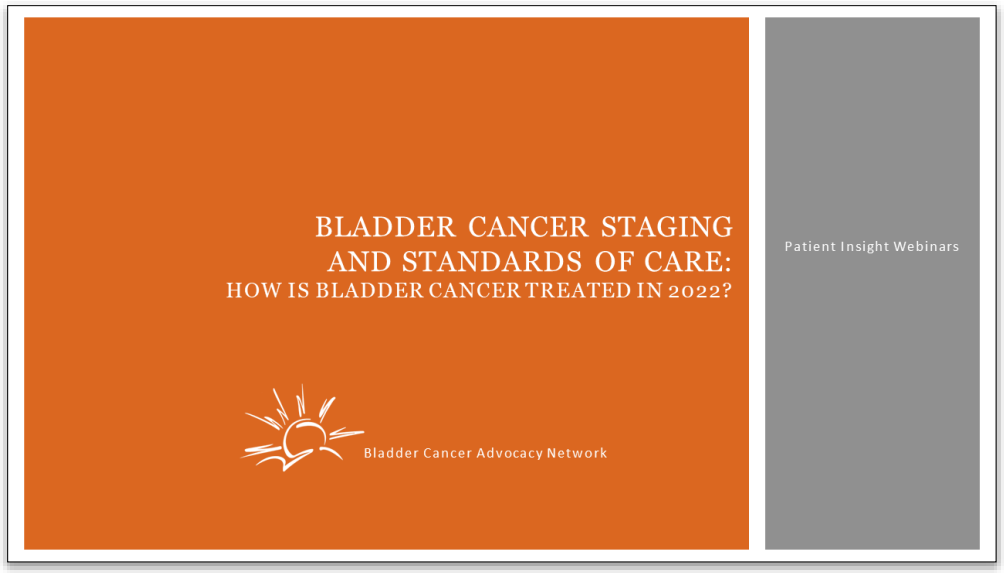


Stephanie Chisolm:

Welcome to Bladder Cancer Staging and Standards of Care. How is bladder cancer being treated in 2022? I want to first point out that everyone's bladder cancer diagnosis is very unique and your doctors are going to work to help understand whether your bladder cancer has spread, what stage is, and how aggressive it is. Your doctor's going to use this stage and grade to help determine your best treatment options. When we talk about treatments that are accepted by medical experts as proper treatment for your type of bladder cancer, meaning your stage and grade, it's really known as the standards of care or best practices. And BCAN is delighted to welcome from the University of Pennsylvania, the professor of urology and oncology, Dr. Trinity Bivalacqua. Who's going to share with you how your cancer is typically staged and what is the best practice for treating the most common types of bladder cancer tumors. Dr. Bivalacqua is a member of BCAN's scientific advisory board. So Dr. Bivalacqua it's a pleasure. I know you had a really busy day. Thank you so much for joining us. And I'm going to turn the screen over to you.

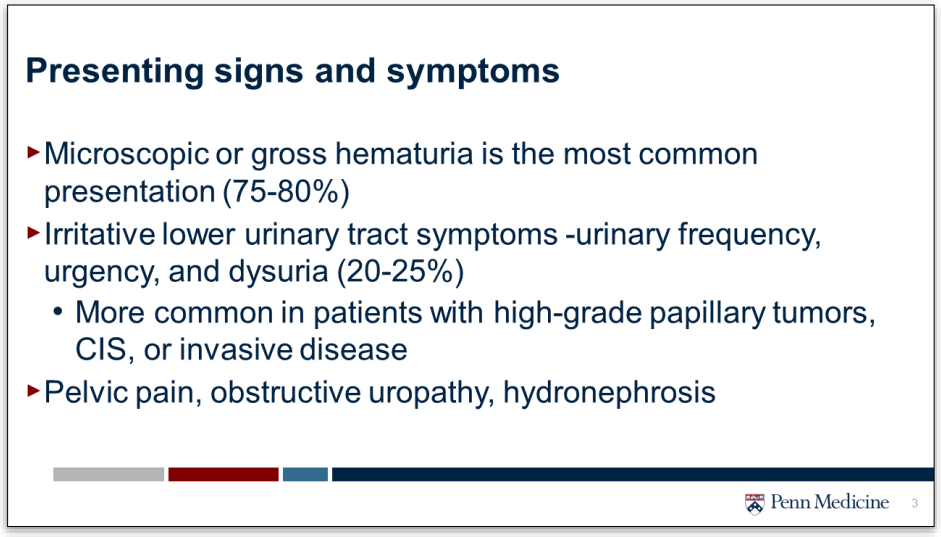
Dr. Bivalacqua:

Got it. Thank you. And obviously I'm so happy to do this and be here. I mean, I just counseled a patient about cystectomy versus more intravesical therapy and giving them the BCAN website. And this is just a phenomenal organization that I'm so honored to be able to be part of it and help patients, which is honestly my ultimate goal. Obviously I'm passionate about bladder cancer and have a clinical practice as well as a research program related around it. So what I was provided by BCAN was some questions that were proposed prior to this, to me starting. So what I've done to the best of my ability is to weave in a lot, if not all of those questions into my presentation. So there will be times when I'm going to talk in very broad strokes and talk a lot about just generalizations, other times when I'm going to talk about specifics, and I will state and tell you that I can talk more about it later in the question and answers if you have it. So please ask questions.

So this is my title. These are my disclosures. And I really have no conflict whatsoever as it relates to this presentation.

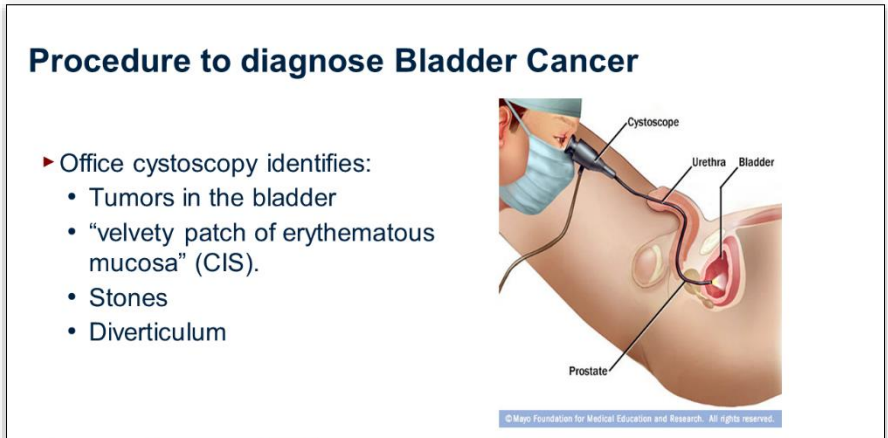
Dr. Bivalacqua:

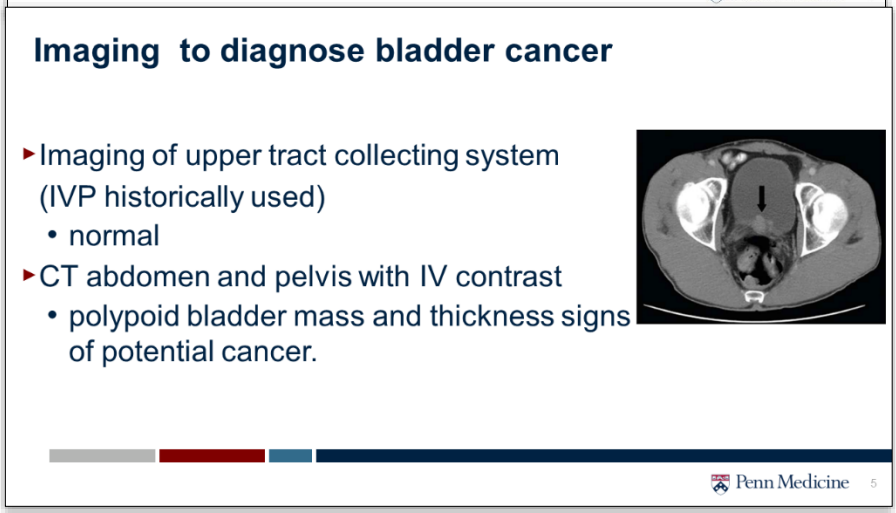
So to start off with the presenting signs and symptoms, unfortunately, I think the people in that I'm speaking to today are unfortunately very aware of these symptoms. And as we are all aware gross hematuria, or just seeing blood in the urine, or even microscopic hematuria is the most common presentation of patients with bladder cancer. What I tell patients all the time, both men and in particular women is that blood in the urine is abnormal and needs to be investigated. I'm not saying that you need to go out and have a PET CT scan, but you do need to see someone that can help determine why you have blood in the urine.



Irritative symptoms in particular, urinary frequency and pain with urination are also the second most common symptoms and this goes along with specifically with a form of bladder cancer called CIS, which we'll discuss. The later really end stage symptoms in patients that present with more locally advanced disease or higher stage cancer is pain, obstruction of kidneys, where the tumor has grown through the bladder wall blocking one of the ureters, which are the tubes that drain urine from the kidney so these are late stage. But really blood in the urine and painful urination and increased frequency.

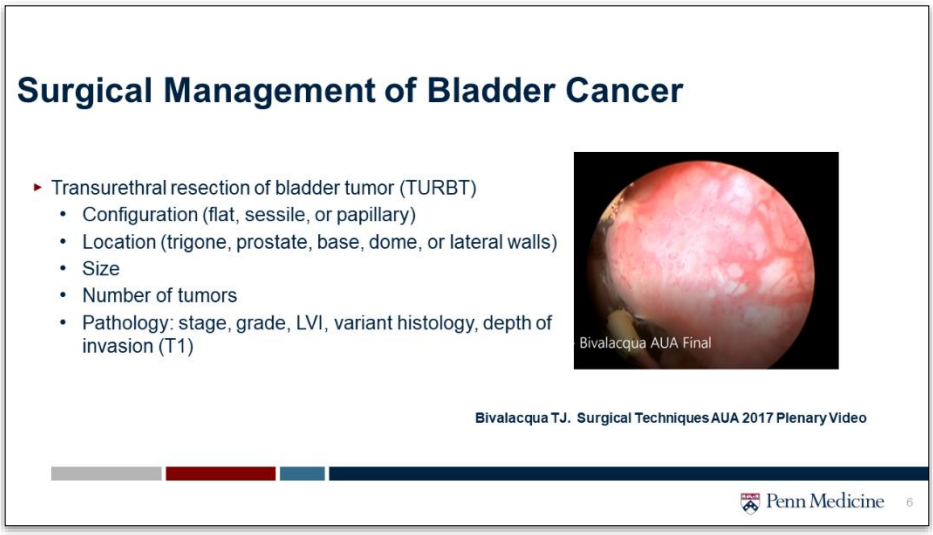
The way we diagnosis is by cytoscopy, it's just a little telescope that we place inside the bladder. It allows us to be able to see stones, outpouching of the bladder or any tumors. So oftentimes this is the way that we diagnose it. The other way is by imaging. Today, a CT urogram or a CT scan with IV contrast, it allows us to be able to see the kidneys, the ureter, as well as the bladder. You can see here, just an example of a little mass that's seen there in the bladder at the base. This is actually a man. And if you have blood in your urine, inevitably, especially if you are seeing blood with your eye, overwhelming majority of people are going to get a CT urogram or endocytoscopy.





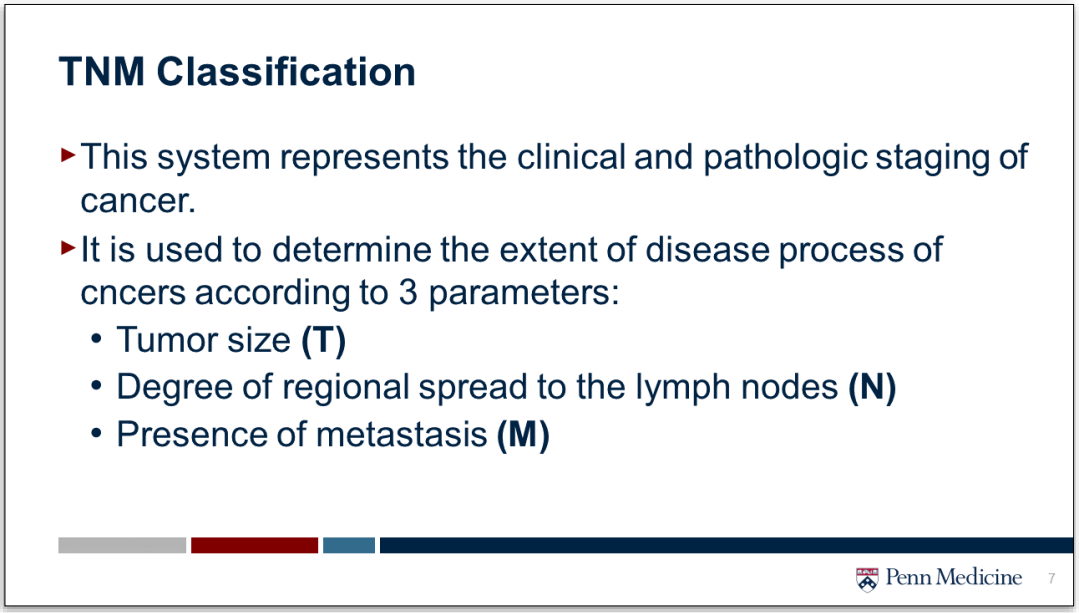
Dr. Bivalacqua:

Now this is where we get into surgical management. So surgical management means if a patient is diagnosed with a tumor in the bladder, which is thought to be bladder cancer, the main state treatment of this and diagnosis, and this goes to what Stephanie was talking about in the introduction, is a transurethral resection of bladder tumor. You'll hear people say TUR, TURBT, I've heard it all. This is where we, once again, place a scope inside the bladder. At the end of the scope is a knife actually that allows us to be able to scrape, cut, remove tumors.



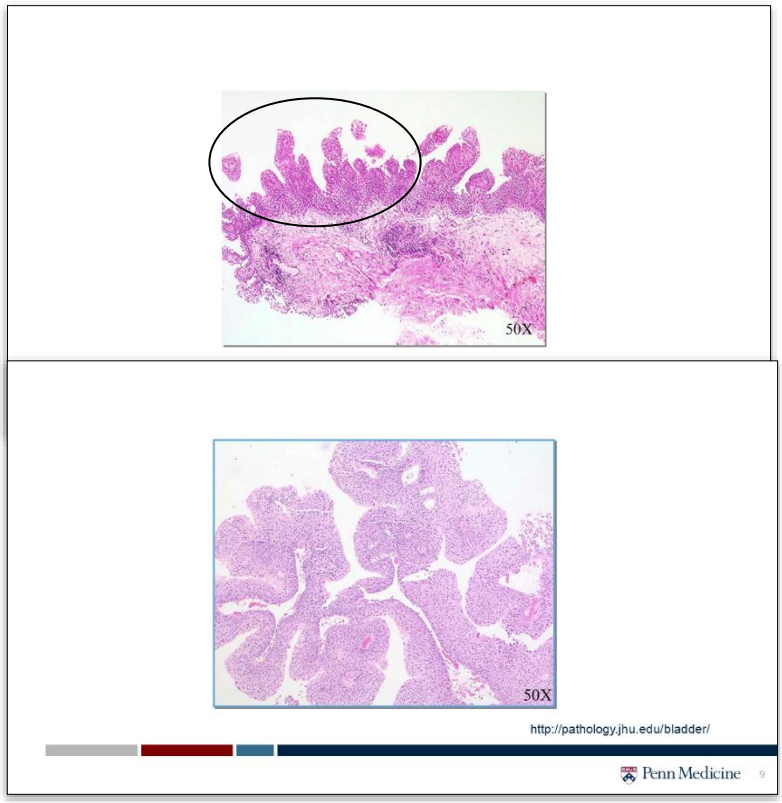
Here you can see what we, as urologists, are actually looking at. We're looking at the configuration of the tumor. Is the tumor flat? Is it broad based? Does it grow out into the bladder? Is it on a tiny little stalk? Is it papillary, it looks like a piece of cauliflower or broccoli? Where is the location? Is it in multiple areas of the bladder? Is it in the prostate, near the prostate, at the sides? How big is the tumor? How many tumors are there? And when we do this, we're able to map the bladder and send this to our pathologists, who look at it underneath the microscope and tell us what is the stage? What is the grade? Is this bread and butter urothelial cancer or is it something called variant histology? What is the depth of invasion, if there is invasion, and something called lymphovascular invasion, which I'll touch upon shortly.

So this goes to the TNM classification system of all cancers. This is a system that represents both the clinical and pathologic staging of cancers. It is used to determine the extent of disease, according to three parameters. Sorry, that's a typo there. So what the TNM stands for is tumor size, the degree or a regional spread into lymph nodes, or N, nodes, presence of metastasis or M. So tumor size. It could be tumor size, a really pathological stage here as it relates to bladder cancer. So when you look at bladder cancer, this is actually a histology of a tumor



Dr. Bivalacqua:

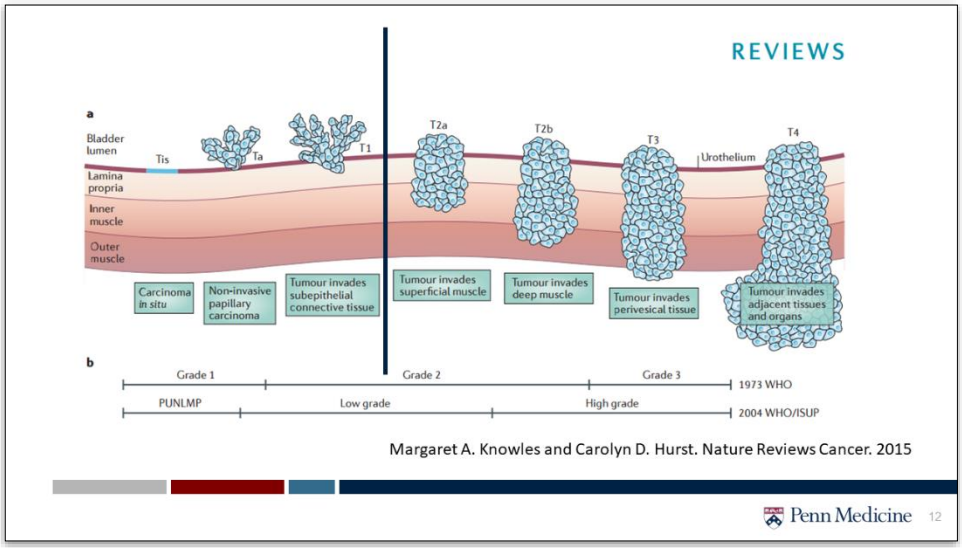
So this is what a tumor looks like underneath the microscope. As you can see, I'll use my mouse here, you can see these fronds or these papillary projections that are coming from the lining of the bladder (circled). You could see these beautiful looking and I call them beautiful, because histologically they look pretty. You could see that the core of these papillary tumors, this is where the blood vessels go to supply blood supply to these tumors so they grow. If you look at it underneath the microscope at high power, you can see that this is a tumor that has these more uniform looking nuclei that are pretty much uniform with these abnormal more dysmorphic looking nuclei. And then you see here where you see a tumor that's now becoming more aggressive, where you have these mitotic signals. These are all the things that pathologists look at underneath the scope. And here's a nasty looking tumor, that's lost all of its morphology, it's undifferentiated is the term.



So when pathologists look at this, what they're looking at is here, which is what are the stage of the cancer. This is actually from Maggie Knowles. This is a paper that's a review for in Nature Reviews and cancer. But I love this slide or this picture, schematic there, because it really goes to the crux of staging of bladder cancer. So if you look here, you could see that on the left of this black line is actually what is termed non-muscle invasive bladder cancer and to the right is what is termed muscle invasive bladder cancer. What I can tell you today is that about 75 to 80% of all patients that are diagnosed with bladder cancer at first presentation are going to be diagnosed with non-muscle invasive bladder cancer. And about one out four are going to be diagnosed with muscle invasive disease up front.

Dr. Bivalacqua:

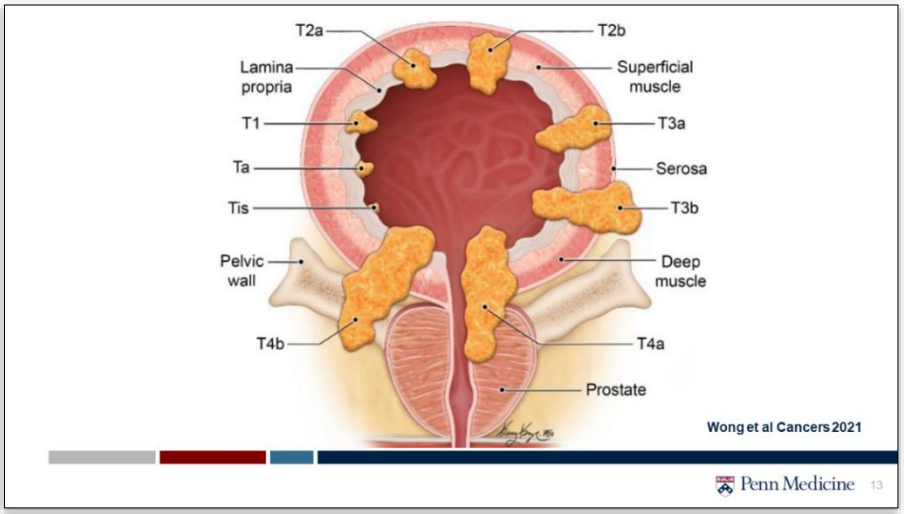
When we consider non-muscle invasive bladder cancer, it comes in three stages or in the TNM stage, T so T for tumor size stage. You can have something called CIS or carcinoma in situ. That is a tumor that is on the lining of the bladder, on the mucosa or epithelium. When a pathologist looks at this underneath the microscope, what they see is a flat lesion. When we look at this by our



eye as urologists, this looks like a red little patch. You will hear urologists say erythematous patch. What to know about carcinoma in situ of the bladder which is very different than in the skin cancer is that CIS of the bladder is actually a high grade cancer. So you can see here, the staging of cancer can be low grade or high grade. All carcinoma in situ lesions are high grade. And if you think about it, what we know at a molecular level, a genetic level, is that CIS is the precursor lesion to invasive T1 cancers.

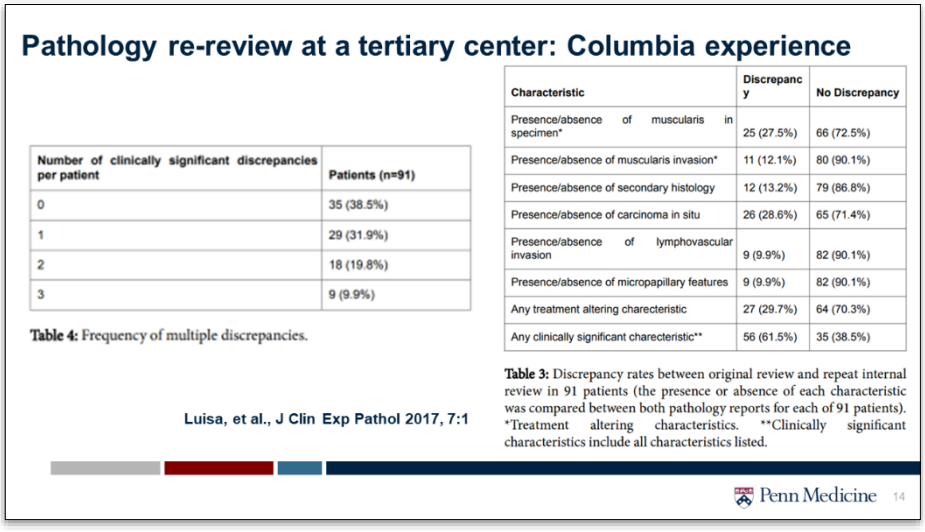
Dr. Bivalacqua:

If the tumor extends into the first layer of the bladder called the lamina propria, this is the supporting layer of the bladder mucosa, I mean, then now we're talking about a stage one cancer. By definition, this is invasive, but it still sits in the non-muscle invasive category because it hasn't penetrated into the deeper wall or muscle. If we have a papillary tumor, this is termed a superficial, is the previous term that we uses, superficial papillary tumors. And this is staged as TA. So most bladder cancer patients are going to be hearing about these stages more than the muscle invasive. Now, if you have muscle invasive disease, it's categorized into stage two, which means it grows into the inner layer of the muscle or the outer layer of the muscle. Stage three, it goes beyond the muscle and into the fat surrounding the bladder. Or stage four is when it goes into adjacent organs.



And if you look at this once again, schematically, here are our early stage cancers right here on the mucosa, CIS, the papillary tumors are going into the lamina propria, but then if you have a higher stage cancer, you could start to see it growing into the fat, beyond the fat or into adjacent organs. For men that's what you see here in this schematic, that would be the prostate. And for women, that could be something like the uterus or cervix.

Now, this is where I think... I work in a tertiary center, I've always worked in an academic tertiary center prior to moving to Penn, I was at Johns Hopkins. And what we always tell patients when they come and see us, and they get very frustrated with this, but we always say, "Listen, we need to get your slides reviewed here at Penn to make certain that the diagnosis is correct." So why do we do this? I love this article. This is a article that was published by the group at Columbia so Jim McKiernan's group with their GU pathologists. So these are pathologists that only look at GU cancers. So if you come and see me at Penn, you'll hear me say, "Okay, I need to get your



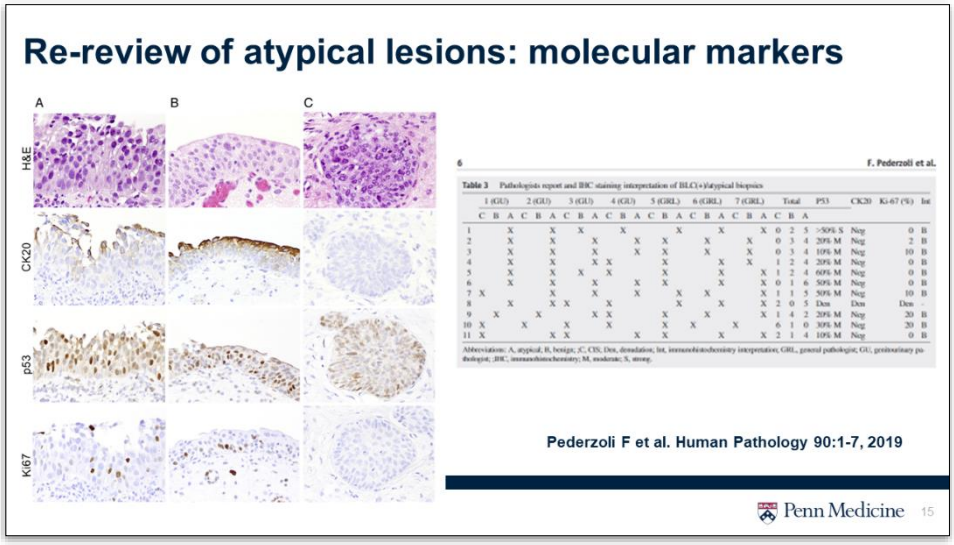
slides reviewed by our pathologist here."

Dr. Bivalacqua:

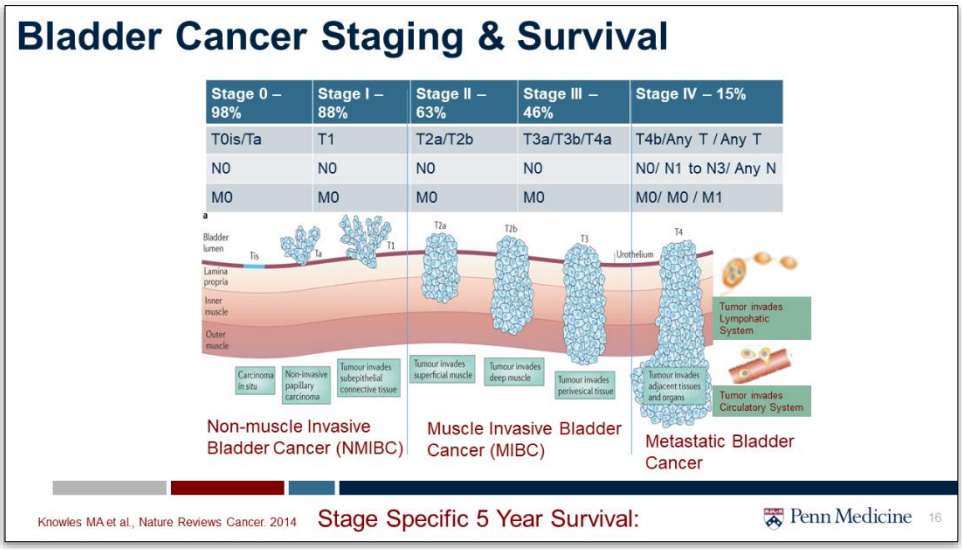
Well, I'm doing that, because our GU pathologists are going to have a very different eye at times than maybe the local pathologist that's doing all kinds of things like breast cancer, colon cancer, bladder cancer, prostate cancer. And this is not a criticism of anyone, but subspecialization makes a difference.

I like this because what they showed in this study was is that when these slides were reviewed at Columbia, 60% of the time, they found that there was a discrepancy actually in the diagnosis of the pathology of the final path that changed clinical recommendations. So said a different way, when the pathology slides were reviewed, it provided me as the urologist that's taking care of that patient with something that changed my recommendation or changed my understanding of their cancer, that meant that we might treat them a little differently. So it's super important, in my opinion, that you have your slides read by a specialist that works in GU pathology, just like you go and see a specialist for a second opinion for management. It's the same thing for pathology.

I put this in here because this has to do with one of the questions that I got prior is what about some molecular markers to be able to determine if this will help guide my treatment of my bladder cancer. I'm going to intertwine that in every section. This is actually for non-muscle invasive bladder cancer. This is work that we did, now I guess three years ago. Felipe, who's a postdoc in my lab, tried to look at molecular markers to see if it would change how we approached things like carcinoma in situ and non-muscle invasive bladder cancer and in reality, it didn't. So we're still not there as it relates to molecular markers for in particular CIS.



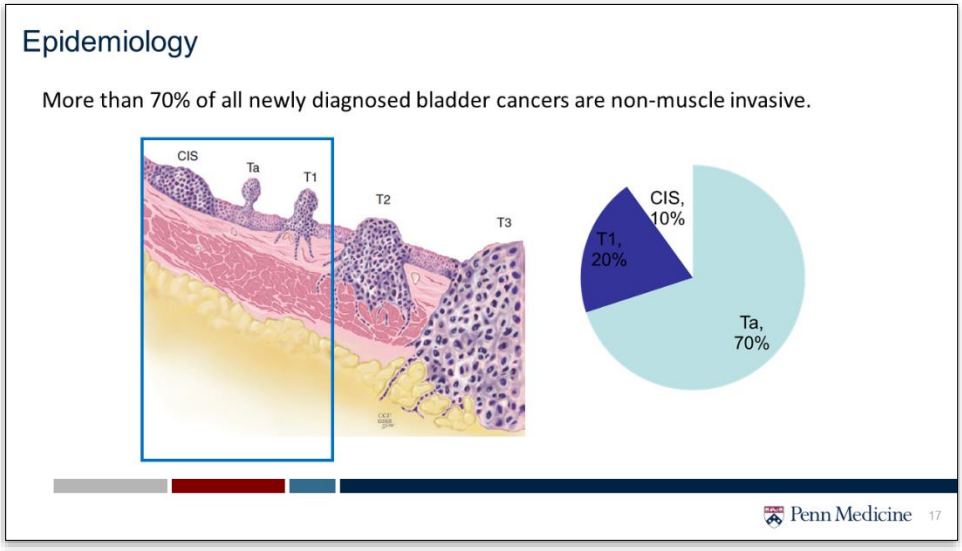
So bladder cancer staging. Remember we talked about TNM. So if we look at these overall survival, this is from SEER-Medicare Database. So this is patients that are 65 years or older. If you have CIS or papillary tumors, and you have no signs of cancer and lymph nodes or spread, then the chances of you being alive and well at five years is almost a hundred percent. So this is early stage so that's a good thing.



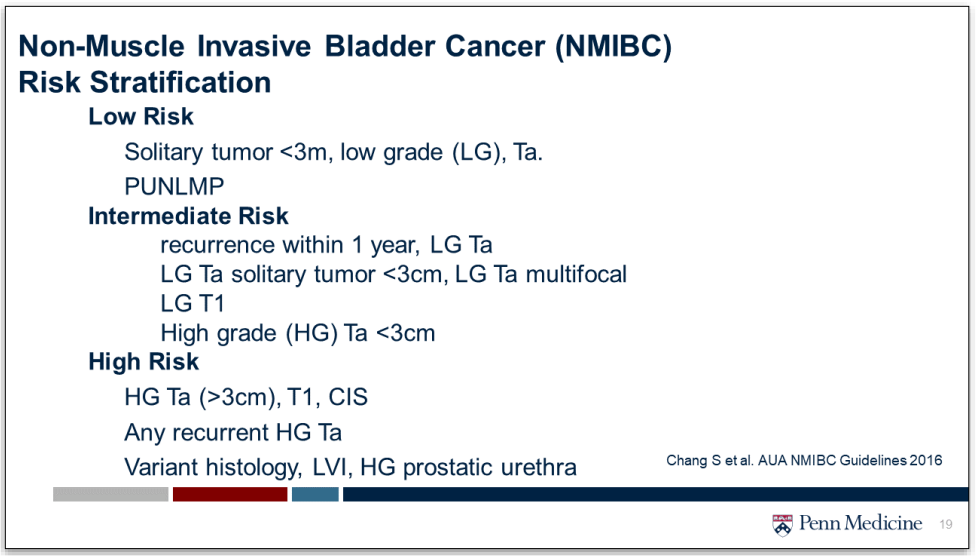
Dr. Bivalacqua:

If you have invasive T1, the chances of survival is stage specific survival at five years drops by 10% to 88%, but still very good. Now this is where it gets daunting and scary for a lot of patients, as well as practitioners and oncologists, is that as soon as you get into stage two, stage three, and in particular stage four, with signs of cancer spread, we start to see that the stage specific five year survival drops pretty significantly as the stage goes up.

So our goal is to obviously diagnose patients early and prevent stage progression. If you are diagnosed at a higher stage, the good news is today in the year 2022, we've got tons more to offer you than we ever did before. As it relates to staging, once again, I'll go start with non-muscle invasive bladder cancer. As I said earlier, about the 75, the 80% of all newly diagnosed bladder cancers are non-muscle invasive bladder cancer. And if you look at how it breaks down, the majority of patients that are diagnosed with non-muscle invasive bladder cancer are going to have this superficial TA tumors. This could be low grade or high grade, which I'll go into. About 20% present with stage one and only 10% present with only stage CIS. What I'm not telling you in this slide is that you can have the combination of TA with CIS, T1 with CIS, TA with T1. So it's a little bit more complicated than this slide presents, but just to give you an idea. The good news is the majority of people diagnosed with superficial disease.

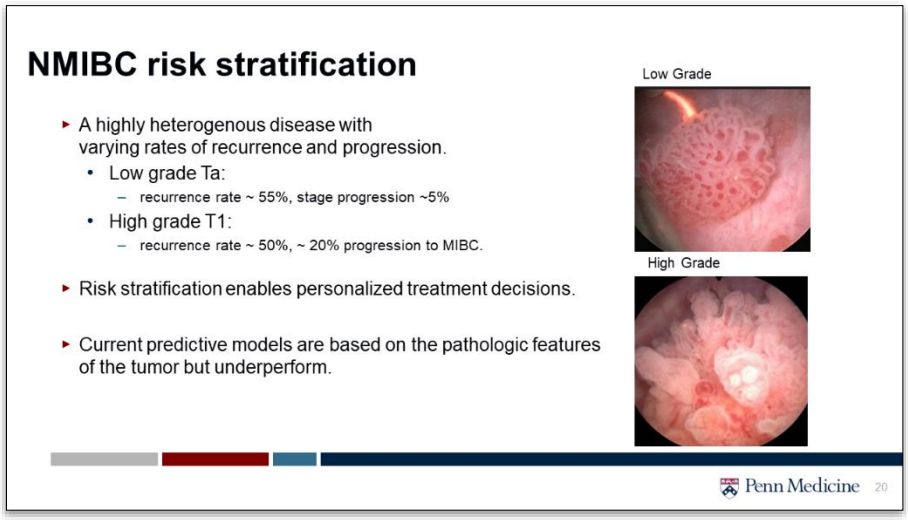


Now we as urologists and oncologists are going to give recommendations as it relates to guidelines. Diagnosis and treatment of non-muscle invasive bladder cancer guideline that was published in 2016, and I will tell you was updated in 2020, is how we manage all of our patients. So one thing that has happened is we risk stratify patients that with non-muscle invasive bladder cancer. So you either have low risk disease, intermediate risk, or high risk.

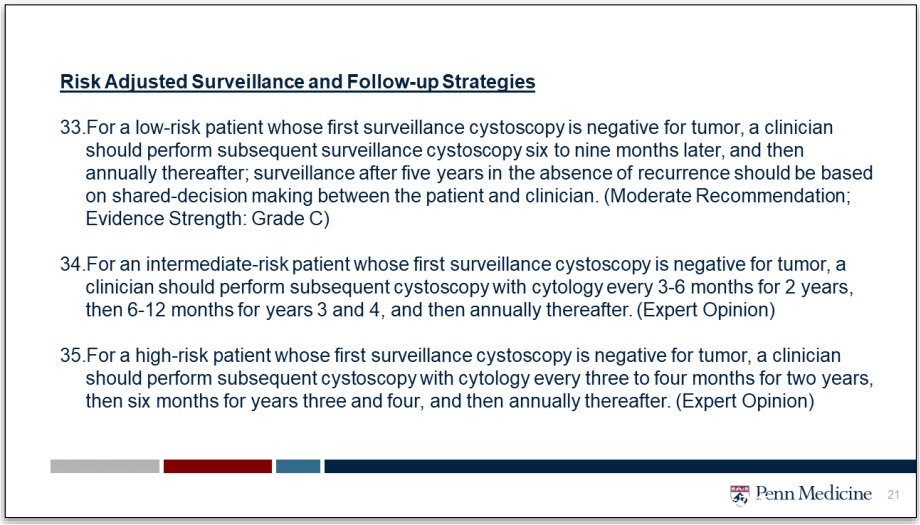


Dr. Bivalacqua:

Low risk patients are patients that have low grade superficial tumors and they're small in size. That's three centimeters, not meters, sorry about that. And they only have one tumor. So these are the patients that undergo removal by a TURBT. We put some chemo inside their bladder and then they don't need any additional treatment.



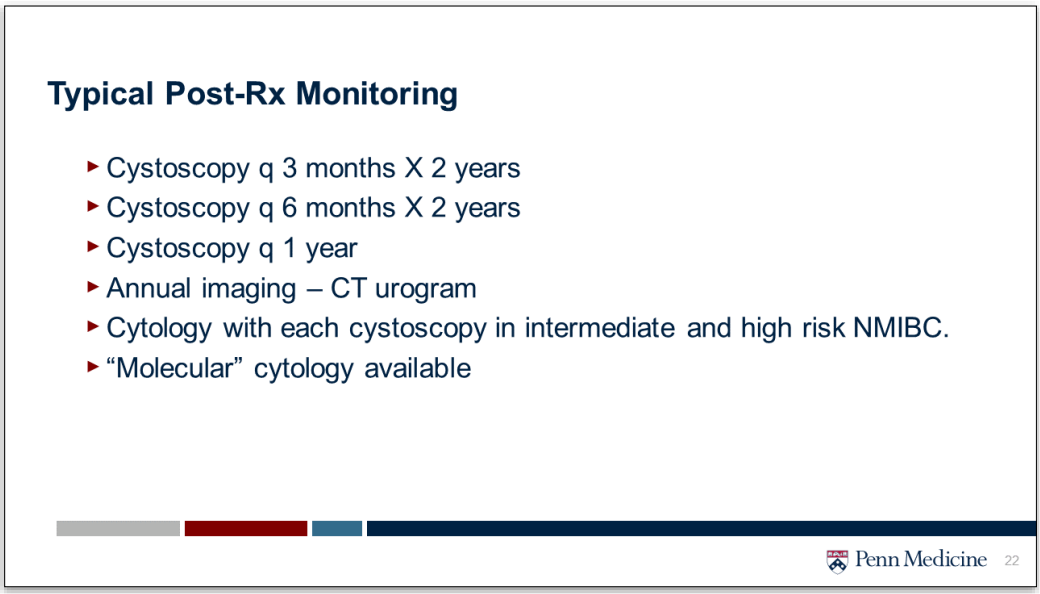
However, that is not the majority of patients that present. A lot of patients present with this intermediate risk, which are patients that have more than one tumor, which is low grade. They may be greater than three centimeters. They could have a recurrence of their cancer, low grade, within one year. So these are the patients that we see a lot in our practice, and I'll go over how we treat those. It's the high risk group that I think gets a lot of attention appropriately, because these are the patients that have high grade cancers, CIS T1 are large TA high grade tumors. They get recurrent or multifocal high grade tumors, and they can have varying histology or high grade cancers in the lining of their prostate. These are all patients that we're going to treat in a specific way, which I'll review.



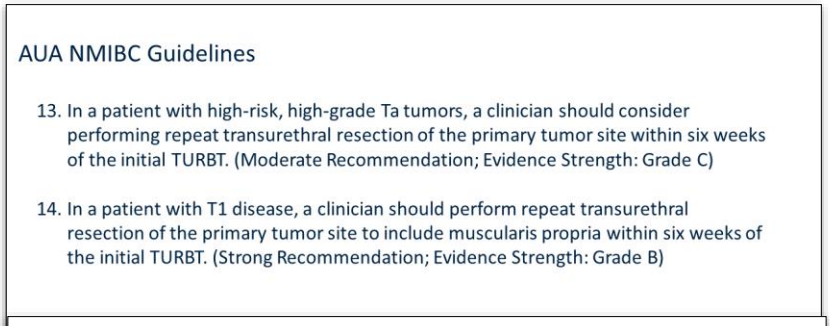
So our goal by doing a TURBT is to figure out, is it low grade? Is it high grade? Is it TA? Is it T1? This allows us to risk stratify patients so we can then make different treatment decisions provided by that pathological information. So if you are a low risk patient and you get your tumor removed, then the majority of those patients, we try our best to put in inside your bladder a medication called Mitomycin C or Gemcitabine in the perioperative period. Once again, I'll review this in a second. Once we've done that, your surveillance for this is actually pretty straightforward. You then come back for your first surveillance about three months later, and then we stretch it out to six months, and then do it yearly for about five years. This is not the majority of patients that we see in practice, but these are the patients that we feel really comfortable that this is a very indolent type cancer and we can manage this very effectively.

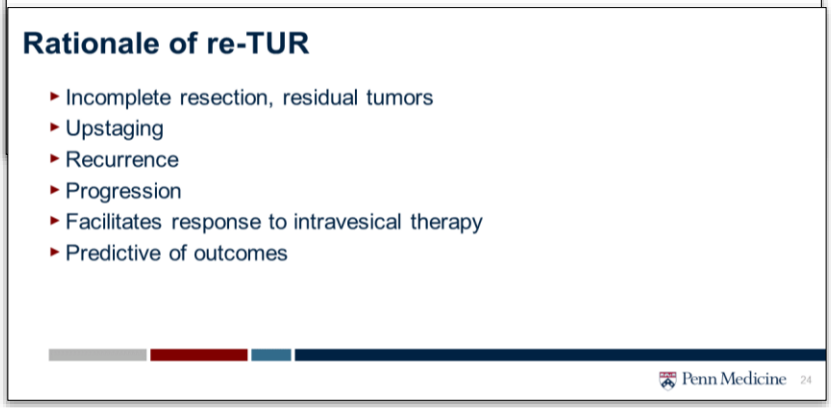
Dr. Bivalacqua:

Patients with intermediate risk disease are those that have more tumors, and we're doing a much more rigorous surveillance cystoscopies and urine tests every three to six months for two years, and then every six to twelve months for the years three to four, and then annually thereafter. I'll make the point that this is an expert opinion. So if your urologist does something a little different it's because it's up to essentially your urologist to how they cater, how they do their surveillance. For high risk patients, we're doing essentially cystoscopies every three to four months for two years, six months for years three and four, and then yearly thereafter. So broken down for a high risk patient. This is kind of what you're looking at. You're looking at two years of pretty intense surveillance cystoscopies then for years three and four, every six months, and then yearly after that.



One thing that I think gets lost sometimes is that we should be performing CT urograms to look for potentially cancers that can occur in the upper tracts of the kidney and urinary every year to 18 months. And in my practice, I do it essentially every 18 months. Cytology is used for patients with intermediate high risk disease, and molecular cytology is available, but I will tell you today that we really don't know if these sort of assays or tests, how to really work it into the clinical practice. As it relates to the guidelines, how do we treat patients with high risk, high grade TA tumors? If you come and see me and you have a high grade superficial TA tumor, I'm going to be repeating another transurethral resection of that tumor bed within six weeks of that first TURBT and I'll explain why in a second. If you have stage one disease or T1 disease, we recommend that you should be doing this because the evidence supports this. This is a strong recommendation.



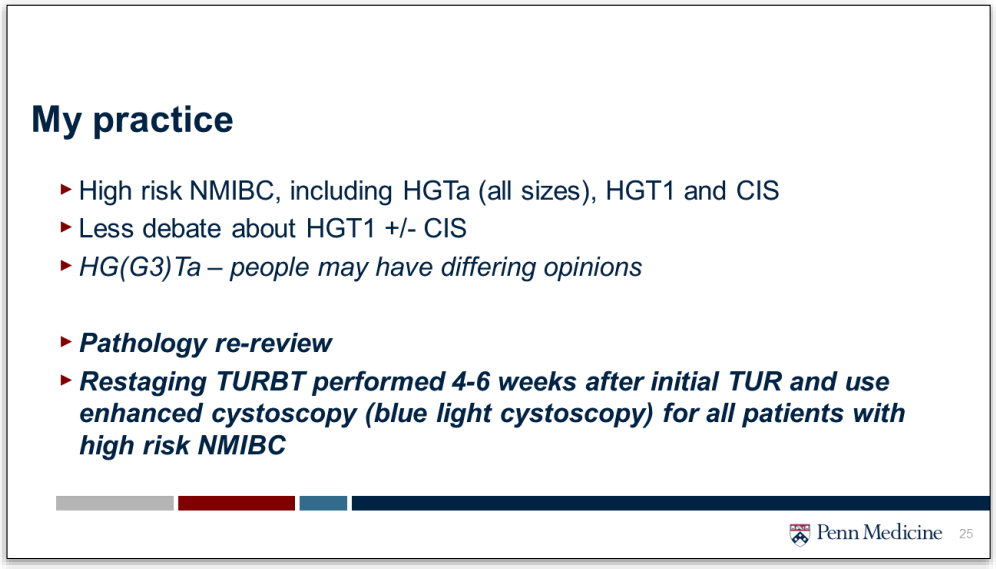


So what is the rationale for a re-TUR? Well, we know that as urologists, we may think we're good, but we're not perfect. It's possible that you had an incomplete resection and there's residual tumor that has to be removed. We are looking to determine that there's no sides of

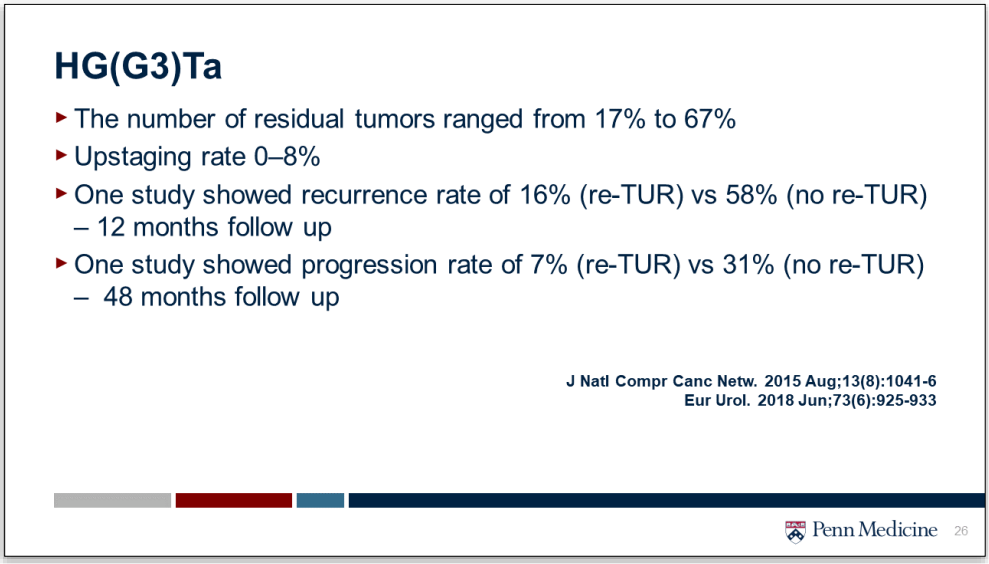
higher stage cancer, for example, stage two or higher.

Dr. Bivalacqua:

We know that a re-staging exam helps prevent recurrence and potentially progression, if you eradicate all of the papillary tumors prior to intravesical treatment, and this facilitates a more effective adjuvant intravesical therapy, which is BCG, our chemotherapy, and some think that it may predict outcomes. So in my practice, if you have high risk, non-muscle invasive bladder cancer, for me, it doesn't matter if it's high grade TA or T1 or CIS, you are undergoing a pathology review for the reasons I described and a re-staging exam about four to six weeks later with using enhanced cystoscopy, which is blue light cystoscopy. We do this because there's strong evidence to support this.

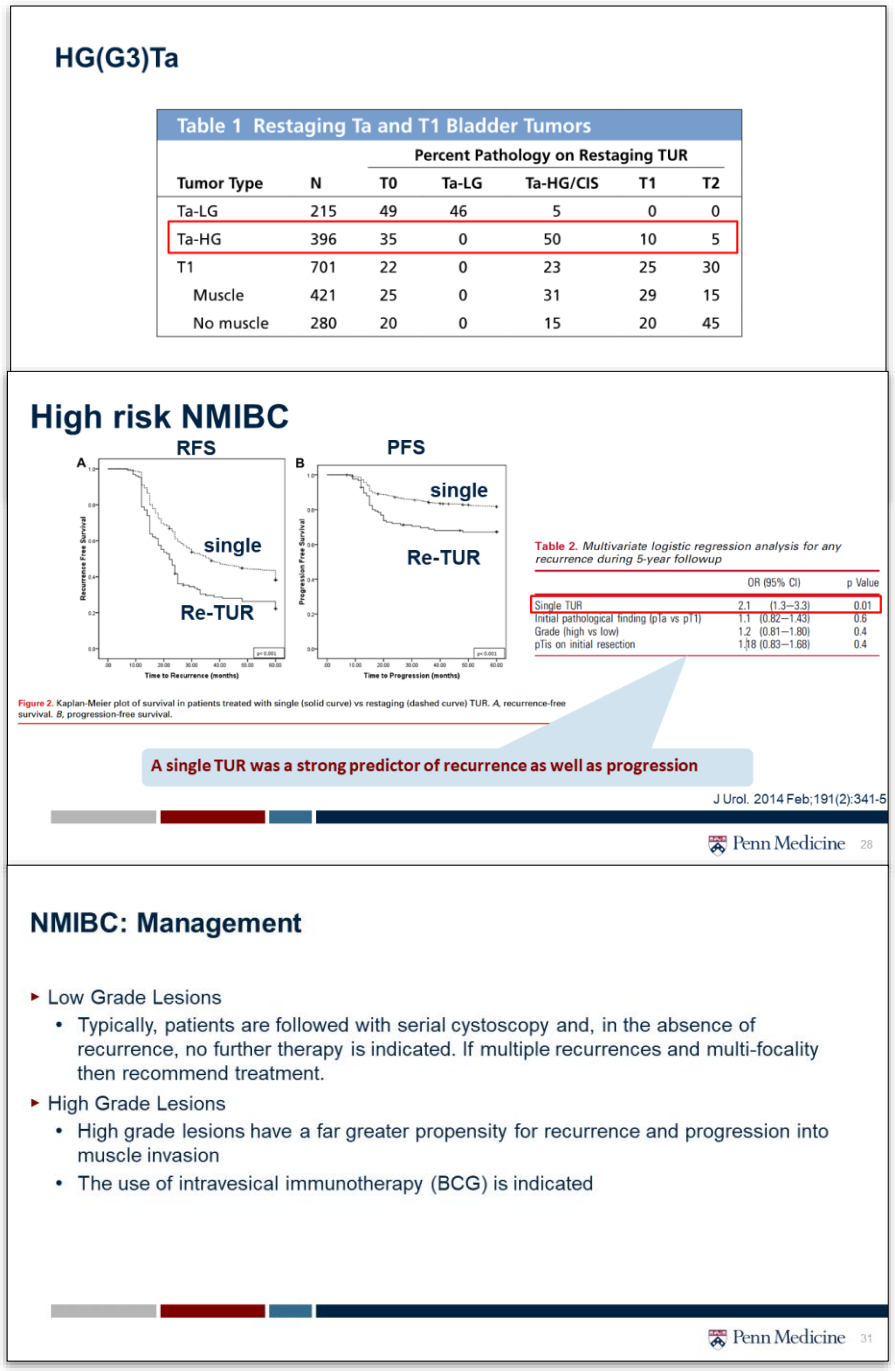


So what is the evidence? Well, this is work that was done by a number of different places. This is just one example. If you have superficial TA high grade cancer, there are reports that upwards of 17 to 67% of patients that undergo re-staging exam, we still find residual cancer. And more importantly, and this is the reason why we do it, is that if you have a re-TUR, the risk of recurrence is much lower than if you had no re-TUR. This tells us that being a hundred percent certain that we've eradicated all the cancer in the bladder prior to intravesical treatment is super important. This is actually a nice study that shows that one of the biggest predictors of recurrence was if you only underwent a single TUR and did not get a re-staging TUR. This is strong evidence to support that your urologist should be performing re-staging TURBTs.



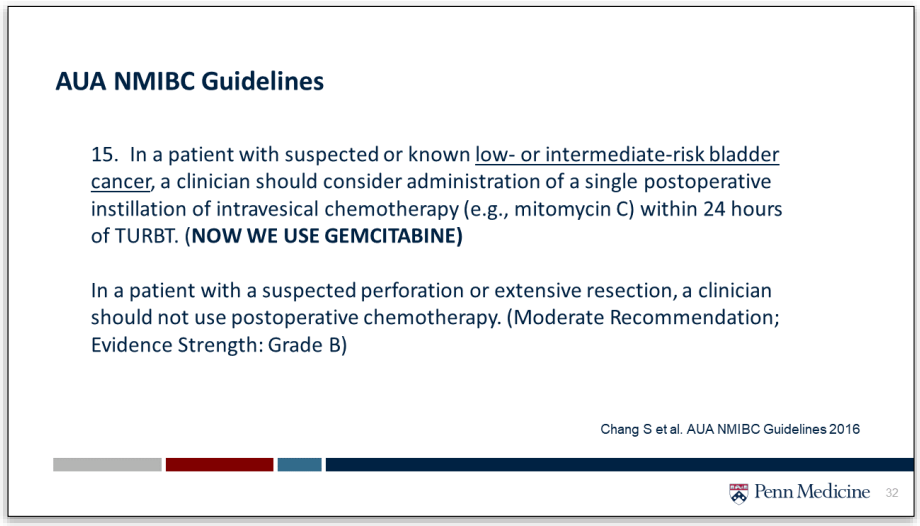
Dr. Bivalacqua:

And more importantly, if you have stage one cancer, this is a study that is a great example that if you have a re-TUR in this patient population, we find upwards of 15 to 20% of patients actually have muscle invasive bladder cancer. So what that means is that if you didn't undergo that re-staging TUR, we could be under-treating your cancer. So that's the rationale. This is actually a randomized controlled trial that randomized patients with high grade T1 to one TUR versus a repeat TUR. And in this randomized controlled trial, they show that the recurrence rates are much lower in those patients that underwent a repeat TUR. All strong evidence of why you need to undergo this as a patient.

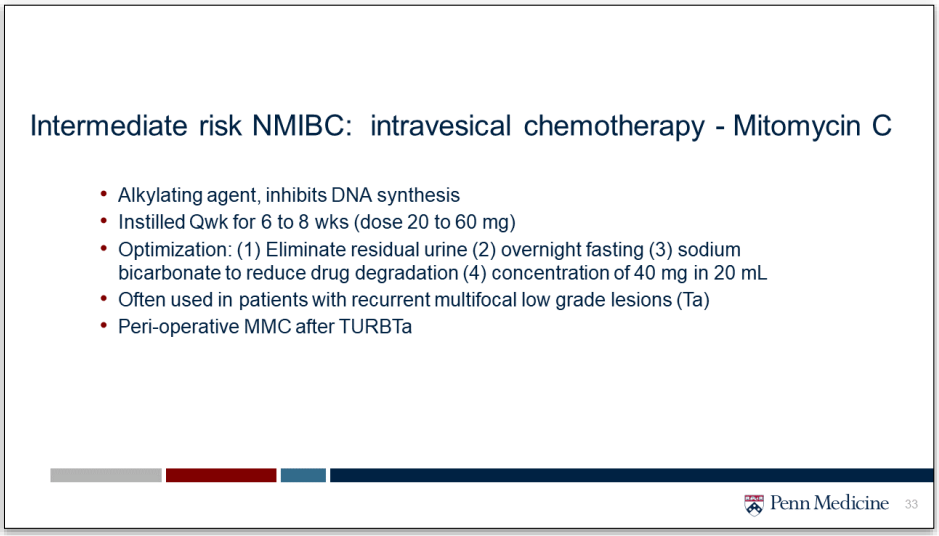


If we look at management of non-muscle invasive bladder cancer, if you look at low grade cancers, these are the cancers that right now in the year 2020, we are treating with intravesical chemotherapy. Prior to all of the BCG shortages, which we're all familiar with, we would also use BCG for low grade intermediate risk, non-muscle invasive bladder cancer. However, now we recognize that chemotherapy is also very effective in this disease state and therefore we use chemotherapy. For high grade cancers, which have a much higher propensity for progression, we know that the number one or most effective treatment for this is intravesical BCG.

Dr. Bivalacqua:



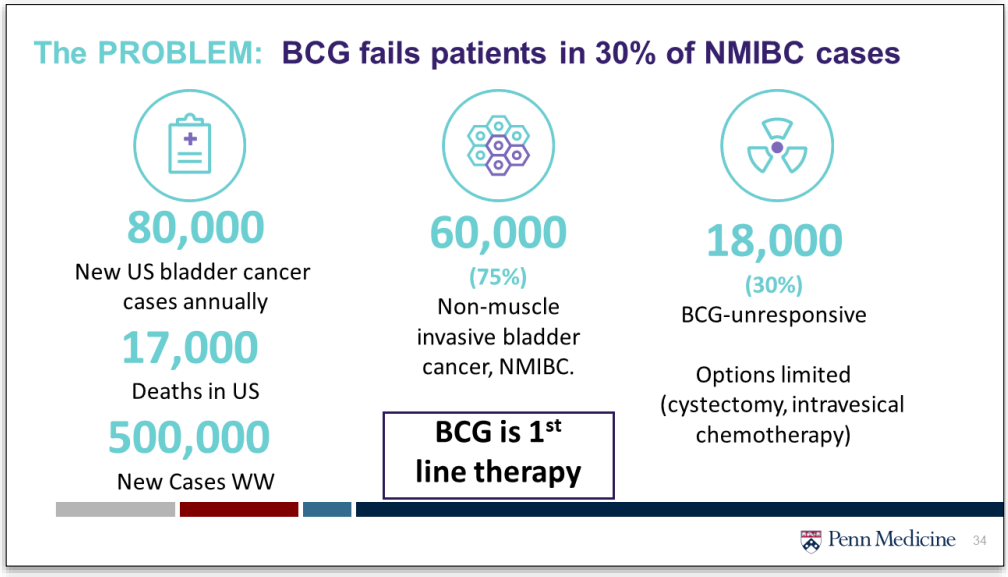
What do the AUA guidelines say about perioperative chemotherapy? So perioperative chemotherapy means that if we believe that the patient has lower intermediate risk bladder cancer. So we look in there and we see this papillary tumor that we believe is low grade, then we should consider a single intravesical installation of chemotherapy within 24 hours of your TURBT. The reason why this is done is, once again, strong evidence to show that there is a significant reduction in recurrence when perioperative chemotherapy is given to patients with low grade are lower intermediate risk bladder cancer. We oftentimes would use Mitomycin C, but now there was a trial that was done by Ed Messing that was published now about probably three or four years ago that showed that Gemcitabine is also effective and actually has a more favorable side effect profile. So this is what I use in my clinical practice. As it relates to management of intermediate risk non-muscle invasive bladder cancer, once again, papillary low-grade tumors, I think what the guidelines recommend is Mitomycin C because there's strong evidence to suggest and trials that show that this is very effective in preventing recurrences of low grade tumors.



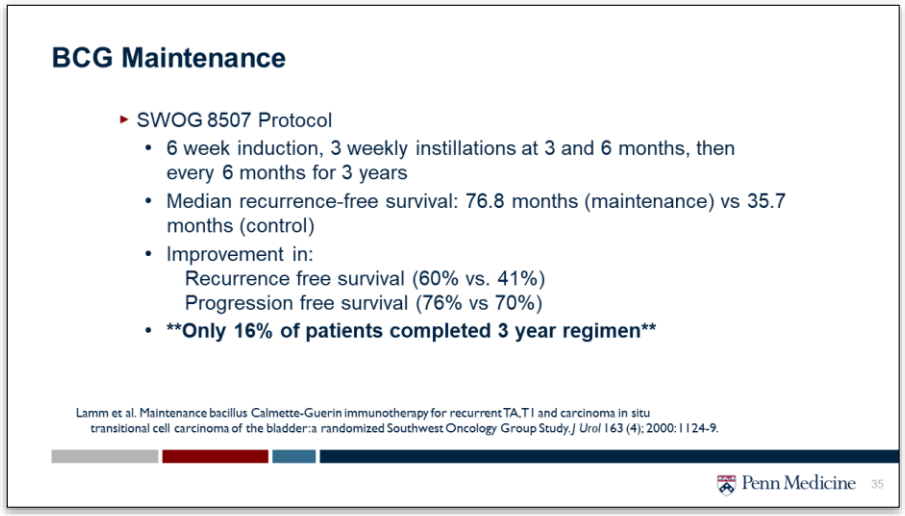
Now, one thing that is oftentimes not really discussed, and I think you see it sometimes on the forums, is that as a patient in order for Mitomycin C to be most effective, you to be dehydrated so you don't want to be drinking a lot of water. You want to alkalize your urine by taking sodium by carbonate. What I tell patients is get one scoop of baking soda in water and take it prior to coming in to the clinic. It helps alkalize the urine and allows Mitomycin C to penetrate and be more effective.

Dr. Bivalacqua:

So this is what we use for patients with intermediate risk, but what scares most patients is the high risk group. So if we look at high risk non-muscle invasive bladder cancer, we know that BCG is the first line of treatment, as I said earlier. And unfortunately, BCG fails patients in about upwards of 30% of patients. They are deemed BCG unresponsive. So the options at this point after BCG has failed you, is things like radical cystectomy, additional chemotherapy inside the bladder or clinical trials. And I'll go over that in detail because I think a lot of the questions that were proposed really go into that.

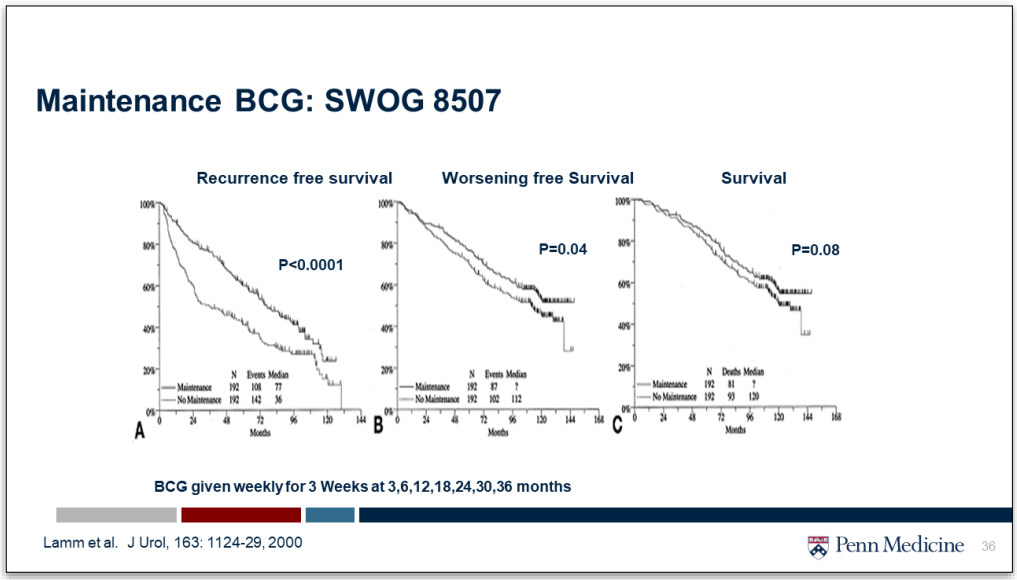


But prior to me talking about it, I think it's important that we acknowledged the important work that was done through SWOG by Don Lamm and colleagues, where he showed that BCG should be given in an induction course, which is weekly for six weeks and then given in a maintenance protocol. The maintenance protocol is three months after finishing the six week induction course, six months after finishing the six week induction course, and then every six months for a total of three years. The reason why this is done is because in this trial, which randomized patients to BCG induction alone or BCG induction with this specific protocol of maintenance showed that it reduced recurrences in patients with high risk disease.

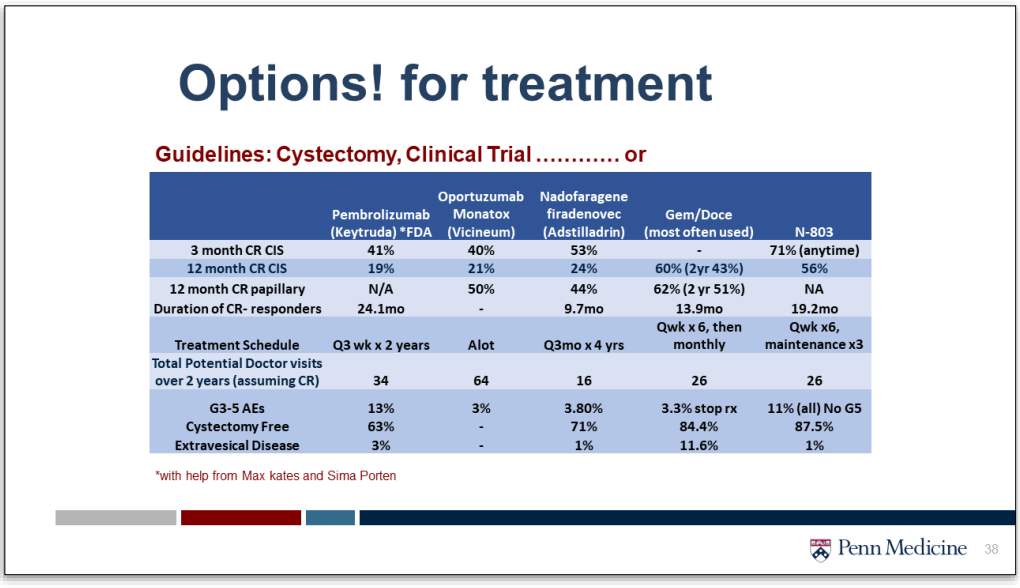


Dr. Bivalacqua:

I think what I always tell patients is that, but what we have to recognize is that this regimen is not easy on you as a patient and only 16% of patients actually completed this three year regimen. My goal in my practice is to get you to two years and then we discuss that additional year because I think it's ultimately a shared decision making at that point. Here is the Kaplan-Meier curves. Patients that got maintenance had less recurrences as well as a significant approval and worsening free survival so progression. So if you get BCG with maintenance and it is something that is unfortunately ineffective and you are deemed BCG unresponsive, the guidelines recommend cystectomy in that patient population. Why do we recommend cystectomy? Because this is a disease, which is unfortunately at high risk of progression to muscle invasive disease, as well as recurrence. So we know that cystectomy is a very effective way to treat this cancer. However, as all patients and practitioners will point out, it also is a very morbid operation and a life changing operation.



So what are our options for treatment at this point? So as a patient, what are your options today? Well, this is a slide that I actually got from Max Kates and Sima Porten. It was actually used at our recent AUA meeting. I think it's a nice slide that actually highlights where the field is today. What I will tell you is that in clinical practice, if you are BCG unresponsive, you either undergo a cystectomy, you enroll in a clinical trial, or you have the following options. The number one option is the use of pembrolizumab or Keytruda, which is now FDA approved for patients that have BCG unresponsive CIS or carcinoma in situ. So the only way that you can get this utilized in its approval by the FDA was for patients that have CIS. Unfortunately, not all patients that have BCG



	Pembrolizumab (Keytruda) *FDA	Oportuzumab Monatox (Vicineum)	Nadofaragene firadenovec (Adstilladrin)	Gem/Doce (most often used)	N-803
3 month CR CIS	41%	40%	53%	-	71% (anytime)
12 month CR CIS	19%	21%	24%	60% (2yr 43%)	56%
12 month CR papillary	N/A	50%	44%	62% (2 yr 51%)	NA
Duration of CR- responders	24.1mo	-	9.7mo	13.9mo	19.2mo
Treatment Schedule	Q3 wk x 2 years	Alot	Q3mo x 4 yrs	Qwk x 6, then monthly	Qwk x6, maintenance x3
Total Potential Doctor visits over 2 years (assuming CR)	34	64	16	26	26
G3-5 AEs	13%	3%	3.80%	3.3% stop rx	11% (all) No G5
Cystectomy Free	63%	-	71%	84.4%	87.5%
Extravesical Disease	3%	-	1%	11.6%	1%

*with help from Max kates and Sima Porten

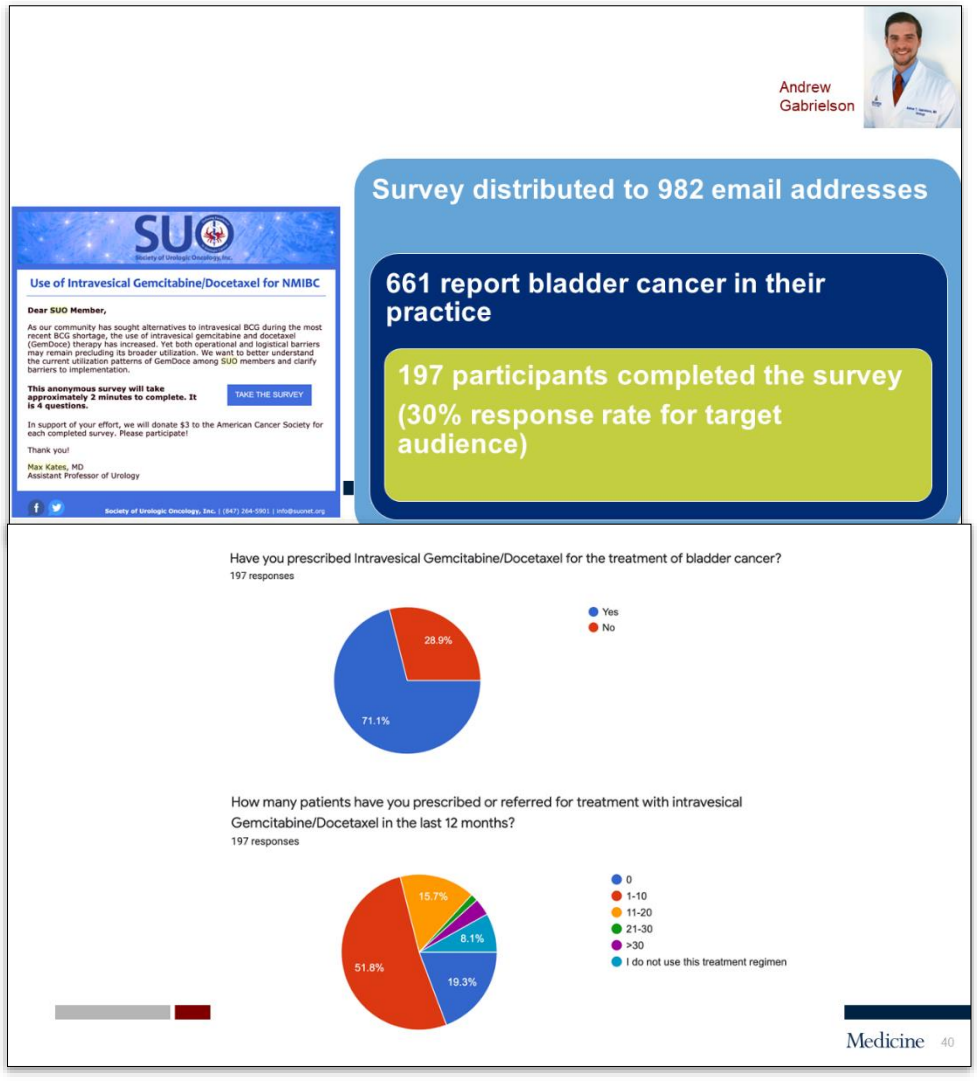
unresponsive bladder cancer have the presence of CIS. But if you do, what we know is, is that the 12 month complete response rate was 19%.

Dr. Bivalacqua:

But unfortunately we still have a lot of patients that are not really benefiting from this treatment. Vaccinium which has been utilized in multiple clinical trials... Excuse me, not multiple. Clinical trials have been performed for FDA approval of vaccinium. It has not been FDA approved, but we see at the 12 month mark, it also is doing a little bit better than Keytruda, but still not significantly better. Nadofaragene which you may have heard is Adstiladrin is also underwent investigation, currently at the FDA for approval. We are now starting to see in the phase three trial for Adstiladrin, a response rate that was 24%. So we're getting better, but still once again, room for improvement.

What has happened in the United States today is that we're using something called salvage chemotherapy or doubling chemotherapy, which is the combination of Gemcitabine and Docetaxel. So this is where patients are given, and BCG unresponsive, Gemcitabine and Docetaxel in the bladder. And in the reports from multicenter studies, we're seeing much better response rates in this cohort. Now, what I need to point out is, is that this was not a randomized controlled trial. This was retrospective studies that were performed, but this has become the salvage therapy because of the high response rates, at least in our retrospective studies. And I will acknowledge that I was part of all of this so clearly I think that this is a good drug combination and the person that started this was Michael Donald.

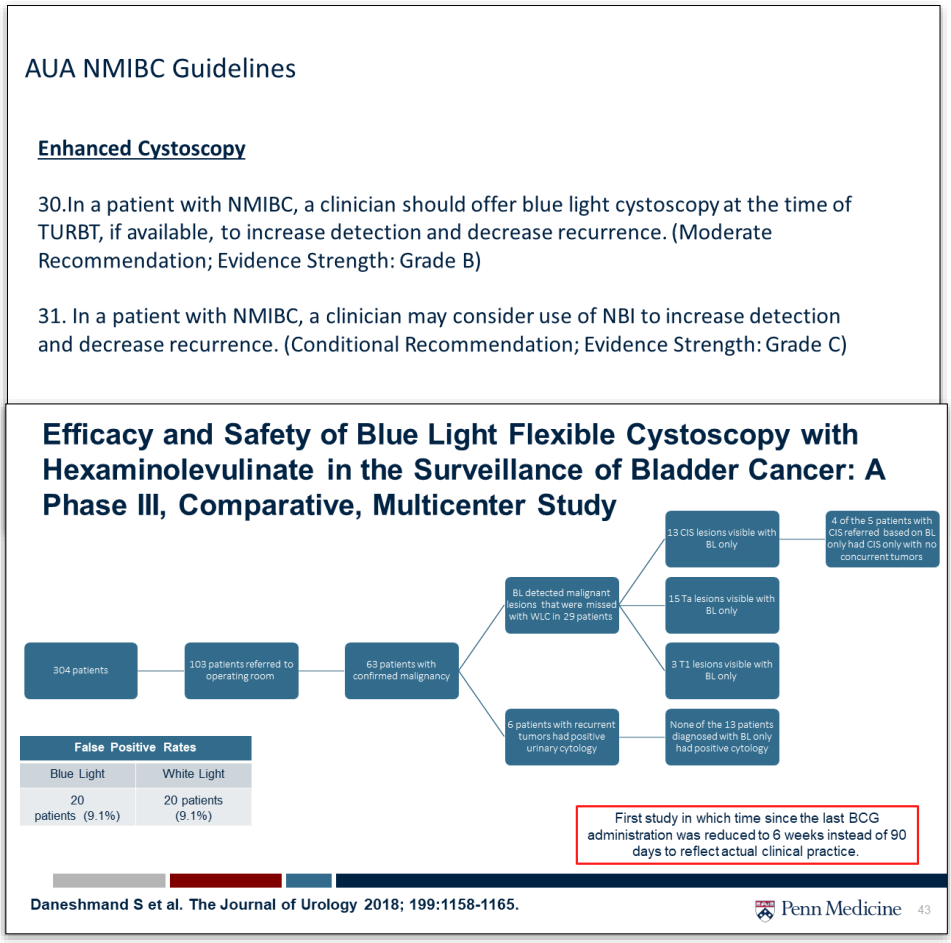
If you use survey the SUO urologist that are all part of BCAN and work with this, this is work that was done by Andrew Gabrielson, who's a urology resident at Johns Hopkins, with Max Kates, as the PI, we see that urologists in the United States today are really using Gem Doce. So almost three quarters of urologists are using this intravesical treatment and they're using it in great quantities. And what we also know is, is that the majority of its use is being used in BCG unresponsive disease, as well as in intermediate disease, patients with intermediate risk, non-muscle invasive bladder cancer. And what we're now learning is, is that if you don't have BCG because of the BCG shortage, it's now being



used in high risk. So a lot of the questions that I were asked is, "Well, what about something else that we can use?" Well, right now in the United States, this is something that's being heavily studied and utilized.

Dr. Bivalacqua:

I'll shift gears now to enhance cytoscopy. So what is enhanced cytoscopy? That's where we, as urologists, will use one of two modalities, blue light cytoscopy, which is something called Cysview or narrow band imaging. Both of these are recommended by the guidelines, both blue light cytoscopy is something that should be used and narrow band imaging may be considered. Why do we use blue light cytoscopy?



Because when we utilize blue light cytoscopy in this study that was published from USC, is that we were able to detect multiple tumors that were not seen with white light. And actually in this study, we used it after intravesical BCG. So it helped us be able to accurately stage and treat patients with bladder cancer. So this is why I use it in my clinical practice.

Another question that was thrown out, "What about molecular subtyping or genomics or molecular profiling of non-muscle invasive bladder cancer?" Well, right now, I'm sad to say it is not part of our clinical practice. It's still very much in the research arena.