Prostate Cancer Canada Network - NEWMARKET

Volume 18, Issue 2, October 15, 2013

A support group that provides understanding, hope and information to prostate cancer patients and their families

Our guest speaker for the October 17th meeting is Dr. Andrew Matthew, Dr. Matthew last spoke to our group in May, 2008 when he helped us "Navigate through the emotional side of prostate cancer." Dr. Matthew is a Co-Founder and Director of the Health Psychology Clinic. He is a Staff Psychologist at Princess Margaret Hospital in the Department of Surgery, and the Department of Psychosocial Oncology and Palliative Care. He is also principal developer of several hospital-based counselling programs for cancer patients. His clinical and research work also includes cancer prevention programming, treatment decision making, sexual rehabilitation, intimacy, quality of life, and survivorship. Dr. Matthew's goal is to use his knowledge and experience to improve the lives of individuals, couples and families confronting the challenges of serious illness beyond the hospital walls. To that end, he also provides assessment and treatment for individuals and couples in crisis and those seeking help because of trauma, grief and bereavement, depression, anxiety, or addictions. October 17th is a meeting you don't want to miss.

Meeting Date: October 17th, 2013

Place: **Newmarket Seniors Meeting Place,**
474 Davis Drive, Newmarket (Side Entrance)

Time: **6:30 pm to 9:00 pm**

Speaker **Dr. Andrew Matthew, Senior Psychologist**
Princess Margaret Hospital and the University of Toronto,

Subject: **Prostate Cancer and Survivorship**

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The Newmarket Prostate Cancer Support Group does not recommend products, treatment modalities, medications, or physicians. All information is, however, freely shared.

September Speaker Notes . . . Dr. Ian F. Tannock, Professor of Medical Oncology, Princess Margaret Hospital and the University of Toronto,

Subject: Open Forum on Prostate Cancer Treatment

Our guest speaker at the September meeting was Prof. Ian Tannock, MD. Professor of Medical Oncology and Medical Biophysics at Princess Margaret Hospital. He was previously Chief of Medicine at PMH and has been Professor of Medicine and Medical Biophysics at the University of Toronto since 1989. Prof. Tannock pioneered the use of pain and quality of life endpoints in clinical trials, especially for breast and prostate cancer. His talk focussed on patients whose cancer has metastasized and spread to the bones Here is what he had to say.

I'm going to be talking, tonight, about men whose cancer has spread to other parts of the body. Its a small percentage of those who have a diagnosis of prostate cancer but it is nonetheless quite a large number of men. I'll try to explain in layman's terms as best I can but, if you have a question, please feel free to interrupt.

I'd like to base this on a hypothetical patient but one who is very typical of men that I see in my clinic at Princess Margaret Hospital (PMH). I'll call this patient Mr. Rodrigues, who is 68 years old with a 3-month history of pain in several bones. His rectal examination shows a hard and enlarged prostate. He has a needle biopsy which shows he has prostate cancer when it's looked at under the microscope. He has a Gleason grade, which is a measure of how angry the disease is. His is between 8 and 10. Very few men have a Gleason of less than five but five or six is usually a slower disease, whereas a Gleason of 9 or 10 is more an angry disease which appears to be more aggressive. It isn't very common for men to present already with disease spread, but it does happen. Mr. Rodrigues could also be a man who had had prostate cancer diagnosed and treated locally with surgery or radiation and had gone on to develope these secondary issues in the bone. His PSA level is very high, 245 where the upper level of normal in men is about four.

Some of you, probably many of you, will have had a bone scan. Normally a bone shows gray on the scan but cancer shows up as black spots. Each of those spots is a secondary tumour. Because those tumours are invading the bone, the commonest cause of pain in men with prostate cancer is from involvement with the bone. Although, in prostate cancer it usually lays down more calcium, so the bones appear thicker, it does weaken their structure, so fractures and other complications can occur.

What is the primary treatment of a man like Mr. Rodrigues, who has prostate cancer spread? I'm not talking about primary treatment now for someone who has localized prostate cancer, which would be surgery, radiation, or sometimes simple observation. The treatment comes from the knowledge that prostate cancer is stimulated by male hormones. The prostate is hormone dependant, stimulated by male hormones. The primary treatment is to reduce the level of the hormones and the technical term for male hormones is androgens, especially testosterone, which is the main one in men. So the strategy is to reduce the level of those hormones in the blood. This is known as ADT, which stands for Androgen Deprivation Therapy, which takes away the stimulation that is needed by those prostate cancer cells. For a man who is receiving first treatment for this, it's remarkably effective. More than 90% of men will respond very well to initial treatment with any strategies that reduce hormone stimulation of the prostate. By respond, I mean that the symptoms such as pain, the pain will get better, the PSA will come down but cancers are, unfortunately, growing cleverer. They can learn to become resistant to every treatment that we give to them and that is the problem. The average time for which men will respond to initial therapy, which is ADT or lowering testosterone levels is about one and half to two years, that's the average but it is a very broad distribution. Some men may respond hardly at all and at the other end of the spectrum, it's not that uncommon to see men who have been treated for a decade and only then start to have further problems. It's variable but the average time is 1 1/2 to 2 years.

So, what are the options for Mr. Rodrigues? Well, there are several ways in which you can reduce the levels of testosterone and other male hormones in the blood. One option which was used until recently was removal of the testicles (orchiectomy), which are the source of the testosterone.

Most men actually don't like having their testicles removed so, largely, that has been replaced by drug treatment. Many of you who have received hormonal treatment, have received injections at one month or three months or sometimes even four or six months intervals with Zoladex or Lupron and there are various others, too. They all do the same thing, lower the testosterone level in the blood. If you use agents like Lupron or Zoladex, they usually give a pill, like Casodex also. Initially these treatments can raise the testosterone before it goes down and raising the testosterone can stimulate the prostate cancer and can cause a flare, like an increase in pain. But that's only very transient. So that's what most of the patients, most of the men, who are receiving hormone treatments in Ontario are getting. You can actually use Casodex alone. It isn't quite as effective, it doesn't last for as long but it does have the advantage that, in men who are sexually potent, it may allow them to retain that, whereas usually the injections don't.

The one phase that we went through about 10 or 15 years ago was using these agents together but that didn't help things. Then, more recently, we moved some people to intermittent therapy. Instead of treating continuously, we treat for a while, the PSA goes down to a low level, we stop treating, let it come up and then we treat again. Those people who are receiving drugs like Zoladex or Lupron are getting it every three months and some men have been getting that every three months for years and years and years. The purpose is to keep the testosterone low but, particularly in older men, once you've been on these agents for a year or more, the testosterone actually stays low quite a long time. Sometimes many, many months. It's inconvenient to keep having these injections and they do have some side effects that are different than having a low testosterone. We have one ongoing study, which is almost complete, where instead of just giving it every three months, we ask men who are volunteers to use the testosterone in the blood as a guide. Instead of keeping injecting, injecting, injecting, (these drugs are very expensive) we started treating them only when the PSA comes up. We already know that we can do that.

These agents do have side effects. You can imagine the side effects if you think of being the opposite of Lance Armstrong. Athletes take hormones, male hormones, to boost muscle, strength, bone density, etc. Some of these effects are doing the other thing, just the opposite of that. First of all, if you reduce testosterone, then you do create a state of impotence in men who already have that from their treatment. You may get some breast swelling or a tenderness, which can be annoying. I know that your spouses will be very sympathetic but many men go through what has been described as male menopause, where you get hot sweats, night sweats, hot flashes and so on. Very familiar to women in their 50's or early 60's. Loss of muscle mass and bone can occur and all men should certainly be taking vitamin D for sure and should have a reasonable amount of calcium in their diet. The best treatment for preserving bone and muscle is exercise. Exercise is pretty much good for everything. I would far rather have somebody who is exercising than have them on medication. The more you can keep your body fit, the less you will lose muscle or bone. Use it or lose it. You can get a little bit anemic and you can become a bit tired or fatigued. More recently, this has only come from studies of large populations, there is an effect to slightly increase the incidence of things like heart disease and diabetes. It's not noticeable usually because these are relatively rare events and it increases the probability of that event by about one and a half times. If it's already there and you go from one and a half percent to half a percent, it can easily be missed. But studies of populations have shown that this can occur and of course, when that occurs, those are very serious diseases.

An overview of survival in 27 trials, including 8,000 prostate cancer patients over ten years, showed no significant benefit of having maximum androgen blockade (Zoladex and Casodex) over androgen suppression only (just Zoladex). With maximum androgen blockade there is an increase in toxicity and considerable cost. Other studies have also shown that survival and delaying the progression of the disease indicate a similar result. People often ask me about using intermittent treatments, "What would you do if you were me?" Assuming you have a good initial response, my response would be, "Yes, I would have this treatment but it has to be that good initial fall in level of PSA." The advantage is you have less time on these injections so, on average, people spend more than half their time free of the injections, free of some of the side effects and a marked decrease in cost. Although the costs are covered by the province, it's still a saving to our health care system. To summarize: Intermittent therapy is similar to continuous therapy in terms of expectation of survival and also delaying progression of disease.

So we come back to Mr. Rodrigues. He gets Zoladex every three months. He is given Casodex for ten days to prevent a flare of his disease and, true to form, he becomes pain free within a couple of weeks.

This treatment can be quite magical. A year later his PSA has fallen from 245 to 1.2. That's not at all atypical of the dramatic responses that occur. However, 15 months after starting, his PSA starts to go up again, to 5, at 18 months it's 20 and at 21 months he's starting to have some pain.

This is the course we see. The timing initially is extremely variable. Sometimes this happens after three to six months, on average after 18 months, sometimes even after five or ten years. Usually it occurs eventually, unless people succumb to something else. At that time when the pain is increasing, it is appropriate to add in Casodex.

One of the reasons that Mr. Rodrigues may be failing this treatment is that the testosterone is not the only source of male hormone in the body. In the normal man, about 85% of the available hormones are testosterone made in the testes. About 10 to 15% are different male hormones made in the adrenal gland, which sits above your kidneys and those are converted to testosterone. Zoladex or Lupron don't do anything about that residual male hormone. Casodex works differently, it counters the effects of the male hormone at the cell level, so sometimes adding it in then can lead to a secondary response. That happens in about 30 to 40% of men but the response is usually shorter. Mr. Rodrigues does that and in this case the response is about six months. His PSA decreases and his pain improves but, about 6 months later, he again has a rising PSA and pain. The Casodex is stopped and he again has a transient response for about 3 months. Strangely enough, sometimes with a drug like Casodex it initially works as a good treatment, it inhibits the effect of those male hormones but strangely, it can even start stimulating things. Fairly rarely about 20% of those who respond to adding Casodex can actually have another response to stop it.

So, summarizing secondary hormonal therapy, about 90% of men respond to removing their testicles or to drug treatment for an average of one to two years. About 30% respond to subsequent addition of an anti-androgen like Casodex for a few months. About 20 - 30% of those who respond to the addition of an anti-androgen will respond to its withdrawal. Some men will still respond to additional hormone therapy. So, until recently, we used things like estrogens (female hormones), and we used a drug called ketoconazole, which is an antifungal agent but it also inhibits the making or synthesis of male hormones. Then, more recently still, we have new drugs that some of you may know of, such as abiraterone and enzalutamide which are even more effective but, at the moment they are only approved for use after chemotherapy in this province. These drugs are hugely expensive. Almost all new drugs cost about $5,000 a month. It's ridiculous but that's the cost.

In answer to a question, Dr. Tannock clarified that if you have an orchiectomy you would never need to take Zoladex or Lupron injections. A second question asked about where metastatic cancer pain usually occurs from prostate cancer. The answer: most of the pain occurs deep in the body. The metastases occur not in the legs and arms usually but it tends to go to the bones in the spine, in the ribs, in the pelvis.

Back to Mr. Rodrigues. He tries abiraterone, this time on a clinical trial for three months but, in his case, he does not respond. Now, 40% of people respond to abiraterone, even after having these other agents. We don't usually think of people being hormone resistant. We tend to use the word castration resistant rather than hormone resistant, now. So he now has hormone resistant prostate cancer. Mr. Rodrigues has pain in his right hip, he's fatigued and he has several other painful areas. So, what should be done for Mr. Rodrigues? The principles of management at this stage. First of all, we, as doctors have to work for pain control. Pain control for people who have wide spread disease in bones that is not responding to hormonal treatment, most of those people need to have narcotic medication regularly. Many men are frightened of taking morphine. They shouldn't be. It is not addictive when used appropriately to control pain. It does have some side effects. Some men can't tolerate it well. It does cause constipation so any time I prescribe a narcotic, I give laxatives. In some men it may cause nausea. It may initially cause some drowsiness but after a while people can adapt to it fairly well.

If you have a dominant site of pain then radiotherapy is extremely good. It is a local treatment and is used to treat the prostate initially or to treat sites of pain. The problem with somebody like Mr. Rodrigues is that he may have a dominant site of pain. You treat that but he's got other sites as well and when this pain is relieved, he starts to feel the other sites and you can't irradiate the whole body. If there are diffusive symptoms or rapid rises in PSA, then we can consider chemotherapy. So Mr. Rodrigues is treated with radiotherapy for his painful hip. "Feel a bit better" he says four weeks later, "but I'm still have achy bones and I'm tired and my PSA is going up again." So Mr. Rodrigues is offered treatment with chemotherapy.

A Canadian group did a randomized trial comparing chemotherapy with mitoxantrone (+prednisone) to prednisone alone for men with hormone-resistant prostate cancer and pain. The trial showed

improved pain control with chemotherapy - and mitoxantrone is well-tolerated - but no difference in survival. It was not large enough to show a survival difference. What are randomized clinical trials (RCTs) and why are they important? In an RCT the patient agrees to accept either of two treatments which are chosen at random (like the flip of a coin) - neither the doctor nor the patient chooses between these treatments. One treatment is the current standard, and the other is a new treatment that might or might not be better. They do not use placebos in cancer trials. Placebos alone are only used if there is no other treatment available. At the end of the trial the two groups are compared to see which is better. These trials recruit about 1000 patients, almost always developed internationally, to show differences of a few months in survival and they cost about $100 million. I shared a trial which was done comparing new chemo with docetaxel and an older chemo with mitoxantrone and everybody received prednisone, which was fairly innocuous. Keeping in mind that these are very advanced cases of prostate cancer, those taking docetaxel survived slightly longer and enjoyed a improved quality of life. Mr. Rodrigues is treated with docetaxel and prednisone every 3 weeks. He has relief of his pain and by the third course of treatment he is able to stop taking morphine. His PSA declines steadily from 150 to 25 with the first 6 courses of treatment but then begins to rise again to 70 after 8 courses. He develops numbness in his hands and feet. His docetaxel is stopped because of this rise in PSA and to avoid further side effects.

Should Mr. Rodrigues receive a drug to prevent bone loss and fractures as well as chemotherapy? Exercise is probably the best protection against loss of bone and muscle. All men with bone secondaries should take calcium and vitamin D. Zometa and Xgeva are approved to be given at 3 - 4 week intervals to prevent bone loss on the basis of clinical trials. They can lead to a delay in radiotherapy but they also have some side-effects of their own. If you have dental work, they can cause some problems with the jaw that can be quite severe and they can lower calcium, sometimes to a dangerously low level, so I think they should be used less often. They are also expensive. We're doing another study with Zometa. It's been our practice, when we use it, to give it every three months rather than every three weeks. If you use Zometa to treat osteoporosis, you can give it once a year, so why every three weeks? Zometa doesn't do anything for the prostate cancer itself, it doesn't change survival, it hasn't even been shown to improve quality of life but it can reduce fractures. Dr. Tannock then said "Goodbye" to his hypothetical patient, Mr. Rodrigues and spent the next ten minutes discussing the various trials being done on chemotherapy for prostate cancer. After the break, he answered many questions from the floor.

A look at your board and it's duties.

We Need Your Help, We Need Your Ideas.

This is our Current Board. (three members below what we would like to have)

Frank Kennedy, - *Serves as Chairman, Treasurer and Newsletter (with wife Jane)* and is Occasional Host

Phil Mahon, - *Serves as Secretary, Website*, and is Occasional Host

Walt Klywak, - *Serves as our Communications/PR person*, Meeting Setup and is Occasional Host

Ulli Baumhard, - *Greeter* and Meeting Setup

Dan Ho, - *Photography and Membership (Newsletter lists etc.)*,

Doug Bowers, - *Member at large* (helping where whatever is needed) and is Occasional Host

We meet once a month, every second Thursday at the Cancer Society office where we label envelopes fold and stuff newsletters and mail them to our mailing list. We also review our finances and the previous monthly members meeting and any thoughts on the speaker. and his/her message. We discuss the next month's meeting to make sure that everything will run smoothly and more important, **we share ideas..** What we also talk about is what we can do to spread our message that we are here to provide understanding, hope and information to prostate cancer patients and their families.

The current board members have all agreed to continue on the executive committee but would gladly surrender or share some of their multiple duties.