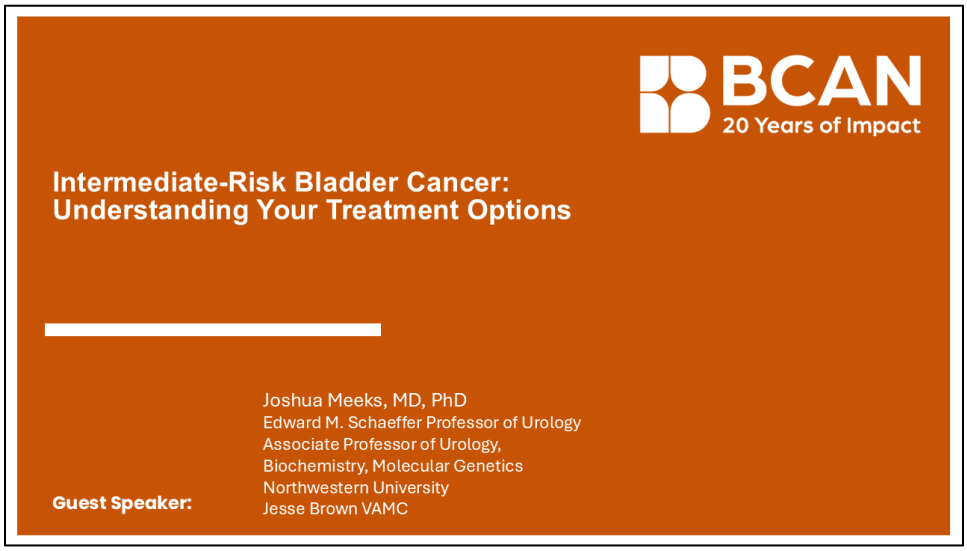
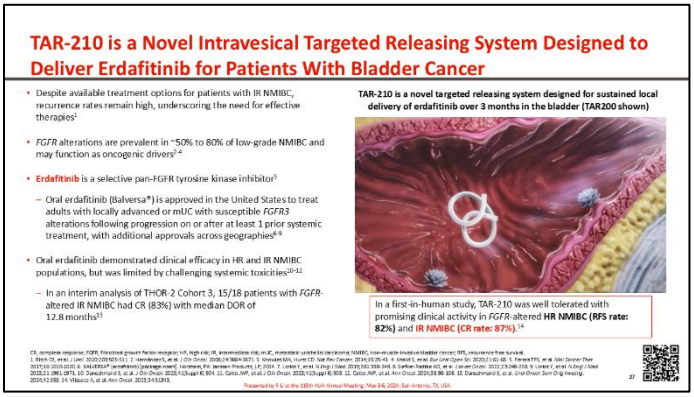


Dr. Joshua Meeks:

And so the first thing is TAR-210.

Dr. Joshua Meeks:

And so, um, TAR-210 here's a nice sort of visual about how it's deployed. It's a device that's put into the bladder and it comes in as a tube and then curls up like a pretzel. People call this the pretzel, um, and now everything I've talked about before is really, um, like a wash. So we put it in your bladder. You hold it for two hours, and then you pee it out. You know, the erda- this pretzel is a device that goes in, and this one stays in for three months. The picture, the video is the other gemcitabine-eluting one, so the colors are a little different. But, you know, the key thing about this and why it's so cool is that this is a therapy that started as a pill. We tried to give it in a pill to people with



advanced bladder cancer. While it worked, um, there was a lot of toxicity, cause it goes throughout your whole body.
So then, J&J was very bright to develop this in something that goes right into the bladder. You get rid of all the toxicity, and you get local therapy. Um, and the cool thing is that many of our early bladder cancers, actually many more, in the neighborhood around 65 to 70% of early stage bladder cancer, intermediate-risk, have an alteration that's directly targeted by erdafitinib. So that FGF receptor mutation, again, is much more common in early stage bladder cancer. Um, and the response rates are very good, and the therapy is very local. And so that's where a lot of us are incredibly excited about this therapy that's there for three months, and it seems to be very specific for their bladder cancer. Um, so, I just want to talk a little bit about the data and try and summarize that as well as I can. So I-

Stephanie Chisolm:
May I just ask a quick question first?

Dr. Joshua Meeks:
Yep.

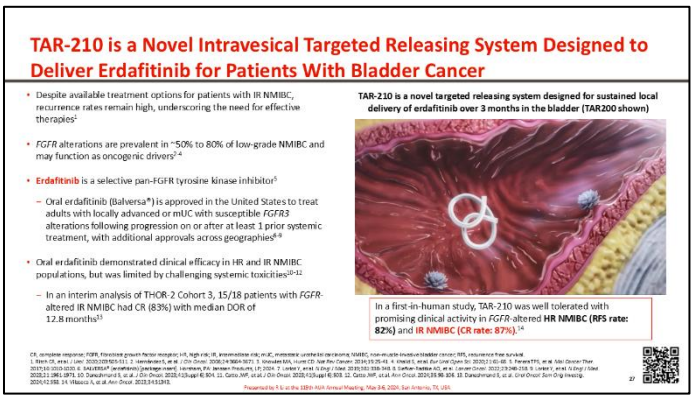
Stephanie Chisolm:
I just want to ask a quick one. Um, how often do you take the tumor, when you remove it with the TURBT through fulguration, and you're taking that tumor out, how often, with this non-muscle-invasive, do you get it tested for these genetic mutations like the FGFR that is what would react better to erdafitinib?

Dr. Joshua Meeks:
So, uh, evolving question. Up until now, we've not been doing it, and the reason for that, Stephanie, is that we've never had a reason to do it, cause I don't have anything specific for it.

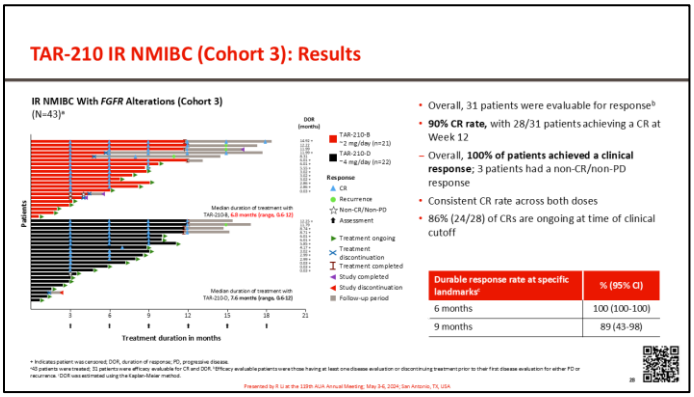
Stephanie Chisolm:
Got it.

Dr. Joshua Meeks:
But now that we have a target, and now that we have something to do specific for those patients, um, you know, I think that that's going to change. And there's two ways to do that. One of that ways is to go get a piece of the tumor and then send that off. The other is a urine test.

Dr. Joshua Meeks:
And so, um, you know, in this first in human trial, we did both. We did both urine and tissue, and it's not perfect, meaning that like just because you have it in tissue doesn't mean the urine's going to be positive. There's some that are positive in one versus the other. But, if you, the good news is that when we look at the results..



Dr. Joshua Meeks:



Which is here, it didn't matter how you tested positive. The response rates were just as good.

Um, the other thing that may be worth questioning, in, for example, in this study, uh, patients didn't have their tumor resected. So they had a tumor, and the device went in.

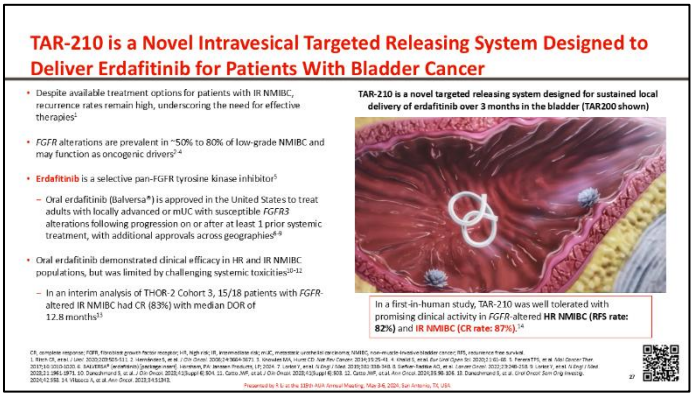
So this is an ablative therapy here. Um, and so, uh, that's also very exciting, because you think about trying to decrease the number of procedures that people had. Because that's one of the huge burdens for intermediate risk, is a lot of surgery, you know, a lot of endoscopy, a lot of procedures. A lot of, whereas this device, when it goes in there, it can just ablate the tumor. Um, that's at least what this data suggests.

So these are swimmers plots, and you look at the time points at the bottom. And so, again, you have a 90% complete response rate at 12 weeks of these tumors that were ablated. So all of these, uh, patients started out with tumor that just went away. And so, you know, again, overall 100% of patients achieved a clinical response. So that's really amazing, and then when you look at the duration of response, that's hitting 89% at, at, nine months. So I think this is a really exciting change to this field. We know a major target, again, found in anywhere from 60 to 70% of patients, and the duration of response seems to be very, very good.

Stephanie Chisolm:

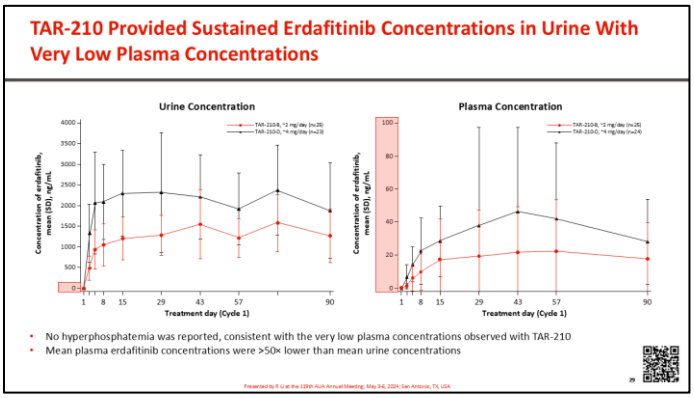
Great. Um, this is a device. The pretzel itself is a delivery mechanism. Right? So they can also use it for other things, like chemotherapy and other medicine that can go into that device?

Dr. Joshua Meeks:



Yeah. So again, this is sort of J&J'S pipeline. So, um, the question would be how it's engineered. I mean, they're incredibly smart people and great to talk to about you know, what you could do with this, but yeah. The pretzel is the shape, and when you actually ... If you ever get to see one up close, there's little small pellets of medication in there, and you're right. Your mind starts thinking about what else you could potentially put in there, you know, as far as medication delivery, and it, it makes sense that you have something that's there all the time as opposed to hold it for two hours and hope it works. Um, this just sits there. Now, I think the downside is, and I don't know that I have a tolerability slide.

Dr. Joshua Meeks:

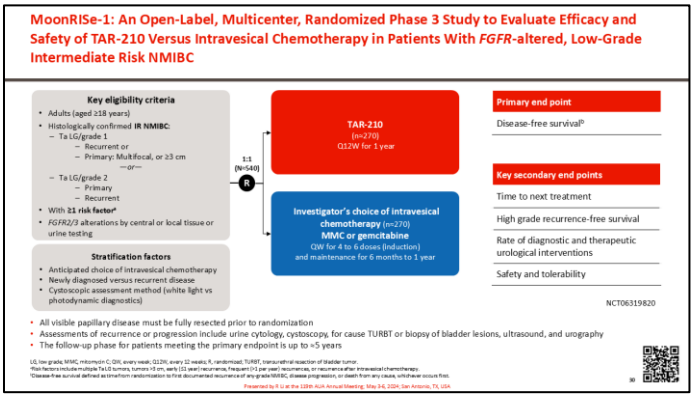


I don't, but, but, you know, there are people who have a little more bladder spasm with this. So I think, you know, again, it's not going to be perfect for everybody, and if you have bladder spasms with it, we're learning how to try to manage that. But, but, some people are going to need breaks, um, and we may have to figure out how to do that. I wanted to just show this. This is like looking at blood versus urine concentrations. And so if you look at the blood concentrations, the red, and blue, and black lines are the two different doses. If you compare those to the urine concentrations, you know, again, we're looking at 40 on the blood, and in the urine, you're getting in the one to 2,000 levels. So the dose is very, very high in the urine, meaning that the drug is working great in the bladder. So it's, you know, 50-fold lower in the blood than it is in the urine, and that's why you're getting the response without the toxicity.

Stephanie Chisolm:

That makes sense when you have that non-muscle-invasive. It really is on that inner lining. So getting it into your bloodstream is not as important, because the odds of there being a cancer cell somewhere else are very slim. So yeah. That makes sense.

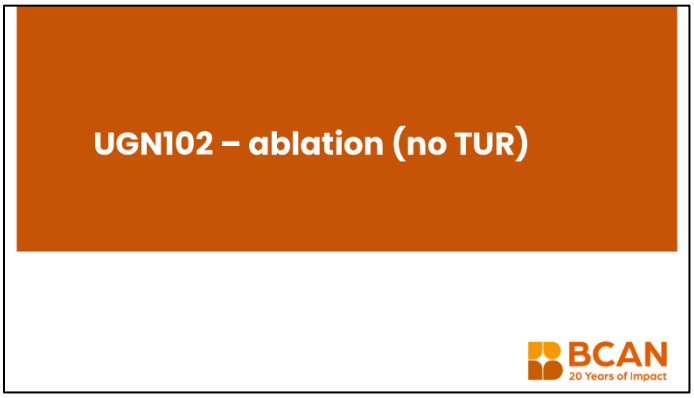
Dr. Joshua Meeks:



And so this is the trial that is ongoing with this now, and this is, you know, a really important trial. So again, this is FGF receptor positive patients. So we've tested their tumor, and it's comparing chemotherapy, which we've talked about, that's a standard of care, versus TAR-210. And it's 270 patients in each arm. Uh, this is, you know, big trial, uh, enrolling now. So we're excited to see, like, is it better? Right? And the question's going to be, how long can people go without tumors in comparing these two drugs, two, two, treatment options. This is how this new standard of care becomes available, um, is that we compare these two. And so this is ongoing. This is called MoonRISe-1. There's more MoonRISes coming, but I think this is a really exciting uh trial in this space and we're really going to be excited to see what it shows.

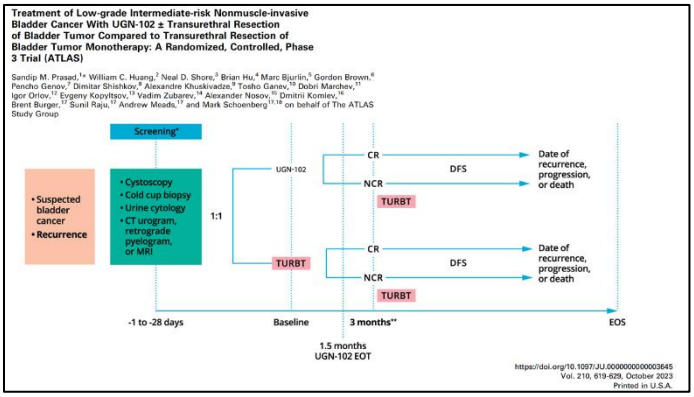
Dr. Joshua Meeks:

UGN-102. So this is another therapy. And so, uh, the really neat thing about this for our patients is that this is an ablative treatment. So the hope is with this, that, again, we can spare patients from TURBT.



Dr. Joshua Meeks:

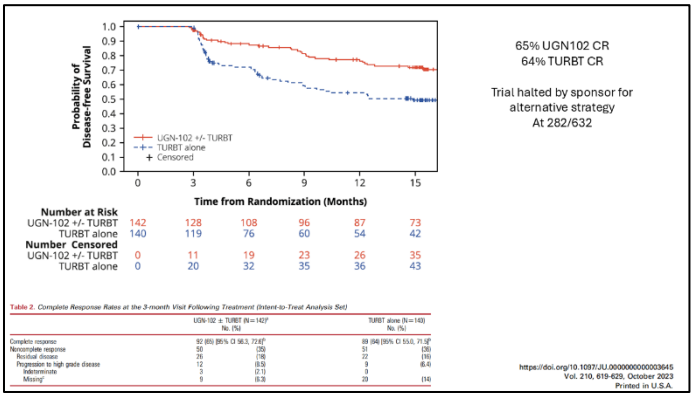
And so the way that this sort of was tested, again, uh, this is the ATLAS trial, so, um, I'm just showing you this so you have a sense of comparison. So this was UGN-102 compared to TURBT. And then if patients had tumor, they could then undergo a TURBT in the UGN-102 arm. And so this is a chemotherapy.



So we talked about mitomycin, and in general, the way that's administered in our clinic is you come in, we put a catheter in, the therapy gets put in, you hold it for, you know, 60 to 120 minutes, and then you urinate it out. This is, you know, more forms of solid gel in the bladder, and it's urinated out much longer. So it's in the bladder for a much longer duration of time. And so because of that, this is the ... If you know about Gelmyto, that's what's used in the kidney, this is ... UGN-102 is a very similar version of that, but, but used in the bladder.

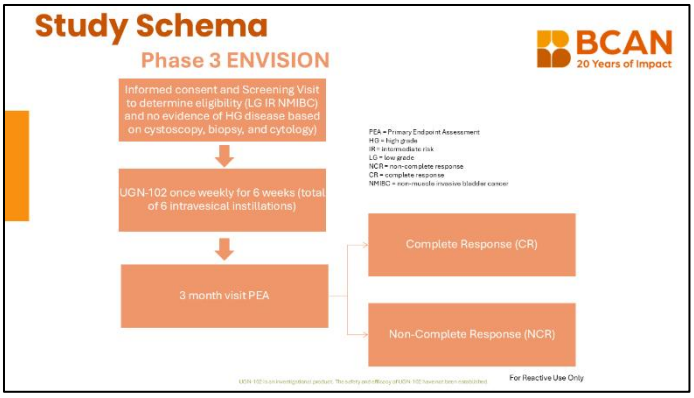
Dr. Joshua Meeks:

And so this is, again, some of those Kaplan-Meier curves comparing UGN-102 versus TURBT rate and even though the response is about the same, uh, when you look over time, you know, people with UGN-102 have less events, and they do much better over time. So this was the ATLAS trial that was published.



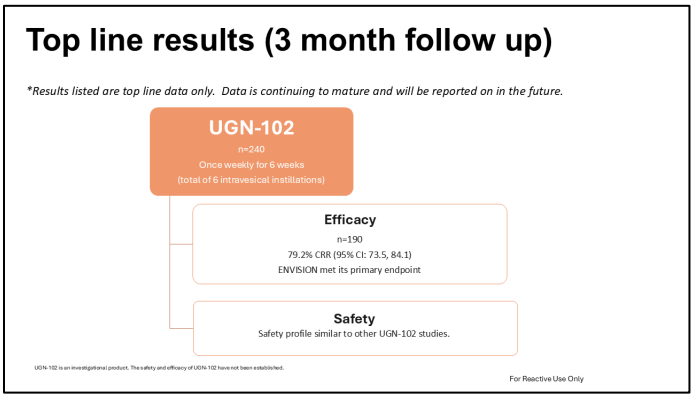
Dr. Joshua Meeks:

And then this led to a single arm trial. This is ENVISION, and again, this is UGN-102, single arm trial, given weekly for six weeks. And then, how did the people do at three months.



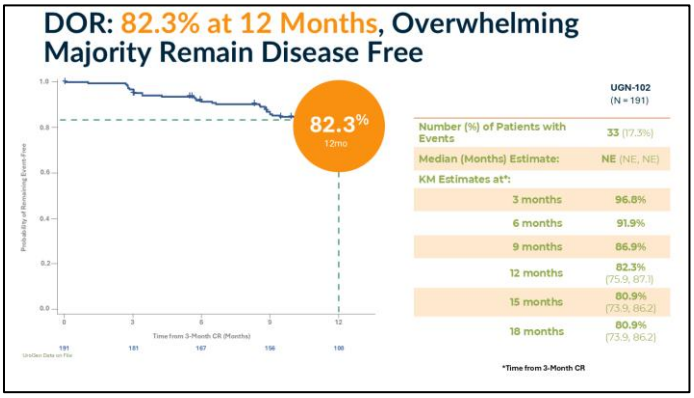
Dr. Joshua Meeks:

And so looking at response rate, 80% complete response rate of almost 200 patients. So that's really good.

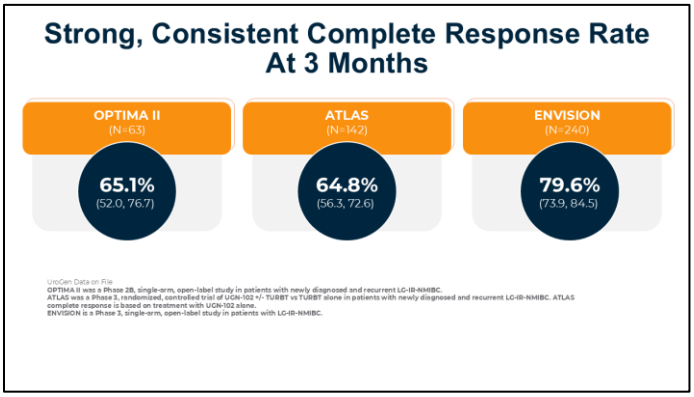


Dr. Joshua Meeks:

So 82.3% with um, remained disease-free of those 90%. So, so again, um, the hope here is that ... Is this going to work for everybody? Hard to know. But we have another therapy for people that, you know, before, are just tired of getting procedures, tired of getting fulgurations, and you're looking at durability of response of 82.3% when you get those um six doses of UGN-102. So I think that that is a real option for folks. I mean, again, it'll be really nice to have more than one option.



Dr. Joshua Meeks:
And you could see why this would be very good for patients because again, if you look across the board, the consistent response rate at three months is somewhere between 65 and 80% of tumors that just go away without the need for a, for a TURBT.



Stephanie Chisolm:
Yeah.

Dr. Joshua Meeks:
Do you, are you hearing that?

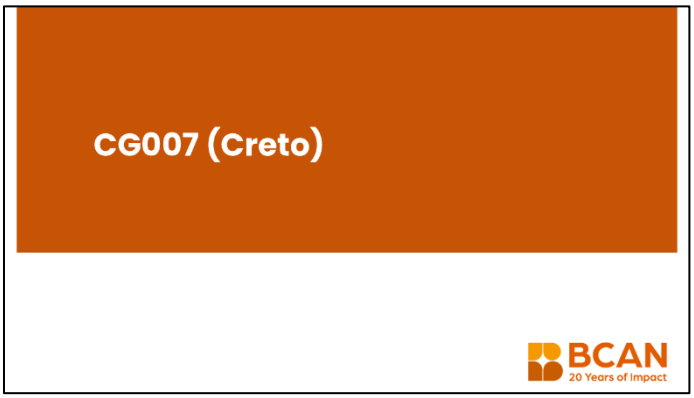
Stephanie Chisolm:
It's great because-

Dr. Joshua Meeks:
Yeah.

Stephanie Chisolm:
Yeah. I think, again, that's also sort of what you get with BCG in the high-risk. It's about 65%, roughly. Right? And so the idea to be able to have that medicine stay against that tumor for a longer period of time makes more sense to be able to have that reaction to get rid of the cancer.

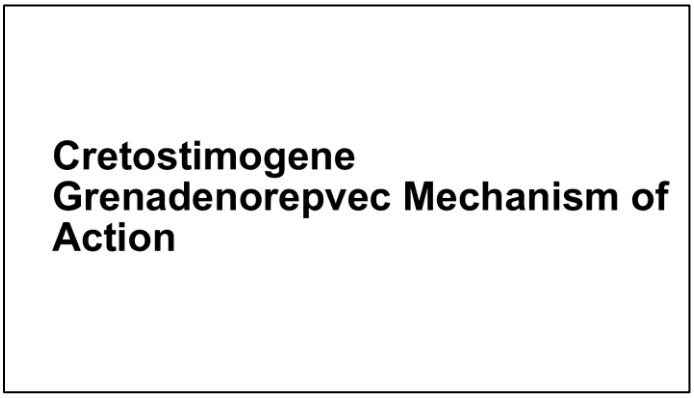
Dr. Joshua Meeks:
Without needing a TURBT, and, and again, some of it is like preference. But as you know, there's a lot of folks that we see that are just not well. And so trying to get the surgery, and stop blood thinners, and you know, ... Even, even, you know, there are, as you know, there are no small surgeries. So, um, if, if. there's a reason to try to avoid that, I think there's also a concern of, you know, how could this be portable? Can this be done well without ... as a procedure first? So I think there's a lot of interest in this going forward.

Dr. Joshua Meeks:
The last thing I'm going to talk about is CG007, or cretostimogene,



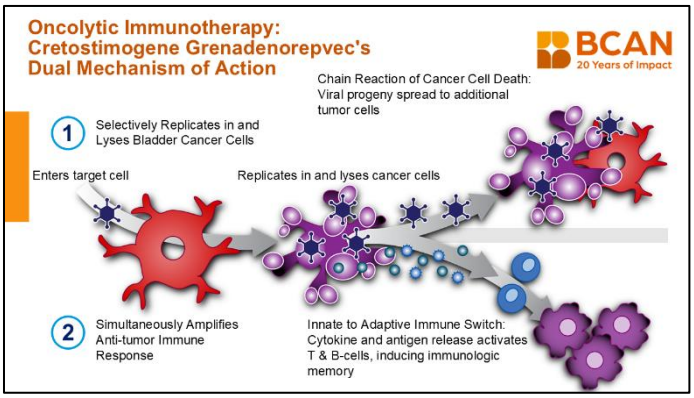
Dr. Joshua Meeks:

And again, this is a pretty, really interesting sort of future-thinking kind of therapy.



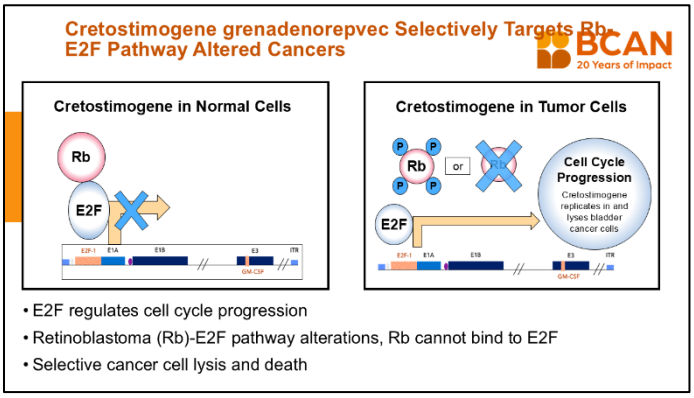
Dr. Joshua Meeks:

And Again, this is a therapy that's put into a viral vector that finds its way into bladder cancer cells. It causes the cells to, to replicate and die, and then that causes more immune cells to come.



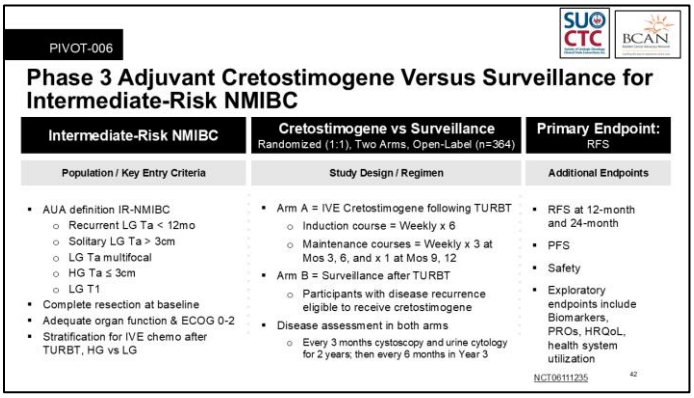
Dr. Joshua Meeks:

So, there is some specificity to that, because it doesn't seem to replicate in normal cells and only replicates in, in bladder cancer cells. So there is some precision involved in that.



Dr. Joshua Meeks:

And, and so this is their Phase III trial. This is what they call PIVOT-006. It does allow some high-grade tumors, but again, it's comparing TURBT to intravesical cretostimogene, six weekly doses followed by three doses at three, six, uh, and 12 months.



So I think, again, this is a really new and innovative therapy. It seems to have really good outcomes in, in BCG-unresponsive folks. And then, we're moving this early into intermediate risk. And so I just think about if you look at these three alone, um, there's so much promise here to be able to offer patients when they say, "I'm tired of having this cancer that keeps coming back. What do you have?" Uh, and, they're all different. Right? So you've got a viral therapy. You've got a ablative gel, and then you've got a device. Um, and so, you know, it's just so many more options that we, we have in the future, potentially, if all of these are effective.

Dr. Joshua Meeks:

And again, these are the sites for PIVOT-006.