September 2015 - Issue #91

Prostate Cancer Canada Network

Montreal West Island

EVERYONE IS INVITED TO ATTEND OUR MEETINGS
We meet every fourth Thursday of each month except July, August and December

MEETING LOCATION

Sarto Desnoyers Community Centre
1335 Lakeshore Drive, DORVAL

Upcoming Meetings:

*On **September 24**, Dr. Guila Delouya will speak on "**Brachytherapy for Localized Prostate Cancer**"*

*On **October 22** Robin Glance will speak to us on "**Food: Fact & Fiction**"*

Make an In Memoriam Donation

Consider making a gift in memory of a loved one who has died of prostate cancer. While flowers are beautiful, many people today prefer to make memorial contributions in honour of a loved one's memory. A tax receipt will be issued upon receipt of a donation.

This Newsletter is available at our website:

http://mtlwiprostcansupportgrp.ca/, as well as at www.pccn.org

Our Upcoming Speakers

Dr. Guila Delouya is a specialist in radiation/ oncology at Hopital Notre-Dame and Clinical Assistant Professor, Department od Radiation, Radiation Oncology and Nuclear Medicine - University of Montreal. Dr. Delouya is also a lawyer and member of the Quebec Bar Association.

Robin Glance is a registered dietitian with over 7 years of experience at the MUHC in oncology. She now has a private practice in the West-Island. Robin has appeared on Breakfast Television Montreal, Global News Morning Show, CBC News and CBS Living as a nutritional expert. In her talk on " Food: Fact & Fiction", Robin will cover such questions as "Should we avoid gluten? Do we really need to drink milk? Is sugar worse than fat? Join registered dietitian Robin Glance to answer all your big nutrition questions and to find out what are the current recommendations for healthy eating.

Support your local prostate cancer support group
PCCN - Montreal West Island . Get Involved!

PCCN - The Montreal West Island Prostate Cancer Support Group

Our Website

Be sure to check out our website. Our internet address is http://mtlwiprostcansupportgrp.ca/ The website provides information about our group, links to PCCN and Procure and gives access to current and past issues of our newsletter as well as up-to-date information about our meetings and other items of interest. Check it out and give us your feedback. Our Director Monty Newborn is the creator and manager of the site and our WEBMASTER.

In Memoriam

POLONCSAK, Leslie M. (1930-2015)

It is with great sorrow that we bring to your attention the peaceful passing of Les on June 15, 2015. As an active member of our Steering Committee, Les will be greatly missed. For many years he served as our librarian and helped in distributing our Newsletter through the postal service as well as set up our meeting hall for our monthly meetings. Medically, Les was a twenty year survivor of prostate cancer but five to six years ago had to deal with lymphoma as well. He was treated by chemotherapy.

Be sure to visit our table, and say hello to our Steering Committee Members, as well as pick up some of the latest information on prostate cancer during the **Pointe-Claire Community Awareness Day** on Saturday **September 19, 2015**, at **Plaza Pointe-Claire**, 269 boul. St Jean.

Biomarker Combo Could Predict Prostate Cancer Survival

News | March 25, 2015 | Prostate Cancer, Genitourinary Cancers
By Anna Azvolinsky, PhD

In a phase III clinical trial, a combination of biomarkers—circulating tumor cells (CTCs) and lactate dehydrogenase (LDH) level—has shown promise as a surrogate for survival in metastatic castration-resistant prostate cancer (CRPC). The combination was "shown to satisfy the four Prentice criteria for individual-level surrogacy," according to the study. The results are published in the *Journal of Clinical Oncology*.

Howard I. Scher, MD, chair of urologic oncology at the Memorial Sloan Kettering Cancer Center, New York, New York, and colleagues analyzed samples from 711 men who took part in the COU-AA-301 phase III clinical trial, a study which tested the efficacy of prednisone plus abiraterone acetate compared to prednisone alone in metastatic CRPC patients who were previously treated with docetaxel.

Both CTCs and LDH level were measured prior to the first dose on trial and at 4, 8, and 12 weeks from trial initiation. This analysis was a planned secondary objective of the clinical trial.

A lower number of detectable CTCs (≤ 4 cells/7.5 mL of blood) has previously been shown to be a sign of favorable prognosis, whereas a higher number of CTCs (≥ 5/7.5 mL) is associated with an unfavorable prognosis. CTC number has also been demonstrated as prognostic and predictive of overall survival in prior clinical trials.

Risk groups were defined according to CTCs and LDH level: high risk (CTCs ≥ 5 cells/7.5mL of blood; LDH > 250 U/L); intermediate risk (CTCs ≥ 5; LDH ≤ 250), and low risk (CTCs ≤ 4; any LDH). Median overall survival was 8.71 months, 12.02 months, and 22.18 months for the high-, intermediate-, and low-risk groups, respectively. The treatment effect on the surrogate was statistically significant ($P < .001$), which satisfied a Prentice criteria, and the ability of the surrogate marker panel to predict mortality was high, according to the study results.
Using biomarker data from the 12-week time point, the probability of 1-year survival in high-risk patients was 25%, compared with 51% for intermediate-risk patients, and 82% for low-risk patients. The probability of 2-year survival in high-risk patients was 2%, compared with 10% for intermediate-risk patients, and 46% for low-risk patients.

CTC count or LDH level alone can predict patient prognosis, and an elevated CTC count or LDH level at 12 weeks is associated with a worse survival time, but alone neither is enough to serve as a surrogate marker for survival, a more stringent criteria. But, CTC count plus LDH level together may provide a surrogate for overall survival. "That LDH level would add to CTC count is plausible, both scientifically and biologically," stated the authors. "Tumors that continue to shed cells into circulation

are likely to be more aggressive than those that do not, and although LDH level, an indicator of tumor burden, is only elevated in a small proportion of men with progressive CRPC, the impact on survival is highly negative when it is."

Surrogate endpoints, wrote the authors, are needed because the currently available treatments—five therapies were approved for metastatic CRPC in the last 3 years—have increased the survival of men with CRPC, making it more difficult to demonstrate an overall survival benefit for newer therapies in development. "Future trials designed with a primary endpoint of survival will have to be larger, longer running, and more costly, with a higher risk of failure," wrote the authors.

"Urgently needed are reproducible and reliable post-treatment outcome measures that are surrogates for survival that can be used to guide patient management and facilitate regulatory approval," wrote the authors. "Using surrogate endpoints would speed up drug development time and costs."

Other phase III trials are also testing whether this biomarker panel demonstrates individual-level surrogacy to confirm these data.

New type of biomarker shows promise in improving prostate cancer care

Date: March 4, 2015
Source: Fred Hutchinson Cancer Research Center

Summary:

Two biomarkers have been discovered by researchers that may improve oncologists' ability to predict which patients' prostate cancer will recur after surgery, long before the development of visible cancer elsewhere in the body.

Many men experience prostate cancer as a curable disease. But in those who recur in the form of metastasis death is inevitable. Pinpointing patients at high risk of relapse is imperative to giving them early treatment options when it's more likely to be effective. Dr. Andrew Hsieh has identified two biomarkers that may improve oncologists' ability to predict which patients' prostate cancer will recur after surgery, long before the development of visible cancer elsewhere in the body. According to Hsieh, "once clinically verified, biomarkers like these have the potential to help clinicians identify patients who are more likely to relapse and therefore may benefit from additional therapy after surgery."

In an upcoming paper in *Oncotarget*, Dr. Hsieh's team showed that the levels of two proteins are closely linked to prostate cancer outcomes. In collaboration with groups at the University of California, San Francisco, and the University of California, Los Angeles, Dr. Hsieh found that patients with higher levels of these two proteins, called YB-1 and MTA1, were much more likely to suffer prostate cancer recurrence and three times as likely to require treatment such as hormone therapy or radiation therapy.
Moreover, adding YB-1 and MTA1 levels to clinical factors currently used to predict prostate cancer recurrence improved their predictive potential.
The search for prognostic biomarkers have primarily focused on changes in DNA and messenger RNA, the intermediate molecule that enables the genetic message encoded in DNA to be translated into proteins. But Dr. Hsieh suspects that a whole field of potential biomarkers remains little studied: proteins whose levels are altered in the absence of gene mutations or changes in messenger RNA expression. In pursuing this hypothesis as a physician-scientist, Dr. Hsieh is navigating uncharted waters.
Proteins are cells' "work horses," said Dr. Hsieh. They underpin how cells live, behave and die. But the process of producing proteins from RNA messenger molecules "is not static," Dr. Hsieh said. "It's not like a factory that does the same thing every time. There are levels of regulation," and changes in how key proteins are produced, independent of alterations to the proteins' genes or messenger RNA, have been shown to drive cancer. YB-1 and MTA1 are just two of potentially hundreds of such proteins, and would never have been discovered if Dr. Hsieh had not ventured beyond traditional DNA and RNA biomarker discovery techniques.
Dr. Hsieh previously identified YB-1 and MTA1 as potential protein biomarkers in a groundbreaking study conducted at UCSF with Dr. Davide Ruggero, using new technology that measure changes in protein production that occur independently of any changes in mRNA. "This work is the clinical application of that finding," he said.
Hsieh aims to uncover how differences in the levels of specific proteins -- without accompanying DNA or RNA changes -- can give clues to how cancers develop and potentially recur. Such mechanisms which control these phenomena could also be the target of drugs, currently in development, that block the key steps in which RNA messages are translated into proteins.
The findings not only have the potential to improve care for prostate cancer patients, but strengthen the hypothesis that the control of protein abundance produces a potentially rich source of biomarkers for many types of cancer. "We have the opportunity to revisit the topic of biomarker discovery in a completely new way," said Dr. Hsieh. "It's great to be working at the forefront of basic research and clinical medicine here at the Hutch."

Story Source:
The above story is based on materials provided by **Fred Hutchinson Cancer Research Center**. *Note: Materials may be edited for content and length.*

Journal Reference:
Davide Ruggero et al. **YB-1 and MTA1 protein levels and not DNA or mRNA alterations predict for prostate cancer recurrence**. *Oncotarget*, March 2015

Update From the ASCO 2015 Genitourinary Cancers Symposium

March 19, 2015 | ASCO 2015 Genitourinary Cancers Symposium, Genitourinary Cancers, Prostate Cancer

By Aaron Falchook, MD

At this year's American Society of Clinical Oncology (ASCO) Genitourinary Cancers Symposium in Orlando, Florida, several high-impact and potentially practice-changing abstracts were presented during the prostate cancer oral abstract session.

The ASCENDE-RT trial is a phase III randomized trial that evaluated high-dose radiotherapy with external beam boost vs brachytherapy boost for prostate cancer. All patients had intermediate- or high-risk prostate cancer as defined by the National Comprehensive Cancer Network (NCCN) and were treated with 12 months of androgen deprivation therapy (ADT), along with 46-Gy pelvic external beam radiotherapy (EBRT) to the prostate, seminal vesicles, and regional lymph nodes. The patients were randomized to receive either dose escalation via an EBRT boost of 32 Gy to the prostate (total dose, 78 Gy) or a brachytherapy boost with low-dose rate interstitial brachytherapy (115 Gy). The primary endpoint was biochemical progression-free survival (bPFS). The trial demonstrated a benefit at 7 years, with a bPFS of 86% in the brachytherapy arm vs 75% in the EBRT arm. There were no differences in metastasis-free survival, overall survival, or prostate cancer–specific survival. The cumulative incidence of grade 3 genitourinary toxicity was higher in the brachytherapy arm (19% vs 5%; $P < .001$), although at 5-year follow-up the difference was smaller (8.6% vs 2.2%). Gastrointestinal toxicity was relatively low in both arms (< 10%). This study showed an impressive bPFS for patients who received brachytherapy boost, compared with higher-risk patients from other dose-escalation trials. Furthermore, this trial gave us additional insight into the value of dose escalation in the setting of ADT use. Although published results in manuscript form are pending, findings from this trial may be practice-changing given the demonstrable benefit of a brachytherapy boost vs an EBRT boost.

Long-term results were presented from the RTOG 0126 trial, which randomized men with intermediate-risk prostate cancer to standard-dose radiotherapy (70.2 Gy) vs dose-escalated radiotherapy (79.2 Gy), with EBRT utilized in both treatment arms. ADT was not given in this study. Previously published results from this study and multiple other dose-escalation studies have shown improved bPFS for men who received dose-escalated radiotherapy. However, the long-term results presented at this year's meeting were the first to show a statistically significant benefit with dose escalation in the reduction of distant metastasis (5% vs 8% at 10 years; $P = .026$). Furthermore, the use of salvage therapy was significantly lower among the dose-escalated group of patients (receipt of any salvage therapy was 13.5% for dose escalation vs 20.6% for standard dose; $P = .0002$). Differences in local progression and overall survival were not statistically significant. These results were significant in that they demonstrated that dose escalation alone (without ADT or any other systemic treatment) reduces the rate of prostate cancer distant metastases.

The final abstract that stood out is the Prostate Cancer Study III trial. This was a three-arm randomized trial of intermediate-risk prostate cancer patients that examined the following regimens: 1) short-term ADT plus prostate EBRT at 70 Gy, 2) short-term ADT plus prostate EBRT at 76 Gy, and 3) prostate EBRT alone at 76 Gy. The benefit of dose escalation in patients receiving ADT has not previously been well-studied. This current trial represents an important effort to fill that knowledge gap. With a median follow-up of 75 months, the addition of ADT improved biochemical control regardless of EBRT dose used. The difference in biochemical failure was not statistically significant between standard-dose and high-dose EBRT for men who received ADT (12.5% vs 8.0%; $P = .187$). Biochemical failure for dose-escalated EBRT without ADT was 21.5%. Rates of metastatic disease were lower among men who received ADT (1.5% for both ADT arms vs 5.5% for dose escalation alone). However, there were no differences in prostate cancer death or overall survival between arms, and the rate of cardiovas-

cular death was higher in the ADT arms (11 patients each in the two ADT arms vs 5 patients in the EBRT-alone arm). These results suggested that from an oncologic outcomes perspective, the addition of ADT provides greater benefit than dose escalation, although the best outcomes were seen among men who received both ADT and dose escalation. Additional studies and longer follow-up are needed to better understand the role of ADT in the era of dose-escalated EBRT for prostate cancer. Baseline patient comorbidities, disease risk features, and patient preferences will ultimately play an important role in the optimal treatment selection for men with clinically localized prostate cancer.

Do Doctors Overscreen for Cancer?

By Quora Contributor

U.S. government committee recommended new mammogram screening guidelines due to over-treatment concerns.

This question originally appeared on Quora, the best answer to any question. Ask a question, get a great answer. Learn from experts and access insider knowledge. You can follow Quora on Twitter, Facebook, and Google Plus.

Answer by David Chan, M.D. from UCLA, Stanford oncology fellowship:

The issues surrounding early diagnosis of cancer are very complicated. The short response is that it depends on which patient and cancer.

The long version is that there are many cancers being diagnosed, including low-grade prostate cancers in older men and preinvasive breast cancers in older women, that don't need to be diagnosed and don't need to be treated. These low-grade cancers have a natural history way beyond average life expectancy, so the large majority of these patients will die of other causes before they have symptoms from their cancers.

This kind of analysis led to the controversial guidelines from U.S. Preventive Services Task Force, the national screening task force, to eliminate PSA blood test screening in the large majority of men for prostate cancer and also to increase the time between mammograms in women to every two years and to stop mammogram screening altogether after the age of 75.

So what we have are two tests (PSA and mammograms) that have been demonstrated to diagnose cancer early, yet a U.S. government committee has recommended reducing their use, dramatically in the case of PSA, because of concerns with overtreatment, costs, and toxicity and morbidity resulting from overtreatments.

The very big problem with these guidelines is that they completely discount those aggressive cancers that are going to be diagnosed too late. Guidelines like those from the task force are population recommendations, but we all know younger men who die of prostate cancer and similarly women of all ages who die from breast cancer. Many cancer specialists and patients would prefer to know about the aggressive cancers and to make educated, informed decisions on not treating the low-grade cancers.

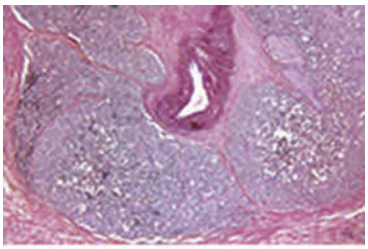
Within the next couple of years, there will be a large number of molecular blood tests that will develop cancer DNA or RNA. These tests are often referred to as liquid biopsies. The tests will be very accurate in finding all sorts of cancer early. Both that's going to lead to a very major problem.

Liquid biopsy technology will often find a cancer way before, maybe many years before, it's detectable by endoscopy, MRI, or CT scan. This will lead to a huge freakout factor for patients and their doctors who find abnormal liquid biopsy tests and multiple normal scans. Although it's certainly possible that the liquid biopsy tests will be so accurate that they can also predict whether the cancer is aggressive or low-grade.

An additional issue is that MRI and CT or PET scans are computer-generated images with low sensitivity.

The software isn't able to detect small areas of abnormality, so the images appear normal when in fact small cancers are present. CT and PET have high levels of radiation and can't be used for routine testing except when cancer risk is high, such as lung cancer screening in older smokers.

Metabolic Syndrome Up With ADT in Prostate Cancer



Microscopic view of prostate cancer

Increases in components of metabolic syndrome, and in prevalence of full metabolic syndrome

Last Updated: June 04, 2015.

For patients with prostate cancer treated with androgen deprivation therapy there are increases in components of metabolic syndrome and in the prevalence of full metabolic syndrome, according to a study published in the June issue of *The Journal of Urology*.

THURSDAY, June 4, 2015 (HealthDay News) -- For patients with prostate cancer treated with androgen deprivation therapy there are increases in components of metabolic syndrome and in the prevalence of full metabolic syndrome, according to a study published in the June issue of *The Journal of Urology*.

Juan Morote, M.D., from Hospital Vall d'Hebron and Universitat Autónoma de Barcelona in Spain, and colleagues conducted an observational prospective study involving 539 prostate cancer patients scheduled to receive three-month depot luteinizing hormone-releasing hormone analogs for longer than 12 months. The authors examined the prevalence of full metabolic syndrome, assessed according to different definitions, and its components.

The researchers found that at six and 12 months after androgen deprivation therapy initiation there were significant increases in waist circumference, body mass index, fasting glucose, triglycerides, total cholesterol, and high- and low-density lipoprotein cholesterol. There were no significant changes in blood pressure of 130/85 mm Hg or greater. There was a nonsignificant increase in the prevalence of full metabolic syndrome, based on National Cholesterol Education Program Adult Treatment Panel III criteria (baseline, 22.9 percent versus 25.5 percent at six months and 26.8 percent at 12 months). At 12 months there were significant increases in metabolic syndrome prevalence with two of the definitions (World Health Organization, 4.1 percent and American Heart Association/National Heart, Lung, and Blood Institute, 8.1 percent).

"Counseling patients on the prevention, early detection, and treatment of specific metabolic alterations is recommended," the authors write.

The study was funded by Ipsen Pharma.

Ref http://www.doctorslounge.com/index.php/news/pb/55691

Dietary Patterns Can Influence Prostate Cancer Risk

A team led by researchers at Duke University Medical Center published a review analyzing the link between **diet** and **prostate cancer** in the journal *BMC Medicine*. The study is entitled "Nutrition, dietary interventions and prostate cancer: the latest evidence."

Prostate cancer is the second most common cancer in men, with almost one million new cases diagnosed every year worldwide. It is a curable cancer that can range from slow-growing tumors (more common) to rapidly progressing aggressive tumors. An early diagnosis of the disease is crucial.

Prostate cancer was found to have a six-fold higher incidence in Western than in non-Western countries, where factors related to lifestyle, diet, genetics and environment are thought to play a role. This review focused on the potential role of dietary patterns in prostate cancer incidence and development.

Researchers found that low refined carbohydrates intake and an increased consumption of omega-3 fat, soy pro-

tein, green teas, coffee, pomegranate, resveratrol (present in raspberries, blueberries, grapes and wine), tomatoes and tomato products may reduce the risk for prostate cancer. Zyflamend, which is an anti-inflammatory mixture of herbs (including ginger, green tea, oregano, rosemary, among others), can also reduce prostate cancer risk. On the other hand, a higher β-carotene status (which is abundant in plants and fruits) and a higher intake of saturated fat can increase the risk of prostate cancer development. A possible 'U' shape relationship (a nonlinear relationship between two variables) may exist between calcium, folate, vitamin C and vitamin D with the risk of prostate cancer.

Although the findings are to some extent inconclusive, there is evidence for a potential role of dietary intake in the prevention of prostate cancer. The team suggests that a combination of all dietary factors found to be advantageous for prostate cancer risk reduction might be beneficial in men. This healthy dietary pattern includes a high consumption of fruits and vegetables and a reduced intake of refined carbohydrates (which can be replaced by whole grains), overcooked red meats and total and saturated fats. Prospective clinical trials should be conducted to establish the benefits of such diet in prostate cancer incidence and development.

Recently, there has been an emphasis on prostate cancer chemoprevention: agents that prevent the progression of prostate cancer. A team of scientists led by Nagi B. Kumar from the Moffitt Cancer Center have recently published the outcomes of a randomized clinical trial that evaluated the effectiveness and safety of the active components existent in **green tea** that can prevent prostate cancer in men who have pre-malignant injuries. The results were presented during the 2015 American Society of Clinical Oncology (ASCO) Annual Meeting, Chicago.

About 20% of green tea is consumed in Asian countries where prostate cancer death rates are one of the lowest in the world. The risk to develop such malignancy seems to increase among Asian men that leave their original dietary habits after migrating to the United States.

Laboratory studies have evidenced that substances in green tea known as "catechins" can inhibit the growth, motility and invasion capacity of cancer cells and stimulate their death. Catechins, of which epigallocatechin-3-gallate (EGCG) is the most powerful and abundant found in green tea, can prevent and reduce the growth of tumors in animal models.

This study evaluated if a 1-year intervention with catechins and green tea could suppress prostate cancer progression in male individuals who had high-grade intraepithelial neoplasia (HGPIN) or atypical small acinar proliferation (ASAP). The investigators used decaffeinated green tea capsules named Polyphenon E with a mix of catechins (mostly EGCG) at a dose of 200 mgs twice daily.

Polyphenon E given to 49 men and placebo tablets given to 48 men were compared during a year of treatment, with results not showing a statistically significant difference in cancer development. However, researchers observed that in those patients who only had HGPIN during the initial phase of the trial there was a lower combined rate of ASAP (group of lesions that can be diagnosed as prostate cancer) and prostate cancer advancement with Polyophenon E. Further, men on Polyphenon E had significant lower levels of prostate-specific antigen (PSA) – a biomarker used to screen patients for prostate cancer.

Importantly researchers noticed a significant increase of EGCG levels in the blood plasma of men on Polyphenon E, and the capsules were well tolerated in this group of men.

http://prostatecancernewstoday.com/2015/06/08/green-tea-may-help-fight-prostate-cancer/

We are currently in need of an individual who is proficient and highly interested in navigating the internet in search of the latest information on prostate cancer, and compile interesting news items into a newsletter for our membership. Some knowledge in the use of Microsoft Publisher – a highly intuitive software, would be an asset, although training would be provided if necessary. We urgently require such an individual to fill the post of Newsletter Editor. If interested please approach any of the members of the Steering Committee.

Newsletter Disclaimer:

All articles appearing in this newsletter are for information purposes only and not intended to be a substitute for the advice of a doctor or healthcare professional or recommendations for any particular treatment plan. It is of utmost importance that you rely on the advice of a doctor or a healthcare professional for your specific condition.

Prostate Cancer Canada Network – Montreal West Island

WE NEED YOUR SUPPORT

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Please note that tax receipts, due to constraints in the cost of processing, will only be issued for contributions of $25.00 or greater.

Telephone Helpline (514) 694-6412

IMPORTANT NOTICES:

- **The PCCN—Montreal West Island Prostate Cancer Support Group encourages wives, loved ones and friends to attend all meetings. Please ask basic or personal questions without fear or embarrassment. You need not give your name or other personal information.**
- **The PCCN—Montreal West Island Prostate Cancer Support Group does not recommend treatment procedures, medications or physicians. All information is, however, freely shared. Any errors and omissions in this newsletter are the responsibility of the authors.**
- **The PCCN—Montreal West Island Prostate Cancer Support Group is a recognized charitable Organization (registration # 87063 2544 RR0001). All donations are acknowledged with receipts suitable for income tax deductions. Your donations and membership fees (voluntary) are a very important source of funds vital to our operations. Together with contributions from several pharmaceutical companies these funds pay the cost of printing and mailing our newsletter, hall rental, phone helpline, equipment, library, etc.**

Your support is needed now! Please help us continue helping you!

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