Prostate Cancer Support Association of New Mexico

Celebrating over 30 years of supporting men and their families

PCSANM Quarterly April 2022 Volume 29, Issue 2

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Our website address: www.pcsanm.org

Email us: pchelp@pcsanm.org

Support Group Meetings

Meetings are held at Bear Canyon Senior Center, 4645 Pitt St. NE in Albuquerque, from 12:30 – 3 p.m. on the first and third Saturday of most months.

Please call 505-254-7784 or email pchelp@pcsanm.org for information. Meeting topics by date may be found at:

https://www.pcsanm.org/meetings/

ZERO – The End of Prostate Cancer (PCa) Prostate Cancer Support Programs and Direct Resources for Those Impacted by Prostate Cancer

ZERO360: Comprehensive Patient Support

1-844-244-1309 (Toll-Free) <u>zerocancer.org/zero360</u> Zero360 is a free, comprehensive patient support service that helps patients navigate insurance, find financial aid resources, connect with support services, and secure access to care. ZERO's experienced case managers are ready to help men and their families through their personal prostate cancer journeys.

Us TOO Support Groups

zerocancer.org/supportgroups

Us TOO Support Groups offer in-person and virtual support. These groups meet regularly to provide peer support, resources, and education to empower men to make informed decisions on testing, treatment, and management of side effects. Groups are also available for special interests, including: Veterans, Black Men, Gay Men and their partners (All LGBTQIA+ welcome), Caregivers, Spanish Language, Deaf Men, and others.

Online Support Services

A variety of online support services are available to help men affected by prostate cancer and their loved ones to connect with others who are going through, or have gone through, similar situations. ZERO Connect is a Facebook-based support group for participants to share stories, ask questions, and connect. The Inspire Online Support Community (<u>ustoo.inspire.com</u>) connects patients, families, friends, and caregivers to enhance the quality of life for all those affected by prostate cancer.

Peer Support

MENtor is a peer support network at <u>zerocancer.org/mentor</u> for anyone who has received a prostate cancer diagnosis or has experienced a recurrence. ZERO's trained, volunteer MENtors represent many different prostate cancer journeys and have a wealth of insights to share based on their experiences. The ZERO Caregiver Connector Program at <u>zerocancer.org/caregiver-</u> <u>connector</u> matches prostate cancer caregivers with others who have been in similar situations. Both MENtor and Caregiver Connectors provide valuable one-on-one support customized to meet individual needs.

Educational Resources

(Covering awareness, early detection, screening, treatment and side effects) zerocancer.org

Special thanks to Presbyterian Healthcare Services for its generous support of this newsletter.

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In Memory

With deep sympathy and regret, we list this name:

Don Moore

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PSMA PET/CT Validated as Imaging Modality in Prostate Cancer

Louise Gagnon

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The use of a nomogram derived from prostate-specific membrane antigen (PSMA) PET/CT findings successfully predicted long-term outcomes in patients with high-risk and very high-risk prostate cancer, according to a multi-center study <u>published</u> in *JAMA Network Open*.

The nomogram was used to estimate the probability of any non-localized PSMA-based upstaging and used four variables — initial prostate-specific antigen level, biopsy Gleason grade group, percentage positive cores, and clinical T category — to predict outcomes in 5,275 patients from 15 tertiary centers in various countries. The outcomes included distant metastasis, prostate cancerspecific mortality, and overall survival.

The accuracy of the nomogram for correctly identifying non-localized disease on PSMA PET/CT imaging was area under the curve (AUC) 0.75 (95% CI, 0.67 - 0.83). Michael Xiang, MD, PhD, lead author and assistant clinical professor in the Department of Radiation Oncology at the David Geffen School of Medicine, University of California at Los Angeles, noted that the nomogram provides indirect evidence of the power of PSMA PET/CT imaging. "PSMA PET/CT imaging technology has been revolutionary for the initial workup and staging and even management decisions of prostate cancer," said Xiang in an interview with Medscape Medical News. "We don't yet have long-term data on how initial PSMA PET/CT findings may influence or prognosticate downstream clinical outcomes such as the emergence of distant metastases, death from prostate cancer, or overall survival, which are the most important endpoints."

As it will be several more years before long-term PSMA PET/CT data become available, Xiang sought to use a UCLA-developed nomogram or risk calculator to assess the prognostic validity of PSMA PET/CT data. "No patients in the present study had PSMA PET/CT imaging," said Xiang. "Everything was predicted using the nomogram as a proxy for the predictive result if they were to get PSMA PET/CT (imaging). It was more of an indirect assessment."

The nomogram differs from other risk-stratification tools because it is confined to use in high-risk and very highrisk patients rather than in all-comers, noted Xiang. The nomogram was compared with the Cancer of the Prostate Risk Assessment (CAPRA) groups, the Staging Collaboration for Cancer of the Prostate (STAR-CAP) stage groups, and the Memorial Sloan Kettering Cancer Center (MSKCC) pre-prostatectomy nomogram for 5-year risk of disease progression.

"This proxy for PSMA PET/CT (imaging) is very, very prognostic and outperforms existing risk stratification and prognostic tools for prostate cancer," said Xiang, who noted one exception: performance of the nomogram was similar to STAR-CAP in predicting prostate cancer-specific mortality.

Xiang acknowledged a major limitation of the study: investigators used a proxy rather than actual results of PSMA PET/CT imaging. Another limitation is that the study was conducted retrospectively.

In the future, additional factors such as molecular and genomic data may be used to help predict risk of outcomes in high-risk and very high-risk patients, according to Xiang. "We would love to incorporate more information such as genomic data and molecular tests," said Xiang. "The combination of our nomogram with genomic data would be even more powerful."

Xiang noted that future directions may involve using the nomogram to help personalize management of patients with high-risk and very high-risk prostate cancer. "The vision ultimately is that with better prognostic information and risk stratification, we can offer more tailored therapies to patients based on their level of risk," said Xiang. "We can translate these prediction tools into actionable items in the clinic."

Thomas Hope, MD, associate professor in residence, Department of Radiology and Biomedical Imaging, School of Medicine, University of California at San Francisco, noted that Xiang's study demonstrates the utility of this particular nomogram as well as reinforces the use of PSMA PET/CT imaging. "This work demonstrates the important prognostic value of PSMA PET/CT and really supports the utilization of PSMA PET/CT in high-risk and very highrisk patients and how [the nomogram] has more value than existing nomograms," said Hope in an interview with *Medscape Medical News*. He was not involved with the study. Hope noted that the use of the nomogram could potentially offer benefit in countries where PSMA PET/CT imaging is not readily available. Reuters: January 12, 2022

Sedentary Cancer Survivors Die Sooner Than More Active Peers

Linda Caroll

Cancer survivors who spent more than eight hours a day sitting are nearly twice as likely to die over the next handful of years as are those who sit for only four hours, new findings suggest.

The analysis of data from more than 1,500 cancer survivors also revealed that being physically active was associated with a much lower risk of cancer-specific death, researchers report in JAMA Oncology. "The combination of prolonged sitting with lack of physical activity was highly prevalent among U.S. cancer survivors, and this sedentary lifestyle was associated with worsened survival," said coauthors Chao Cao and Dr. Lin Yang with Alberta Health Services in Calgary, Canada.

"The exact biologic mechanisms are unclear but the negative effects on metabolic and sex hormones, inflammation, and immunity are some of the main hypothesized pathways," they told Reuters Health in a joint email. "Experimental studies have shown that uninterrupted sitting for long periods is associated with impaired glucose metabolism and increased systematic inflammation, and these can be attenuated by breaking up prolonged sitting."

To take a closer look at the impacts of long hours spent sitting and little exercise, the two researchers and a colleague turned to a nationally representative sample from the U.S. National Center for Health Statistics' National Health and Nutrition Examination Survey (NHANES), which has been conducted on biennially since 1999.

NHANES collected cancer information - including cancer type and age at diagnosis - during in-person interviews. Participants were asked "Have you ever been told by a doctor or other health professional that you had cancer or a malignancy of any kind?" Those who responded yes were defined as cancer survivors and were asked, "What kind of cancer was it?" and "How old were you when this cancer was first diagnosed?" The participants reported their total daily sitting time and their leisure-time physical activity (LTPA) through the Global Physical Activity Questionnaire (GPAQ). They were also asked about moderate- and vigorous-intensity recreational activities during the in-person interviews.

The researchers defined LTPA as minutes of moderateintensity recreational activities plus twice the minutes of vigorous intensity recreational activities. They linked participants' NHANES data to mortality data from the National Center for Health Statistics. The analysis was based on data from 1,535 cancer survivors; 57% reported an LTPA of 0 minutes per week during the previous week (inactive group); 16% reported an LTPA of less than 150 minutes per week (insufficiently active group); and 28% reported an LTPA of 150 minutes or more per week (active group).

Thirty-five percent reported sitting for six to eight hours per day and 25% reported sitting for more than eight hours per day. During the follow-up period of up to nine years (median, 4.5 years), 293 of the cancer survivors died, 114 from cancer, 41 from heart diseases and 138 from other causes.

On multivariable analysis, the risks of both all-cause death (hazard ratio, 0.34) and cancer-specific death (HR, 0.32) were significantly lower in physically active people than in the inactive group. More sitting, on the other hand, was quite deleterious. Sitting more than eight hours a day was associated with significantly higher risks of all-cause mortality (HR, 1.81) and cancer death (HR, 2.27) compared with sitting less than four hours a day.

When the researchers looked at the combined effects of sitting time and amount of physical activity, they found that inactive and insufficiently active survivors who reported sitting more than eight hours a day had the highest risk of dying from any cause (HR, 5.38) and from cancer, specifically (HR, 4.71).

Reuters: January 12, 2022

Sedentary Cancer Survivors Die Sooner Than More Active Peers

Linda Caroll

Continued from page 4

"The findings of the present study showed that the negative effect of sitting too long appeared to be offset by meeting the Physical Activity Guidelines for Americans (150 minutes/week moderate-to-vigorous intensity leisure-time physical activity)," Cao and Dr. Yang said. "The critical issue here is that nearly three out of four U.S. cancer survivors did not meet the Physical Activity Guidelines. These data mean that guidelines and interventions need to not only promote physical activity but also include a focus on sedentarytime reduction due to different behavior-change techniques that may be required."

The new study "highlights the importance of incorporating behavioral interventions aimed at both increasing leisure-time physical activity and reducing daily sitting time into comprehensive cancersurvivorship care," said Dr. Carissa Low, an assistant professor of hematology/oncology, psychology and biomedical informatics at the University of Pittsburgh and the UPMC Hillman Cancer Center. It, "provides strong evidence that sitting for eight or more hours per day is associated with increased risk of mortality among cancer survivor, particularly survivors who do not engage in moderate or vigorous physical exercise," Dr. Low told Reuters Health by email.

The study points to the need to "find the right interventions to modify behavior in cancer patients to promote a healthier lifestyle and decrease the chance of the cancer recurring," said Dr. Ashwani Rajput, a professor of surgery and director of the Johns Hopkins Kimmel Cancer Center-National Capital Region, in Baltimore, Maryland.

But the focus on a healthy lifestyle should start much earlier in life, Dr. Rajput said. "We need to teach kids to make the right choices - to be active and to maintain a healthy diet," he added. "If you can prevent obesityrelated cancers you don't have to worry about a recurrence." New York Times: December 17, 2021

Chicago-Based Clinic Focuses on Gay, Bisexual Men with Prostate Cancer

The New York Times recently reported on a Chicagobased clinic's program that focuses on gay and bisexual men grappling with the aftermath of prostate cancer. Headed by Dr. Channa Amarasekera, it is the Gay and Bisexual Men's Urology Program at Northwestern Medicine. The program, which began taking patients only in August, is the first of its kind in the United States, and Dr. Amarasekera, who has focused his career on urologic care for gay and bisexual men and other sexual minorities, is the program's first leader. It is an emerging field of study driven in part by the increasing number of prostate cancer patients who identify as gay or bisexual.

Dr. Amaresekera told The New York Times, "Historically, the medical system has sort of operated in a don't-ask-don't-tell environment, and that's been problematic. Fortunately, that's changing. Patients are increasingly open about who they are."

The article explains that gay and bisexual men in their 50s and 60s who are now entering the prime demographic for prostate cancer also lived through the worst of the AIDS epidemic. That experience has left many of them more experienced in dealing with the medical establishment and more distrustful of it.

"It's important now to reassure patients who came of age through that time that things are different, and they can expect better care," Dr. Amarasekera said.

To read the full article by Steve Kenny, please visit:

https://www.nytimes.com/2021/12/07/health/prostategay-sex-cancer.html

Cancer Support Now of New Mexico offers LGBTQ+ Cancer Peer Support

Reach New Mexico Cancer Support Now LGBTQ+ Cancer Peer Support with a call to its 24-hour line, 505-255-0405. Prostate Cancer Foundation: January 24, 2022

Could More Testosterone Be the Hidden Key to Fighting Prostate Cancer?

Janet Farrar Worthington

Androgen deprivation therapy (ADT) has been the bedrock of treatment for advanced prostate cancer for more than half a century. But investigators at Johns Hopkins are rethinking it – in a way that sounds counterintuitive – and driving new approaches to tackle treatment resistance. They're discovering that **shaking up prostate cancer with high-dose testosterone makes it more vulnerable to other treatments.**

ADT slows prostate cancer's progress by shutting off testosterone. Eventually, however, cancer adapts to this new environment and PSA levels start to rise; this stage is called castrate-resistant prostate cancer (CRPC). ADT is not a curative treatment, and long-term ADT causes significant side effects, including fatigue, hot flashes, weight gain, and loss of sexual function.

Several years ago, medical oncologist Samuel Denmeade, M.D., Co-Director of the Johns Hopkins Prostate Cancer Program, and colleagues came up with a remarkable concept for attacking prostate cancer: alternating ADT with high-dose testosterone. "It had been known for a long time that something weird happened when you gave testosterone to prostate cancer cells," says Denmeade. "Yes, with low doses you could get the cancer cells to grow – but plenty of reports said that paradoxically, at high doses the cancer cells **don't grow as well, or they die.** Even Charles Huggins, who won the Nobel Prize for discovering hormonal therapy, said in his Nobel acceptance speech that another way to kill cancer would be to give **too much hormone**. I was always interested in that idea."

About 10 years ago, Denmeade conducted a small study to test the concept of using testosterone *against* prostate cancer. "At the time, it seemed like all the data and literature suggested that the dose was really important; **it had to be a high dose**." The hypothesis: Prostate cancer cells adjust to a very *low*-testosterone environment (created by ADT) by making *very high levels of the androgen receptor (AR)*. And here, as he says, "too much of a bad thing can be a good thing." These high levels of the AR **now make cancer vulnerable** to very *high* levels of testosterone. Cancer cells that survive this respond to high-dose testosterone by turning the AR back down – and making the cancer once again susceptible to very low testosterone. "The idea is to screw up the cancer cell's ability to adapt." Denmeade and colleagues coined the term, Bipolar Androgen Therapy (BAT), "to capture these polar extremes of very high and very low. Not just making the testosterone high, but cycling between high and low." It's this cycling that seems to be the key to keeping the cancer off-balance, slowing its ability to flourish. In BAT, men experience high testosterone levels that decrease over a 28-day period, then bounce back up with the next testosterone injection.

In that early study, of just a handful of patients, "we were very cautious, because we didn't want to make the disease worse. We built in all these safety parameters. But we were surprised: it didn't seem we made anybody worse. It seemed very safe. The patients did very well, and some of them stayed on the testosterone for a year or more. Most of them felt really good. A number of them did not want to come off of it when it seemed they were progressing: they were just so happy to have more energy, and some of them could have sex again."

Armed with this initial clinical data to show that BAT was safe and to show some response, Denmeade received funding for additional proof-of-concept studies from PCF, among other sources. Larger studies at Johns Hopkins have followed, including RESTORE, TRANSFORMER, and COMBAT. Other trials testing this concept have been completed or are under way at the University of Washington, University of Colorado, and in Australia, Brazil, and the Netherlands.

Prostate cancer-related bill before U.S. Congress

A bill introduced by Rep. Bobby Rush (IL) seeks to make it easier for men with prostate cancer to have access to lowor no-cost screening.

Titled PSA Screening for HIM Act, the bill seeks to amend Title XXVII of the Public Health Service Act to require group health plans and health insurance issuers offering group or individual health insurance coverage to provide coverage for prostate cancer screenings of high-risk men without the imposition of cost-sharing requirements.

The legislation, which has been introduced in previous sessions of Congress, resides in the House Energy & Commerce Committee's Subcommittee on Health. It also has broad bi-partisan support of 30 co-sponsors (23 men and 7 women) from 19 states.

AI Holds Its Own vs Pathologists for Prostate Cancer Diagnosis

Bianca Nogrady

Artificial intelligence (AI) performs as well as expert uropathologists – and in some cases better than general pathologists – in diagnosing and grading prostate cancer, suggests a new study.

AI has shown promise in the diagnosis and grading of prostate cancer. However studies so far have been siloed, "with limited proof for generalization across diverse multinational cohorts, representing one of the central barriers to implementation of AI algorithms in clinical practice," the investigators wrote in <u>Nature Medicine</u>.

Wouter Bulten, from the Radboud Institute for Health Sciences, Radboud University Medical Center, Nijmegen, the Netherlands, and coauthors reported the outcomes of the international PANDA histopathology competition, in which 1,290 deep learning algorithm developers were challenged to come up with reproducible algorithms that could match the findings of human experts. Deep learning is a form of machine learning in which artificial neural networks "learn" from large datasets and apply that learning in a similar way to the human brain. At least one AI product for detecting prostate cancer – the Paige Prostate system – has already been approved for clinical use in the United States. The Food and Drug Administration authorized marketing it in September 2021, as an adjunct to – but not replacement for – pathologist review.

The developers of the new algorithms participating in the competition were given a set of 10,616 digitized prostate biopsies to learn from, then were tested against a panel of either one to six – depending on the country – experienced uropathologists on a set of 393 digitized slides. A selection of 15 teams were then invited to take part in a validation phase with an additional 1,616 slides. Within the first 10 days of the competition, one algorithm already achieved greater than 0.90 agreement with the uropathologists; by day 33, the median performance of all the teams in the competition was greater than 0.85 agreement with the human experts.

Algorithms Correctly Detected Tumors in 99.7% of cases. The algorithms selected for validation showed even higher levels of agreement. These algorithms correctly detected tumors in 99.7% of cases (95% CI, 98.1%-99.7%), and correctly identified 92.9% of negative results (95% CI, 91.9%-96.7%). When it came to classifying the prostate cancers based on Gleason grade, the algorithms showed significantly more agreement with uropathologists than did an international panel of 13 or 20 general pathologists. "This higher sensitivity shows promise for reducing pathologist workload by automated identification and exclusion of most benign biopsies from review," the authors wrote.

The study found that the AI algorithms missed 1%-1.9% of cancers, but the general pathologists missed 1.8%-7.3%. The algorithms demonstrated a sensitivity of 96.4%-98.2% and specificity of 75%-100% for tumors, whereas the pathologists showed a sensitivity of 91.9-96.5% and specificity of 92.3%-95%.

The main error that the algorithms made was misclassifying benign cases as the International Society of Urological Pathology (ISUP) Gleason Grading (GG) 1 cancer. The authors commented that this was likely caused by a shift in the distribution of cases between the training data given to the algorithms and the data set they were validated on.

They also noted that, in one validation set, the algorithms over-graded a "substantial proportion" of ISUP GG 3 cases as GG 4, whereas general pathologists tended to undergrade cases, particularly in the higher-grade cancers. "These differences suggest that general pathologists supported by AI could reach higher agreements with uropathologists, potentially alleviating some of the variability associated with Gleason grading," they wrote.

The authors also pointed out that the algorithms were validated on individual biopsies from each patient, whereas in the clinical context, a pathologist would likely have multiple biopsies from a single patient.

"Future studies can focus on patient-level evaluation of tissue samples, taking multiple cores and sections into account for the final diagnosis," they wrote.

The study was supported by the Dutch Cancer Society, Netherlands Organization for Scientific Research, Google, Verily Life Sciences, Swedish Research Council, Swedish Cancer Society, Swedish eScience Research Center, EIT Health, Karolinska Institutet, Åke Wiberg Foundation, Prostatacancerförbundet, Academy of Finland, Cancer Foundation Finland, and ERAPerMed. The authors declared a range of grants and funding outside the study, including from Philips Digital Pathology Solutions. Several authors declared patents related to prostate cancer diagnoses, and 10 were employees of Google.

This article originally appeared on <u>MDedge.com</u>, part of the Medscape Professional Network.

Medscape Medical New: January 1, 2022

Research Backs Abiraterone for Treating Locally Advanced Prostate Cancer

Peter Russell

Abiraterone acetate with prednisolone should be added to standard treatment for men with high-risk nonmetastatic prostate cancer, research suggested. Combination therapy was associated with significantly higher rates of metastasis-free survival compared with androgen-deprivation therapy (ADT) alone, according to the <u>study in *The Lancet*</u>.

Abiraterone with prednisone is <u>currently recommended</u> <u>by NICE</u> in some cases of metastatic prostate cancer. However, questions have remained over its benefits and impact on survival in earlier-stage disease.

Using abiraterone (Zytiga, Janssen) for patients with locally advanced prostate cancer, where the cancer has a high chance of spreading, will now be considered by NHS England, based on the research led by University College London and the Institute for Cancer Research (ICRS).

Researchers on the <u>STAMPEDE trial</u> analyzed data from two randomized controlled phase 3 trials involving 1974 patients in the UK and Switzerland with a median age of 68 years.

In the first trial, 459 participants were randomly allocated to receive combination therapy with abiraterone and prednisolone in addition to androgendeprivation therapy (ADT), and 455 to a control group receiving androgen-deprivation therapy (ADT) alone.

In the second trial, 527 received the combination therapy plus enzalutamide, while 533 were allocated to a control group.

After a median follow up of 6 years, results showed that adding abiraterone alone, or with enzalutamide, to standard prostate cancer treatment improved survival and decreased the chance of cancer spreading.

Metastasis-free survival was 82% (95% CI 79 to 85) in the combination-therapy cohort compared with 69% (95% CI 66 to 72) in the control group.

There was no evidence of a difference in metastasis-free survival when enzalutamide and abiraterone acetate were administered at the same time compared with abiraterone alone. Prof Gert Attard, from the UCL Cancer Institute, who co -led the investigation, said: "This is the first time we've seen a treatment for this kind of prostate cancer that can do more than extend life. We're seeing clear and convincing evidence that some people who would have died of prostate cancer, the third leading cause of cancer death in the UK, will no longer die from it."

Nick James, Professor of Prostate and Bladder Cancer Research at the ICRS, and Chief Investigator of the STAMPEDE trial, said: "The next step is for NICE to consider and implement our findings, so that men can benefit from abiraterone before their cancer has spread, drastically improving their quality of life and preventing many unnecessary deaths."

The study was funded by Cancer Research UK, the Medical Research Council, the Swiss Group for Clinical Cancer Research, Janssen, and Astellas.

Michelle Mitchell, Chief Executive of Cancer Research UK, said: "These results are the latest in a long line of practice-changing findings from our STAMPEDE trial. It's recruited over 10,000 patients and has led to 29 changes in clinical practice across the world, directly influencing the treatment of people with prostate cancer. "It's great to see that yet more people with prostate cancer could soon see benefit from this innovative research." Medscape Medical News, UK: January 6, 2022

Blood Test Accurately Detects Cancer in People with Non-Specific Symptoms

Tom Broder

A new type of diagnostic blood test has been shown to accurately detect cancer in patients with non-specific symptoms, such as unexplained weight loss and fatigue, as well as differentiating between patients with localized and metastatic disease. This makes it the first bloodbased cancer test to determine the metastatic status of a cancer without prior knowledge of the primary cancer type.

In a study published this week in the journal Clinical

<u>Cancer Research</u>, researchers from the University of Oxford analyzed blood samples from 300 patients with non-specific but concerning symptoms of cancer using a technique called nuclear magnetic resonance (NMR) metabolomics. Unlike conventional blood-based tests for cancer, which look for genetic material from tumors, the NMR-based technique uses magnetic field and radio waves to analyze levels of metabolites in the blood as biomarkers to distinguish between different cancer states.

Dr. James Larkin, one of the study's authors, explained: "Cancer cells have unique metabolomic fingerprints due to their different metabolic processes. We are only now starting to understand how metabolites produced by tumors can be used as biomarkers to accurately detect cancer."

NMR-based metabolomic analysis correctly detected the presence of solid tumors in 19 out of 20 patients with cancer in the study. It also identified metastatic disease in these patients with an accuracy of 94%.

The authors emphasize that the techniques will need testing in a larger cohort of patients to confirm the results and evaluate the utility of the test in a wider clinical context. But the technique shows promise as a rapid and inexpensive test to enable early detection of cancers in patients before conventional imaging is performed. It could also allow doctors to more promptly identify patients who can benefit from drugs designed to treat metastatic disease. NMR metabolomic testing may be particularly helpful for diagnosing cancer in people with vague or nonspecific signs and symptoms, such as unexplained fatigue or weight loss, persistent nausea, or new atypical pain.

Current cancer referral pathways rely on organ-specific symptoms such as haemoptysis or haematuria, or clinically palpable abnormalities such as breast lumps. If symptoms are non-specific, it can be difficult to know to which specialist a patient should be referred. Patients can go back and forth between GP and hospital many times before a diagnosis is made.

<u>NHS Rapid Diagnostic Centres</u> are being rolled out across England to speed up cancer diagnosis and provide a referral pathway for patients who might not otherwise qualify for urgent referral. But cancer can still be difficult to diagnose without organ-specific symptoms to direct investigations.

Metabolomic testing has the potential to offer a quick and easy-to-administer way to triage patients with more vague signs and symptoms without needing to pinpoint a specific site, allowing doctors to prioritize those patients who require more invasive investigations.

Dr. Fay Probert, lead researcher on the Oxford study said: "This work describes a new way of identifying cancer. The goal is to produce a test for cancer that any GP can request. We envisage that metabolomic analysis of the blood will allow accurate, timely and costeffective triaging of patients with suspected cancer, and could allow better prioritization of patients based on the additional early information this test provides on their disease."

Larkin JR, Anthony S, Johanssen VA, et al. Metabolomic Biomarkers in Blood Samples Identify Cancers in a Mixed Population of Patients with Nonspecific Symptoms. Cedars-Sinai (blog): February 25, 2022

Scientists Target Protein to Lower Risk of Prostate Cancer Spread

Wei Yang, PhD

Cedars-Sinai Scientists Found That Attacking a Protein in Prostate Cancer Cells Can Stop Disease From Spreading to Other Parts of the Body in Mice

Targeting a specific protein that is often overexpressed in prostate cancer can help prevent or delay the disease from spreading to other parts of the body, according to a study led by Cedars-Sinai Cancer investigators.

The research, published in the peer-reviewed journal *Nature Communications*, opens the possibility of using available commercial drugs, including one approved by the Food and Drug Administration for leukemia, to shut down a protein known as receptorinteracting protein kinase 2-;or RIPK2. If confirmed in human clinical trials, the finding could have a major impact on the treatment of men with advanced prostate cancer.

"About 90% of cancer deaths are caused by the recurrence of metastatic cancer, which occurs when cancer spreads to other organs. So, if we can prevent the occurrence of metastatic cancer, we can substantially extend the lives and improve the quality of life for men with this disease," said Wei Yang, PhD, Associate Professor of Surgery and Biomedical Sciences

To better understand the genetic drivers of disease development and potential treatment targets, the Cedars-Sinai team examined the molecular profiles of cancer tissue in men with advanced prostate cancer. The investigators discovered that RIPK2 was amplified in about 65% of lethal prostate cancers, which kill approximately 34,000 U.S. men each year.

"We found the amplification of the protein RIPK2 increased along with cancer progression, which showed us that this protein may have a very important role in cancer progression," said Yiwu Yan, PhD, a project scientist in the Yang Laboratory and first author of the study.

While this protein has been studied in inflammatory disorders, little is known about its molecular functions in the context of cancer progression and metastasis, Yang said. Once the protein was identified, the team conducted a large-scale analysis to help decode how RIPK2 might alter the activity of other functions in the cell. Investigators found that RIPK2 activates another protein, which in turn triggers a crucial driver named c-Myc that fuels the progression and metastasis of many cancer types, including prostate cancer.

In a series of experiments in mice, investigators found that inhibiting the RIPK2 function with both small molecular inhibitors (drugs) and a gene-editing system, known as CRISPR/Cas9, substantially reduced the spread of prostate cancer.

They found that targeting RIPK2 with ponatinib, an existing FDA-approved protein inhibitor, reduced prostate cancer metastasis by 92% in mice.

"Administrating RIPK2 small molecular inhibitors is a high-value strategy that reduced the metastasis in mice by over tenfold," Yang said. "If we can translate this to human patients, we may extend patients' lives by several years, instead of just several months."

The next step is to identify biomarkers that can help guide investigators and clinicians to select the group of patients that would benefit most from this treatment. In addition, investigators will evaluate the effects of RIP-K2 inhibition on immune cells to see if the protein can potentially improve immune cells' ability to attack tumors.

"Targeting RIPK2 in preselected patients, either alone or in combination with standard or emerging therapies, might hold the potential for improving the survival time and quality of life of cancer patients," Yang said.

Additional Cedars-Sinai co-authors are Bo Zhou, Chen Qian, Alex Vasquez, Avradip Chatterjee, Yeon-Joo Lee, Xiaopu Yuan, Leigh Ellis, Dolores Di Vizio, Edwin Posadas, Beatrice Knudsen, Ramachandran Murali, Arkadiusz Gertych, Sungyong You and Michael Freeman. Collaborators at Purdue University and Mount Sinai Hospital also contributed to the study.

NOW ENROLLING – New Mexico Cancer Center Has a Radiopharmaceutical Trial Open for Patients with Metastatic Castration-Resistant Prostate Cancer Who Have Progressed After Hormone Therapy

WHY IS THE SPLASH STUDY IMPORTANT?

Metastatic castration-resistant prostate cancer (mCRPC), is prostate cancer that has metastasized, or spread to other areas of the body, and that has progressed after hormone therapy. When metastatic prostate cancer does not respond to treatments such as surgery, radiation, and hormone therapy, there are very few treatment options.

The SPLASH study is testing an investigational therapy (called ¹⁷⁷Lu-PNT2002) against the current standard treatment (either abiraterone or enzalutamide) to see whether ¹⁷⁷Lu-PNT2002 is safe and effective when prostate cancer reaches this point.

Biopharmaceutical companies use clinical research studies like this one to learn more about investigational therapies before they are made available to the public. Your participation in this study, if you are eligible, can help improve the understanding of this therapy, potentially helping make it available to others in the future.

New Mexico Cancer Center Research Contact Email: <u>research@nmohc.com</u>

To learn more about the study, visit <u>https://www.splashtrial.com/#AboutSplash</u>

What Will Happen in the SPLASH Study?

Everyone Receives Treatment

During the study, all participants will be treated with either ¹⁷⁷Lu-PNT2002 or with the current standard of care therapy. Everyone receives active treatment in this study. There is no placebo (inactive treatment).

2 parts to the study:

- 1. The first 25 patients will receive 4 doses of ¹⁷⁷Lu-PNT2002, spread out over 32 weeks (7 months).
- 2. The next 400 patients will be randomized to either receive ¹⁷⁷Lu-PNT2002 or one of two existing approved therapies, abiraterone or enzalutamide, over 32 weeks (7 months) or until disease progression.

Ensuring Access to ¹⁷⁷Lu-PNT2002

Participants who are receiving standard of care and experience progression of their disease (confirmed by radiologic testing) may be eligible to switch therapies to ¹⁷⁷Lu-PNT2002.

Participants from both parts of the study will receive long-term follow up for up to 5 years.

¹⁷⁷Lu-PNT2002 is an investigational therapy. Investigational therapies have not yet been approved by the U.S. Food and Drug Administration (FDA) or any other regulatory agency. ¹⁷⁷Lu-PNT2002 is also known as ¹⁷⁷Lu-PSMA-I&T in previous studies.



PCSANM *Lifeline* Newsletter Celebrating over 30 years of supporting men and their families

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A Message from the Chairperson

April 2022

Since we've been keeping track, your wonderful monetary contributions tend to come during the final quarter of a year, which is great. We also have data about typical contribution totals for other quarters in the year. Well, we're behind on that first-quarter benchmark as we enter the second quarter of 2022.

Here's a catch up plan:

You may not know – I didn't until recently – that months have cancer-connected themes. So at any point in the year, you can write a paper check or punch a computer button that gives a cancer-related 501(c)(3) organization a boost. For instance, January was Cervical Cancer Awareness Month, February was National Cancer Prevention Month, and Prostate Cancer Awareness Month is not until September. But, you don't have to wait for a specially themed month to invest in PCSANM–just go to www.pcsanm.org now and click the donate button.

And please remember to adjust your Amazon account to <u>Smile.Amazon.com</u>, where you can easily designate a portion of every purchase be donated to a 501(c)(3) organization of your choice, including our support group.

Finally, thank you for your other types of contributions, such as volunteering your time, attending our twice-a-month Saturday meetings, and very importantly, for providing direct input and suggestions which translate into better support to all who are involved with this organization. We appreciate your contributions.

Rad Ger

Rod Geer Chairperson of the Board, PCSANM