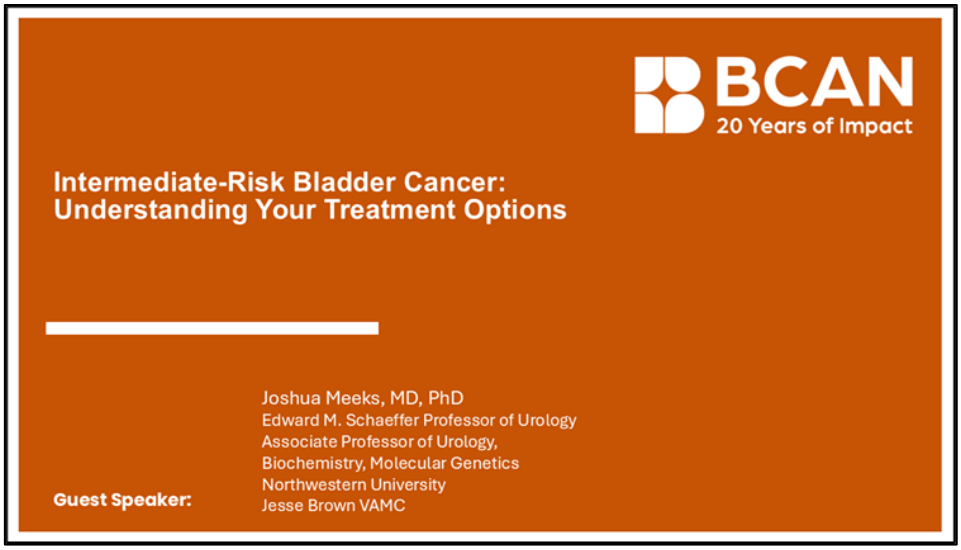


Dr. Joshua Meeks:

So, I just want to kind of summarize what I do and kind of how I approach it, and this is really just kind of a beginning of the discussion for what I would anticipate someone with ... you know.. If you have intermediate-risk bladder cancer, and you were just diagnosed, this is kind of how that discussion should go. So number one, hopefully you had a TURBT. I usually do a blue light. Hopefully, you got a single dose of chemotherapy, because that decreases the risk of recurrence. I usually meet with people at around a week, and we talk about their pathology and next steps. I talk about what we found, and I usually do give them evidence of like, "This is what your risk score is, you know, zero, one to two, three or greater."

I put this in the notes so it's clear to my partners, it's clear to the patient. If someone travels, gets a second opinion, they see all that information. But I think that really begins to have a backbone of like, just based on these factors alone, what's your chance of this cancer coming back? Um certainly, there's people who are going to want to do less. There's some people who are going to want to do more. But I think the key point is if our outcome is recurrence, you know, what do we expect to have happen? I think that just levels the playing field for, you know, where are we, and what do we anticipate this next year is going to look like?

And that's really where we come up with a plan. The two questions that we need to leave with are, what's the rate at which we're going to take a look in your bladder, and then, are we going to do therapy or not? And again, that's where the risk factors kind of help us make that decision. But again, I have a lot of folks who say, "I just want to do scopes, and if it comes back, I'm willing to escalate it." I, personally,

think that's totally appropriate um, as long as we kind of know exactly what the risk is. And from there, we just kind of schedule it out. So, I mean, is there anything, Stephanie, that you think I'm doing wrong or that you would say that we should be doing? But this is kind of how much of that, that first visit discussion will go.

Stephanie Chisolm:
Yeah. I think it's really important, first of all, for patients to just understand their risk levels. So if they don't know, maybe the next time they go in, they might inquire, they might ask-

Dr. Joshua Meeks:
Absolutely.

Stephanie Chisolm:
"What are my risk factors, and would you classify me as low risk, or intermediate risk, or high risk?" And you know then, you can sort of stimulate a discussion that way by getting it started, by finding out, because I think many patients don't have that level of detail. This is still a new concept, to have those risk factors kind of scoring you and putting you in a category that now gives you some other options. Because I think many patients don't have that information, and I'm not sure that as many in the community that aren't in large academic centers for treatment are getting people to look at that and to share that information. So it would be a good thing for people to ask about.

Dr. Joshua Meeks:
That's a great point, just to start there. I do find that in general, um, when folks are going to providers that don't see a lot of patients with bladder cancer, there's a little too much and a little too … you know .. so we're probably doing too many scopes, oftentimes, right, too many scopes in low-risk patients, and then maybe offering BCG to low-risk patients which may or may not need it, um and then, when something comes back as like a Stage 1, a T1, and we're like, "Oh. That's a high-risk cancer," maybe not having the discussion about escalating treatment. So you're right. That so I think from the beginning, to your point, I would say if people could walk away from this intermediate-risk talk with anything, it would be know your risk status. Then, if you are intermediate-risk, maybe start having that discussion about, you know, "Where am I within that, and what do I expect for this year?"

Stephanie Chisolm:
Yeah. Great. Okay. So we did get a couple of questions that came in with the Q&A box.

Dr. Joshua Meeks:
Great.

Stephanie Chisolm:
Is UGN using mitomycin C? Is that what's in there?

Dr. Joshua Meeks:
Yeah. That's the chemotherapy. That's the mito gel, and uh it's obviously a very special compounding. But the active agent is mitomycin. Yep.

Stephanie Chisolm:
Mm-hmm. Okay. There's a couple of other questions that might be leaning a little more towards high-grade. Um... When is treatment considered complete? For instance, is treatment considered complete after therapy with BCG, or is it a certain amount of time after therapy and a set number of cystoscopies? This is important when it comes to VA benefits. So let's take out the BCG, because that wasn't one of the real things we discussed, but is it considered complete after a certain period of time or number of cystoscopies?

Dr. Joshua Meeks:
Well, so you can do BCG for intermediate risk. Um and it is there as a possibility, and it is effective for patients with intermediate risk. Again, I think a lot of places ... like we don't offer it, because we don't have as much to offer patients. But certainly, for someone who's seen chemotherapy, who doesn't want gemcitabine-docetaxel, BCG as possible. So it actually is reasonable for intermediate risk. Usually, therapy is 12 months for intermediate risk. Uh so you know if you're going to get chemotherapy, that looks like usually six doses of induction, and then monthly doses of maintenance. For BCG, it's six doses of induction and then maintenance at three, six, and 12 months.
So it's usually a year of therapy, and then we stop. And again, to contrast that with high-risk patients, um, ideally, we're giving three years of therapy for high risk, but again, in our shortage, everybody's at a year. So you know it's kinda, it's brought the ceiling down to the floor, and everyone's at 12 months. And that, you know, works for a lot of people, but oftentimes, the high-risk patients are much more likely to recur.

Stephanie Chisolm:
There's another question that was in there, again, talking about BCG and are you all at Northwestern doing a partial dose?

Dr. Joshua Meeks:
Yes. A hundred percent. So um, we're allotted 39 doses of BCG a month. Um, that's our allocation downtown. Um ... We have four other affiliates across uh Chicago, and some of them actually have more than we do and um ... We've tried to develop this network where we're either sending doses, asking them to split and increasing their capacity, or asking people to go you know 12 miles to another facility, but we do split. Um that's been the guidance from the SUO and the AUA, how to manage that, and you know honestly, we've never seen a difference in outcome. I know, again, Ashish has looked at his data.
I would say that the tolerability seems to be just as good, if not better. Um, I rarely think people actually do a little bit better on split-dose BCG, uh and I think the recurrence rates are the same. So I actually think it's ... Not only is it a way to manage the shortage, but I think it's actually probably a better outcome from a tolerability perspective. Um I do have patients who say they really want full-dose BCG, that's how the dose is intended, and I say that I just can't offer them therapy here. So I usually you know refer them out to one of our sites in the city that I know have been giving full-dose BCG, and um you know that's just what we'd have to do.

Stephanie Chisolm:
Yeah. So um I know back in the beginning of the shortage, we would get calls from patients that said, "My doctor said I have to call the pharmacy to see if they have BCG." Actually, that, that did happen. I answered a call, and they said, "My doctor said I have to call the pharmacy. I don't know where to start." But the question that came in was, "Can patients source BCG on their own through specialty pharmacies?"

Dr. Joshua Meeks:
I've never seen that happen, um, where people show up with their own BCG, and we put it in. I don't know that that's feasible. Um so I've never seen, because it's a biologic. But I've never seen that done. Uh again, in our place, it's given by our nurse providers, and we get it from the hospital pharmacy. I know we've had other sites where it's given through the infusion centers, um and it's a little bit different. But I've never seen a patient get the drug and show up with it.

Stephanie Chisolm:
Yeah. Okay, and because it comes frozen. You have to defrost it, and yes. It's distributed not through a specialty pharmacy, but through the entire pharmacy network, through the large suppliers.

Dr. Joshua Meeks:
Yes.

Stephanie Chisolm:
So I did learn something interesting a little while ago in speaking to one of the people at Merck, was that they're building that second plant, and hopefully the BCG shortage will be over um when that is complete. But what I didn't know, and this makes a little more sense, was that BCG was first approved by the FDA 40 years ago, and the technology that creates the BCG was 40 years old.

So they're building a new facility that they must build with 40-year-old technology. So they're like retrofitting back to that, because if they changed anything, they wouldn't get FDA approval. So that explains it. Doesn't make it any better, but it explains why it's taking so long.

Dr. Joshua Meeks:
Well, and again, I think all of it comes back to how it's made, right, so the processing. Uh so it came due in bladder cancer in like 1974, were some of the trials. Right? So that's like fifty-some years. But the vaccine dates back to turn of the century, and the sort of way it's grown has really not changed. Now, it's kind of different by strain, and um that's why I'm optimistic that different strains, combinate strains, strains like you know Tokyo-172, all of these have different ways of being made, may add to that. Right? Because at the end of the day, we just want to be able to give people BCG and give them adequate BCG. Now, we'd love to know if those strains obviously, this is a whole another discussion, but do people have a different response to different strains, and could we, again, give the right person the, the right strain?

Stephanie Chisolm:
Yeah. Other countries have approved um BCG that's brought in from India and the Tokyo strain, many different strains. Unfortunately, the FDA is still studying whether it's as effective and as safe for patients. We have time for maybe two more quick questions. What are your thoughts on single agent gemcitabine without docetaxel?

Dr. Joshua Meeks:
Again, I think that is sort of the standard. So when someone shows up with intermediate risk, and we say, "Okay. What would you like to do?" Uh, I always talk to them about a trial. Um but I think the comparison for that is uh single-agent gemcitabine or mitomycin. The two are, you know, never been compared head to head in intermediate risk. Um I-I usually talk to patients about, "Well, let's start with mitomycin,

because it tends to have a little bit more activity." Um Gemcitabine is actually tolerated probably better right after surgery, but it can cause some nausea.

I have a really high fraction of patients that are women that I care for with intermediate risk, and I will tell you that uh nausea is very common in women with intermediate risk that I treat. I don't know what that is. Never really been described in a manuscript, but that's my experience just kind of caring for folks. Women, intermediate-risk, enriched, and then gemcitabine tends to make a little bit of nausea. So I start with mitomycin uh just based on sort of my own experience, but I think they're both ... And then, I'll also use docetaxel as another drug to give people.

Stephanie Chisolm:
Mm-hmm. Yeah. That's interesting. Since it's intravesically-administered, you would think that nausea wouldn't be a big deal. That's fascinating.

Dr. Joshua Meeks:
You know, and It can be real, Stephanie. I mean, I know a patient that uh would be out for like three days after getting gemcitabine, which is just unreal. Right? I mean, you think, that goes back to this, the burden of this, and like you think about one option is we full grade tumors every six months versus being down for three days after therapy when it's given six weeks in a row. That's awful. So um it's just, it's probably not an acceptable alternative therapy.

Stephanie Chisolm:
Thank you. One last question, and then we have one more question, too. But um is high grade always considered high risk?

Dr. Joshua Meeks:
So it depends on your definition. So in, again, in the US, a small high-grade tumor is considered intermediate risk. Now, in the European system, they would consider high risk, and that patient would get BCG. I kind of have that, again, have that discussion with patients. So if they have a single small high-grade tumor, um, I usually start with chemotherapy, because I'm trying to save the BCG for patients that are multifocal, a Stage 1 with CIS. Um so it really depends on the system and discussion with the patient. I think, again, the key point is they're probably going to get scopes every three months for two years, um, and then we're definitely going to treat them. Again, we'll have a discussion about, do they want to try chemotherapy or BCG? "Here's the risk, benefits. What do you think?" Um I would say that the only problem with starting with BCG for patients, again, with like a 3, a small high-grade tumor is that if they don't respond, they're BCG-unresponsive, and then you're sort of in a very different group of folks.

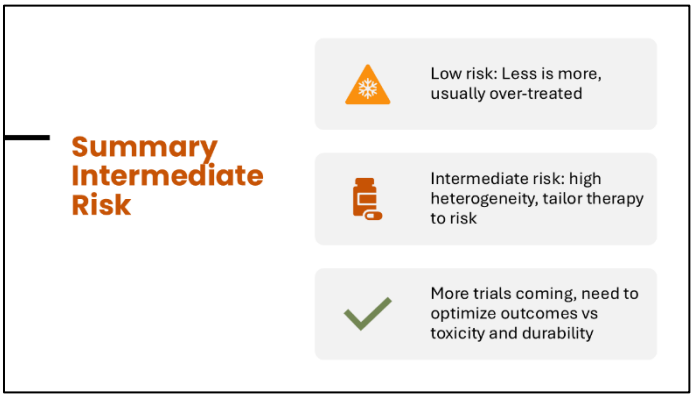
Stephanie Chisolm:
Right. Right. Yeah. Then, you've got to escalate, maybe, some of the other options.

Dr. Joshua Meeks:
Right.

Stephanie Chisolm:
Okay. Well, this has been incredibly informative. I'm so excited to have this as a resource for our patients, and I greatly appreciate your expertise and your time. And you've seen so much in the 20 years since

you've been in the bladder cancer space. So if you could sum it up, what would be one takeaway that you would want patients to know.

Ah. Look at that. You've already got it.



Dr. Joshua Meeks:
Yeah. Yeah. No. I think this is it. Right?

Stephanie Chisolm:
Yeah.

Dr. Joshua Meeks:
So, I loved your concept about if you can walk away and at least just know your risk status, like when you walk into your scope, say, "Okay. I'm this," you know I think that that just begins to empower you to think about, "What should we be doing?" um and so having these discussions with your provider. Right? Again, I think that you know our all is the same is probably changing, and there's a lot more coming. So, you know this is a very optimistic place. If you're a patient with an intermediate-risk bladder cancer, I would walk out thinking that the glass is half full, and there's a lot of good stuff coming… and you know I think the hard thing, again, for the patients that I care for with this is that they're mostly … you know they're looking for a way to treat this with the least amount of toxicity, and I'd say that there's a lot of people thinking about you and you know I'm very optimistic that we're going to be there very soon.

Stephanie Chisolm:
Yeah. I always try to remind patients that a clinical trial is a viable treatment option. It gives you an opportunity to use an investigational medicine that's still being finalized, but you also get much better observation. They're really watching what's happening with you with that medicine. So clinical trials are a treatment option, and now, there are so many to, this is…

Dr. Joshua Meeks:
But clearly, you know this space is … I just showed you three groups that … These don't work without participation of this group. You know?

Stephanie Chisolm:
Yeah.

Dr. Joshua Meeks:
If people aren't taking an active role to try to make this better, then we don't get answers, and we can't say this works and this doesn't. So um unless communities are bought in to make things better for people, then that's just not possible and BCAN's really the responsible party for that.

Stephanie Chisolm:

Yeah. I always say no new treatments happen without clinical trials. So that's really important. And again, it's so exciting. Because of all the clinical trials and all the individuals that really committed to giving their bodies to these new drugs, and trying them out, and working on fine-tuning them, we do expect some of them to get approval in the next six months. That's really exciting, and obviously, BCAN will announce those things as they come through. Dr. Meeks, thank you so much. This has been a phenomenal resource and a wonderful program.