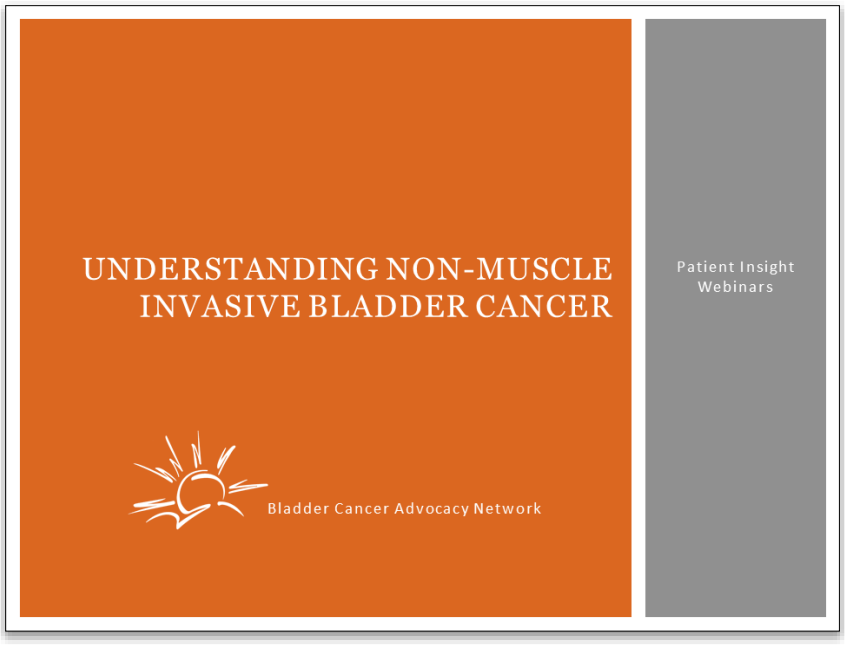

Stephanie Chisolm:

Thank you so much, Dr. Luckenbaugh. That was really comprehensive. And I think you covered a lot of some of the questions that came in. So, this is wonderful. And we have a little bit of time, so we will definitely get to the questions. I'm going to just go back to one of the first ones that we received, **how fast typically does bladder cancer develop?** And likewise, the transition from non-muscle invasive to muscle invasive, in the case of those patients with high grade, what is the usual expectation as far as how quickly it can convert and become more aggressive?

Dr. Amy Luckenbaugh:

That's a tough question. That's a great question. So, we never know how long you have had it. It could have been in there for a long time and slowly growing. And people who have high grade disease and T1 disease, the evolution can be pretty quick. And so, those people we tend to be fairly aggressive. I know that when I give BCG to those patients, high grade T1 disease, I oftentimes instead of looking after the BCG is done in my office, I have them go straight to the operating room and look with them under anesthesia, and repeat biopsies right then and there to make sure that there is nothing there, to kind of save that time.

There's no like crystal ball with how fast it can progress, but it certainly can be fast in some people. And some people can go years and years and nothing progresses, and then at year four of surveillance, all of a sudden, poof, they have a new tumor. And that's I think the frustrating thing for us and for patients.

Stephanie Chisolm:

Thank you so much. Yeah, that is very frustrating. **So, when you're doing regular routine cystoscopy, it's a pretty invasive procedure. How often do you recommend that people have urine cytology done to check for free floating cancer cells, or things like that? And is it really something you do in conjunction with your cystoscopy, or you can do that at a different time?**

Dr. Amy Luckenbaugh:

That's a great question. So, for low grade cancer, we do not do cytologies at all, because the cytologies are usually negative. It only really works for high grade cancer. And cytology is very good if it is positive. If it is positive we can say there's probably something somewhere, and we definitely should be looking. If it's negative though, unfortunately, it's not very reliable. And so, we usually do, for people with any type of high grade cancer, we do the cystoscopy and the cytology together, so in conjunction. There's not a great thing in the urine yet that can say, "Do we really need to have this cystoscopy?" That's an area of research that is very like ongoing and warranted, because it is an invasive procedure. But right now there's nothing that says, "Hey, your urine looks okay, we won't do the cystoscopy this time," we have to do both.

Stephanie Chisolm:

Okay. Great. This is very important information. **Can you talk a little bit about those patients that have mixed grade, predominantly low grade, but maybe there's a few high grade?** What is the concern there from your perspective as the urologist?

Dr. Amy Luckenbaugh:

That's a frustrating question. I think that our tough question as urologists is, do we treat those people as if they are low grade, or do we treat them as if they are high grade? And I think if it is a single time that they have a low grade and it says, "Focal high grade," then I usually treat those people if it's a small tumor like they are low grade, but if it comes back, then I immediately switch to treating them as if it is high grade. And in those people I do check a cytology when I look in their bladder, even though it was predominantly low grade just to make sure that there isn't something else going on.

Stephanie Chisolm:

So, when you go in and you do a TURBT, if there are multiple tumors, you would take all of the tumors that you could see out? So, when they do the pathology report and that patient is seeing that pathology report, how do they summarize that? How do we understand if you've got all these different sizes and shapes of tumors and sometimes even different grades, how should a patient look at that pathology report? And how does that drive the recommendations of their individual urologist?

Dr. Amy Luckenbaugh:

A good question. As urologists, we all do it differently, but if there are multiple tumors in different places, I like to make sure to separate them all out for the pathologist. Because what we send the pathologist is kind of just a pile of junk, and it's not very easy for them to look at. So, separating it out helps them do a really good job of looking at each individual spot. And then as the patient, I would take into account, but what is the worst one, or the highest grade one? And that is what we as urologists will be looking at in deciding our treatment based on.

The multifocal, meaning multiple tumors, does kind of bump you into that either intermediate risk or high risk category, and not the low risk category, because they're multiple.

Stephanie Chisolm:

That's a great answer. know from a patient perspective, any TURB is too many TURBs. **But is there such a thing as how many TURBs a patient can endure**? What is the general rule of thumb before you begin

to think, "Well, maybe we need to go on to something bigger and more heavy duty to attack this cancer, to treat this cancer"?

Dr. Amy Luckenbaugh:

That is tough. I think in low grade cancer, many patients can endure TURBTs indefinitely, in low grade cancer. And sometimes even low grade cancers now we look in the office and just burn them, because it's been low grade for five years and we know it's low grade, instead of taking people to the operating room.

In high grade cancer it isn't necessarily that we worry that their bladder can't handle it, it's just that we worry what will happen if they keep coming back. The more they come back, the more deep they're likely to go, and the more likely they are to spread. So, it isn't per se your bladder is resilient and can handle it, it's more we just want to get to it before those cells start to creep outside.

Stephanie Chisolm:

That's a great answer. I appreciate that very much. **So, I know that sometimes patients are sent home with BCG and asked to hold it for the two hours before they naturally void it out on their own. And then they have instructions for how to keep it safe and clean. But what about intravesical chemotherapy?** Is the patient ever sent home with chemotherapy still in their bladder and expected to take care of that? Is that something that commonly happens, or is it different with chemo?

Dr. Amy Luckenbaugh:

It actually it does commonly happen. If it's the chemotherapy that we give right after the procedure, the single dose oftentimes the patient's still waking up from anesthesia and everything. So they don't have to worry about that, because we drain it out in the recovery area before they're ready to go home. But with something like gemcitabine where you're getting it weekly for six weeks, we can also send you home with that chemotherapy in the bladder with similar guidelines on what needs to be done and how to do it.

Stephanie Chisolm:

So, in general, and I know we're in the middle of a BCG shortage right now, but when patients are able to get BCG, **are there long-term side effects that we see with the BCG installation inside the bladder?**

Dr. Amy Luckenbaugh:

Yeah. The BCG side effects are often cumulative. So they can get worse with more BCG, unfortunately. Some people rarely have side effects at all, and that's great. And other people gradually start to develop side effects, like frequency of urination, urgency of urination, burning. And some people very rarely can develop almost what we call an N stage bladder from BCG, that it's so small and so contracted, that they are urinating constantly. It's not common, but it's something that can happen. And so, it's common as you're getting the BCG for things to kind of... They starts off okay, and then you slowly have side effects that are altered. And we can give medications to help with that, and we can also reduce the dose, and that sometimes can help with that as well.

Stephanie Chisolm:

Thank you very much. So, given that the BCG shortage isn't getting any better anytime soon, I know you have a bigger practice at Vanderbilt, so I'm sure you're getting an adequate supply of BCG to treat your

patients, but I know not everybody is being seen in the large academic institution where they might have an adequate supply. So, when they're being treated in their community, **do you have a sense of what the community urologist is able to provide to them in lieu of BCG if they can't get it? What are some of the things that are being used in the community?**

Dr. Amy Luckenbaugh:

Gemcitabine is being used instead of BCG in the community. And some practices are reducing the dose, and cutting the dosage in a third and splitting the rest of the thirds amongst other patients to get some BCG rather than non. That is kind of my limited knowledge of what goes on. Yeah.

Stephanie Chisolm:

Here's a particular question. **How does the FISH test fit into monitoring?**

Dr. Amy Luckenbaugh:

That's a good question. I don't often use the FISH test. Some of it is a financial reimbursement thing. But I think that if we have doubts or questions about abnormalities and cells, specifically the cytology, getting the FISH can give additional information about whether there is an area of concern we should be focusing on. Because sometimes the cytology can not be perfect, and FISH can help provide backup for the cytology. But I wouldn't use it as routine monitoring, or routine testing, or anything like that.

Stephanie Chisolm:

There's been a lot of talk about some of the discomfort that goes along with both a cystoscopy and even for the BCG. **Does topical lidocaine help in your mind, when you see that? Do you use that with patients if they have challenges with the cystoscopy or with the BCG installation? And does that impact both?**

Dr. Amy Luckenbaugh:

We do use it. I do not think it impacts things negatively at all. And if people have difficulty, we use it prior to assist you, also we use it prior to our cystoscopies, and it does not impact the effectiveness. That's like somewhat of a controversial topic, but I do not think it does.

Stephanie Chisolm:

Okay. Great. **So, does the risk of recurrence and progression lessen in high grade T1 cancers with the passage of time once it's successfully treated with the TURBT and the BCG?**

Dr. Amy Luckenbaugh:

Yes. Yes. It still exists, but of the biggest predictors is, after BCG, the first time you've gotten it, if we look in your bladder and there is cancer back, that is one of the biggest predictors of future progression and future cancer coming back. So, as we get further out we feel better that it is less likely to happen, and that's why we decrease that frequency of cystoscopy and everything like that.

Stephanie Chisolm:

Great. there's a question that came in about the AUA, the American Urological Association, treatment and monitoring protocols for high grade bladder cancer seem to be based on experience with BCG. **If you're having chemotherapy and still the gem and docetaxel, should the monitoring protocols be**

about the same as they would be for the BCG, or more aggressive, more frequent scoping, or less aggressive? What's the general take on that? What is your thought?

Dr. Amy Luckenbaugh:

Some of it is nuanced and provider-specific, but I think if BCG hasn't worked, I tend to survey people a little more closely than the guidelines suggest, because BCG hasn't worked and I want to make sure whatever subsequently is being used does work.

Stephanie Chisolm:

So, if somebody were to have experienced something like cystitis that came about from their BCG, what are their options for treatment?

Dr. Amy Luckenbaugh:

So, in terms of their cancer, they could still get BCG at reduced dose. In terms of their side effects, there are things that we can use. There's things over-the-counter such as Azo or Pyridium that can be used to help reduce the burning that can be given concurrently with BCG. There are things for bladder spasms that can be given. Like oxybutynin is an example, or Mirabegron is another form, that can be given to reduce bladder spasms.

Some people have significant spasms when the BCG is instilled. And so, there are people that we have them on long-term bladder spasm medication, but we also ask them to take an extra as needed dose before they come to get the BCG so that that BCG can be helped better. Sometimes in people who have spasms so severe, sometimes we leave a catheter in, and send them home with it. And then they take it out once they've drained the BCG so that they're able to hold the medication in. So those are kind of some options both to help continue to get BCG, but also for management of the symptoms from the BCG.

Stephanie Chisolm:

Sort of an interesting question, **what size is considered a large tumor?** And we're still going to stay in the non-muscle invasive. What would you consider a large tumor? And do you have any sense of the largest tumor that people have seen? And most of them, if you were thinking about the average tumor size, is usually what?

Dr. Amy Luckenbaugh:

Let's say the average tumor size is somewhere between two and five centimeters, about. The guidelines use three centimeters as the cut-off to move someone from the intermediate risk category to the high risk category, and some of that is based on research that has been done. But I would say two to five centimeters on average is its average. And there are times where bladders are completely full of tumor. And those patients, I think one thing to keep in mind if you are one of those patients is that that sometimes requires multiple trips to the operating room to get your bladder to be not completely full of tumor. And that's in part because we can only safely scrape for so long because of things that happen with fluid and everything like that.

Stephanie Chisolm:

So, are there any contraindications for the practice of physical exercise after a TURBT, or during intravesical therapies that you can recommend, or that you've seen patients have challenges with?

Dr. Amy Luckenbaugh:

I usually tell people right after a TURBT, depending on the size, to take it easy in terms of no heavy lifting for greater than 10 pounds for about 48 hours. There's no data behind that, but I think your bladder is forming a scab, and so that straining or pressure can kind of burst the scab off and increase the risk of bleeding. But otherwise, I would say there's pretty limited physical activity restrictions. And during intravesical therapy, you can continue physical activity. You shouldn't have intercourse within about 48 to 72 hours of receiving it. But besides that, you can continue normal physical activity during the intravesical therapy.

Stephanie Chisolm:

Great, okay, good. **Does an evidence of a prostatic urethral carcinoma in situ in addition to what might be in the bladder affect the prognosis?**

Dr. Amy Luckenbaugh:

It affects the prognosis a little bit, because carcinoma in situ in the prostatic urethra is a little harder to get rid of. It doesn't respond quite as well to the BCG, because the BCG sits in your bladder, but it can't sit in the urethra tube. And so, it doesn't have as much contact with the urethra tube as it does with the bladder. It's not to say that we don't try often to use it, but it just doesn't work quite as well as it does in the bladder.

Stephanie Chisolm:

There's a medication-specific question, and I'm not sure if you have the answer. **But if you're taking tamsulosin, does that impact or affect BCG?**

Dr. Amy Luckenbaugh:

No. No, it does not. Not at all. Actually, a lot of people we wind up, men specifically, putting them on it throughout the course of the treatment.

Stephanie Chisolm:

Okay. That's excellent. Thank you. **Can BCG failure be due to steroid drugs being taken while having the infusions, if you're on steroids?**

Dr. Amy Luckenbaugh:

It is a little bit dependent on how high of a dose of the steroids. If it's a low dose, like daily prednisone kind of thing, typically not. But if you're on big doses of prednisone, or big doses of steroids, or big drugs that affect your immune system for arthritis or things like that, we may work with your rheumatologist or primary doctor to help adjust those, just to make sure to get the maximal effect of the BCG. It usually takes a pretty high dose though for it to not be effective.

Stephanie Chisolm:

I have two location questions. **When the CIS is in the dome of the bladder, which is assumed to be the thinner part of the bladder, does that mean it's a higher risk of progression into the muscle?**

Dr. Amy Luckenbaugh:

No. So, the dome of the bladder is slightly thinner, but what really is important about the dome is it's the hardest to biopsy or scrape tumors off of because it can rupture like a water balloon. And so, the real concern with stuff at the dome is on us, making sure that we get as deep as we can safely. It doesn't increase the risk of progression to muscle invasive, though.

Stephanie Chisolm:

If you have more than one tumor, but they're all clustered in the same location, same area of the bladder, is that a good sign, or maybe more of a risk? What's the risk there?

Dr. Amy Luckenbaugh:

It's hard to say. We treat multiple tumors as multiple tumors, and we associate it all the same. But the question is a good one, because are there multiple tumors and they're just little satellites popped off of the main tumor, and that's why it's all clustered in one location? Possibly. But we don't have quite enough information about that to know.

Stephanie Chisolm:

This is kind of a timely question. **When on immunotherapy like BCG, is there any concern about vaccinations for flu, or for COVID?**

Dr. Amy Luckenbaugh:

No. I do not think so. I tell everyone they should go ahead and get their normal vaccinations, and do all of that regardless of the BCG, or intravesical chemotherapy being administered.

Stephanie Chisolm:

Okay. And then the last question has to do with BCG. **I know that it in some cases needs to be mixed under a hood, because it's the attenuated virus and everything. But the question is, does it have to be administered in a negative pressure room with an N95 on?**

Dr. Amy Luckenbaugh:

The people who administer it generally do wear an N95 for their safety. They do not do it in a negative pressure room, it's administered in our normal clinic rooms in general. But they do wear gown, gloves, and an N95, and face shield to protect themselves.

Questions submitted that were answered in writing:

How do you know if a CIS is or is not already Muscle Invasive Cancer?

They determine this by doing biopsies and TURBTs that take samples of muscle as well as the tumors. This shows whether the cancer is in the muscle.

Why is CIS considered high risk?

You can read more about CIS at: https://bcan.org/facing-bladder-cancer/bladder-cancer-types-stages-grades/. Generally it is considered high risk because pattern of the cells.

Why wouldn't blue light cystoscopy be used on all patients if it picks up the cancer better than the white light cystoscopy?

Blue light is a "newer" technology and the equipment for it is quite expensive, so not every clinic/hospital is able to purchase this equipment.

If cytology is negative for High Grade cancer, how can one be sure that the bladder does not have Low Grade cancer?

They use TURBT to determine this. Generally speaking, biopsies and TURBTs are more accurate than cytology. Cytology is not accurate or often used for low grade cancers.

When on immunotherapy like BCG is there any concern about vaccinations for flu or Covid?

Patients are encouraged to receive vaccinations like the Covid or flu vaccine, while they are undergoing intravesical treatment. Always consult your healthcare provider if you have concerns about side effects from vaccines. You can also listen to a more in-depth here: https://bcan.org/what-you-need-to-know-about-covid-vaccines-and-bladder-cancer-with-dr-seth-lerner-and-dr-laila-woc-colburn/