are critical related to this. What do we do in the patient who has very low volume oligometastatic disease? Is that a patient who, in addition to these agents, needs local therapy? There's some data showing that local therapy may help. That's a really pressing question in the metastatic space.

In the localized space, are these agents useful earlier on as adjuvant or neoadjuvant therapy? That's going to be a big question that we see over the next 5 to 10 years. It used to be that we had dismissed neoadjuvant hormonal therapy prior to local therapy for prostate cancer. Nowadays, people are saying that maybe with the new agents, it will be effective. That's one of the big questions out there that is going to be answered.

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One of the things you have to recognize is a lot of these drugs have the same mechanism of action. You can't combine, for example, apalutamide and enzalutamide. You're hitting the same note on the piano. We want to mix things up a bit.

Is there potential for immunotherapy in the prostate cancer space?

[There are] PARP inhibitors, specifically in the hormone-resistant space with metastatic disease, but immuno-oncology is clearly the future. We can use them earlier when the patients have metastatic hormone-sensitive disease, and perhaps as adjuvant or neoadjuvant therapy with localized disease.

What ongoing trials are happening in prostate cancer?

There are a lot of trials going on, more than I can count. I am really interested in the trial looking at the oligometastatic disease and the role of surgery, the TRoMbone trial. That's going to be very interesting.

There are all these ongoing trials looking at the various checkpoint inhibitors in this space. The future is really interesting. Compared to 10 to 15 years ago when we had almost nothing, now it seems like we're finding new agents and new ways to treat this disease and really getting towards a chronic disease, maybe even cure.

References

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3. Armstrong AJ, Szmulewitz RZ, Petrylak DP, et al. Phase 3 study of androgen deprivation therapy (ADT) with enzalutamide (ENZA) or placebo (PBO) in metastatic hormone-sensitive prostate cancer (mHSPC): The ARCHES trial. *J Clin Oncol.* 2019;37(suppl 7, abstr 687). doi: 10.1200/JCO.2019.37.7_suppl.687.

4. Chi KN, Agarwal N, Bjartell A, et al. Apalutamide for metastatic, castration-sensitive prostate cancer. *N Engl J Med.* 2019;381:13-24. doi: 10.1056/NEJMoa1903307.

Agarwal N, McQuarrie K, Bjartell A, et al. Patient-reported outcomes (PROs) from TITAN: a phase III, randomized, double-blind study of apalutamide (APA) versus placebo (PBO) added to androgen deprivation therapy (ADT) in patients (pts) with metastatic castration-sensitive prostate cancer (mCSPC). *Ann Oncol.* 2019;30(suppl_5). doi: 10.1093/annonc/mdz248.008.

Prostate Cancer - New strategies against bone metastases

sciencedaily.com

https://www.sciencedaily.com/releases/2019/12/191202140610.htm

When prostate cancer spreads, it most often spreads to bone. And while the 5-year survival rate for prostate cancer that has not spread is nearly 100 percent, once the disease reaches bone, the 5-year survival rate is only 29 percent. Now a University of Colorado Cancer Center study published in the *Journal for Immunotherapy of Cancer* suggests a new approach, or, possibly two new approaches against these bone metastases: While targeted therapies and anti-cancer immunotherapies have not been especially successful against primary prostate cancers, the study suggests that both these approaches may be effective against the bone metastases that grow from primary prostate cancers, and, in fact, the type of bone metastasis may dictate which targeted therapies and immunotherapies work best.

There are two types of bone disease from metastases: lytic metastases, which destroy bone tissue, and blastic metastases, which build new bone-like tissue with cancer cells. Currently, it doesn't matter if a bone metastasis is lytic or blastic -- they are both treated the same way. But the current study shows that the genetic and cellular landscapes of these two types of metastases are different, providing different drug targets and suggesting different treatments.

"The genetic and immune checkpoint changes are like those seen in other solid tumors, making it potentially possible to apply new strategies to prostate cancer patients with metastatic bone disease," says paper first

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author Claire Ihle, PhD student in the lab of CU Cancer Center investigator and paper senior author Philip Owens, PhD.

Lytic metastases were characterized by over-activity in a genetic signal called pAKT and its larger signaling pathway called PI3K-AKT, both of which have been targets for drug development in other cancers. Meanwhile, blastic lesions had over-activity in another genetic signal called pSTAT3 and its signaling pathway JAK-STAT, for which FDA-approved drugs already exist.

"I was really shocked by the increase in pSTAT3 in the blastic patients. I expected that these bone-producing (blastic) lesions would have little to no specific targets. I am glad I was wrong as these are the most common lesions in prostate cancer patients," Ihle says. "I would love to see STAT3 inhibitors go to blastic-type patients if we have more data showing a good response."

Importantly, both types of bone metastases also had characteristics that predict response to immunotherapy. Doctors and researchers call primary prostate cancers "cold," meaning they tend not to provoke an immune response. However, both blastic and lytic bone metastases had high levels of the protein PD-L1, which could mean they are more likely to respond to the class of anti-cancer immunotherapy known as checkpoint inhibitors.

"The other interesting point of our studies is that we developed a test that can directly measure immunotherapy and pathway targets in bone metastases," Owens says. "This is significant because we could potentially use this as a test to determine which of the many immunotherapies could be best for an individual patient, one at time, and truly provide a personalized therapy. If I had metastatic disease in bones, I would like a pathology department to know that the immunotherapy they wish to treat me with has a good level of target in the tissue they are hoping to treat."

The group is now focused on testing therapies in mouse models of lytic and blastic bone metastases to determine the most promising drugs and drug combinations.

"The pathway-targeted therapies could be used in combination with immunotherapy or alone and we really don't know if or how to combine them," Owens says.

Previously, the field assumed that bone metastases could be treated the same as the primary prostate cancers from which they grow. Now, the current study shows that's not the case, and even pinpoints signaling pathways and immunologic weaknesses of various types of metastases. If these findings stand the test of ongoing work, the line of research may point to new therapies and drug combinations for these metastases that represent the most dangerous aspects of prostate cancer.

acs.org

Saccharin derivatives give cancer cells a not-so-sweet surprise - American Chemical Society

"`A Sweet Combination': Developing Saccharin and Acesulfame K Structures for Selectively Targeting the Tumor-associated Carbonic Anhydrases IX and XII" *Journal of Medicinal Chemistry*

Saccharin received a bad rap after studies in the 1970s linked consumption of large amounts of the artificial sweetener to bladder cancer in laboratory rats. Later, research revealed that these findings were not relevant to people. And in a complete turnabout, recent studies indicate that saccharin can actually kill human cancer cells. Now, researchers reporting in ACS' *Journal of Medicinal Chemistry* have made artificial sweetener derivatives that show improved activity against two tumor-associated enzymes.

Saccharin, the oldest artificial sweetener, is 450 times sweeter than sugar. Recently, scientists showed that the substance binds to and inhibits an enzyme called carbonic anhydrase (CA) IX, which helps cancer cells survive in the acidic, oxygen-poor microenvironments of many tumors. In contrast, healthy cells make different — but very similar — versions of this enzyme called CA I and II. Saccharine and another artificial sweetener called acesulfame K can selectively bind to CA IX over CA I and II, making them possible anti-cancer drugs with minimal side effects. Alessio Nocentini, Claudiu Supuran and colleagues wondered whether they could make versions of the artificial sweeteners that show even more potent and selective inhibition of CA IX and another tumor-associated enzyme, CA XII.

The team designed and synthesized a series of 20 compounds that combined the structures of saccharin and acesulfame K and also added various chemical groups at specific locations. Some of these compounds showed greater potency and selectivity toward CA IX and XII than the original sweeteners. In addition, some killed lung, prostate or colon cancer cells grown in the lab but were not harmful to normal cells. These findings indicate that the widely used artificial sweeteners could be promising leads for the development of new anti-cancer drugs, the researchers say.

NETWORKING

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

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

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

FINANCES

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

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

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

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

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