REMINDER

ANNUAL PHCSG MEMBERSHIP $20

Join our Monthly meetings on the third Tuesday (Feb – Dec) 10am – 12:30pm

EFT Payments to:
Prostate Heidelberg CSG
BSB 083 256
Acct 583244292

Prostate Heidelberg

March 2021 Issue 204

For Education, Information and Support

Meeting Hall: Ivanhoe Uniting Church 19 Seddon Street, Ivanhoe
POB 241 Ivanhoe Victoria 3079
Email: prostateheidelberg@gmail.com
Website: www.prostateheidelberg.info

Next PHCSG Meeting – Tues 16 Mar (via Zoom)
10am – 12:30pm

Join Zoom Meeting: Copy link and paste into your browser
https://us02web.zoom.us/j/87660247785?pwd=eTlHNHZKYURUK0hURTlzeFpWUFlLdz09

Meeting ID: 876 6024
Passcode: 821427

PHCSG's First Meeting for 2021

At our first meeting of 2021 in February, we welcomed a new member and were, of course, pleased to see those of you who had renewed membership and were able to join us for a very informative Zoom. Our sincere thanks to Carla D'Amico (PCa nurse at the Austin), who regularly attends our meetings, for answering the myriad questions from members. It wasn't planned that way but the support she provided was invaluable.

So, with the safety of our leaders and group members front of mind, our advice remains the same. Cancer Council, along with many other cancer organisations, continues to recommend that Cancer Support Groups not meet face to face for the foreseeable future.

We also understand that not everybody is particularly internet savvy. If you would like individual help with the process of setting up your PC or mobile to join us via Zoom, please let me know. We really do want you to be able to participate.

In this month's newsletter we highlight:

If there is anything you want to talk through in relation to your treatment or wellbeing please don't hesitate to ring:

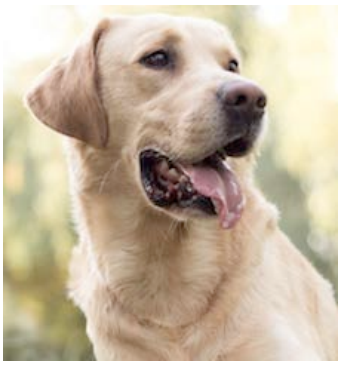
Max Shub	0413 777 342
Mike Waller	0438 616 240
Michael Meszaros	0407 837 538

Prostate Heidelberg Cancer Support Group

PHCSG provides information, education and support for those affected by Prostate Cancer. At our meetings we are committed to:

- showing respect to members, speakers and guests
- allowing members to speak without interruption
- respecting confidentiality

Cancer Gets One Paw Closer to a 'Robotic Nose'



"Imagine a day when smartphones can send an alert for potentially being at risk for highly aggressive prostate cancer, years before a doctor notices a rise in PSA levels. The incredible work of the [cancer-sniffing] dogs is critical as we advance this program to develop an improved method of early prostate cancer diagnosis" said Dr Claire Guest, Co-Founder and Chief Scientific Officer of Medical Detection Dogs.

This new research from a multi-national, cross-disciplinary team of scientists from Medical Detection Dogs (MDD) in the UK, the Prostate Cancer Foundation (PCF), Massachusetts Institute of Technology (MIT), Johns Hopkins University – and a friendly pair of specially trained cancer-sniffing dogs at MDD – has scientifically validated that a dog's nose may hold the key to prostate cancer detection: a more accurate, non-invasive early diagnostic tool able to differentiate between potentially lethal high Gleason Grade cancers and low-grade, less dangerous cancers.

This is the first truly controlled study – both human researchers and dogs were double-blinded on which samples were from cancer patients versus otherwise healthy patients. The findings demonstrate that canines can be trained to detect the most aggressive and lethal form of prostate cancer from volatile organic compounds in urine samples.

It's Worthwhile Challenging an Insurance Decision

There are several products on the market to address ED. Pills, pricks and pumps.

One of our PHCSG members had tried all three with varying degrees of satisfaction (and dis-satisfaction). An internet search put him onto a web site (atouchysubject) recommending a particular medical grade vacuum pump and showing a demonstration video. Looking better than many others on the market, from sex toys to medical devices, he knew that the only way to try it was to buy it. Unfortunately, there was no money back guarantee.

It arrived in a discrete white cardboard tube and after some practice selecting the correct size restriction ring it was put to use. Voila! No need to abandon it to a back corner of the wardrobe or send it to the op shop!

At a cost of nearly $350 our member wondered if his private health extra's insurance would accept a claim. After all, they paid out towards his prescription glasses and dental checkups and, if he needed it, physio and psychology sessions. A quick call to the insurer revealed that vacuum pumps were not on their approved list, although the friendly operator did agree that it seemed not much different to the standard of support a female with breast cancer received. He was told to get his GP to write a convincing letter.

With due respect to his GP and the amount of time she can spend with each patient, the letter was not a resounding success. The claim was rejected in 3 days. Not to be daunted our member decided to write to the health insurance managing director. In it he stated *"…as a company that claims to have "health and wellbeing at our core", there is a clear and compelling case for [insurance compny] to provide financial support for medical grade penis pumps. These are not sex toys. They are a proven remedy for rehabilitating and re-establishing male sexual function in the face of the many challenges and side effects of prostate cancer treatment."*

He hoped it was convincing.

It took just over a week, but he received a phone call from an insurance company representative agreeing to reimburse around two-thirds of the cost, and saying that they will be re-assessing their extras criteria for prostate cancer patients.

So, now we will not only tell you to get a second opinion on your diagnosis and treatments, but also on any insurance rejections!

How Research is Prioritised

Increasing the reliability of cancer trials

Source:
Dr Norman Swan on
ABC Health Report

Most medication trials are paid for by pharmaceutical companies to get their drug registered so it can go on the market. You're probably now an expert in clinical trials, having watched the COVID vaccine studies. But cancer drugs are approved after phase 3 trials which have all kinds of what are called end points - predefined outcomes - and the trial finishes when the patients have been recruited and the end point reached. But what happens after that in the years that follow - and does the cancer drug get better results or perhaps not show its initial promise.

Guest:

Prof Ian Tannock

Medical Oncologist, Princess Margaret Hospital, Toronto

JAMA Oncology: Updating Reports of Phase 3 Clinical Trials for Cancer

A group in Canada has looked at the trials in breast cancer, lung and prostate, to see how many have in fact been updated as time passes and what the results look like then. The findings are both disturbing and illuminating. Ian Tannock is a medical oncologist at the University of Toronto.

Ian Tannock: We found in this series that only about 20% of the trials were ever updated, so you didn't have access to the mature results. And what we found was that of those 20% that were updated, there was a trend for the results to get less statistically important. That is, the size of the effect, the size of the difference got a bit less with time as you got more mature data. We have no idea of course what happened in the other 80%.

Norman Swan: So there's two things that could be the case here. One is that the phase 3 trial was badly designed and therefore not really designed for a valid endpoint and therefore the regulator should be cracking the whip on phase 3. Cancer trials are notorious for not necessarily having endpoints that really matter to patients.

Ian Tannock: Exactly.

Norman Swan: Does the tumour come back, progression-free survival, when actually I want to know am I going to be alive in five years, and very few trials in cancer tell you that. So one is the design of the phase 3 trials, and the other is what's in it for the drug company to continue sponsoring the follow-up of the data when they've got the answer they want. So that's a long question, but let's start; is the problem here that we are pretty poor at designing phase 3 trials?

Ian Tannock: I mean, there have been some good trials, let's not throw all of them out. And if the effect that you see early on, the difference is big, then you are probably okay. This particular study didn't look at endpoints or outcome measures. What you say there is exactly right.

Norman Swan: But these drugs are costing hundreds of thousands of dollars and billions on the drug bill, and immunotherapy was touted as this great result, and indeed for some people who respond to them it's fantastic. But the average, when you look at the trials, is pretty poor. Some people get a great result, cure, long-term survival, and some people don't. Governments like the Canadian government and the Australian government are spending a lot of money on drugs that may actually not in the real world be working as well as they should.

Ian Tannock: That's right, and there have been a couple of papers, one is in the *British Medical Journal*, for example, that looked at EMA approvals of cancer drugs over a 10-year period, and only about a half of them were ever shown to improve either the duration of survival, how long people lived, or the quality of survival. And when it comes down to it, there are only two aims in any medical treatment; either to help patients live longer or help them live better. And only half of the anti-cancer drugs that have been approved have actually ever shown that.

And of those that were approved, that did show a difference in

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Learn to be your own researcher to make the best treatment decisions, by being proactive and an advocate for your own health

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survival, the average improvement in length of survival was just under three months. There are some clear winners, and immunotherapy for people with melanoma, which is obviously very important in your country, that has been a very dramatic improvement. But those unfortunately are the exceptions rather than the rules, and most of the other types of treatment give much less benefit than you see with immunotherapy in melanoma.

Norman Swan: What do you think should be the response to this? Only 20% of trials in your study have any sort of update. When you update there is what's called regression to the mean, I suppose, which means that the effect is not as great as you originally thought. This is serious, it's serious for people's expectations about cancer treatment, and it's serious in terms of tax payers' money. What should happen, what reforms should occur?

Ian Tannock: I think several. First of all, I think the ethics board should actually demand that mature results of trials should be published. They should also be more critical of the endpoints which you brought up, and certainly concentrating on survival and its quality. And then I think the registration agencies are hugely to blame. I've criticised pharmaceutical companies extensively, but at the moment you have to say that they've done a pretty good job, some of them, developing Covid vaccines, so sometimes they do good things.

But I think that the registration agencies like FDA and the EMA, and you probably have a local one in Australia as we do in Canada, but they tend to follow along mainly the same lines, they need to set the bar higher. They need to look for larger effect sizes, and they need to be more critical of trials that use supposedly surrogate endpoints, as is the tumour responding or delay in the tumour progressing. That's not the same as improving survival or its quality.

But I think we need to be more critical in the way that clinical trials are done. Unfortunately I don't see much sign of that happening. If the FDA is going to essentially give approval to any anti-cancer drug that gives a statistically significant rather than clinically important difference in an approved outcome, and they generally allow outcomes like progression-free survival, time without the tumour progressing, then pharmaceutical companies are going to do the trials to allow them to market the drug. And at the moment I don't see any sign in either the FDA or the EMA, being the two biggest, that they are moving to raise the bar on what is approved for marketing. And like you say, once the drugs are approved for marketing, there is absolutely no relationship between the cost at which they are sold, the price at which they are sold, and their efficacy. Basically every new drug is currently being sold in the United States for something like $10,000-$15,000 a month, which is utterly obscene.

Norman Swan: Ian Tannock, thank you for joining us.

Ian Tannock: It's a pleasure.

Norman Swan: Ian Tannock is a medical oncologist at the Princess Margaret Cancer Centre at the University of Toronto.

Source:
JANUARY 15,
https://pubmed.ncbi.nlm.nih.gov/33452455/
DOI: 10.1038/s41388-020-01613-4

Implications for bone metastases:

Melatonin interrupts osteoclast functioning and suppresses tumor-secreted RANKL expression

Cancer-related bone erosion occurs frequently in bone metastasis and is associated with severe complications such as chronic bone pain, fractures, and lower survival rates. In recognition of the fact that the darkness hormone melatonin is capable of regulating bone homeostasis, we explored its therapeutic potential in bone metastasis. We found that melatonin directly reduces osteoclast differentiation, bone resorption activity and promotes apoptosis of mature osteoclasts. We also observed that melatonin inhibits RANKL production in lung and prostate cancer cells by downregulating the p38 MAPK pathway, which in turn prevents cancer-associated osteoclast differentiation. In lung and prostate bone metastasis models, twice-weekly melatonin treatment markedly reduced tumor volumes and numbers of osteolytic lesions. Melatonin also substantially lowered the numbers of TRAP-positive osteoclasts in tibia bone marrow and RANKL expression in tumor tissue. These findings show promise for melatonin in the treatment of bone metastases.

Metastatic Prostate Cancer: Don't Accept Complacency!

You have metastatic prostate cancer, and your doctor has said you're doing all you can do. How can you be sure?

Source:
February 16, 2021
By JANET FARRAR WORTHINGTON
https://www.pcf.org/c/metastatic-prostate-cancer-dont-accept-complacency/

"This is all we can do" is a phrase no cancer patient wants to hear, especially someone with metastatic disease. Medical oncologist and PCF-funded investigator Andrew Armstrong, M.D., M.Sc., hears those six words a lot – from patients who have come to see him at Duke University's Cancer Center, a comprehensive cancer and clinical trial center. The patients are hoping their local doctor was wrong – that this is, in fact, *not* all that can be done.

And here's some good news: Often, there *is* something more, and the list of options is growing even as we speak. "The FDA has approved many new therapies for advanced prostate cancer," says Armstrong. The challenge, he adds, is in knowing which of these might be helpful for you – and which are likely a waste of your time and money.

Why don't all of these drugs work for everyone? Because underneath the umbrella diagnosis of metastatic prostate cancer are many factors that make the response to treatment different in each man. Understanding whether or not you have some of these factors could not only save you thousands of dollars, but could point you away from treatment that is not going to work, and toward better, more promising options.

Do you need a "liquid biopsy?" Armstrong and investigators at five centers recently completed the PROPHECY trial, funded by a Movember-PCF Global Challenge Award. The study's goal was to use a "liquid biopsy" – a blood test that can detect circulating tumor cells (CTCs) shed by prostate cancer – to evaluate a biomarker called AR-V7 as a predictor of response to androgen receptor-blocking drugs such as abiraterone (Zytiga) and enzalutamide (Xtandi). AR-V7 is a variant androgen receptor that some men develop over time. "AR-V7 does not show up when you're first diagnosed with prostate cancer," says Armstrong, "and it generally does not show up before you start hormonal therapy. It only shows up when a patient has developed resistance to commonly used hormonal therapies like leuprolide or degarelix, and more commonly after he has been taking an androgen receptor pathway inhibitor like enzalutamide or abiraterone."

The results of the PROPHECY study, published in the *Journal of Clinical Oncology* and updated this past year in *JCO-Precision Oncology*, showed that AR-V7 is a "negative predictive biomarker" for response and outcomes to abiraterone or enzalutamide. In other words, if a blood test shows that your cancer cells have detectable AR-V7, these drugs are not likely going to be helpful for you. There are two blood tests for AR-V7: one is an mRNA assay developed at, and offered by, Johns Hopkins, and the other is a more widely available CTC protein-based assay made by Epic Sciences. Both tests are good, says Armstrong. "It's common practice," he explains, "that if a man has been on enzalutamide and his cancer has progressed, to try another hormonal agent such as abiraterone, and vice versa. But that strategy can lead to cross-resistance," where neither drug is effective in this patient. "These drugs are very expensive." Abiraterone is now available in a much less expensive generic form, but enzalutamide can cost more than $10,000 – per month! That's a lot of money, particularly if it's not going to help you.

New Strategy: Shotgun *and* Sniper Rifle!

If you have AR-V7, what should you do instead? Think shotgun – many pellets aimed at the disease – *and* sniper rifle – a highly focused, precision medicine approach. "The answer is not to give up, but also not to give therapies that don't work," says Armstrong. "Right now, drugs that are more effective would be chemotherapy: docetaxel and cabazitaxel, and radium-223," a drug that mimics calcium – and, like calcium, gets absorbed into areas of bone with a lot of cell turnover, particularly areas where bone metastases are forming." Treating

PLEASE NOTE:
Treatments may vary in Australia. Please ensure you discuss your diagnosis and treatment options with your consulting specialist

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cancer in the bones not only improves quality of life, but has been shown to increase survival. Another experimental way to treat areas of metastasis is with stereotactic ablative radiotherapy (SABR, or SBRT), an intense, focused dose of radiation directly to a metastatic site.

Gene-targeted treatment is another option for some men. "I look at AR-V7 as not the only blood test you're going to do, but as part of a broader plan to find a therapy that fits the patient," says Armstrong. A small percentage of men have microsatellite unstable (MSI-high) prostate cancer – defects in one or more "spell-checker" genes involved in DNA mismatch repair. This can be identified by tumor genomic sequencing biomarker tests. "About 5 percent of men have microsatellite unstable prostate cancer, and those patients can do very well on immunotherapy such as pembrolizumab – and may even get complete remission of their cancer!"

Another small percentage of men – those who have a defective BRCA1 or BRCA2 gene – may have an excellent response to a PARP inhibitor drug like olaparib or rucaparib and to off label platinum-based chemotherapy. "Ongoing trials are exploring a range of combination approaches of both immune therapies and these targeted agents, as well."

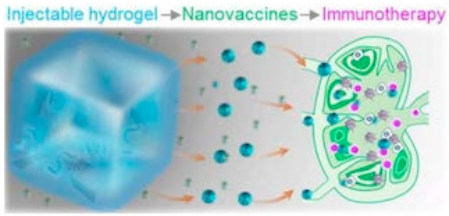
Armstrong is an investigator in clinical trials for still other treatments: newer immunotherapies, targeted molecular agents, newer AR degraders and other inhibitors of hormone signaling, and PSMA-targeted radionuclides, which can detect and attack areas of prostate cancer throughout the body. "A negative test (such as a blood test finding AR-V7) doesn't mean you close all doors. It just means that other doors may open to you, and if those doors are more likely to help, those are the doors you should open. But the first step is going to see an expert who can open those doors for you." Look for a Comprehensive Cancer Centre.

And don't forget: you can help your body fight prostate cancer, as well! Exercise can help minimize side effects and maximize the effectiveness of treatment. The stress hormone, cortisol, plays a role in some forms of prostate cancer, and lowering stress can help slow down cancer's growth. Foods that lower inflammation and insulin resistance can also slow cancer's growth, and new evidence suggests that caloric restriction can decrease metastasis and increase overall survival.

To sum up: Don't accept complacency. "I see it all the time," says Armstrong, "and I've heard stories you wouldn't believe," of patients who have been told there is nothing more that can help them. "Sometimes, if you just do some of these tests, you can find really actionable results." There is almost always something else you can do. There are clinical trials under way and entirely new avenues of treatment, such as PSMA-targeting radionuclides, that offer tremendous promise.

So, consider this: If your doctor doesn't mention new tests or experimental treatments – or even different uses for existing treatments that might be helpful for you, then it's up to you to start this conversation. And even during the pandemic, some clinical trials are still enrolling patients.

It never hurts to ask. Don't give up.



Credit: American Chemical Society

An mRNA vaccine for cancer

Source:
FEBRUARY 17, 2021
https://phys.org/news/2021-02-mrna-vaccine-cancer-immunotherapy.html

Messenger RNA (mRNA) vaccines to prevent COVID-19 have made headlines around the world recently, but scientists have also been working on mRNA vaccines to treat or prevent other diseases, including some forms of cancer. Now, researchers reporting in ACS' *Nano Letters* have developed a hydrogel that, when injected into mice with melanoma, slowly released RNA nanovaccines that shrank tumors and kept them from metastasizing.

Cancer immunotherapy vaccines work similarly to mRNA vaccines for COVID-19, except they activate the immune system to attack tumors instead of a virus. These vaccines contain mRNA that encodes proteins made specifically by tumor cells. When the mRNA enters antigen-presenting cells, they begin making the tumor protein and displaying it on their surfaces, triggering other immune cells to seek and destroy tumors that also make this protein. However, mRNA is an unstable molecule that is quickly degraded by enzymes in the body. For cancer immunotherapy, researchers have tried using nanoparticles to protect and deliver mRNA, but they are typically cleared from the body within 1-2 days after injection. Guangjun Nie, Hai Wang and colleagues wanted to develop a hydrogel that, when injected under the skin, would slowly release mRNA nanoparticles, along with an adjuvant—a molecule that helps activate the immune system.

To develop their system, the researchers used ovalbumin (a protein found in chicken egg whites) as a model antigen. The team mixed ovalbumin mRNA and an adjuvant with other compounds to form a hydrogel. When injected under the skin of mice with melanoma tumors engineered to express ovalbumin, the hydrogel slowly released mRNA and adjuvant nanoparticles over a 30-day period. The mRNA vaccine activated T cells and stimulated antibody production, causing tumors to shrink in the treated mice. Also, in contrast to untreated mice, the vaccinated mice did not show any metastasis to the lung.

These results demonstrate that the hydrogel has great potential for achieving long-lasting and efficient cancer immunotherapy with only a single treatment, the researchers say.

Life after treatment: Wellness program helps cancer survivors find their 'new normal'

Adapting to life after treatment is always a challenging time for cancer survivors.

That's why, with your help, Cancer Council's Cancer Wellness and Exercise program helps cancer survivors live well by prioritising their wellbeing.

How the program helps

The Cancer Wellness and Exercise program aims to increase a patient's ability to take charge of their own health and wellbeing.

It also gives cancer survivors the skills and education to know more about their own health, and demonstrates how exercise and implementing small lifestyle changes can improve quality of life.

The program was developed based on clinical research (such as data from the Clinical Oncology Society of Australia) that shows exercise is a safe and effective way to counteract many of the physical and psychological effects of cancer and its treatment.

The program also increases knowledge and understanding of survivorship; encourages survivors to participate in discussion in a safe and supportive environment; and increases a participant's ability to transition from clinical care to supported self-management.

One participant said they were "grateful" to have access to the program.

"The program helped show me concrete things that I can do to help myself," they said.

Another said it helped adapting to life after treatment.

"It was a great benefit to both my physical and mental wellbeing. It increased my fitness and positive outlook," they said.

How the program works

The Cancer Wellness and Exercise program gives participating cancer patients access to eight weeks of group education and exercise led by trained facilitators who are also exercise psychologists, occupational therapists or physiotherapists.

Each participant takes part in one hour of group exercise and a one-hour group education session each week.

Cancer Wellness topics include:

- Cancer survivorship
- Exercise and fatigue
- Healthy eating and nutrition
- Emotions and wellness
- Maintaining physical health
- Your GP and your health
- Finances and work
- Relationships and intimacy
- Local services
- Foot health
- Complementary therapies
- Bone health

Sessions take place at hospitals, clinics and other health services across Victoria. Thanks to Cancer Council supporters, there are more than 200 trained Cancer Education Program facilitators ready to support cancer patients at 70 health services across Victoria.

These trained facilitators are health professionals who work in oncology, radiotherapy, occupational therapy, exercise physiology/physiotherapy, social work and allied health in both a clinical and community settings.

Cancer Council supporters are crucial in making sure the program is available to people affected by cancer.

Cancer Council's 13 11 20 information and support acts as a referral service for cancer patients and carers – any cancer patient interested in joining the program can call our nurses on 13 11 20 to be connected with their closest participating health service.

Plus, Cancer Council's Education and Training team review and update the program bi-annually, provide resources as required to trained facilitators, and deliver any other support that the facilitators may need to run their program.

The history behind the program

The program started in 2016 as a pilot project funded by the Department of Health and Human Services with an aim to educate more cancer survivors about the benefits of exercise and wellness – particularly in regional and rural Victoria.

Pilot programs took place at five health services across the Grampians and Hume regions with education programs held through telehealth.

By the end of 2018, the pilot programs had helped 110 participants.

Data showed that one third of participants had increased their physical activity levels by 86%, while 48% had increased their intake of fruit and vegetables.

After the success of the pilot project, and with the help of generosity like yours, Cancer Council launched the official Cancer Wellness and Exercise program in January 2019.

In its first year, 40 programs were delivered at 13 acute and community health services across Victoria helping 350 participants.

Throughout 2020, due to COVID-19 and an increase in demand by participants, many facilitators used telehealth and other online resources to continue running exercise and education programs.

If you or someone you know is interested in participating in the Cancer Wellness and Exercise

Source:
Tuesday 9 February, 2021
https://www.cancervic.org.au/about/stories/exercise-and-wellness-program.html

Source:
Jan 16 2020
By Janet Farrar Worthington
https://www.pcf.org/c/focal-therapy-for-prostate-cancer-if-it-sounds-too-good-to-be-true/

Focal Therapy for Prostate Cancer: If It Sounds Too Good To Be True…

If you have been diagnosed with cancer that is contained within the prostate, you may be thinking:

"Hey, there's just a spot of cancer that showed up on the MRI," or:

"Only three of the needles came back with any cancer at all."

And this may lead you to think: "Why do we have to treat the whole thing? Why can't I just get a prostate version of a lumpectomy?"

Or: "Why not just zap that one spot of cancer?"

Wouldn't that be great?

This is called focal therapy – just treating part of the prostate. In just a few seconds on the internet, you can see that there's a lot of this focal therapy out there, and it all sounds great! No erectile dysfunction (ED) or urinary incontinence! If your PSA rises, no problem! Treat it again! A lot of doctors are offering focal treatment, using methods including cryotherapy (freezing the tissue), high-intensity focused ultrasound (HIFU), or even with highly focused radiation.

There's just one problem with every type of focal therapy for prostate cancer, says University of Michigan radiation oncologist and Prostate Cancer Foundation (PCF)-funded investigator Daniel Spratt, M.D.: "I would say, strongly, that it's experimental. There's a very high risk of recurrence, usually within the first three years and it may increase your risk of side effects if you later need curative treatment. There is a reason it is not considered a standard-of-care treatment by most national and international guidelines."

Prostate cancer is usually a multi-focal disease, meaning it is in more than just 1 or 2 spots in your prostate. This is true even if your biopsies or MRI show only 1 area being involved with cancer. Some studies suggest >40% of patients have MRI-invisible tumors, and standard prostate biopsies sample <1% of your prostate gland. This is why focal therapy is often ineffective – it treats only part of your cancer.

Also, a lot of what they say about not having side effects is not true. "Side effects are often lower than men experience with a radical prostatectomy, but there are side effects," says Spratt. "There's still the potential for erectile dysfunction (ED) and other side effects, and one of the biggest concerns is that with subsequent treatment, if the patient needs surgery or radiation, sometimes you can have severe or unexpected side effects. I've seen it in patients who previously had focal therapy," including one man after HIFU, whose entire urethra (the tube that carries urine from the bladder through the prostate and into the penis) became necrotic – the tissue died. "He had to have emergency surgery. They killed healthy tissue."

That's why focal therapy for prostate cancer is still considered experimental. "At the PCF, 'experimental' means 'not proven,'" says molecular biologist and medical oncologist Jonathan Simons, M.D., CEO of the PCF.

Why is it not yet proven? This requires well-designed studies to see how patients do in the short run and then over several years. "There's so little evidence in the literature," says Spratt, and most are retrospective studies or small single arm trials. "No well-powered trials with long-term follow-up have been done to even inform us of how effective these therapies are, and to show the safety of doing subsequent curative treatment (surgery or radiation)."

Spratt has seen many men in recent years who have come from around the country to see him after focal therapy has failed. "Most of the patients I see who have had it are very upset. Insurance often does not cover it, and they have spent $20,000-$30,000 out of pocket, thinking they're going to get a cure with no side effects. But some do get side effects and *all* of them who see me were not cured. And when I tell them, 'Look, you need a second treatment and you're at a higher risk of having more side effects,' they are very upset."

The best way to try focal therapy, Spratt continues, is in a clinical trial, "where you are fully informed of all the risks. Many top centers offer focal therapy, and they should be offering it in the context of a clinical trial. If not, this is concerning. These trials are critical to learn how to quantify and optimize focal therapy. Maybe if they improve it, in the years to come, it will be better than surgery or radiation. But right now, it's definitely not. We're learning. There's a lot of misinformation out there. We must remember that if patients want a non-invasive option other than radical surgery, there are multiple forms of radiotherapy that are completely non-invasive and have better cure rates and long-term potency rates than focal therapy."

In a recent trial of HIFU, "within one year, about 30 percent of men developed ED and 25 percent still had cancer in their prostate. Most of these men had low- or intermediate-risk disease, and could safely have been monitored on active surveillance. In comparison, in a similar risk group of patients receiving radiotherapy, one would expect close to zero percent chance of recurrence within one year, no incontinence, and fewer than 10 percent would experience ED so soon. Similarly, surgical removal of the prostate would also have excellent long-term cure rates.

"So why do centers and providers offer focal therapy? This is very complex. I fear it comes back to money, trying to advance one's academic career with something different, and the pervasive avoidance of working as a multi-disciplinary team. A lot of doctors are trying to offer something less invasive than removal of the prostate for patients looking to avoid the risks of incontinence or impotence, rather than simply offering radiotherapy. Focal therapy is new and it entices patients – like they found the magic bullet. However, external-beam radiotherapy has extensive, high-quality evidence with very long-term follow-up beyond 20 years, and has essentially zero percent incontinence and superior erectile function outcomes compared to the focal therapy literature."

Spratt says, "Bottom line: the two standard-of-care treatments for prostate cancer are surgery and radiotherapy. Lots of emerging treatments and technologies, including focal therapy and proton-beam therapy, may have a role for the management for prostate cancer. Well-done randomized trials are necessary to determine what, if any, role they will have in the management of prostate cancer. Until then…proceed with caution."

Source:
February 22, 2021
https://www.urotoday.com/recent-abstracts/urologic-oncology/prostate-cancer/126138-expression-of-immune-checkpoints-on-circulating-tumor-cells-in-men-with-metastatic-prostate-cancer.html?ct=t(EMAIL_CAMPAIGN_3_7_2021_8_19)&mc_cid=58f4f30e9d&mc_eid=ab8e58b4d4

Expression of immune checkpoints on circulating tumor cells in men with metastatic prostate cancer

A subset of men with metastatic prostate cancer (mPC) responds to immune checkpoint inhibitors, and there is an unmet need to predict those most likely to benefit. We characterized circulating tumor cells (CTCs) for expression of immune checkpoint ligands in men with mPC as a non-invasive biomarker of immune evasion and immunotherapy benefit.

Three cohorts of patients were enrolled: 1) men with mCRPC starting abiraterone acetate/prednisone or enzalutamide (pre-ARSI), 2) men with mCRPC who were progressing on enzalutamide or abiraterone acetate/prednisone (post-ARSI), and 3) men with newly diagnosed metastatic hormone sensitive prostate cancer (mHSPC) starting androgen deprivation therapy. CTCs were captured using the CellSearch® system and stained for PD-L1, PD-L2, B7-H3, and CTLA-4 at baseline, on treatment, and disease progression. Summary statistics on mean CTCs per cohort, as well as rates of ligand positivity were used to analyze CTCs by cohort and by timepoint.

Men in all cohorts and timepoints had prevalent CTC B7-H3 expression (> 80%). We found evidence for CTC PD-L1 expression across disease states, in which > 1 positive CTC or > 50% of CTCs were positive for PD-L1 in 40 and 30% of men with mHSPC, respectively, 60 and 20% of men with mCRPC pre-ARSI, and 70 and 30% of men with mCRPC post-ARSI. CTC PD-L2 expression was present in 20-40% of men in each disease state, while CTC CTLA-4 expression was rare, present in 20% of men with mCRPC pre-ARSI and 10% of men with mCRPC post-ARSI or with mHSPC. CTC immune checkpoint expression was heterogeneous within/between men and across disease states.

We have identified that CTCs from men with mPC heterogeneously express immune checkpoints B7-H3, PD-L1, PD-L2, and CTLA-4, and the detection of these immune checkpoints may enable monitoring on immunotherapy.

New Prostate Cancer Approvals

Orgovyx First FDA-Approved Oral Hormone Therapy for Patients with Advanced Prostate Cancer

February 2021

In December 2020, the FDA approved Orgovyx (relugolix; from Myovant Sciences), an oral hormone therapy called gonadotropin-releasing hormone (GnRH) receptor antagonist, for the treatment of men with advanced prostate cancer. Orgovyx is the first oral hormone therapy approved for patients with advanced prostate cancer. However it has not yet been approved by the TGA for use in Australia.

"Today's approval marks the first oral drug in this class, and it may eliminate some patients' need to visit the clinic for treatments that require administration by a health care provider," said Richard Pazdur, MD, Director of the FDA's Oncology Center of Excellence. "This potential to reduce clinic visits can be especially beneficial in helping patients with cancer stay home and avoid exposure during the coronavirus pandemic."

The American Cancer Society estimated that more than 90,000 cases of prostate cancer would be diagnosed in the United States in 2020.

The FDA approved Orgovyx based on the results of a clinical trial of 930 patients with prostate cancer who required at least 1 year of androgen-deprivation therapy because of prostate cancer recurrence after radiation or surgery, or who were newly diagnosed with castration-sensitive advanced prostate cancer.

The patients received 48 weeks of either Orgovyx or another GnRH receptor antagonist, Lupron Depot (leuprolide acetate). The main measure of the benefit of therapy was medical castration, which was defined as maintaining blood testosterone suppression to castrate levels by day 29 through 48 weeks of treatment. Among the 622 patients who received Orgovyx, 97% of them reached medical castration rate, an almost complete efficacy rate, demonstrating the benefit of this new oral therapy.

The most common side effects with Orgovyx were hot flushes, musculoskeletal pain, fatigue, diarrhea, and constipation.

Prostate Heidelberg Cancer Support Group Meetings

While we are having to distance ourselves and are unable to hold face-to-face group meetings we are engaging speakers via video conferencing.

We are planning to recommence our regular monthly meetings at Ivanhoe Uniting Church. When this happens we will also try to continue to provide for attendance via Zoom for those who cannot attend in person.

Learn to be your own researcher to make the best treatment decisions, by being proactive and an advocate for your own health

New Prostate Cancer Trials

CAR T-Cell Therapy, MB-105, Shows Promise in Metastatic CRPC Patient in Phase 1 Trial

Source: https://patientahead.com/car-t-cell-therapy-mb-105-shows-promise-in-metastatic-crpc-patient-in-phase-1-trial/

A heavily pretreated patient with metastatic castration-resistant prostate cancer (mCRPC) showed significant benefits, including a 94% decrease in the levels of the prostate-specific antigen (PSA) biomarker, one month after receiving MB-105 in a Phase 1 clinical trial.

The promising initial data from Mustang Bio's investigational CAR T-cell therapy were shared at the 27th Annual Prostate Cancer Foundation Scientific Retreat, which was held virtually from Oct. 20–23.

Tanya Dorff, MD, an oncologist at City of Hope National Medical Center in California, and the trial's principal investigator gave the presentation, titled "Clinical Development of PSCA-Targeted CAR T Cells for Advanced Prostate Cancer."

The trial (NCT03873805) is actively recruiting adult mCRPC patients, who progressed while receiving a second-generation androgen receptor inhibitor, at the City of Hope center in Duarte. Additional data are expected by 2021.

"We are encouraged by the initial data presented by City of Hope from the ongoing Phase 1 trial of Mustang's CAR T cell therapy MB-105," Manuel Litchman, MD, president and CEO of Mustang, said in a press release.

mCRPC refers to a form of prostate cancer that is both metastatic, meaning it has spread to distant locations, and castration-resistant, which means that the tumor continues to grow even when the amount of testosterone is reduced to very low levels.

Mustang's MB-105, initially developed at City of Hope laboratories, is a type of immunotherapy with the potential to treat prostate, pancreatic, gastric, and bladder cancers by directly attacking tumor cells.

MB-105 consists of a patient's own T-cells, immune system cells with the ability to fight cancer, that have been genetically engineered in the lab to more efficiently attack tumor cells.

These engineered cells, called CAR T-cells, are specifically modified to produce a man-made chimeric antigen receptor, or CAR, that helps them recognize and kill cells containing the prostate stem cell antigen (PSCA) protein, without harming healthy cells.

The PSCA protein is found at higher levels in cancer cells, with limited expression in normal tissues, and is found on the surface of the cells, making it an ideal target for this immunotherapy approach.

Following the genetic engineering step of the CAR T-cell process, these cells are allowed to grow under laboratory conditions before being administered as a therapy via blood infusion. Some form of immunosuppression, such as chemotherapy, is typically administered with CAR T-cells, to reduce the likelihood of an immune response to the modified T-cells.

Researchers launched a Phase 1 clinical trial (NCT03873805) into MB-105, which will recruit a total of 33 patients with mCRPC that expresses the PSCA protein.

Its primary goals are to investigate the safety of MB-105, and to determine a proper dose for future study. These steps are incorporated into the design of the trial, which is a dose escalation study, meaning that subsequently enrolled patients are given higher treatment doses until the side effects become too severe.

The researchers will also assess treatment efficacy, by measuring the persistence of the CAR T-cells and by evaluating the patients clinically, namely the proportion of those who respond to treatment, their survival outcomes, and changes in cytokines, or proteins that regulate immune responses.

The recent presentation reported the case of a 73-year old man given MB-105 after failing eight previous treatment courses. Four weeks after receiving the CAR T-cell therapy, the man showed a 94% reduction in PSA levels, a near-complete elimination of soft tissue metastasis — assessed via computerized tomography (CT) imaging — and an improvement in bone metastasis seen via magnetic resonance imaging (MRI).

The patient did experience cytokine release syndrome, a potential side effect of CAR T-cell therapy in which cytokines are rapidly released in response to the treatment, causing symptoms that can range from mild to life-threatening.

In this case, clinicians managed his response with Actemra (tocilizumab), an antibody that targets and reduces the activity of the cytokine IL-6. He also had a hemorrhagic cystitis, or an inflammation of the bladder, which required a blood transfusion and was ultimately resolved within 30 days.

Given the improvement in the patient's mCRPC, Mustang was encouraged by the report, and will be providing further details about MB-105 toward the end of next year.

"We see potential for this PSCA-targeted CAR T in the treatment of prostate cancer, as well as other difficult-to-treat solid tumor cancers," Litchman said. "We look forward to the continued progression of this trial and anticipate providing further data in the second half of 2021."

Internet Resources

Members have found the following websites useful

Prostate Cancer Foundation of Australia for guides & help
https://www.pcfa.org.au
https://onlinecommunity.pcfa.org.au/

Australian Cancer Trials Information on clinical trials
https://www.australiancancertrials.gov.au

USA Prostate Cancer Foundation (Guide) PDF guide for men newly diagnosed with PC
https://www.pcf.org/guide/

Us TOO International PCa Education (USA) USA PC support groups' information & newsletter
https://www.ustoo.org

Cancer Council Victoria for general support services
https://www.cancervic.org.au

ExMed Cancer Program Melbourne based 'best practice' exercise medicine program
https://www.exmedcancer.org.au

ProstMate (PCFA) A companion to record PC results

Beyond Blue for help with depression and anxiety
HELPLINE 1300 22 4636

Continence Foundation of Australia for assistance with incontinence aids
HELPLINE 1800 33 0066

PCRI Prostate Digest (USA) Prostate Cancer Research Institute supporting research and disseminating information to educate and empower patients, families and the medical community
https://pcri.org/insights-newsletter

PAACT Newsletter (USA) Patient Advocates for Advanced Cancer Treatments
http://paact.help/newsletter-signup/

A Touchy Subject
https://www.youtube.com/channel/UCdyuxGuAuCWJbe-kZvwVSzQ

The internet is a good source for research but it should not be trusted to give you answers for your personal care. Always speak to your doctor to clarify any medical advice.

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PHCSG Correspondence

Mike Waller Convener
Max Shub Co-Facilitator
Peter Anderson Treasurer
Spiros Haldas Library
David Bellair Web Site
Michael Meszaros Welfare Officer
Sue Lawes Secretary/Newsletter

PHCSG Meetings 2021 10am – 12:30pm

Tues 16 Feb
Tues 16 March
Tues 20 April
Tues 18 May
Tues 15 June
Tues 20 July
Tues 17 August
Tues 21 September
Tues 19 October
Tues 16 November
Tues 14 December (including Xmas lunch)

Please note that all face-to-face meetings have been cancelled until further notice. Please check your email regularly for updates from the PHSCG Committee.

2021 PHCSG Articles

If you have any feedback or wish to include articles on specific aspects of Prostate Cancer please contact Sue at:

prostateheidelberg@gmail.com

January 2021

- Exercise Infographic
- Sexual Dysfunction & Shared Decision Making
- FDA Approves first Oral Hormone Therapy
- Prolonged ADT Reduces Cardio Fitness
- Reducing the Burden of Out-of-Pocket Expenses
- BAT Sensitizes CRPCa to Subsequent Therapy
- Targeting Bone Mets with Radiation in Oligorecurrent Men

Prostate Cancer Trials

- PEACE V:STORM
- UpFront PSMA Phase II
- NINJA

February 2021

- Advantages of Coffee
- Our Biological Clock
- Statins tied to Better Outcomes
- What's New in Inflammation
- New PC Management Techniques
- About the Patch Trial
- Eating a Colourful Diet
- Dose Painting
- Advancement in Focal Therapy

Prostate Cancer Trials

- Enza-P
- DASL-HiCaP Trial
- Lu-177-PSMA-617
- Adding Apalutamide to Radiotherapy & LHRH Agonist

March 2021

- Challenging Your Private Health Provider
- How Research is Prioritised – Norman Swan podcast
- Metastatic PCa – Don't Accept Complacency
- An mRNA Vaccine for Cancer
- Life After Treatment – Wellness Program
- Focal Therapy – If It Sounds Too Good to be True
- Immune Checkpoints on CTCs

2020 PHCSG Articles

If you have any feedback or wish to include articles on specific aspects of Prostate Cancer please contact Sue at:

prostateheidelberg@gmail.com

March 2020
- PCFA Consumer Advisory- Coronavirus and Cancer

April 2020
- Telehealth & Delayed Hospital Treatments due to COVID-19
- Fexapotide Triflutate (FT) injection – a new kind of focal treatment to extend time on active surveillance

Prostate Cancer Trials
- DASL-HiCaP Trial
- Evaluation of a mainstream model of genetic testing for men with prostate cancer

May 2020
- ADT May Offer Some Protection From COVID-19 in Men with Prostate Cancer
- TULSA – Novel MRI-guided ultrasound treatment destroys prostate cancer
- Whack-a-Mole A Treatment of Oligometastasis
- Long-term adjuvant ADT improves results of brachy boost therapy in unfavorable-risk prostate cancer patients
- Harnessing the immune system to control prostate cancer spread to the bone

Prostate Cancer Trials
- A study to see whether PET scans using a chemical called Exendin can detect metastatic PC
- Evaluation of a mainstream model of genetic testing for men with prostate cancer

June 2020
- Evaluating the Outcomes of AS in Gleason Grade 2 Prostate Cancer
- Advancing precision medicine for metastatic prostate cancer
- Impact of Primary Prostate Cancer Treatment with Subsequent Metastatic Disease
- Comparative Analysis & Survival Outcomes in a Real-World Practice Setting
- Fexapotide Triflutate (FT) injection – a new kind of focal treatment to extend time on AS

Prostate Cancer Trials
- Impact of 18F-DCFPyL PET scanning in patients undergoing post-prostatectomy Radiotherapy

July 2020
- Testosterone Therapy does not Increase the Risks of PCR or Death after Definitive Treatment for Localised Disease
- Association of Pre-Salvage Radiotherapy PSA Levels after Prostatectomy with Outcomes of Long-term Antiandrogen Therapy in Men with Prostate Cancer
- Testosterone Replacement in the treatment of Advanced Prostate Cancer
- Memorial Sloan Kettering Cancer Center PCa nomograms Prediction Tools

August 2020
- Advanced Prostate Cancer Algorithm
- Blood Test Predicts Response to PC Treatment (liquid biopsy)
- The Perils and Pitfalls of Treating PSA in PCa
- Reprogramming Immune Cells could Switch Defence into Attack in PCa
- Maintenance of Sexual Activity Following ADT

September 2020
- ProtecT Trial showing patient outcomes after AM, RP & EBRT
- Changes in Penile Length after RP
- Active Surveillance for PC – is it right for you?
- The final part of The Perils and Pitfalls of "Treating PSA" in Advanced Prostate Cancer
- Managing Erectile Dysfunction – A Patient Guide

Prostate Cancer Trials
- Efficacy and Safety of Pembrolizumab (MK-3475) Plus Enzalutamide Plus Androgen Deprivation Therapy (ADT) Versus Placebo Plus Enzalutamide Plus ADT in Participants with (mHSPC)
- Navigate: An online treatment decision aid

October 2020
- World Osteoporosis Day
- Lifestyle Factors and Chronic Disease
- Hormone Therapy for PC
- Early ADT for Recurrent PC Challenged
- Unexpected aPC weakness can be targeted by drugs
- Hijacking an Epigenetic Program
- New PC Research: Immunotherapy; Gut Microbiome
- Veyonda New Research on Survival Rates

Prostate Cancer Trials
- MIndonline - mindfulness

November 2020
- Life insurance & Genetic Testing
- World First Surgery in NZ
- Melatonin increases survival
- SBRT disease control
- Public vs Private Hospitals
- Early ADT for Recurrent PC challenged
- Enzamet trial results

Prostate Cancer Trials
- Randomised Phase 2 of sequential 177Lu-PSMA & Docetaxel
- Exercise for Heart Health

December 2020
- ACTA Trial Award
- Rethinking Metastasis
- ESMO Phase 1 AMG160
- Five Ways to Get it Right
- Immunotherapy Offers Hope
- SBRT Doubles Pain Response
- Elevated Streess Hormone Levels

Prostate Cancer Trials