



Stephanie Chisolm:

I think you really nailed it on explaining all of these different things. There have been quite a few questions that have come in. Some of them that we've been able to answer on our own with other information from BCAN, but also you really did a great job of really addressing a lot of the questions that were covered early on when people were putting in their registration. So I'm going to just ask a couple of questions we have about 10 minutes left. You mentioned a lot about the five year survival rates and a few people had questions about, "Well, what happens after five years?" How do we find out what the 10 year or 15 year rates would be for some of the different diagnoses that people can have?

Dr. Bivalacqua:

We actually have that. We actually do have that data and we can provide that. What I tell my patients is if you've gotten to five years and wherever you are at five years, you could pretty much state that that's kind of where you're going to be probably in 10 years. And it's likely that you're probably going to potentially have a new problem, like heart disease, like diabetes or whatever happens to all of us as we get older. One thing that I think we oftentimes...

Why I continue to follow patients after five years with things like CT scans and the like, is that we do see that patients that have... And I'm talking specifically about muscle invasive bladder cancer right now, so please, to make sure I clarify. So if I've done a cystectomy in a patient and they have muscle invasive bladder cancer, and they do well, they're five years out. There's no signs of cancer spread or recurrence. I'm still imaging them because we know that they're at risk of developing potentially cancers in the upper track so in the lining of the kidney and ureter so I still follow them. Once again, it's a shared decision making as to how often we do CT scans. But it's pretty safe to say that wherever you are at five years, good chance you're going to be right there at eight years and a good chance at 10 years. That's why you always hear five years, because we know that correlates pretty well. I'm overgeneralizing this, but that's in essence what we know.

Stephanie Chisolm:

Okay, great. I think that's really helpful because again, a lot of people said, "Well, you're saying five years, but does that mean I'm done in five years and I got nothing left?" I think it's really important that where you are at five years is probably going to give a good indication of where you're going to be. So I hope that provides a little bit of reassurance for folks. We had a lot of good questions. I did drop in to the question and answer thing about people were asking about the blue light and why isn't it available in more places. And I did drop the Cysview address where you can find blue light and find out if it's in your neighborhood on the chat box. I'll make sure that we get that and put that in there for you later on. Here's a patient who is diagnosed with non-muscle invasive bladder cancer in 2011 with the recurrence in 2013 and they have annual cystoscopies. Should they be getting cytology along with that when they're having their cystoscopy? Is that just enough for them?

Dr. Bivalacqua:

Yeah. So if this patient had low grade papillary disease, a low grade TA bladder cancer, we know that cytology doesn't help. We don't really use it. Oftentimes urologists will get it, but it really doesn't help. But if you have high grade cancer, the guidelines recommend that you get surveillance cystoscopies with urine cytology annually, once you've gotten beyond five years. When you hit 10 years, last time you had a recurrence was 2013 when you hit 2023, you're at that 10 year mark, once again, it's a shared decision making with your urologist, if you continue with surveillance cystoscopies. And we always, with patients with high grade disease, check a cytology with it.

Stephanie Chisolm:

Okay. And that's also including the FISH test?

Dr. Bivalacqua:

No, it's okay. So what we know about the UroVysion FISH test is that it is another test that is used to detect recurrent bladder cancer cells. What we know about the test is that it's very specific. So what does specific mean? If it's positive, it's likely you have a tumor, or a cancer, or a lesion, all the different terms we use. It doesn't necessarily mean that we're going to be able to find it right then.

Stephanie Chisolm:

It's maybe too small to see.

Dr. Bivalacqua:

Yeah. So how do we do that? Well, we investigate. We use things light cystoscopy to help us find it. Typically when people have a positive cytology or a UroVysion FISH test, that's positive, it's usually something called CIS or carcinoma in situ, which are hard for us to see visually with our eye, with white light. And that's when we start to use things like blue light to help assist us. So yes, it is used in clinical practice.

Stephanie Chisolm:

Okay. So if somebody were to have a TURBT and all that information, the tumor goes out to the pathologist and they had multiple tumors. If there was 80% low grade, 20% high grade, how is that going to be treated? How does that influence how you treat? Do you treat to the worst grade that's out there in terms of the highest grade, or do you just aim for low hanging fruit? How do you guys make that decision as medical professionals?

Dr. Bivalacqua:

Yeah. So great question. So it's not an easy decision because when a tumor has a mixed high grade low grade component, what we can tell you right now is we, as urologists, we cannot say what percentage 5%, 20%, 50% high grade means it's going to behave like a high grade tumor and not behave like a low grade tumor. So what I use in my clinical practice is if I've got multifocality, multiple tumors, they're 3, 4, 5 centimeters. They are throughout the bladder, three or four tumors in different places. And I get a tumor that comes back as low grade with a high grade component, and I've got increased size and multifocality, I'm treating that as a high risk patient. So I'm treating to the high grade component because it's behaving like a high grade cancer. So that's how I make that decision. So it's actually, we make the decision on a case to case basis. It's not just as simple as a certain percentage means you could treat it like intermediate risk versus high risk. So it's up to your practitioner.

Stephanie Chisolm:

Okay. And a good question to ask your doctor as well.

Dr. Bivalacqua:

Right, absolutely.

Stephanie Chisolm:

So again, keeping that communication open as the patient, hopefully your doctor will answer all of your questions and if they don't, find another doctor.

Dr. Bivalacqua:

Yeah. I mean, get a second opinion. Yeah. Get a second opinion. There's no harm in that.

Stephanie Chisolm:

A second opinion is always a good idea. And I think, you're a urologist, I know that you're consulted for second opinions often and I don't think you're insulted when somebody else says that-

Dr. Bivalacqua:

No. I ask almost every patient that has a diagnosis that it's hard to come up with what I want to do. You know what I mean? Like, "Oh, I'm not sure." The first thing I ask them is, "Who do you want to see? What city do you want to go to? Let me give you the name or I'll even contact them and give you their name and get you referred." I mean, absolutely. You should seek a second opinion and if your practitioner is offended by that, don't worry about it. Just go get a second opinion.

Stephanie Chisolm:

Right. Okay. Well, here's a question, I think for a lot of people that have had a few years between their tumor removal and now, that are wondering, based on what you said, "Can I have my tumor reevaluated?" How do you find out if your slides are available so that the new technologies that they have could be applied to the tumor to really do a deeper dive into what's going on.

Dr. Bivalacqua:

Absolutely. Yeah. So that's a lot easier than you think. So what I will tell you is, as it relates to non-muscle invasive bladder cancer, there's no role in getting, for example, sequencing to look for a

mutation in X, Y, or Z. There's no role for that. However, if you have muscle invasive bladder cancer, getting your original tumor or recurrence or whatnot, if you want to get it sequenced, all you have to do is contact the pathologist or the pathology department, excuse me, where you had your initial tumor, these are all saved in something called paraffin. They just have to recut you your tumor and send it to a place like Foundation Medicine, for example. And they're able to do the genetic analysis, whatever that may be.

Doing things like RNA sequencing and where you're doing a little bit more in depth, next generation sequencing, that's a little bit harder, but not impossible. But once again, that's not clinical practice just yet. We use a lot of sequencing of tumors in the muscle invasive state, but more importantly in patients that have metastatic bladder cancer. So that's something that we do almost in everyone now. Unfortunately, once again, not going to necessarily change what drug we use, but it's still information that allows us to be able to look for something that's a third line, fourth line if God forbid things aren't working. The other thing that I will say is if you want to have things like looking at, for example, PDL1 status, which is what we use to help maybe think that if a patient's going to respond to immunotherapy. Once again, contacting the pathology core and saying, "I need my slide stained for PDL1." And they can do it. That is standard of care now.

Stephanie Chisolm:

Okay. So this is good because again, the research is advancing on a regular basis. There are always new things. In the last six or seven years, there's just been an explosion of options in the bladder cancer space, which I hope gives people hope going forward. And so the fact that if your slides are still available, you might be able to go back and just get a better understanding of what new options might be available to you is certainly something.

Stephanie Chisolm:

So here's a quick question. It's very specific, but when you've gotten a histology where telomeres stain is positive, what does that mean?

Dr. Bivalacqua:

Oh my God. What is that? What does that mean? Well, first of all, clinically, it doesn't mean anything. That's a research question and really honestly, wouldn't be involved in any type of treatment decision making. So that's really just looking at the actual, the cancer cell, if the telomeres have been lost, gained whatnot. And that kind of helps us determine the aggressiveness of the cancer, I think in layman's term, I guess is the best way to state it. But it does not help us, in any way, tell you what the next steps are or what your outcomes are going to be. That's way too much TMI.

Stephanie Chisolm:

So in this case, reading that on your pathology report is almost a bit of TMI because it's not going to really-

Dr. Bivalacqua:

Way too much TMI.

Stephanie Chisolm:

Okay. So that's something-

Dr. Bivalacqua:

That's too much information, right? That's what TMI-

Stephanie Chisolm:

Yes, TMI, too much information. Yeah.

Dr. Bivalacqua:

My kids do it to me all the time, Stephanie, it drives me crazy and I'm like, they text me and I have to reply back, "What does that mean?"

Stephanie Chisolm:

Yeah, exactly.

Stephanie Chisolm:

I appreciate that. I certainly do. All right. So good. So just take that into consideration. If you have a question about your report, talk to your doctor, that's a really important thing to bring up that just because you're getting a copy of your pathology report doesn't mean you are going to be able to understand it. So find out how that is being used to recommend the treatments for you and what are they learning from that pathology report? I think that's really an important thing to keep in mind. So here's another good question. Why aren't more radical cystectomies offered, at least as a choice, when staging is still at the T1. I know you mentioned between the low grade and the high grade, what is the general thought behind that? If you've got just an intermediate grade tumor, that's still T1, why don't you offer the cystectomy more often?

Dr. Bivalacqua:

Yes. So I didn't put this in the talk because, I was just trying to cover all bases. So let's break it into two things. If you are diagnosed with stage one bladder cancer as your first diagnosis, in the guidelines we do state that you could consider a radical cystectomy. The reason why you would consider it is that we could have under-staged you, which means you actually have more extensive disease, because our TURBTs are not perfect. We try to be, but we're not perfect. Additionally, if you have invasive T1 disease up front, we also know that those are the groups of patients that are less responsive to things like BCG. The guidelines do state, however, if you received adequate BCG, which means you got two induction courses and you recur with stage one or T1 cancer that we do recommend radical cystectomy. So that is the recommendation.

However, a lot of patients desire bladder preservation for the reasons that I kind of alluded to because it's a life changing event. So the reason why we offer radical cystectomy in that setting and recommend it in the guidelines is because we know that our second, third, fourth line treatments, as I pointed out, are really not that great. And it puts you at risk of progression. So we want to use that window of opportunity to cure you so we do that. I guess there are some urologists that may be pushing the limit a little bit and just continue to try intravesical therapy. But that's honestly, I will make a plug here that God forbid BCG fails you and you recur with invasive T1, that's actually the time point when you want to go see a specialist. That's where you need to look at that risk benefit of cystectomy versus additional treatment inside the bladder or a systemic treatment for that matter.

Stephanie Chisolm:

Thank you. So you mentioned treatment guidelines frequently and you actually showed some of the guidelines and they had evidence grading on there. There's a question that came in, "Treatment guidelines and medicine are varying quality. What assurance do we have as to the strength of the evidence?" And by the way, everyone, I did put in the chat a link to our page, which has all of the common guidelines that are currently available to treat bladder cancer. So if you go and you open that page, you can take a look at it later. But now if you could just talk about that strength of evidence. [inaudible 01:06:00] decided? Because it's a big process and I don't [inaudible 01:06:04] people understand that.

Dr. Bivalacqua:

Yeah, my God, it's a wonderful question. Brilliant question, actually. Okay. So I know a lot about this because I've been part of multiple guidelines for the AUA, we're the American Urological Association. And when we write guidelines, as you've appropriately pointed out, we do what's called a systematic review where we ask questions for our statisticians epidemiologists who provide us with the literature with the level of evidence for each of the different treatment options for the question we're asking. So let's use BCG as an example. There is strong evidence, like level one evidence, which is the highest level of evidence, grade level A, that BCG is the most effective compared to chemotherapy in patients with high risk non-muscle invasive bladder cancer. So I could tell you with strong confidence that the evidence supports that. There are other scenarios, for example, once again, I'll use BCG and non-muscle invasive bladder cancer. Where we as urologists, the literature does not support, for example, a treatment option after a patient does not respond to BCG. So we will recommend something for example, therapy X, and then we state, "This is an expert opinion or this is level C evidence, which means not very strong, but there is some evidence for it." And then we will give what we call a recommendation, strong, moderate, weak.

So what you have to do as a patient, and this is hard because patients don't know what to ask because just like I wouldn't know what to ask my car mechanic how to replace my engine. But what you have to ask is to your doctor, your urologist, oncologist, what does the evidence support for your recommendation? And you can ask them that and then if they can't provide that to you, then maybe you need to see somebody that can. And as Stephanie said, you could go online and actually look at the evidence, the level of evidence to support all of our recommendations. If you go back, I know I went quickly, but I showed you what that in the guidelines for each of the things that I was talking about.

Stephanie Chisolm:

Great-

Dr. Bivalacqua:

I hope that answers your question. It's not an easy one as a patient to understand, but it's a great question.

Stephanie Chisolm:

Yeah. And again, not every doctor... Are they generally all up to date on the guidelines. They're out there, but does every doctor know what the most recent guideline is? What is your opinion on that? So on our website that I put that link into the chat so you're welcome to open that up. We've got the microhematuria guidelines and the EAU, the European Urology Association, we've got non-muscle invasive and metastatic and National Cancer Center Network bladder cancer guidelines. We have a number of different guidelines there. It just helps you to be better informed, to think about better

questions to ask your doctor about the treatments that they're recommending. So I think it's really important. There were a couple questions that came in and we'll wind this down in just a minute, but some questions about BCG. Why don't people get or complete all of their maintenance and what if they had an issue like cystitis or irritation with that? Is there a protocol for cutting back? And then also, maybe can you mention a little bit about what we're doing now with the shortage of BCG? And I don't know if at Penn you are having a lot of BCG or if you have to use that one third dose that's recommended, can you just talk a little bit about that?

Dr. Bivalacqua:

Sure. So the reason why patients are not able to tolerate the maintenance for the three years that are recommended from the trial is because of exactly what you said, they get cystitis. Cystitis is just a catchall term for irritation of the bladder. And the reason why patients get irritation of the bladder is because BCG, when it's in contact with the urothelial lining or epithelial lining, the mucosa, it actually activates your immune system, which is going to bring in these wonderful, beautiful immune cells, which are going to help prevent the cancer from coming back, hopefully. But guess what that also does? It also causes inflammation. It also causes a lot of irritation. And when the body sees this repeatedly over time, it honestly can't tolerate it and the bladder gets progressively more irritated and more inflamed. And a lot of patients, and this is very much the case, just can't tolerate it.

My conversation that I have with my patients is that I say, "Okay, how bad is it?" "Well, the day after I really go to the bathroom every two or three hours, I have pain, but then 48 hours later, I'm essentially back to normal." Well, for me, I'm like, "Okay, well, let's try to get you through that 24 to 36 hour period." And we use medications to help with that. If the patient says, "For seven to 10 days until my next treatment, I'm miserable." Then at that point I'm like, "Okay, we're stopping." Because you can actually cause "permanent damage" or irritation to the bladder where patients don't recover. And that's what we want to try to prevent.

If you have horrible symptoms and it could take months before that bladder recovers. And what I do in my practice is, and I will be the first... The level of evidence for this is poor. Okay, this is voodoo, but I like it. I do a cocktail of three drugs, which is an antibiotic, a medication that stabilizes the urothelium and causes your urine to change different colors. And then I give you a medication that quiets the bladder. It's an antimuscarinic, it's like a antispasmodic medication. I find that helps with the process. At Penn, we are unfortunately had the same problems of everywhere else with BCG shortage. We've come up with a risk adapted protocol where we have patients that are getting full dose and some that are getting reduced dose.

Stephanie Chisolm:

Yeah. So that would certainly look at patients who have a recurrence after BCG or more likely to have a recurrence after BCG...

Dr. Bivalacqua:

Yeah. Those are patients with invasive T1 cancer, CIS, they're getting BCG full dose. And unfortunately as like other places, we don't have the ability to do maintenance right now because of the shortage. We just don't have that amount. And if we do have it, when we do maintenance, we do a reduced dose. That way we can give it to more patients.

Stephanie Chisolm:

Great. Well, I think this has been incredibly informative. I'm going to close it down now. So I think what I heard you say through today's program is obviously looking at that stage, how far that cancer has progressed, how big is that tumor, where is it, and then the grade of how aggressive it is, are part of the criteria that you, as a physician, are going to use to recommend treatments. And then you are also going to look at what is the general patient's health. So if you have an 80 year old, who's an active avid biker and kayaker and doing all kinds of physically active things, they might be given a different recommendation than somebody who's more frail, correct?

Dr. Bivalacqua:

Absolutely. I mean, I'll use an example from my clinic today. I mean, I saw a patient who is 89 years old and he has unfortunately muscle invasive bladder cancer. He can't get chemoradiation to preserve his bladder because he's already had radiation therapy previously. And I signed him up for cystectomy because he chose that. But he chose that because he is the upper echelon of health. He's exactly what you talked about. But I also saw a patient who's in their fifties that is not fit for cystectomy that I can't offer that surgery to. So it's really about coming up with who is the right person for the right treatment and what are their goals of care. So that's always really important to discuss. What are your goals of care and medically are you fit to undergo what we are asking you to do. That's a big part of what we do. One size doesn't fit all.

Stephanie Chisolm:

Yeah. So again, inform yourself, ask questions, get a second opinion and really be an active partner in your care. I think that's really the general gist of this, that you are an active participant. It's not just you're just following what your doctor says, but you have a voice here as well. And I think it's really important to just remember that and make sure that you're getting what you need to have the best care possible. So Dr. Bivalacqua this has been phenomenal. I'm really excited about having this as a resource to our patients.

Dr. Bivalacqua:

Bye.

