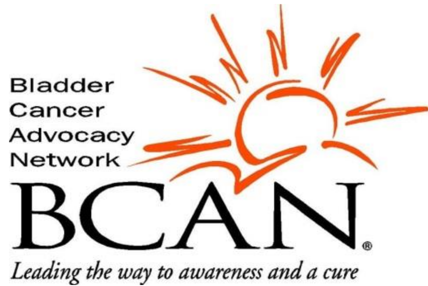

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Bladder Cancer: A Multidisciplinary Approach

Diane Zipursky-Quale: Welcome to Conversations About Bladder Cancer. I'm Diane Zipursky-Quale, the co-founder of the Bladder Cancer Advocacy Network, or BCAN as we like to call it. Today we're going to talk about the team approach to bladder cancer, also referred to as the multi-disciplinary care for bladder cancer. I'm so happy to be joined by 3 specialists today, all of whom are engaged with BCAN as members of our scientific advisory board.

I'm joined by Dr. Jason Efstathiou, a radiation oncologist from Massachusetts General Hospital in Boston. Dr. Gary Steinberg, an urologist from the University of Chicago and the chair of our scientific advisory board. Dr. Jeannie Hoffmann-Censits, a medical oncologist from Thomas Jefferson in Philadelphia. Welcome to you all, thanks so much for being here.

Dr. Jason Efstathiou: Thank you.

Dr. Jeannie Hoffmann-Censits: Thanks for having us.

Diane: Most people consider bladder cancer to be treated only by urologists but today we're joined by a medical oncologist and also a radiation oncologist. Jeannie, as the medical oncologist, can you tell me what is your role in bladder cancer care?

Dr. Jeannie Hoffmann-Censits: Sure, thank you. My urology colleagues, like Gary, will refer me patients when patients have tumors that are invading into the muscle layer of the bladder. I really think of that almost like a line in the sand, because for patients that have tumors that are non-muscle invasive, those are predominantly taken care of by urologists, but for tumors that are able to grow into the muscle layer of the bladder, those really have a very different phenotype. Those are much more aggressive tumors and they need that multi-disciplinary, multi-modality approach.

As a medical oncologist I give systemic chemotherapy for those patients, and that's considered standard of care for patients to come into the clinic, be evaluated, and for patients who are fit to receive systemic chemotherapy we deliver that chemotherapy prior to the surgery, prior to cystectomy.

Diane: Okay. Jason, as a radiation oncologist, why are you involved, or how are you involved, in bladder cancer care?

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Dr. Jason Efstathiou: As a radiation oncologist we're actually the least likely typically to be seeing bladder cancer patients. But in the spirit of total informed decision making, patients do have options as far as treatment. As Jean was describing muscle invasive bladder cancer, for some patients there is indeed the option for what we call bladder preservation, or sparing the bladder by using chemotherapy and radiation together with resection of the tumor to try and both cure the cancer and keep the bladder and maintain excellent quality of life.

Diane: How would you best define what I've referred to as the team approach, or multi-disciplinary care? Why is it important for bladder cancer patients, and specifically for the patients with muscle invasive disease?

Dr. Gary Steinberg: There has to be accurate diagnosis, staging and grading. I think that the garden variety patient with bladder cancer has a low grade, non-invasive tumor, and in that regard that's great news in that they don't need to see a medical oncologist or a radiation oncologist. But there's no question in my mind that the high grade cancers, and there are a fair number of patients that present with high grade cancer.

Diane: When you say high grade, just for people, would that be with what we call T1 tumors or T2 tumors, or just any who's diagnosed as high grade?

Dr. Gary Steinberg: The grade is what the actual cells look like under the microscope. The T1 or T2, that's more the staging, that's the depth of penetration. I personally believe that anybody with a high grade cancer, I think those are the aggressive actors, those are the tigers in the tank, and that all too often in the past urologists have not appreciated the aggressive nature of high grade cancer. I think that the best form of treatment is going to entail a systemic approach as well as a surgical approach to make sure that you diagnose and stage the patients most appropriately.

Being in bladder cancer for 25 plus years now, I've seen the tremendous growth in the field when we became inclusive and started adding the medical oncologists and the radiation oncologists. There's no question that we are light years ahead of where we were just 10 years ago because of all the newer innovative systemic approaches, the big tent that we've created that has included other disciplines. Our pathologists are better now, our radiation oncologist, our medical oncologists, our radiologists. We're beginning to treat bladder cancer like the real life threatening disease that it is and I think we're making a lot of progress.

Diane: When you say progress, improving outcomes? Saving lives?

Dr. Gary Steinberg: Absolutely.

Diane: Okay. In terms of this team approach, what kind of patient and when should a bladder cancer patient first see a medical oncologist or first see a radiation oncologist? How does that happen? How does it work at Jefferson?

Dr. Jeannie Hoffmann-Censits: Like I said earlier, most of the patients that I see are referred by our urology team because many patients present to the urologist with the initial symptoms of bladder cancer, blood in the urine or urinary frequency. As Gary said, the staging and radiographic staging, as well as the grading of the tumor is so important. Even though there's 3 of us today, this team approach is really much bigger and it does include our pathologist and our radiologist to help us really understand what's the best approach for the patient. But I do see patients that have muscle invasive disease who are in the locally advanced setting intended to go on

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to cystectomy for a discussion about whether or not they should get preoperative or neoadjuvant chemotherapy.

Diane: Neoadjuvant chemotherapy is what refers to as the standard of care. There have been trials demonstrating that neoadjuvant chemotherapy before removal of your bladder does improve patients outcome, correct?

Dr. Jeannie Hoffmann-Censits: That's correct.

Diane: Okay. I just wanted to make that point because we know it's the standard of care and yet unfortunately it's not what all patients are being offered. We want to make sure that we can inform the patient that these are the treatment options that are available, and actually are recommended for them.

Dr. Jeannie Hoffmann-Censits: Yes.

Diane: Great. Jason, tell me a little bit more about bladder preservation and what patient is eligible. Is there an ideal patient for that? Is that something that should be offered to all patients who might need to have their bladders removed?

Dr. Jason Efstathiou: I think what we see nationally is that a lot of muscle invasive bladder cancer is indeed under treated. Not all patients are good candidates for bladder removal or a cystectomy.

Diane: Who's not a good candidate for bladder removal?

Dr. Gary Steinberg: To reiterate what Jason just said, there are too many patients in the United States and throughout the world that are receiving inadequate or no care for their life threatening bladder cancer. Why that is, it's unclear. I think that BCAN has done a tremendous job of trying to educate patients, educate physicians, and that work is still ongoing. But bladder cancer is a disease of the elderly; it's a disease of aging. The average age of diagnosis in the United States is 73 years old. The median age is I think around 68 or 69 years old.

Bladder cancer patients come from all walks of life but many of them have multiple other medical issues, heart disease, lung disease, diabetes, peripheral vascular disease, cerebral vascular disease. There's no question that radical cystectomy, or removal of the bladder, is a major operation. This is not like going in for a hernia repair, this is a major operation where you're removing a number of internal organs and then reconstructing the urinary tract using the gastrointestinal tract.

It's a major undertaking. The complication rate even in centers of excellence is not trivial and I think that we need to think long and hard about what's the best approach for patients. I think that there's no question that bladder preservation is something that's under-utilized in the United States and that we need to figure out better ways to incorporate bladder preservation, potentially in combination with chemotherapy, potentially in combination with some of the new immunotherapy drugs in trials. But to really serve the entire population, I think that bladder preservation is critically important.

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Diane: Jason let's get back to you and talk a little bit more about when patients are referred to you. Should all cystectomy patients be referred to you at least to know that there's that option available?

Dr. Jason Efstathiou: I do believe so. I'm fortunate to work at a hospital where we have multi-disciplinary, or team based, clinics. Those clinics are tended by urologists, by medical oncologists and by radiation oncologists. Most muscle invasive bladder cancer patients would be seen in that environment, with all 3 doctors in the room at the same time. We would review the options for the patient, and if we thought one option were better than the other we would convey that to the patient.

Indeed there are muscle invasive bladder cancer patients who are either better served or good candidates, for bladder preservation. Just do describe a little bit what that means, the urologist remains very centrally involved in that. There's the original removal of the tumor, what's called a transurethral resection of the bladder tumor or TURBT. That should be done as best as possible, ideally remove as much if not all of the tumor.

Then those patients that don't have very advanced disease, who've been able to have a maximal removal of the tumor in that fashion, who have good kidney function for the use of chemotherapy, who don't have blockage of the kidneys and the ureters, what's called hydronephrosis, and who don't have a lot of other types of disease throughout the bladder, things like carcinoma in situ, or other types of forms of bladder cancer. That patient may actually be an excellent candidate for the option of bladder preservation. That patient would go through a course of chemotherapy and radiation that are given together.

Diane: It's chemo during the same 3 weeks, 6 weeks, whatever it might be?

Dr. Jason Efstathiou: Correct, there are different ways to do this. Let's say it's basically about a 7 week course of chemotherapy given at the same time as radiation. These are low doses of chemotherapy; Jeannie can talk more to that. They're goal is to sensitize the radiation, to give a little extra bang for your buck with the radiation treatment. Patients then get through that course. They would then have a discussion with a medical oncologist whether or not it's worth doing high doses of chemotherapy thereafter on its own.

They would continue to have very close surveillance with an urologist, doing cystoscopies, looking in the bladder, making sure there's no recurrence of the tumor. That would go on, there would be imaging as well. The hope and expectation for these patients would be that there would not be recurrences of their bladder cancer, and yet they've been able to retain their native bladder.

We've learned in longer term studies that, again for well-chosen patients for this kind of treatment this can work extremely well, perhaps as well as upfront removal of the bladder. That indeed in many of these patients quality of life remains excellent, bladder function remains excellent. What we found is that patients who've chose this route, who've had the opportunity of having discussions with all the relevant specialists, they remain very satisfied with their ability to have been offered reasonable alternative treatments for their kind of cancer, and to have been able to engage in informed decision making as far as what their treatment should be.

Diane: For a patient who's had bladder preservation and if later with monitoring and following a new bladder tumor comes up, has the chemo radiation impacted the urologist's ability then to remove the bladder?

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Dr. Gary Steinberg: No, but certainly that type of operation is probably best performed at a center of excellence that does a lot of bladder removals, because there are a fair amount of technical nuances and changes in the surgical anatomy that can happen from radiation specifically. I think that the reconstruction can be more difficult, and I think that some of the continent urinary reconstruction options can be a little bit more difficult.

Diane: You're talking about a neobladder or what people refer to as an Indiana Pouch, that might be more difficult if you've had radiation before.

Dr. Gary Steinberg: I think that there are still some centers that will go ahead and try to perform a neobladder in somebody's who's had radiation for bladder cancer. My own personal preference is to not use a neobladder, and I prefer to use something we call an Indiana Pouch, which also an internal bladder that has continence so that patients have control over when they eliminate their urine, but to eliminate the urine they have to catheterize themselves and like everything you learn how to swim, you learn how to ride a bike, it becomes second nature very quickly and that patients can catheterize themselves very easily.

In general they have to catheterize themselves as often as everybody else would urinate, so they would have to catheterize themselves every 3 to 4 hours depending on how much they've had to eat and drink. But again it can become quite natural. The concern about a neobladder in somebody who's been radiated is that there may be a lot of additional scarring and the urinary continence rate may not be very good, if you're trying to hook something up to the native urethra.

Diane: Why do you think, Gary you mentioned just a few minutes ago that this idea of bladder preservation has become more accepted, certainly in the last 10 years, I'd say maybe even in the last 5 or 6 years?

Dr. Gary Steinberg: I think that the family members and the patients themselves as well as referring internists, non-bladder cancer specialists, removing a patient's bladder, patients can have a feeling of loss of sociability, loss of sexual function, feelings of inadequacy, it really can be body image altering experience. I've seen patients that say, "You know, I'd rather die than have my bladder removed." Again we have so many potentially life-saving treatment options today, that I think we need to eliminate that impression that patients and referring family physicians may have. I think that all too often bladder cancer, today patients are getting palliative treatment because we've waited too long.

Diane: Palliative means just to make them comfortable.

Dr. Gary Steinberg: To make them comfortable, where we're operating on patients with much more advanced disease, treating them with radiation therapy and chemotherapy with much more advanced disease than we should. If we were much more proactive and everyone was on board and everyone says, "I can deal with my bladder cancer," because it doesn't necessarily mean that I have to have my bladder taken out. I think that we can just change the overall impression of what we're doing and how beneficial and life-saving that can be, and yes potentially using multiple tricks in the armamentarium this huge number of patients that are not getting treated or are getting inadequate treatment or getting late treatment, we can prevent.

Dr. Jason Efstathiou: To backup Gary's point, we know as he mentioned this is a disease where the average age is about 73. If you look at patient who are over the age of 70, and especially those over the age of 80, fifty percent, sixty percent of those are not getting the radical cystectomy, the bladder removal. There are other

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treatments that can help fill that gap. The beauty about team based care is that we as physicians, we have to be honest with ourselves. We all have biases of our own. When we operate together as a team it helps rid ourselves of some of our own biases and some of our levels of maybe not full comfort with certain treatment paths.

We know that nationally neoadjuvant chemo, chemo given before surgery, is way under-utilized. I think it's only maybe up to 20% of muscle invasive bladder cancer. That's perhaps because not all patients are seeing the medical oncologist and there isn't this idea of team based care. Then similarly as Gary's saying, a lot of patients are under treated and therefor are being under served. Perhaps again that's because there hasn't been an engagement of team based care that can try and help fill those gaps.

Diane: Mass General, I see, has been one of the leaders of team based care, specifically for bladder cancer. You all have been doing bladder preservation for a long time. Other institutions are coming along now. How can we help ensure that this change becomes more widespread so that the team based approach becomes the norm, as opposed to the exception?

Dr. Gary Steinberg: One thing that we have to remember is that we're not living in a healthcare vacuum, and that a lot of what we're doing is tremendously labor intensive. There are a lot of places that they say, "Yes we can do bladder preservation," but they're not giving the chemotherapy with a radiation, or they're not using what we would think we would be the best chemotherapy with the radiation, or they're not using the full radiation dose and there's gaps and they're not being followed up by the urologist. To truly do this correctly it does require a commitment of everybody, the patients and the healthcare team, as well as it is labor intensive and I think that that's one of the hurdles that we have to get passed as well.

Dr. Jason Efstathiou: We also have to be honest; this is not a means of delivery of care that's feasible in all environments. There are community settings that don't have the benefit of having all specialists in one building. Indeed, it's one thing to say at Mass General we're able to do it, but we've a very large academic medical center and have had support internally to build these clinics. That is not necessarily feasibly everywhere, nor is it reimbursed everywhere.

Diane: Let me ask that question specifically because one of BCAN's missions is to make sure that patients have the information that they need and we want proactive patients because we believe that a proactive patient leads to a better outcome. For patients who don't necessarily have access to a comprehensive cancer center, like each of you come from, and are being treated by say a urologist in their own community, is there something the patient can do to help ensure that he or she is getting this kind of team approach, even if the patient has to create the team by herself or his-self?

Dr. Jason Efstathiou: I'll start, but I think we should all give our thoughts to this. I think a patient who's advocating on their behalf is the best. I think this is where BCAN is really serving the bladder cancer community extremely well. It's arming patients, engaging patients in a dialog where they know what questions to ask. Some of those questions should be, "Should I see a medical oncologist? Should I see a radiation oncologist? I understand perhaps you don't have one in your building or in your clinic here but could you please refer me to those specialists for an opinion?"

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Ask the questions of, "Should I get chemotherapy before surgery?" Ask the question, "Am I a candidate for trying to spare my bladder, to keep my bladder?" I think as long as ... when patients start asking those questions, they'll probably be able to build a network of a team on their own, even if it doesn't naturally exist in the clinic or in the center where they're being seen initially.

Diane: You had mentioned the insurance issue, Jeannie as far as you know from your own practice, has this team approach been covered by most insurance companies?

Dr. Jeannie Hoffmann-Censits: Yeah, I think absolutely. Many patients too will come often times to our multi-disciplinary clinic to get our team approach and team recommendation, and many insurance companies will cover a second opinion at a major cancer center, and then go back closer to home with a recommendation. Both Gary and Jason have pointed out that bladder cancer is under treated, and I think as a medical oncologist one of the under treatments that we see is I think the biases that we talked about in terms of our elderly population in terms of whether or not those patients can really tolerate chemotherapy.

For patients with muscle invasive disease, for many that is a life limiting disease. That is their most important, most threatening disease that they have. They may have a history of heart disease, they may have a disease of peripheral neuropathy, but as a medical oncologist I feel that it's my job to assess them as best as I can, to see whether or not they're a candidate for the chemotherapy.

In terms of other under treatment, there's also patients who are not getting what we believe is the best chemotherapy, which is a cisplatin based chemotherapy. Another role that I feel like that I have to play is to again assess patients, look at their medication list, talk to them about their comorbidities and have a full discussion about what we think are the risks and potential benefits of getting that chemotherapy. But I think not everybody has the comfort level of delivering that kind of chemotherapy everywhere. If a patient is going to get preoperative chemotherapy, we really endorse 1 or 2 regimens, as well as discussing potential opportunities for clinical trials for patients as well.

Dr. Gary Steinberg: I think that one of the most important roles of the academic physician is to try to not only change practice patterns within your own institution but within your own region. I'm happy to say that that's happening. All too often in the past when patients would get chemotherapy it would be regimens that were not exactly the top of the line, or standard. The way the urologist would manage non muscle invasive bladder cancer would be not necessarily following the standard guidelines or algorithms.

I think that over the 25 years that I've been at the University of Chicago that that's changed, and that the urologists that send me patients, the preliminary work that they've done prior to sending them to me and to the medical center has been spot on. I think that the patients have benefited from that tremendously.

Dr. Jason Efstathiou: I also think we should think even further about, should the system of healthcare delivery change a little bit to really support this environment. We've gotten through all kinds of exercises in recent years, meaningful use and other things that perhaps haven't panned out as hoped. But one simple thing for serious illnesses that life threatening like muscle invasive bladder cancer, perhaps there are quality metrics that each patient should have achieved in their process of care. Perhaps that is being able to see all the various specialists that could be involved with their care to get a consensus opinion of what may be best for them. Hopefully the

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way in which healthcare is delivered and the way in which healthcare is valued, starts to show more emphasis on this team based kind of care.

Diane: Thank you all for being here. This has been a great conversation. I think it indicates it's an exciting time for the bladder cancer field and we've seen new developments. For me to see the increased team approach, putting the patient first and really letting the patient have the benefit not just of one bright mind but of a team of bright minds looking to improve their outcomes is really very exciting and I encourage everybody listening to seek out the best opinions you can, go get a second opinion. If you're being treated by an urologist and they're telling you need to have your bladder out, talk to them about seeing a medical oncologist first. Make sure you're getting the best care possible. Again, thank you all for being here and thank you all for watching.

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