ANNUAL MEMBERSHIP

PHCSG 2021 annual membership fees are due. Jan – Dec $20. A renewal form will be sent out shortly with payment details. If any new readers are interested in joining, please send an email to: prostateheidelberg@gmail.com

Prostate Heidelberg

December 2020 Issue 201

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 15 Dec (via Zoom)
10am – 12:30pm

Copy link and paste into your browser
https://us02web.zoom.us/j/84682723223?pwd=ek80b21KV1prRTFtMVlNK3RhVk91dz09

Meeting ID: 846 8272 3223

Passcode: 130217

This month… HAPPY CHRISTMAS

A smaller group gathered via Zoom to discuss members' progress and diagnoses and we were delighted to have Sheryl (co-ordinator for Warnambool) join us. Some of the discussion revolved around the benefit of exercising while on ADT (hormone therapy) so we are going to include this information on the PHCSG website. We also learnt the importance of finding the most comfortable saddle for bike riders – to which Mike & I can attest after hiring bikes recently on a short trip into country Victoria.

We would normally finish the year with a Christmas lunch after our December meeting. However until our meeting venue reopens we will not be meeting face to face but look forward to organising a get together in the New Year.

In this month's newsletter we highlight:

I'm sure we're all happy to be out of lockdown and able to catch up with friends and family Australia wide but, as always, please don't hesitate to contact us if there is anything you want to talk through in relation to your treatment or wellbeing.

Wishing all members & readers an enjoyable Christmas and healthy New Year.

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

Clinical trial for prostate cancer awarded 2020 ACTA Trial of The Year

The Australian Clinical Trials Alliance (ACTA) has recognised the remarkable Australians who advance the health system through clinical trials at the virtual Clinical Trials 2020: National Tribute and Award Ceremony.

The Awards honour those who design, conduct and participate in ground-breaking clinical trials, and promotes the importance of clinical trials and the expertise and complexity of the work involved.

One trial scooped the pool at the Awards. The winner of the 2020 ACTA Trial of the Year Award, the ACTA STInG Award for Excellence in Trial Statistics and the Consumer Involvement Award was the ENZAMET Trial. The trial looked at whether adding enzalutamide to hormone therapy right at the beginning of treatment would improve the survival of men with metastatic prostate cancer.

Led by the Australian & New Zealand Urogenital and Prostate (ANZUP) Cancer Trials Group, the ENZAMET Trial showed impressive results including a 33% relative reduction in the risk of dying for men who received enzalutamide added to hormone therapy right at the beginning of treatment, compared to men who received the treatment after waiting for the cancer to grow after prior hormone treatment.

Professor Ian Davis accepted the Trial of the Year Award.

I Am And I Will: Together, all of our actions matter

When we choose to come together, we can achieve what we all wish for: a healthier, brighter world without cancer. Together, all of our actions matter. This World Cancer Day, who are you and what will you do?

Each year on 4 February, World Cancer Day empowers communities and individuals across the world to show support and raise the profile of cancer in a positive and inspiring way.

The campaign theme for World Cancer Day 2019-2021 is **'I Am and I Will'.** Whoever you are, you have the power to reduce the impact of cancer for yourself, the people you love and the world.

Get involved any way you can. Because together, we can create change.

To find out how you can get involved visit - https://www.worldcancerday.org/about/2019-2021-world-cancer-day-campaign

Rethinking Metastasis

Source:
https://www.pcf.org/c/rethinking-metastasis/?utm_source=NewsPulse&utm_medium=email&utm_campaign=NOV20NP

10Nov 2020

News flash: It's a spectrum. All metastasis is not alike, and the basic category of "metastatic prostate cancer" is being redefined by doctors and scientists even as we speak. In fact, it is very likely that there's wiggle room – and still the potential for cure – between cancer escaping the local area around the prostate and full-blown, widespread, metastatic cancer.

That makes sense, right? And yet, for a very long time, many doctors believed, and many still believe, that if we don't cure cancer while it's confined to the prostate, then that's it. Game over, it's not curable. Note: *That doesn't mean it can't be treated, sometimes for many years!* But in terms of treatment, traditionally, metastasis has meant **bye-bye, local therapy, and hello, systemic therapy** – androgen deprivation therapy (ADT), androgen receptor-blocking drugs such as apalutamide or enzalutamide, and chemotherapy. For patients with metastatic prostate cancer who see their doctors every three months for just a few minutes at a time, that can feel, as one patient's son put it, like **"Lupron and a handshake."**

But a lot of things have come together recently to make doctors and scientists say, **"Not so fast! Maybe there's a window, and maybe the window is wider than we thought."** One of these things is the recent **ORIOLE study**, led by Johns Hopkins radiation oncologist and PCF-funded investigator Phuoc Tran, M.D., Ph.D. Another is the development over the last decade of better imaging, such as PSMA-PET, which allows tiny bits of cancer to be seen months before they could be seen on conventional imaging, such as a CT scan or bone scan. Better imaging has sparked an idea: **"If we can see it, we can treat it."** Is it true? Can treating little spots of cancer, before full-blown metastasis develops, prolong life?

Earlier this year, PCF brought together some of the country's best and brightest – experts in radiation oncology, oncology, urology, and basic science – for a worldwide exchange of knowledge, a webinar attended by more than 300 scientists around the world. The topic was oligometastasis. **Oligometastasis is just a little bit of metastasis**; definitions vary, but generally, scientists who use this word are generally talking about fewer than 3 or 5 spots of cancer that have escaped from the main tumor. It's not widespread; it's limited. That doesn't mean it can't go on to cause trouble later. If your kids or grandkids are into Pokémon, it's like catching a little monster before it evolves into something more powerful.

Is oligometastasis treatable? It is in some other cancers. In colon cancer, for example, oligometastasis is treated with surgery or spot radiation in addition to removing the primary tumor, and sometimes it's cured! Phuoc Tran's ORIOLE study, and now promising early results from other studies, including ORIOLE's successor, the RAVENS study, suggest that treating oligometastasis – in Tran's case, with SABR (stereotactic ablative body radiation, also called SRBT, a highly focused, intense dose of radiation therapy) – *in addition to treating the primary prostate tumor* **can change the course of metastasis- in some patients.**

Patients reach oligometastasis in different ways. Some reach it by biochemical recurrence – the dreaded rise of PSA after treatment of the primary tumor in the prostate with surgery or radiation. Others are diagnosed from the get-go with cancer that has already spread outside the prostate. **The standard of care for most of these latter patients is not only *not* to treat the main tumor, but *not* to zap or surgically remove the few sites of metastasis.**

Why not? Why the heck not? Or, as Tran says, "It makes so much sense, so why don't we do it? Because we have tried periodically over the past five decades to treat metastatic disease aggressively with local therapies, and *because of lack of imaging*, treatment technology and just general lack of our ability to take care of patients, this approach did not work." In fact, he continues, "it was actually a resounding failure, and made many who lived through these periods very scared of doing much more harm than good. One of the first texts on this concept, called 'Solitary Metastases,' actually started out with a chapter called "Illusion or Reality.'"

But that was then. Even now, there's

not yet definitive proof that it works. **But take heart: the winds of change are blowing!**

This brings us to the PCF 2020 Global Knowledge Exchange on Oligometastatic Prostate Cancer. Eric Klein, M.D., Chairman of the Glickman Urological & Kidney Institute at the Cleveland Clinic, who moderated the discussion, set the stage with a story about a patient. The man was in his 50s, diagnosed with Gleason 9 cancer that extended slightly past the prostate, into the seminal vesicles. He also had cancer in a lymph node. The man received ADT for six months, had a radical prostatectomy, then was on abiraterone plus prednisone for a year afterward. A bone scan showed one spot of cancer; it was treated with radiation at MSJCC. "He's about eight or nine years out now," says Klein. "He has an **undetectable PSA and a normal testosterone**."

As PCF's CEO, Jonathan Simons, M.D., says, "One clinical case well studied can change the course of medical history." This patient's exceptional clinical course has led Klein ask to the big question: "If we can seemingly cure one man with metastatic prostate cancer, can we cure others? And are we at a place now in the field to be asking the right questions, with the right trial behind them?"

Ralph Weichselbaum, M.D., Chair of the Department of Radiation and Cellular Oncology at the University of Chicago, is the radiation oncologist who coined the term, "oligometastasis." He specializes in treating it in various forms of cancer. Not only does metastasis represent a spectrum of disease, he says, "depending on the **number of metastases, the organs involved, and the pace of progression**," but patients represent a spectrum, too. "There are subsets of patients who are potentially curable with metastasis-directed therapies" (treating breakout tumors directly, and not relying on systemic therapy alone). What accounts for these subsets? Genetic factors, and also the robustness of the patient's immune system. Weichselbaum's research suggests that patients with a well-functioning immune system are better able to hold metastasis in check than others. In other words, whether oligometastasis responds to treatment depends on "the complex relationship between tumor and host."

Mary-Ellen Taplin, M.D., medical oncologist and Director of Clinical Research at the Dana-Farber Cancer Institute's Lank Center for Genitourinary Oncology, collaborated with other physician-researchers on the design of a multi-arm, multi-modality therapy clinical trial with funding from a PCF Challenge Award. "Our focus is the patient with high-risk localized disease, or low-volume or recurrent metastatic disease," said Taplin. The trial will be looking at many things, including potential biomarkers for sensitivity and resistance to treatment. But one of the objectives is of particular interest: "to eliminate all disease in patients largely incurable with *any single* treatment."

In other words: to kill prostate cancer that has escaped the prostate, these doctors and others believe, *in addition to targeting the primary tumor* with prostatectomy or radiation, it may well take *a short course of ADT*, perhaps also *chemotherapy*, maybe further external-beam *radiation to the area around the prostate*, and then *radiation or radiofrequency ablation to the metastatic sites themselves*. But then, the hope is that these patients will have an undetectable PSA and that they will get their testosterone back.

There are several other important trials underway to treat oligometastasis in prostate cancer. Of all the things scientists hope to learn from these trials, perhaps most important, says medical oncologist Ana Aparicio, M.D., of MD Anderson Cancer Center, is "**how do these site-directed therapies work?"** Will the success come from messing up the circulating tumor microenvironment? One idea is that, as cancer spreads, it sends messengers back for supplies to the other sites where cancer is already established, using the bloodstream as a liquid version of Fed Ex. "Or, are we modulating the immune response? Does the primary tumor have an immunosuppressive effect that limits the ability of the patient's immune system to control the disease? Or, are we having an immune- stimulatory effect with treatments? We may need to build on that, and combine radiation with some novel immunotherapies. Or, are we decreasing the tumor burden," by zapping sites of oligometastasis?

Aparicio draws a picture for her patients to help explain: There are two icebergs, one blue, one yellow. "The blue one, most of it is above the water," she notes. "If you get rid of what you see, it is likely that the iceberg is going to take a long time to grow again and become a problem. So, if what we see on the scans is most of the disease that's present, then yes, addressing all the sites we can see can be beneficial. But if it's just the tip of the iceberg (like the yellow picture), and there's a large burden of tumor we are not able to detect with our imaging tools, we'll find that the disease grows very quickly."

Better imaging, such as PSMA-PET, will undoubtedly help determine the true state of tumor burden, "particularly when the PSA is rising, but it's less than 10; conventional imaging really is not useful when the PSA is 5 or 10," says Phuoc Tran. He believes the number of patients with oligometastasis in the U.S. is huge, "much higher than the number of men diagnosed each year." Right now, "systemic therapy is the standard of care for patients with metastatic disease," says Tran. "But in that gray area of biochemical recurrence (PSA creeping back up after prostatectomy or radiation of the primary tumor), as men are approaching low-volume metastasis, there's a perfectly reasonable period in which you can ask the question, does local therapy change the metastatic process?" That was the question behind the ORIOLE trial.

"If the oligometastatic state didn't exist, if this were not a spectrum, and if local therapy could not alter that natural history of metastasis, then we shouldn't be able to affect progression at all with local therapy alone. **Patients should progress no matter what. We did not see that.** Obviously, stronger evidence is needed," but the results of the ORIOLE trial and early results of the RAVENS trial have been very encouraging.

It may be, says Weichselbaum, that we are dealing with multiple, different disease states, "requiring entirely different kinds of treatments. We need to define really what metastasis is, and how the systemic treatments and ablative treatments fit together for optimal therapeutic outcome."

And maybe one day, says Tran, "we can alter the natural history of metastasis, and cure these patients with formerly incurable disease."

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

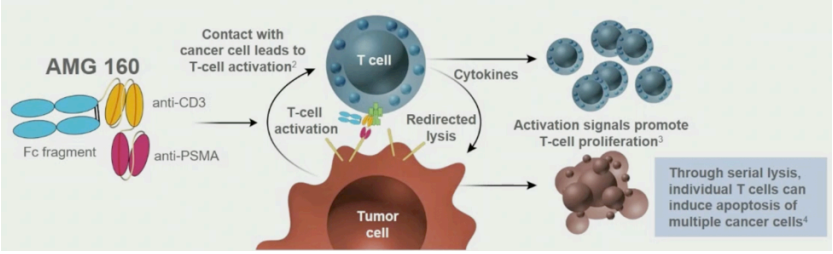
Source:
https://www.urotoday.com/conference-highlights/esmo-2020/prostate-cancer/124630-esmo-virtual-congress-2020-first-results-from-a-phase-1-study-of-amg-160-a-half-life-

ESMO Virtual Congress 2020: Phase 1 Study of AMG 160

The following article was presented by Ben Tran, Medical Oncology Department, Peter MacCallum Cancer Centre, Melbourne, Australia. Although a phase 1 Study it's good to see local expertise on the world stage

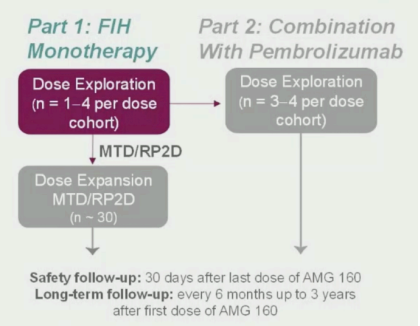
First Results from a Phase 1 Study of AMG 160, a Half-Life Extended, PSMA-Targeted, Bispecific T-Cell Engager (BiTE®) Immune Therapy for Metastatic Castration-Resistant Prostate Cancer

There is an urgency to develop therapies with novel mechanisms of action to treat prostate cancers resistant to chemohormonal and radiation therapies. Unfortunately, to date, immune therapies have offered limited efficacy in patients with metastatic castration-resistant prostate cancer (mCRPC). More recently, there has been excitement regarding PSMA as a clinically validated therapeutic target in prostate cancer. AMG 160 is a targeted half-life extended, bispecific T-cell engager (BiTE®) immune therapy that engages a patient's own T cells to kill prostate cancer cells via binding of CD3 on T cells and PSMA on cancer cells:



At the prostate cancer session during the virtual ESMO 2020 annual meeting, Dr. Ben Tran and colleagues presented their preliminary results from the dose exploration portion of an ongoing phase I study of AMG 160 in mCRPC (NCT03792841).

For this study, eligible patients had mCRPC refractory to prior novel hormonal therapy and 1–2 taxane regimens, as well as evidence of progressive disease. Key exclusion criteria included active autoimmune disease or requiring immunosuppressive therapy, prior PSMA-targeted therapy (however, patients treated with PSMA radionuclide therapy were eligible), as well as patients with CNS metastases, leptomeningeal disease, or spinal cord compression. AMG 160 was administered as a short IV infusion every two weeks at doses of 0.003–0.9 mg. The combination of AMG 160 plus pembrolizumab was also evaluated (results not presented). The primary objectives of this study were to evaluate safety and tolerability, as well as the maximum, tolerated dose, and recommended phase II dose. Secondary objectives were to characterize the pharmacokinetics and to evaluate preliminary antitumor activity. Finally, exploratory objectives were to evaluate biomarkers of activity and to identify potential patient selection biomarkers. A summary of the trial design is as follows:



As of the data cutoff of July 20, 2020, 43 patients had received ≥ 1 dose of AMG 160 monotherapy at 6 dose levels, and 19 patients (44.2%) were still on treatment (6 for ≥ 6 months). The median age was 66.0 (range: 49–78) years, the majority of patients were Caucasian (79.1%), and 26 patients (60.5%) had received ≥ 4 prior lines of therapy. The median number of prior lines of therapy was 4 (range: 1-9), and the median PSA at baseline was 79.2 (range 0.1-4035) ng/dL; 34.9% of patients had RECIST-measurable disease. Among the 43 patients, 41 (95.3%) experienced a treatment-related adverse event, most commonly cytokine release syndrome (n=30, 90.7% all grade; n=11, 25.6% grade 3). Cytokine release syndrome was reversible, manageable, and most severe in cycle 1, with associated fever, hypotension, transient transaminitis, nausea/vomiting, and/or diarrhea. There were 26 patients (60.5%) that had grade 2 cytokine release syndrome as the worst grade, and 11 patients (25.6%) that had grade 3 cytokine release syndrome as the worst grade; 4 patients (9.3%) experienced reversible atrial fibrillation in the setting of cytokine release syndrome/ tachycardia. Prophylactic mitigations to improve the cytokine release syndrome profile in the cycle 1 priming cohort included:

- Dose priming: lower run-in dose before maintenance target dose
- Dexamethasone premedication: 8mg PO and 8mg IV before AMG 160 dose
- Prophylactic IV hydration: 1L normal saline after the AMG 160 dose

There were no grade 5 events and none of the treatment-related adverse events resulted in treatment discontinuation. Six of 30 patients (20.0%) assessed developed antidrug antibodies affecting drug exposure between cycles 1 and 10, however, no adverse events associated with antidrug antibodies were observed.

At the data cutoff, the maximum tolerated dose had not been reached. AMG 160 demonstrated efficacy with long-term responses. There was a confirmed PSA response in 27.6% of patients, an unconfirmed PSA response in 11.4% of patients, and a CTC0 response in 23.1% of patients. Among patients with RECIST measureable disease, 13.3% had confirmed partial response, 6.7% had unconfirmed partial response, and 53.3% had stable disease. A summary of efficacy is as follows:

PSA reductions (best response) were dose-dependent and occurred in 24/35 (68.6%) of evaluable patients at the data cutoff of July 20, 2020, whereas PSA reductions >50% occurred in 12/35 (34/3%) of evaluable patients:

Dr. Tran then provided three patient examples of particularly deep responses to AMG 160:

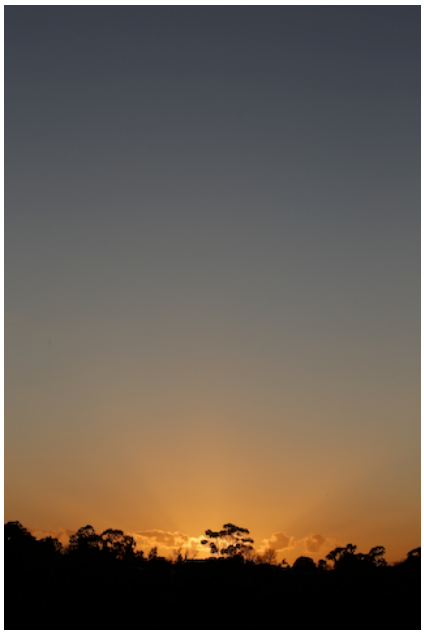
- Patient 1: had prior surgery, radiotherapy, and four systemic therapies (docetaxel, enzalutamide, bicalutamide, and talazoparib) – treated with 0.09 mg AMG 160 with cycle 1 priming who had a rapid PSA drop in 1 month with a durable PSA response
- Patient 2: had prior surgery and three systemic therapies (docetaxel, enzalutamide, and sipuleucel-T) – treated with 0.09 mg AMG 160 with cycle 1 priming who had a rapid PSA drop in 1 month with a durable PSA response
- Patient 3: had prior radiotherapy and four systemic therapies (apalutamide, docetaxel, sipuleucel-T, and radium-223) – treated with 0.3 mg AMG 160 with cycle 1 priming who had a rapid PSA drop in 1 month (limited longer-term follow-up)

Dr. Tran concluded his presentation of the phase I AMG 160 trial with the following take-home messages:

- AMG 160 had a manageable safety profile as monotherapy: cytokine release syndrome was reversible and manageable with priming doses and standard mitigations, and there were no grade 5 treatment-related adverse events or treatment discontinuations
- In heavily pre-treated patients, AMG 160 showed preliminary evidence of efficacy: 68.6% of patients showed a PSA decline across all monotherapy dose cohorts, 34.3% had a PSA reduction >50%, and among 15 patients with measurable disease, there were 3 partial responses and 8 patients with stable disease
- 44.2% of patients remained on AMG 160 at the time of data analysis, with 6 (14.0%) of patients continuing treatment for more than 6 months
- The maximum tolerated dose had not been reached and dosing optimization of AMG 160 continues as the study nears the recommended phase II dose
- Investigation of AMG 160 in combination with pembrolizumab is in progress

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

Five Ways to Get it Right



Source:
https://www.pcf.org/blog/5-ways-al-roker-got-it-right-regarding-his-prostate-cancer-diagnosis/?utm_source=NewsPulse&utm_medium=email&utm_campaign=NOV20NP

Get screened before showing symptoms. If an early-stage prostate cancer is confined to the area of the prostate it significantly increases your odds of survival. But it is important to note that prostate cancer can only be found early if you undergo a PSA (prostate specific antigen) screening at a routine checkup. It is important for men to talk to their doctor about getting screened for prostate cancer even if everything feels fine. It is recommended that men talk to their doctor about screening at age 45, but that drops to 40 if you have a family history of.

Practice shared decision making with your doctors. Talk frankly with your urologist/surgeon and get second opinions, including from radiologists specialising in PC. Find out if you are a good candidate for active surveillance (monitoring the cancer closely and deferring treatment only if and when the cancer shows signs of progression).

It is important to remember that not all prostate cancers are the same, and therefore, not all treatment options will be right for every man. It can be easy to get swept up in personal opinions from friends and family who have gone through a similar experience. But each prostate cancer, each man, and each family is unique.

Share your experience to help educate and save others. All too many men choose to keep their prostate cancer diagnosis a secret, or worse, they are too embarrassed to even discuss regular screening with a doctor. It is important to educate other men about this disease so that they can proactively talk to their doctor about prostate cancer screening. Talking with other men about your diagnosis has the potential to inspire others to be open about their own diagnosis and save lives. Join a support Group or better still start one if there isn't one meeting locally. It's very likely that there are many other men in your vicinity who will be pleased you did.

Maintain a positive attitude. Be confident. You can acknowledge the seriousness of the disease, but also acknowledge that prostate cancer is one of the most treatable cancers, particularly when found early. Do not view your diagnosis as a death sentence but allow yourself to focus on all you have to be grateful for, and set yourself up to be in the best possible mental place for your recovery.

Prioritise your health and take time off to heal. This may seem obvious but it can be an underappreciated step in the recovery process. It can be tempting to put off screening or treatment for as long as possible. In some cases your doctor may advise you that it is okay, or even preferable to wait for treatment. Many men don't have to rush into treatment and have time to research their options.

Based on an article about Al Roker (TV personality on the NBC The Today Show) who had a PC diagnosis in Sept 2020.

Prostate cancer: immunotherapy offers hope

Source:
https://www.pcf.org/blog/5-ways-al-roker-got-it-right-regarding-his-prostate-cancer-diagnosis/?utm_source=NewsPulse&utm_medium=email&utm_campaign=NOV20NP

An antibody for treating advanced prostate cancer improves progression-free survival in patients with metastasised, castration-resistant prostate cancer.

This is the finding of the long-term analyses of an international phase 3 clinical trial, recently published in *European Urology*.

The study showed that overall survival was 2 – 3 times higher than in the placebo arm.

Ipilimumab is a humanised monoclonal IgG1 antibody that is active against CTLA-4. CTLA-4 is a molecule that controls part of the immune system by down-regulating it.

"Cancer cells can evade the endogenous defence of the immune system by deactivating it.

An antibody that targets CTLA-4, a so-called checkpoint inhibitor (CPI), can block this deactivation, thereby reactivating the immune system once again.

This reactivated immune response can then help the body to destroy cancer cells," explains oncologist Michael Krainer from the Department of Medicine at MedUni Vienna/Vienna General Hospital and from the Comprehensive Cancer Center (CCC).

The internationally renowned "Urological Tumours" working group from the division led by Krainer was invited to participate in the first global clinical phase 3 trial of a CPI in prostate cancer CA184-043, the long-term results of which have now been published in *European Urology*, the world's most influential urology journal.

The recent trial included a total of 799 men.

It was conducted globally: in the USA, Canada, South America, Australia and European countries.

Patients were randomised in a 1:1 ratio to receive bone metastasis radiotherapy (a single 8 Gy fraction) followed by either ipilimumab 10 mg/kg or a placebo every three weeks via up to four injections.

Although in the first planned analysis, the survival advantage in the treated group was present it was not significant, whereas the recent analysis shows that long-term survival after 3, 4 and 5 years is two – three times higher in the immunotherapy arm as opposed to the placebo arm.

Ipilimumab is already licensed by the European Medicines Agency to treat melanoma, lung cancer and bladder cancer.

However, there is still a lack of reliable data for approval to treat prostate cancer, since the first planned analysis did not show any significant survival advantage.

In the light of the new long-term results, Krainer says: "Immunotherapy is highly promising and can be used, for example, when chemotherapy options have been exhausted or are undesirable.

It can also be expedient to start it at an early stage, since any treatment is more effective if there is little cancer present and the patient is in good general health.

We are the first group in Austria to gain such valuable experience and we are now attempting to incorporate immunotherapy into the treatment in the context of international clinical trials."

The working group will soon start on two study protocols using immunotherapy before a chemotherapy that is currently the standard treatment for patients with castration-resistant prostate cancer.

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

SBRT Doubles Pain Response Over Usual RT in Spinal Metastases

Source:
Abstract LBA-2, on Medscape Medical News 29 October 2020

A 2-day course of high-dose stereotactic body radiotherapy (SBRT) doubles the complete pain response for patients with painful spinal metastases vs. conventional palliative RT. It is also safe and non-destabilizing, conclude researchers reporting a phase 3 Canadian trial.

"Conventional RT has historically not achieved high rates of complete response to pain or long-term local control," commented lead author Arjun Sahgal, MD. "So many years ago, we started building on the idea of using highdose SBRT for the spine." Sahgal, who is professor and deputy chief of radiation oncology at Sunnybrook Health Sciences Center, the University of Toronto, Ontario, Canada, explained that his team devised a plan to use SBRT with 24 Gy in 2 fractions. This involves only 2 consecutive treatments, which is very convenient for patients. Conventional RT requires 5 or more sessions. "Now we have shown a doubling of the complete response rate to pain at 3 and 6 months compared with conventional palliative RT, and patients appreciate fewer treatment sessions, too, so we are helping our patients financially," Sahgal told Medscape Medical News.

He presented the new results during the 2020 virtual annual meeting of the American Society for Radiation Oncology (ASTRO). Patients enrolled in this trial had de novo (recent onset) painful spinal metastases with metastatic involvement in 3 or fewer consecutive spinal segments arising from a primary tumor causing pain that was scored at least 2 on the Brief Pain Inventory. "The median baseline worst pain score was 5 in a range of 2 to 10. The median total spinal instability and neoplasia score (SINS) was 7 in a range of 3 to 12," Sahgal noted. "The primary endpoint was complete pain response rate at 3 months," Sahgal told a press briefing held within the context of the virtual meeting. Patients were randomly assigned to receive either SBRT with 24 Gy delivered in 2 fractions over 2 consecutive days or conventional palliative RT with 20 Gy delivered in 5 fractions. "The trial was launched as a phase 2 study initially, but once investigators could demonstrate that patient accrual was possible, they converted the trial into a phase 3 study," Sahgal noted.

A total of 114 and 115 patients were enrolled in the SBRT and conventional RT arms, respectively. All were included in the intent-totreat analysis. "We found that at 3 months, the complete response rate was 35 vs. 14% in the SBRT and conventional RT arms, and the difference was statistically significant," Sahgal reported. The complete response rate was sustained at 6 months. It remained at 32% in the SBRT arm and 16% in the conventional RT arm. There was also a reduction in the total SINS score at 6 months that favored the SBRT arm. Adjusted for age, sex, performance status, primary cancer, and total baseline SINS, SBRT was almost 3.5-fold more likely to result in a complete pain response rate at 3 months and was about 2.5-fold more likely to yield the same response at 6 months compared with conventional RT – "which was highly significant at both endpoints," Sahgal noted.

However, there was no difference between treatment groups in either radiation site-specific progression free survival (PFS) or overall survival (OS). After 3 months, 92 and 86% of patients in the SBRT and conventional RT arms, respectively, were cancer free at the treated site, and at 6 months, 75 and 69%, respectively, were cancer free at the treated site. As for adverse events, 17% of patients who received conventional palliative RT developed a vertebral compression fracture following treatment, compared with 11% of SBRT-treated patients, but the risk for adverse events of grade 2 or higher was essentially the same in both treatment arms. Importantly, those treated with SBRT reported a better quality of life (QoL) than those treated with conventional RT. "Patients are dealing with metastatic disease. Now they have to come to the hospital for another treatment, and the financial burden of coming to the hospital is not inconsiderable," Sahgal said. "So patients appreciate fewer treatment sessions and, even if it costs our department more, because treatment with SBRT needs so much more planning and resources, we are helping our patients financially, and this will push our departments to say, even if it costs more to do, SBRT is better for our patients," he said.

Special Advantage Commenting on the study, session moderator Sue Yom, MD, PhD, professor of radiation oncology, otolaryngology-head and neck surgery, University of California, San Francisco, reminded the press that with SBRT, very high doses can be delivered very safely to precise areas of the body with a small number of treatments. "This has obvious advantages over conventional RT," she noted, "and may be especially an advantage now in the midst of the COVID pandemic, as it reduces the risk [for viral exposure] to patients and hospital personnel.

"With this study, the additional resources and expense involved in offering SBRT in comparison with conventional RT appear to be justified," Yom said. "The increased dose that was given in only 2 fractions of SBRT produced results that allowed significantly more patients to achieve complete pain relief than patients who got conventional treatment with 5 fractions to the same site," Yom reaffirmed. "And the complete resolution rate of the spinal tumors at 6 months was also superior with SBRT, so the oncologic benefits with SBRT vs. conventional RT are also better," she said. Yom also felt that the QoL surveys that were filled out by patients during the study – not reported during the press briefing, but alluded to by Sahgal during his interview with Medscape Medical News – were also quite revealing. "It's easy to dismiss any difference between 2 and 5 treatments as not being significant, but there was a real quantifiable difference between 2 and 5 treatments in terms of patients' QoL," she noted. "So being able to have fewer treatments is significant to patients, and that significance buttresses this study's importance," she said. Presented at the ASTRO 2020 Annual Meeting,

Elevated stress hormone levels could reawaken dormant cancer cells

Source:
By SHRADDHA CHAKRADHAR
@scchak DECEMBER 2, 2020

The recurrence of cancer months or even years after successful treatment is an all too common phenomenon, and scientists have been chipping away at understanding how undetectable cells can once again unleash disease on the body — often more aggressively than the first time around.

In a new study published Wednesday in Science Translational Medicine, one group of researchers describes how a cascade of events set off by high levels of a stress hormone could cause dormant tumor cells to reawaken to once again cause cancer.

The hormone, norepinephrine, is naturally found in the body, but more of this chemical is released into the bloodstream when the body detects higher levels of stress. In some cancer models, scientists found that an elevated level of norepinephrine led to the activation of cells known as neutrophils, which help shield tumor cells from the body's immune system. Activating neutrophils in turn led to these cells releasing a special type of lipid — which then awakened sleeping cancer cells.

"It's sort of a triangle," said Michela Perego, a molecular biologist at the Wistar Institute in Philadelphia and lead author of the study. "And it's a chain of events that ends up being very powerful in reawakening dormant tumor cells."

Perego and her colleagues observed this mechanism in mice that were injected with dormant lung cancer cells. The mice were placed in a setup where they had less room than usual to move around, which likely made them feel trapped and spiked their stress levels.

A subset of these mice were also treated with an experimental beta blocker, a class of medications used to treat blood pressure. Dormant tumor cells in mice treated with the drugs remained so, the researchers found.

The team also examined 80 lung cancer patients who had had surgery to treat their disease. In this group, 17 patients saw their tumor return within three years of surgery — a recurrence that's considered early. Compared to the other 63 patients whose cancer came back later or didn't return at all, the 17 patients with early recurrence had higher levels of the chemical that indicates activated neutrophils.

If this preliminary finding holds true through more studies, "you could potentially monitor stress hormones in a patient undergoing therapy for cancer," Perego said, emphasizing that it would be in addition to regular treatment and not in place of it.

STAT spoke with Perego to learn more about the research. The conversation has been lightly edited and condensed for clarity.

What does it mean for a tumor cell to be dormant?

It means there are still cancer cells around, but they are undetectable. They can be in the primary tumor location or somewhere else. If the cells stay that way and don't start regrowing, it's fine because you don't have symptoms and you don't have growth. But if cells come back, then there's often resistance to the first therapy or sometimes it's hard to do surgery.

How can dormant cancer cells be a problem?

Dormant cells are not a problem until they wake up. There's big progress that has been made in the last few years in cancer therapy, but we know that some of them only last for some time before the cancer comes back. And we know very little about how cancer comes back, why it comes back, and how we can control cancer for longer before it comes back. We also can't predict when it is going to come back.

Is this true for all cancers?

It can happen in all cancers. We know, for instance, that breast cancer patients can experience relapse after 20 years of being in remission. It doesn't happen at the same rate across cancers, though, or even for all patients with a type of cancer.

How are you defining stress for this study? And is it any stress or certain levels of stress that reactivate sleeping tumors?

When we say stress, we mean stress hormones, and there are tons of those in the human body. We looked at this specific one, norepinephrine.

We all undergo stress, and some handle it better and some handle it worse. What is very important is that stress alone doesn't reawaken dormant cells. You need stress hormones, but you also need neutrophils, *and* you need them to be activated *and* then for them to produce this specific lipid to turn on tumor cells.

Aren't neutrophils part of the immune system? How do they help cancer cells?

Neutrophils are important for how organisms fight pathogens. They are good for us, but there is also an evil counterpart to them. Depending on the presence of cancer, neutrophils switch and become bad and support cancer cells. They seem to support tumor growth because they can block the other cells of the immune system that kill tumors. But we don't fully understand this.

What was surprising about what you found?

That these hormones were so powerful in influencing the immune system was such a surprise. The whole idea that these stress hormones could show a physical effect, and take a physical toll, on cells was unexpected.

You tested beta blockers in mice as a way to stop this "triangle" of activity — why?

Beta blockers are already used in clinics to block norepinephrine, for people with heart failure and other stress-sensitive conditions. It's nice because it's not a new drug that has to be developed. And it could be something to add in to existing cancer therapy to help with patients' stress hormones.

What's next?

Every time you find a mechanism, you open up another 10 questions. There are a lot of other hormones that we don't know about and how they interact with the mechanism we described. There's also a lot to learn about the tumor environment, and how that might influence [dormancy].

The final goal of this research is to get it to the clinic, so I would be very happy to see some of this translate that way. For example, we could develop techniques to detect lipids or stress hormones to indicate when a relapse may be occurring.

New Prostate Cancer Trials

DASL-HiCaP Trial

The purpose of this study is to see if a new tablet drug, darolutamide, combined with the current best treatments, can improve outcomes for men with high risk prostate cancer that has not spread beyond the prostate area. Previous studies have shown promising results for darolutamide preventing disease progression and improving survival for men with advanced prostate cancer. This is a randomised controlled trial, which means that, in addition to best standard treatments, half the participants on the study will receive darolutamide, and the other half will receive placebo. The trial is being led from Australia by ANZUP in collaboration with the NHMRC Clinical Trials Centre. We plan to enrol 1,100 men from Australia, New Zealand, Canada, the US, Ireland, and the UK.

The trial is open and recruiting.

DASL-HiCaP trial details from the Australia New Zealand Clinical Trials Registry

ENZA-p Trial

Enzalutamide is a potent hormone therapy that prevents testosterone from reaching prostate cancer cells, thereby stopping cancer growth. It is already widely used in men with prostate cancer that has stopped responding to standard hormone treatments (castration-resistant prostate cancer). However, most cancers become resistant to enzalutamide over time, with almost 1 in 4 being resistant from the start of treatment.

Many prostate cancers, in particular those that have spread or become resistant to hormonal therapies, have a substance on their cell surface called prostate specific membrane antigen (PSMA). Lutetium-177 PSMA (Lu-PSMA for short) is a new treatment in advanced prostate cancer. Lu-PSMA is a radioactive molecule that attaches to the surface of prostate cancer cells throughout the body. This drug is given as an injection through the vein and allows targeted radiation to be delivered directly to prostate cancer cells.

Smaller pre-clinical studies have demonstrated synergistic effects by combining Lu-PSMA with enzalutamide. It is possible that Lu-PSMA can prevent early resistance to enzalutamide, extending the time that men benefit from treatment.

The ENZA-p clinical trial aims to compare the effectiveness of enzalutamide in combination with Lu-PSMA, versus enzalutamide alone for the treatment of prostate cancer. This is a randomised study, so half the men in this trial will be randomly allocated to receive Lu-PSMA and enzalutamide, and the other half will be randomly allocated to receive enzalutamide alone. We plan to enroll 160 participants across Australia.

The trial is open and recruiting.

Interested in this trial? Print off the ENZA-p trial details from the Australia New Zealand Clinical Trials Registry and take it to your GP.

PSMA-PET Scans now available in the USA

While there are always areas for improvement of treatment for prostate cancer in Australia, we can be very thankful for our Medicare system and the services available.

On 2 December 2020, the ^{68}Ga-PSMA-11 PET was finally approved in the United States by the FDA but still only at two institutions and costing around US$3000 if health insurance won't pick up the tab.

The "PSMA PET" scan can detect prostate cancer metastases much earlier, when they are much smaller, which may help to improve treatment of patients with prostate cancer.

PSMA, short for Prostate Specific Membrane Antigen, is a protein that is found in relatively larger amounts on the surface of prostate cancer cells. PSMA PET is an imaging technology that allows doctors to "see" PSMA using a PET scanner. Compared to other scans used for prostate cancer detection, such as CT, bone scans, and MRI, PSMA PET is more sensitive and can detect much smaller prostate cancer metastases. PSMA PET can be used for initial and subsequent management decisions in patients with certain types of prostate cancer, in order to determine if and where they have metastases. Researchers are studying how PSMA PET may change treatment and, ultimately, patient outcomes like disease progression and survival.

How does it work? The strategy is based on a small-molecule PSMA binding chemical attached to a radioactive reporter [radioactive element gallium-68 (^{68}Ga)]. This conjugate (PSMA-binder + ^{68}Ga = PET tracer) is introduced into the circulation of a patient where the conjugate accumulates at sites of prostate cancer and the unbound conjugate clears rapidly from circulation. The patient's body is passed through an imaging camera that records areas where the PET tracer accumulated.

The cancer can be observed earlier, and in smaller amounts, so that Clinicians can use PSMA PET to direct radiation therapy in patients who have recurrent disease in the pelvis, or just a few metastases that may improve outcomes.

Eventually the FDA may approve PSMA targeting agents as part of a therapeutic strategy – not just to "see" the cancer, but to deliver drugs or radiation directly to sites of prostate cancer metastasis, killing tumor cells while generally sparing normal tissue. (see PHCSG November Newsletter).

Other PSMA PET imaging agents, including ^{18}F-DCFPyL PET, which was developed by PCF-funded investigators at Johns Hopkins University, also may become FDA-approved in the near future.

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 have a great line up of guest speakers for 2021 when we also hope that we can meet face-to-face.

Support Group Leaders are particularly welcome to attend meetings when we have guest speakers.

We are awaiting news on the reopening of the Ivanhoe Uniting Church for our regular monthly meetings. When this happens we will also try to continue to include Zoom for those of you who cannot get to the venue.

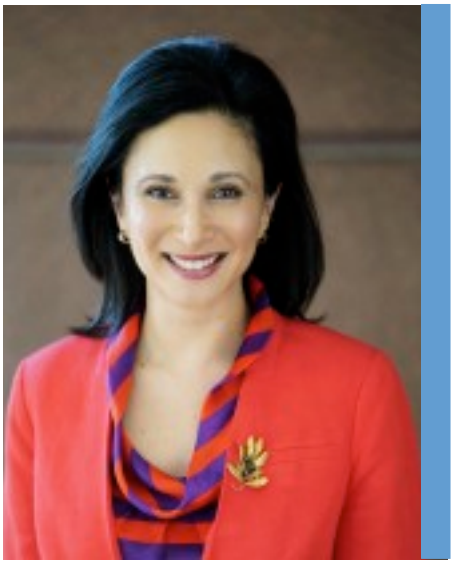
Guest Speaker

Tuesday 15 December 2020

Dr Cleola Anderiesz is an experienced senior executive with 18 years of experience in health across the research, not-for-profit, and government public sector.

Committed to quality in healthcare, Dr Anderiesz holds a PhD in Medicine and a Senior Executive MBA. She is skilled in policy, strategy, innovation, program development and implementation, stakeholder engagement, and evidence-based decision making.

Dr Anderieesz will be talking about Cancer Australia's work on national data to improve cancer outcomes.



Dr Cleola Anderiesz
Deputy Chief Executive Officer
at Cancer Australia

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/

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 Correspondance

Mike Waller Convenor
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.

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