

MAN TO MAN – SARASOTA

Prostate Cancer Patient Support

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Man to Man

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Man To Man – Sarasota is a not-for-profit group organized to educate and inform its members on matters concerning prostate cancer. The organization does not dispense medical advice. Meetings are normally held on the fourth Monday at 2 p.m. in Sarasota Memorial Hospital although exceptions to this schedule do occur. Call the number above for further information.

Dr. Winston Barzell, a urologic surgeon here in Sarasota with a national reputation, has come to speak to our January Man To Man meeting. Today his topic is the use of cryotherapy in the treatment of prostate cancer. Dr. Barzell:

Introduction

We want to talk to you today about cryosurgery. Also, I'm going to talk to you about mapping – 3D mapping. I want you to understand that in our office we do all the procedures, whether it's radical prostatectomy, seeds, radiation, robotic or cryosurgery. I am going to emphasize this a few times. There is no best treatment for every patient. These are not competing treatments, where one or another is the best treatment. Every patient, when you consider age, co-morbidity (which means other illnesses), the type and extent of cancer, has two or three choices that are the best. Sometimes the best option is a radical robotic. Sometimes the best option is seeding. Sometimes the best option is cryo. So what I am going to do today is try to explain to you where cryo fits in this armamentarium that we have. I think we need to shy away from someone who is wedded to one treatment because they tend to put everybody in the same slot. So, it is important to know that there are various options for prostate cancer. And, the reason that there are various options is that they all work. Unfortunately, the answer to the real question that patients need to know is not available. None of the studies has put one treatment against another in a randomized study. That's the only way that you would know which is better.

It's hard to randomize studies with prostate cancer. The reason being, if you have prostate cancer, it's the rare patient who is going to say o.k., I'll get randomized. You tell me which treatment comes up on the computer and I will do it. The patient usually wants to understand all of the options. They'll choose one that fits them. All of these studies that you see comparing one treatment to another are based on historical reviews. And, any smart statistician will tell you that those are usually confounded with all sorts of potential errors. The reason is that they were based on retrospective studies. When they do prospective studies a lot of our impressions are no longer true. So I just wanted to start and tell you that I am not

saying that cryo is by far the best treatment. But for certain patients it is.

When Does Cryo Fit In?

The topic today will be two-fold. The first thing is I am going to talk about is where cryo fits in the treatment of prostate cancer. This is early prostate cancer (visual slide), and this is advanced prostate cancer. There is a spectrum. And it turns out that cryo actually works quite well in the early cases, where we can do a lumpectomy. I am going to show you where, I think, it is the best treatment for advanced cases; where you have a lot of cancer, such as with a high Gleason score. I'm going to show you that it fits in the early and in the late stages. In the middle, cryo is a good option, but so are the other treatments. I think where cryo comes out ahead is in the very early cancers and in the very late cancers.

The other thing that I am going to talk to you about is 3D pathologic mapping. I know this wasn't on the roster. But, this is important in the management of prostate cancer. It's important in being able to do a lumpectomy. This is something that I started back in 2001 here in Sarasota, and now it is getting wide recognition. I have been asked to speak on this topic to the American Urologic Association in May of this year and to go to a consensus conference in Orlando. I also just made a presentation to the Society of Urologic Oncology, and will share some of this with you, and how it affects treatment.

Cryo-therapy

So, let's talk about cryo-therapy. Cryo is the Greek work for cold. Therapy is healing. So, it is really cold healing. The advantages include no major incision, no major blood loss, and no radiation. It destroys cancer cells during the procedure. The dead cells are re-absorbed by the body and then some of them are urinated out. Usually it's an outpatient procedure unless done late in the day, in which case it is an overnight stay. But most of the patients are outpatients. There is rapid return to normal activity. And it is, as you have heard, a repeatable procedure unlike radiation, where if it fails, you can't radiate more because the body reaches toxicity. The way we do it is, we use an ultrasound in the rectum to visualize the prostate which tell us where to put the needles. We put six to eight

cryo-probes which deliver Argon gas at minus 40 degrees. Actually Argon gas comes out at minus 100° at the tip. We like to get the prostate and the surrounding tissue to a minus 40°C. And we do a double freeze. We freeze it, thaw it, and freeze it again because they found that cell kill after just one cycle is not enough. You can visualize the process. You can see the ice form. Computerized imaging tells you where to put the probes, with each probe giving you an oblong pear-shaped, if you will, ice ball. The initial technology did not have a warmer in the urethra and produced significant complications. In fact, cryo got a very bad rap about 10 to 12 years ago. Before they had the urethral warmer it used to be a real problem.

The other thing is there was really no way to protect the rectum and sometimes the rectum got frozen. So what we have now is a urethral warmer that warms the urethra. So that while you are freezing the prostate, the urethra, which is the passage that you urinate through, stays warm and healthy. That's why you can get the catheter out and get back to normal earlier. We also put saline between the prostate and the rectum and that protects the rectum. So, in the last five years cryo has become a much safer procedure and that is why we are doing it. We knew that you could kill cells by freezing them. You can imagine if you were up North and it was minus 40° just how long you last out there. And we do this to the whole prostate. You are basically getting a complete destruction of the prostate. So, we know ice works. We just didn't know how to protect the normal tissues and make it safe.

Various Ways to Use Cryo

There are two ways to freeze the prostate. You can freeze the whole prostate or you can freeze just part of it. So, let's talk about who is eligible to have freezing of the prostate. These are the primary cancers. Primary, being cancer just diagnosed. Another example relates to patients with recurrent prostate cancer after radiation or seeds, with moderate risk disease, where the goal is to completely ablate the gland. As noted earlier, we place six to eight probes and totally freeze the prostate and the surrounding tissue beyond the gland. This is why I think cryo works well in advance cases because you are not only just freezing the prostate but you are freezing the tissue around it.

The focal prostate freeze is where we are only freezing half the gland. The reason we freeze half the gland is that this way we can preserve the neurovascular bundle. This is the so-called lumpectomy. We are talking about primary or recurring cancer confined to one side. You only freeze one side. The incidence of incontinence is very low, with a significant chance of preserving potency. Reports say that 87% are maintaining erectile function. I think that's overstating it. I believe if you do one side there's probably a 50-60% chance of preserving potency. That is a little high. I just want to make my case that cryo is good for advanced cases.

Interesting Statistics

Dr. Duke Bahn, who is in California, has done hundreds and hundreds of cryo's, probably 800. He is one of the biggest cryo proponents who looked at his cancer survival statistics which showed little difference between lower-risk, moderate-

risk and high-risk disease. In every other treatment it's the high risk patients that just don't do as well. It doesn't seem to be the case with cryo. We are not sure why. But the following may be one explanation.

We know when we do a radical that 30% to 40% of patients have a positive margin. And this is why you can have a radical prostatectomy and 10 years or 15 years later you have a PSA that's rising because the knife cannot go outside the prostate. I've done probably 2000 radicals in my life. I started doing them in 1985. I certainly have huge experience, but every now and then you get fooled. You think the patient has minimal cancer, and you go in and find he has a lot of cancer. And indeed the margin is positive. A number of my patients have had recurrences and they have had to have radiation. So that happens.

With cryo, if there is cancer outside the capsule, because cryo goes outside the gland and freezes outside, is why you do not see the statistical fall-off as with the higher-grade cancer. This is just a theory. So, what I have said so far is that cryo is probably no better than any other treatment if you do whole gland treatment for low-grade cancers or moderate-grade cancers; but, for higher-grade cancer it seems to do better.

What Is Considered High Risk?

We define low-risk as PSA under 10 with Gleason 6 or less, and no more than 50% involved in any one of the biopsies. High-risk is Gleason over 7, PSA over twenty, palpable lesion that is obviously outside of the gland when you do a digital rectal; therefore a stage C. This is considered advanced cancer. And, intermediate is between. So, the high-risk cancers are patients who have a very high risk of failing treatment. No matter what you do.

3-D Mapping

I want to now switch for a bit and talk about 3-D mapping. We will get back to cryo. 3-D Mapping is when many biopsies are performed on the prostate. It is used in the diagnosis of patients with proven cancer and in management of patients with established cancer.

Let me give you some historical prospective here. In 2001, Mayo Clinic published an article by Dr. Igel who performed transperineal saturation biopsies. I was very intrigued with this because I had a lot of patients with a rising PSA. I suspected that they had cancer but I couldn't prove it with multiple biopsies. So in 2001 I started doing transperineal biopsies for diagnostic reasons. This past November I attended the Society of Urological Oncology at the National Institutes of Health in Bethesda where they had a panel discussion of what to do with patients with low volume cancer. This is a direct quote from one of the panel members. "We face a dilemma when advising patients on therapy in the absence of controlled trials." If you go to the doctor with a minimal cancer and he says you could do nothing or we could do a radical surgery, radiation, or seeds, it's a hard choice for a patient. Therefore, we do mapping for people wanting focal cryo or lumpectomy.

So, what's involved? It's just like doing a seed procedure where it can be done in the office, but usually done in a hospital, and takes about half an hour. You place an ultrasound probe and visualize the prostate, and whenever you see prostate tissue you take a biopsy. We do anywhere from 70 to 110 biopsies per prostate. When you finish a 3D mapping you are pretty sure that if it is negative the patient doesn't have more than 1 or 2 mm. of cancer, which is not significant. Plus you've mapped the cancer and you know where the cancer is. We divide the prostate into distal and proximal halves. Each half is divided into four quadrants. So, you have eight octants. And each octant is divided into three zones. So you end up with 28 to 32 different zones, and probably do 80 to 100 biopsies. This way you can map the cancer and you can tell exactly where the cancer is in that patient. The reason that this is getting a lot of attention is that a lot of people are interested in doing focal treatment or intensity modulated treatments. I have had people call me from GE and various people that do radiation wanting to know if we can do a map like this of the prostate. We can then give it to the treatment planner, the physicist, and they can put it in the computer. When you radiate your prostate, you would not just radiate the whole prostate with the same amount of radiation. You would do a dose escalation where the cancer is. So, this is the new thing; to do dose escalation. If you have a prostate of 60 grams and you only have two or three spots with cancer, presently we treat the whole gland because we don't know where the cancer is. But if you could precisely locate where the cancer is you can do a dose escalation. This approach is getting more and more interest.

Benefits of Mapping

Let me just give you an example of a couple of patients of how this works. Here is a 60-year-old patient who came with a rising PSA. Between 1999, when his PSA had gone up to 15, and 2004, it went from 15 to 50. During this period he had five sets of truss biopsies. These are transrectal biopsies at a major teaching institution. I cannot mention its name, but it is one of the top three or four institutions in the country. All were negative. Finally in November of 2004 they found one out of 12 had a small focus of Gleason 6 cancer. This didn't fit. How could you have a PSA of 50 and just a small cancer? So, they did a very extensive evaluation including bone scans, CT, MRI's, including a Ferumoxtran 10 Scan (which is only available in this one institution). It is an experimental scan that tells you if your lymph nodes are positive. It is a pretty amazing scan and it is going to be available in the next two or three years. All tests were negative!

I first saw him in February of 2005. At that time his PSA was 48 with 4.1 free. I did a 3D map on him. All the biopsies toward the rectum were negative. The anterior half, the part that the rectal biopsies don't get, was full of cancer. He received conformal cryo for this Gleason 7 cancer which had been sitting in the same anterior zone for whatever – five, six, seven years. PSA kept rising. But the transrectal biopsies couldn't get it. We didn't do much cryo below because they had no cancer. We just treated the upper part of the prostate. I last saw him in September and his PSA was 0.2, down from 50. So

this is an area where 3D mapping really helped show where the cancer is and help treat it.

Here is another patient who came to me in 2003 at age 59. This patient had a small amount of cancer on the left side. I said, you know you should have a radical prostatectomy and not fool with it. You are only 59. He said no. He wanted to have focal cryo. I said I couldn't do that without a mapping. At that time that was a new thing. I was the only urologist doing that in the country, and the world actually. Now, a lot of people are starting to do it. 3-D mapping showed he had extensive, gland confined cancer in the right lobe which would have been missed if we had done cryo on the left side, which was what he wanted, and we would have missed all of this cancer. He would have failed. We ended up doing a radical prostatectomy. So, this is just to show you where 3D mapping can help both in diagnosing the cancer, and then how to manage it.

At N.I.H. in November 2006, I discussed how to use mapping on patients with low volume prostate cancer. What to tell patients who have minimal cancer when they are first diagnosed. If you do mapping, 33% of the patients with low volume cancer can be spared any treatment. Studies show that if you relied on trans-rectal biopsy on individuals with a micro-focus cancer rather than mapping, a 64% false negative rate can be expected. In other words, if a patient has a small amount of cancer and you repeat his biopsy in the office, 64% of the time you are going to miss the tumor. In patients with low volume cancer, Gleason less than 6, 3D mapping enabled the separation of low-risk, clinically insignificant cancer, from the intermediate and high-risk cancers. Treatment can be withheld in the lower-risk group while it can be more appropriately tailored in the high-risk categories.

I want to take it back to cryo to show how the two are related. There is a lot of talk now about the male lumpectomy, also known as focal cryoablation, cryolumpectomy, unilateral, or conformal cryo. If you take a patient who has had radiation and it fails and now you do cryo on the whole gland, the risk of complications is very high because it has already been radiated or seeded. That is too much insult for the patient. So, if you can do just half of the gland, or one-third of the gland, you are much better off. That is why we do a lumpectomy. Then, in the early cases, where a patient comes in with a very small cancer, and he says doctor, I do not really feel comfortable about doing nothing. On the other hand I don't want to have a radical prostatectomy, seeds, or radiation if I don't need to. So this is where you would say, let us see where the cancer is and we will treat that one cancer. That is where this one-sided lumpectomy comes in. Remember I said that cryo is good for the early cases and the late cases. We are talking about the early cases here.

Conclusion

So, it is an alternative to watchful waiting versus whole gland treatment. There is a safety net here because we do PSA's, we repeat biopsies, retreat if the cancer comes back or goes on the other side. This all comes from lessons that we have learned from breast lumpectomy. The aim is preserving function with-

out compromising the results. In other words, can you do a lesser treatment, still get good cancer control, but have fewer problems with urinary function and sexual function. This is what I want to leave with you because it is very important. There is no best treatment that can be universally applied to everyone. A clinician should not be wedded to any particular technology where you only think that this is the only way to go. Remember this quote? If your only tool is the hammer, you tend to treat everything like a nail. We will end it here.

Our speaker for the month of March, Dr. Laurence Klotz, was introduced by Dr. Alan Treiman, as follows: Dr. Klotz is chairman of the Canadian Urology Research Consortium, chairman of the World Urology Oncology Federation, and Editor and Chief of the Canadian Journal of Urology. He has published probably in the hundreds of articles and contributed to all aspects of the urologic literature.

Prostate Cancer in Transition

Thank you for that introduction. My talk today is about the transition of states of prostate cancer inasmuch it has been changing a lot over the last 17 years due to the advent of PSA. That has really transformed the face of the disease. I am Canadian. The Canadian medical system is different from what you have in this country. It's got advantages and disadvantages, and I'm not at all a proponent of how great our system is. It's got some real problems. But, it does have some advantages. One, is that medicine is less of a business. And we have the luxury of dealing with patients without the issue of the finances, and the patient's ability to pay. It is less of an issue in Canada, although we have other problems. For example, we don't adopt new technologies. We have a waiting list and so on.

So, what's happened in prostate cancer? The disease has undergone something called stage migration, which means there has been a shift with this diagnostic test (PSA) to earlier diagnosis of earlier disease in younger patients. Just overall, there has been a general shift to younger age in diagnosis. There has been a shift towards earlier disease of TIC.

TIC means no palpable nodule. And, TIC in 1990 was only a small percentage. It is now about two-thirds of newly diagnosed patients with a highly elevated PSA. Their prostate basically feels normal or benign. It could be enlarged. It is now rare to see a patient with metastatic disease at the time of presentation unless they have not seen a doctor at all in the last period of time. The average PSA at the time of diagnosis, which used to be relatively high, has come down steadily. So, for example, proportion of PSA in the range of 4 to 10 has increased dramatically. That's now, by far, the commonest group. So, everything has come down. Curability has improved. Mortality has dropped by 25% in most constituencies. It's really a dramatic change.

There's a major debate over why that is. I think it is in part due to screening, and early detection. But, there's a cost. The cost is that a lot more prostate cancer has been identified and it has been shown, for example, that with wide spread use of

PSA screening you find a lot of disease that might not be clinically significant. PSA screening has resulted in the disease being much more curable at the time diagnosis, and we've got this falling mortality to prove it.

Interesting Study Observations

A study done on men in their 30's and 40's, who succumbed to trauma, had serial biopsy sections performed on their prostates, whereupon many were found to have micro foci prostate cancer. This is not a cancer like other cancers. These men, the majority of them, would never have known they had this. They would have lived the rest of their lives, barring other problems, with these micro foci, where the mortality likelihood is only somewhere around 3%.

This incidence of micro foci of prostate cancer occurs in all races and all regions in the world. So, for example, the Chinese have a mortality rate that is only 1% of the North American rate. One in 100 has as much of likelihood to die of prostate cancer if you are Chinese in China, compared to Caucasians, and particularly African-Americans, living in North America. They all have the micro foci but these don't seem to progress in China; whereas in Canada, Australia, United States, and Scandinavia, something is happening to cause progression of these micro-foci of cancer. So, here is a phenomenal natural history experiment because you have differences in genetic, environmental, and in micro-nutrient ingestion (diet), that are probably responsible for this huge difference between Asia and the West in terms of prostate cancer progression. Now, it was thought for the first ten years of the PSA era, which was 1990 to 2000, that although it was known that many had these micro-foci prostate cancers, that it didn't cause the PSA to go up. If the prostate was biopsied, you were unlikely to find these microscopic foci of cancer.

The Prostate Prevention Trial

The Prostate Prevention Trial was the largest intervention trial ever done in the field. Eighteen thousand men, who were randomized between Proscar/finasteride (a mild hormonal agent that causes shrinkage by reducing level of the active form of testosterone), and a placebo, were biopsied at seven years after they were entered on the study. Now, the surprising thing is that although PSA has been around now for 15 years, no one had actually biopsied a large group of normal men. That was the first time it was done. The striking finding is that one in four men on placebo (these are completely normal men, normal PSA, normal everything), were found to have prostate cancer. So, what this showed us (and this is high quality evidence because it is a huge, carefully done trial by a national cooperative clinical trials group), that the strategy of biopsying men results in finding a lot of these micro-foci of cancer. The other striking thing from the trial, (a strongly positive trial), was the cancer detection rate dropped by 25%. So, Proscar does work to prevent prostate cancer.

Perspective on Current Strategy

A lot of patients who are diagnosed with prostate cancer using the current strategy which is mild elevation of PSA, leading to

a biopsy, are found to have cancer that may not really pose a threat to their survival if it was never diagnosed or treated.

There is some other data to confirm there is a low grade cancer; more specifically, Gleason 6 or less (that's the grade or microscopic appearance), PSA of 10, or less and no large palpable nodule. This is now roughly half of newly diagnosed patients who fall into this group because of the staged-migration effect. So, about half of new patients fall into favorable risk category. A Gleason 6 in a 60 to 64-year-old followed for 20 years, has about a 25% chance of dying of prostate cancer without treatment. That means a 75% chance that the patient will not die of prostate cancer. Now, a lot of them die of other causes because obviously nobody lives forever. Now, with higher grade cancer you die of prostate cancer if you live long enough. So, once you are up to Gleason 7, 8 – 10 you're very much at risk. That's why PSA screening is a good thing. Because you find these cancers earlier and you can treat them.

In a Swedish study they managed to randomize more than six hundred patients between radical prostatectomy and no treatment. Now, actually you think about how amazing an accomplishment that is. You take a patient who has just been diagnosed with prostate cancer, and you say "we are going to flip a coin, heads you have radical prostatectomy, tails, you have nothing (watchful waiting). It's not up to you or me". Most patients (certainly most Americans), would rebel at that. It has been tried. It hasn't panned-out in the United States very well. But, they did it in Sweden. It showed a dramatic reduction in cancer mortality at 10 years with radical prostatectomy. So, for the right patient, the surgery works.

We've had some other interesting observations that you might find interesting. Vitamin D is a very powerful vitamin. It looks like it has some favorable activity in prostate cancer. Toronto Canada at least is hot and sunny in the summer and miserable in the winter. So, we looked at Vitamin D levels and they correlate with the PSA fluctuation. We found that the PSA went down in the summer in these patients and it went up in the winter.

Hormonal Therapy

I'm going to now switch gears and talk a little bit about hormonal therapy. About one-third of patients who are treated radically, in spite of the best efforts, still have a recurrence. Typically the PSA starts to go up. And that's the sign of PSA recurrence. We've learned in the last few years about what you can expect with these patients. It turns out that not all patients who have PSA recurrence are at risk from dying of prostate cancer. It's a very diverse group. You can use some parameters like the PSA doubling time, and the Gleason score, which is the other important clinical feature of prostate cancer that's predictive, allowing you to really stratify patients according to the risk of prostate cancer death at 10 years. The bad group is where the doubling time is less than three months, usually encountered with higher grade cancer. Even with lower grade cancer almost all of these patients die of prostate cancer within 10 years. In contrast, the group which has a slow doubling time of nine months, or in the range of a

year or more, have almost no chance of dying of prostate cancer in 10 years.

Hormone therapy usually means using drugs that are called LHRH agonists. Zoladex is the one that is most widely used in the United States. The other one is called Lupron, and there are a number of others that lower the level of testosterone in a man's body, basically close to zero. Prostate cancer is dependent on the male hormone for growth and survival. The cells that are hormone sensitive when the hormones are withdrawn mostly die or go into a dormant state. So, that has been the mainstay of treatment for advanced prostate cancer now for 65 years. There are a lot of questions about it. One question is does it matter when you treat the patient. We still don't really know the answer to that. There are a number of studies. You can see basically they're just about all positive; comparing early to late hormonal therapy that show patients are better off being treated before they have metastatic disease that's symptomatic. If you wait till the disease has spread and is causing symptoms, usually bone pain, there's a decrease survival with that strategy. But what we don't know is, short of having metastatic disease, if the PSA is going up, when the hormone therapy should be started. So, this is something that might be of interest to some people in the audience. I thought I would review it briefly.

One of the problems is that with hormone therapies, the loss of testosterone has a lot of side effects in men, particularly long term. It's understandable that losing testosterone, you'd lose libido, or interest in sex, you would get an erectile dysfunction, and some decrease of energy. But, you also see a lot of other metabolic and constitutional alterations; osteoporosis can be accelerated, loss of muscle mass, there is something called the metabolic syndrome which includes things like hypercholesterolemia, decrease glucose tolerance, and hypertension, all associated with loss of testosterone in men. There are also cognitive changes. So, regarding what is good for prostate cancer may not be the best thing for the patient, particularly if they are not at risk of dying of prostate cancer.

There have been only two studies that really address the issue of what the PSA should be when you start the treatment. There is one that showed overall no difference between early and delayed treatment, unless the doubling time was less than a year, or the patient had high-grade cancer. In these patients the PSA was somewhere around 5 to 10 when treatment was initiated. There was no advantage treating earlier. There was only advantage in those patients with these high-risk features. Then another study relevant to this is from Europe; about a thousand patients. This one randomized between immediate and deferral hormonal therapy. Essentially this showed some benefit in the patients treated early. But, for reasons that aren't clear most of that benefit was in non-prostate cancer deaths. Not so much in prostate cancer deaths. But the other thing it showed is that the PSA threshold for treatment in this randomized study ... the PSA point where it looked like the patients were having benefit in terms of survival in men under age 70, was a PSA in the range of 20. PSA that was more than 20, they benefited. Less than 20, they didn't benefit. In older men

above 70, it wasn't until the PSA hit 50 that they started to show a benefit compared to deferred treatment. That is the best data that we have on this question at the moment. Now, if there are men in this audience who have been treated for a rising PSA with hormonal therapy, my bet is that they were treated long before their PSA was 50. There's been a real trend to early treatment of hormonal therapy. I don't think it can be justified by the data anymore. So, the approach I use now is for the high grade patients or the short doubling time less than a year, which is about 25% of these patients, you treat when the PSA is somewhere between 5 and 10; but for all the patients with lower grade cancer, with doubling time of more than a year, you should wait until the PSA is somewhere between 20 and 50, depending on the age of the patient.

Another point I am just going to address briefly is intermittent therapy. Again, the same problem exists in trying to reduce the impact of treatment without compromising patient survival. There are a number of reasons for considering intermittent therapy. There is evidence that testosterone may actually have a favorable effect under some circumstances in prostate cancer. It's actually a minority view, and considered very radical, that very high doses of testosterone might be favorable. In advanced prostate cancer, that's not as totally off the wall as you might think. There is some pre-clinical data from the lab, that testosterone at high doses can shut down prostate cancer growth. Now, as some of you might know, testosterone is the pre-hormone. It is converted to dihydrotestosterone which is the active one. Dihydrotestosterone causes proliferation and cell growth. Testosterone may be the one that is actually causing the inhibitions. That's an area of active research at the moment. So, the ideas of intermittent therapy is one, to reduce side effects, two, to reduce the cost of the drug, and three, maybe to have the testosterone come back is a favorable thing. One of my claims to fame was that the first article on intermittent therapy was written by me. This is now 20 years ago.

~~~~~Note: The opinions expressed herein are not necessarily those of the American Cancer Society ~~~~~



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The final point for those of you who may be on hormone therapy or contemplating intermittent therapy; you can really prolong the duration of 'off treatment' interval by using a drug called Proscar or Avodart which is widely used to shrink the prostate in men who have benign prostatic enlargement. But, it also slows the recovery of the PSA. Just keep in mind about seven times as many men harbor prostate cancer as die of it. In the patients treated with hormonal therapy with rising PSA, using the doubling time, and the grade, to separate out the ones that are really at high risk from dying of the disease, treating them aggressively, and being much more conservative both with timing of treatment, and the duration of therapy.

**A special thanks to all of you who generously contributed to the Man to Man Relay for Life. A total of approximately \$4,000 was raised.**

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