

# **Keynote Luncheon**

**William Catalona, MD**

**Northwestern University**

## **I. Translational Cancer Research**

Translational research is distinguished from regular laboratory research where you have a scientist in the laboratory working with test tubes to research that would go from the laboratory to clinical practice. There is a major initiative by both the National Institutes of Health and the National Cancer Institute to try to fund and stimulate research where the end result is what it will do for patients.

## **II. Background Information**

In the United States, cancer is responsible for about 560,000 deaths a year close behind heart disease as a major cause of death in the U.S. population. Prostate cancer is the most common cancer in men followed by lung cancer, colorectal cancer and bladder cancer. In women, breast cancer is the most common cancer. Both account for roughly the same percentage of cancers, about 25%. One in six men will face the diagnosis of prostate cancer in his lifetime, and anyone who has been diagnosed with prostate cancer very quickly realizes that it is a big fraternity. With the introduction of PSA screening, the incidence of prostate cancer went way up, and now it has leveled off at a higher level than it was before PSA was introduced. In terms of deaths, prostate cancer is the second leading cause of death from cancer in men. By far the leading cause is lung cancer. Lung and colorectal cancer rates are coming down, but the death rate that has dropped most dramatically is that of prostate cancer. More men die from cancer than women, and in terms of the war on cancer, the American Cancer Society has looked at the overall cancer death rate, how rapidly it was rising, and where it would now be if we had not introduced some of our screening techniques. There has been a little bit of a win in that war against cancer, and it is greater in men than it is in women. When you are dealing with cancer, early diagnosis is a good idea, and it saves lives. It allows for better treatment results.

When I was a medical student, more than half of the men with prostate cancer had metastases when they were diagnosed, but now nearly 90% of men diagnosed with prostate cancer have localized disease. Very few have metastatic disease at the time of diagnosis, which is largely due to PSA testing. The percentage of men that have PSA testing, however, is a little over 50%. Death rates related to prostate cancer are falling in places where it is actively treated aggressively with surgery and radiation, and where PSA testing is not utilized the death rates are continuing to rise.

## **III. Latest Guidelines for PSA Testing**

The National Comprehensive Cancer Network indicates that “PSA testing is effective and needs to be more rigorously conducted in high-risk men.” A study from Sweden showed

that a single PSA test taken before age 50 gave powerful information about the man's likelihood of developing prostate cancer later in life. The prostate biopsy should be considered in any man whose PSA is higher than 2.5 especially if it seems to be going up every year greater than 0.35. The Preventive Service Task Force has recommended against PSA screening in men over the age of 75, and I think that this is a problematic recommendation. In the 2010 NCCN Guidelines, they say "Screening in men over 75 years should be considered individually." Additionally, if a man has a rising PSA, it is nice to know why, but one does not have to go on to treatment. "It is neither the intent nor the suggestion of the panel that all men diagnosed with prostate cancer require treatment."

#### **IV. Active Surveillance**

The uproven hypothesis of active surveillance is that it may reduce over treatment while retaining the option for curative treatment if the cancer is progressing. In the Toronto active surveillance update, 47% whose cancer was found to be progressing were free of tumor recurrence after five years, but less than 50% had cancer that was still contained in the prostate at the time of surgery.

According to the Swedish watchful waiting series with 20 years of follow-up, almost 50% died of prostate cancer.

In the Johns Hopkins program, which is the most strict active surveillance program in the country, of the patients who failed active surveillance and required surgery a third of them had cancer that had already extended outside of the prostate gland, 15% had positive surgical margins, and 6% had seminal vesicle invasion and lymph node metastases.

#### **V. Familial and Genetic Factors**

Prostate cancer certainly does run in families. To date, about 31 genetic variants have been identified that exist in the population, and people who carry a larger number of these are at a greater risk for having prostate cancer. In translational research, we try to identify these risk alleles and put them together to create a clinical test that would improve our ability to identify men with prostate cancer and especially men who have the more aggressive forms of prostate cancer. Additionally, anybody who has any type of cancer is slightly more susceptible to get other types of cancers.

A very controversial issue is whether genetic factors determine prostate cancer aggressiveness, and I'm sure that they do though there are some research groups that say yes they do and others that say no they don't. The most important goal right now in prostate cancer research is to identify tests for aggressive prostate cancer. The Prostate SPOREs Genetics Working Group is a resource for identifying genetic factors that may differentiate aggressive and non-aggressive prostate cancer. When we discover all 100 of the high-risk alleles, it will allow us to divide the population into independent populations with a little bit of overlap.

## **VI. Pipeline**

In the past month, the FDA has approved the immunotherapy Provenge for prostate cancer. There is a new chemotherapeutic agent that has been approved for prostate cancer, and there are a number of other drugs that are pretty far down the pipeline and will probably become available as well. One of the things in development from Northwestern is a nanotechnology PSA test, which is 300 times more sensitive than anything that is available commercially. It redefines “undetectable” PSA and biochemical recurrence after radical prostatectomy. We are not allowed to give patients information until we are sure it is valid, which requires FDA approval. We wouldn’t want a patient to go out and get radiation therapy unnecessarily on the basis of a nanotechnology assay that wasn’t accurate. It will be a couple of years at least before that would be commercially available. The Pro-PSA assay has been approved in Europe and is under review by the FDA. It’s a more accurate PSA test, and it appears to be more useful in detecting the aggressive forms of prostate cancer. It is helpful in identifying the patients in an active surveillance program whose cancer is going to progress. A chemical has also been identified in soy protein that prevents prostate cancer cells from spreading. It decreases the genes that cause cell motility. That will be worked on in the future, and it may be a way of preventing the prostate cancer from spreading throughout the body. The sub-protein is called Genistein, and the real active ingredient is a small part of that.

## **VII. Questions**

### **1. Supplements and Diet**

#### **Participant**

I’ve read that when soy is introduced to an American in his or her sixties, it isn’t going to work like it has in Asia. Is there any research to support that?

#### **William Catalona, MD**

We have an IRB-approved protocol right now, and we are soon going to be giving men who are coming in for surgery this supplement. We have some preliminary studies looking at biochemical markers that look like it is doing good things.

#### **Participant**

Going back six or seven years, we believed that vitamin E and selenium would be great cancer-preventing agents, but we saw ultimately that too much selenium wound up causing diabetes and a whole host of other things. We are now talking about the introduction of more vitamin D, 5-ARIs and Genistein. How do we know that we are doing good?

#### **William Catalona, MD**

We don’t. When my patients ask me what they should do about their diet and supplements, I tell that that a heart-healthy diet is also a prostate-healthy diet. In terms of soy, people have been eating soy for thousands of years, and I don’t think there is an indication that it will do anything bad for them.

## **2. Risk**

### **Participant**

When we talk about risk assessment, where would you put a T1c with a Gleason of 8 or 9?

### **William Catalona, MD**

T1c indicates a patient whose prostate feels normal, which is the most favorable state. Gleason 8 or 9 indicates that it is highly aggressive. It would appear to be a potentially highly aggressive tumor that has been detected early before you can feel anything.

### **Participant**

How do you feel about women having their breast removed when they don't have cancer?

### **William Catalona, MD**

I think you are probably referring to women who have had the breast cancer mutation test. The genetic markers that I was talking to you about are called low penetrance markers. The more of these markers that a man inherits, the greater his risk of prostate cancer. There are some high penetrance markers like BRCA-1 and BRCA-2. If a woman carries those markers, she has nearly a 100% chance that she will develop breast cancer, ovarian cancer or some other type of cancer.

### **Participant**

If one has an aggressive cancer without much PSA, would you advise getting a prostatic acid phosphatase test?

### **William Catalona, MD**

We do that in patients who have aggressive prostate cancer. If they have a high Gleason grade, I also measure the acid phosphatase.

### **Participant**

If someone has radiation first, what could they follow that with?

### **William Catalona, MD**

You can have radiation after surgery, but you can't really safely have surgery after radiation because the radiation tends to damage the blood supply to the tissues. They don't heal as well, and the complication rates are ten times higher.

### **Participant**

If you are the first in your family and there is no history of prostate cancer, what are the odds of your brother having it? Also, what are the odds of your granddaughter's sons having prostate cancer?

**William Catalona, MD**

They are probably the same as the general population, but it really depends on what your family pedigree is. If your father had no brothers and your mother had no sisters, who knows what your grandparents had because people didn't know what they had in those days. In that case, having a negative family history is a lot less informative. If, on the other hand, your father had six brothers and your mother had six sisters and none of them had prostate cancer or breast cancer, you would think that the risk would be the same as the general population. We traditionally thought of a father passing prostate cancer to a son and a mother passing breast cancer to her daughter. It is possible for a father to pass breast cancer susceptibility to his daughter and for a mother to pass prostate cancer susceptibility to her son.