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Prostate cancer research yields hope, disappointment



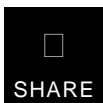
LARRY PYNN

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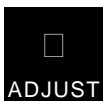
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Michael Izen has tried experimental drugs for prostate cancer but it has spread through his body and he has only a matter of months to live. NICK PROCAYLO / PNG



Michael Izen wrote the book on prostate cancer. And now he's dying of the disease.



The Vancouver labour-market analyst consultant jokes that he had "softwood lumber" problems and was diagnosed with prostate cancer in 2012. He had it removed shortly thereafter, but the aggressive cancer — caused by the defective hereditary gene BRCA2 — always returned.



It spread to his liver, spine and, now, to his brain.

COMMENT

"It's moved everywhere," explains 51-year-old Izen, who self-published the book, *Finger Up The Bum*, which sought to educate and add levity to an otherwise grave situation. "That's an issue, to say the least."

PRINT

He's received hormone treatments, two rounds of radiation, chemotherapy, and, as an experiment, the drug Olaparib, normally used for ovarian and breast cancer and which worked well for a year with few side-effects.

The problem is, cancer adapts to treatments. New research is looking at ways to target the disease during these temporary periods of dormancy when drugs have success at arresting its progress.

"I've known I had a limited horizon for a while," Izen said. "Two and a half years ago, after the cancer moved to my liver, I was told that people in my condition last about a year."

He now estimates he has six months to live. "I said if I could live three years that would be fantastic. And it looks like that wish will be granted."

Researchers are working feverishly to find treatments for men like Izen with late-stage prostate cancers, with a special emphasis on genetics and the search for customized drug treatments for an individual's specific cancer.

Research has shown that the same gene mutations are responsible for several cancers, including prostate, breast and ovarian, which means a man may stand a greater risk of getting prostate cancer if his mother has had breast or ovarian cancer. The cancer gene can also be handed down from man to child.

"This has been under-recognized," said Dr. Kim Chi, a medical oncologist with B.C. Cancer in Vancouver. "A man can carry the same altered gene, which can predispose them to developing prostate cancer. And it affects all races.



"This is going to become more and more important as time goes on. It's an exciting time. We're on the verge of so much."

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Currently, the B.C. medical system does not cover a screening test to determine if a man carries a parent's gene mutation, but one can go to private companies to have the determination made.

If a man is found to have the gene, then he can start being more vigilant, including getting regular PSA tests, to catch the prostate cancer early should it surface.

One company that performs the test is Color, a California-based genomics company that charges US\$99 to screen for two of the more prominent defective genes — BRCA1 and BRCA2 — and US\$249 to screen for a suite of 30 genes.

A couriered package contains a test tube for collecting saliva, which is mailed back and tested within a month. A consultation with a genetic counsellor is included.

Should the saliva test reveal that a man carries a defective gene that might be passed on, it is recommended that his children also be tested. If they, too, have the gene, they can get regular tests for cancer.

It is a fast-growing medical enterprise given the continuing improvements in the cost and efficiency of such tests.

"Lower costs translate into higher access," said Scott Topper, the company's vice-president of clinical operations. "It allows you to personalize the family risk. If you have the mutation yourself, there is a 50 per cent chance that each of your children will inherit the mutation."

The National Comprehensive Cancer Network, an alliance of leading cancer centres in the U.S., recommends that men with advanced or metastatic cancer receive genetic screening for BRCA1 and BRCA2 — but that does not apply in Canada.

"I recommend it, but we can't afford," Chi said. "It would rapidly overwhelm our system. We're doing it through research dollars now, but really it should be a standard test. Eventually it will get so cheap, we can apply this at population levels."

Chi said that of those men with localized prostate cancer, only one to two per cent are genetically predisposed to the disease, but for those with the more aggressive prostate cancers, that number can rise to about 10 per cent.

Currently, researchers at B.C. Cancer and Vancouver Prostate Centre are inviting men from across B.C. with metastatic prostate cancer to be tested for the defective genes as part of a research study. Where the tests are positive, men are referred to B.C. Cancer's hereditary cancer program for counselling and further information.

Men who are interested in participating should talk to their doctor to see if they might be eligible for the study.

"It may open up different treatment options, and we'll watch that man more carefully," Chi said. "For every patient, at least three family members on average will come in and get tested. It's big. Prostate cancer is common so there's a lot of people. It gets beyond prostate cancer, it's women and



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families.”



Angelina Jolie carries the defective gene that can cause cancer. JORDAN STRAUSS / JORDAN STRAUSS/INVISION/AP

Oscar-winning actress Angelina Jolie had a preventive double mastectomy in 2013 followed by removal of her ovaries and Fallopian tubes in 2015 because she inherited a defective gene from her mother, who died of ovarian cancer at age 56.

In some cases, there is little time to wait. “A man signed up for our program a couple of years ago, and by the time we found out he had the gene he had already passed away from his cancer,” Chi said. “I called his daughter and just that week she had been diagnosed with breast cancer. That hit me. If we’d known about it earlier ...”

Chi recalls that in the late 1990s men with metastatic advanced prostate cancer would survive an average 10 to 12 months. Now it’s closer to three years because of medical advances.

An estimated 620 men died from prostate cancer last year in B.C.

The latest research in Vancouver involves blood tests that isolate and sequence DNA to provide detailed information on a man’s specific prostate cancer — far less invasive than a biopsy, which requires taking tissue samples from the prostate.



Vancouver researcher Alexander Wyatt of the Vancouver Prostate Centre is seeking to tailor drugs specific to a patient's late-stage cancer. LARRY PYNN / PNG

Alexander Wyatt is a senior research scientist with the Vancouver Prostate Centre who oversees a 12-person lab conducting research on metastatic cancer, which, he explains, happens when prostate cancer cells overwhelm other organs in the body.

“If your liver is being colonized by prostate cancer, you can look down a microscope and those cells actually look a little bit like prostate cells. It’s a strange concept for patients to deal with.”

That’s also why the PSA (prostate-specific antigen) blood test is used to help track the advance of prostate cancer.

Because most metastasis goes to the bone, obtaining biopsies would be painful for patients. Wyatt is looking to blood samples as a way to study such cancers.

“Everything in the cancer cells is in the blood,” said Wyatt, whose grandfather died of metastatic prostate cancer. “If you have the appropriate technology you can profile that. And that’s what we do.”

The goal is to produce specific drug treatments based on an individual’s cancer, and to get a better idea of how aggressive it is. “Everyone’s cancer is a bit different, a unique combination of their genetics and the evolutionary path of that cancer,” he said.

Gaining approval from pharmaceutical companies to allow drugs that are used in other applications to be tested in experimental prostate-cancer research can be challenging, since they don’t want the drug to be associated with failure.

“We’re dependent on company goodwill to provide the drug free of charge ... so they do hold the balance of power to some extent.”

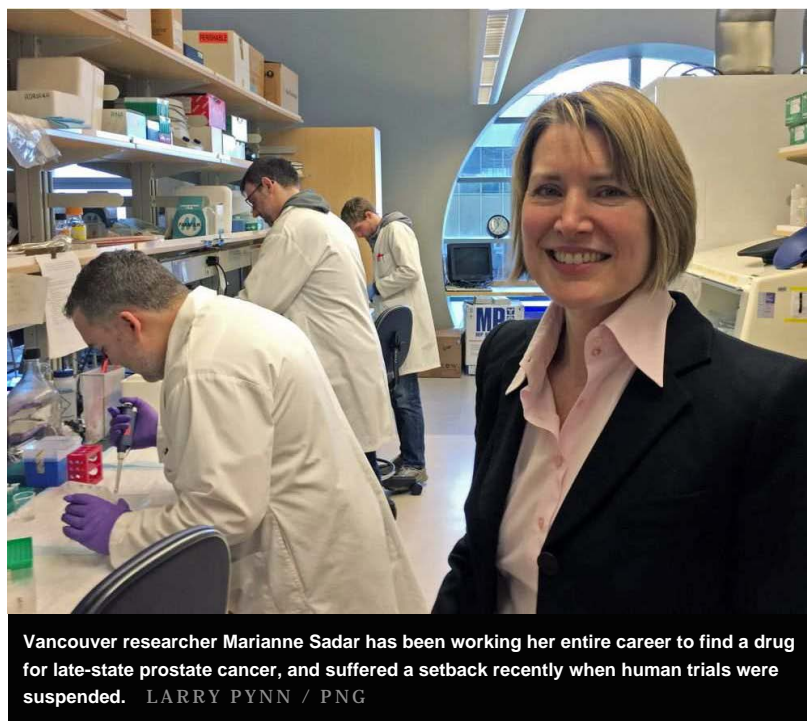
All medical research is launched with optimism. Over time, the harsh reality of a genuine breakthrough takes hold.

Along the way, medical institutions are quick to shout out their latest promising

research, and news organizations are only too eager to publish the findings.

Postmedia News medical reporter Pamela Fayerman received a 2012 grant from the Canadian Institutes of Health Research to study “knowledge transfer” — the way research findings are adapted into medical practice for the benefit of patients.

“Breakthrough is a word used far too often in the reporting of medical research,” Fayerman said. “There are starts and spurts, full stops, dead-ends, U-turns and even reversals.”



B.C. cancer scientist Marianne Sadar started her research in 1995, focusing on finding treatments for “the difficult ones” — those men with the most advanced prostate cancers.

One headline in 2007 on her research shouted: ‘B.C. find raises hopes for curing advanced prostate cancer,’ after Sadar’s research showed promising results in mice. Her findings, published in *The Proceedings of the National Academy of Science*, involved manufacturing a decoy to “confuse” prostate cancer cells so they will die before they can proliferate.

In 2015, Sadar’s continued research into the drug — derived from a Papua New Guinea marine sponge — received more publicity as it was about to undergo human trials, a first for B.C. Cancer.

“If this one works, it could be a billion-dollar drug,” said Chi at the time. He also ran the North American trial for the drug, known as EPI-506.

Looking back, Sadar allows: “We got a lot of press. You guys were very good to us.”

Then, late in November 2017, human trials were suspended — without the usual news releases.

Participants in the trial were taking 18 pills per day — saturated in castor oil, which, of course, has its own complications — and even then the drug wasn’t

sticking around.

“They take the pill orally and we measure the amounts of drug in their blood. It goes quickly up and then it quickly comes down. Between dosing there’s nothing in their blood. It’s all gone.”

Disappointing? Of course.

But rather than calling it quits, researchers hope to tweak the drug in hopes that it can one day prove useful. “We think we know how to fix the problem,” Sadar says. “It’s metabolized differently in humans than animals. Our chemist is modifying the drug. Let’s (still) hope we have a blockbuster.”

Sadar is also a director of ESSA Pharma Inc., the publicly traded company producing the drug and raising money for additional clinical trials. B.C. Cancer owns the patent. If the drug proves to increase survival and be of clinical value, B.C. Cancer, lab members and Sadar also stand to benefit. She says the arrangement is not unusual.

Research funders have ranged far and wide, and include the U.S. army, U.S. National Cancer Institute, and Country Meadows golf club in Richmond, which bought medical equipment.

“The public gets skeptical about breakthroughs,” Sadar acknowledges. “I remain very optimistic. It’s my life’s work.”

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Prostate Cancer: Life, Death and the Unknown

A five-part series

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Part 2: [Early detection and the PSA test controversy](#)

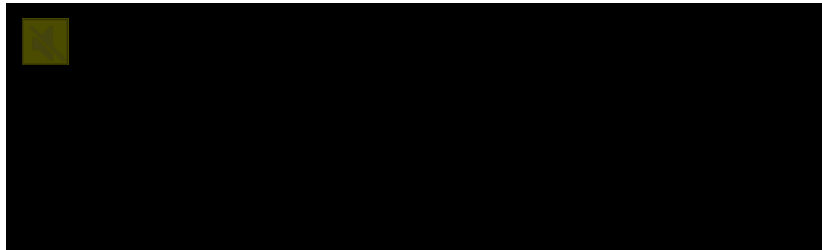
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