



Bladder Cancer and COVID-19 | Treatment and Vaccine Update for Patients & Families.

This program was recorded on April 23, 2020



BCAN | Stephanie Chisolm:

Welcome. My name is Stephanie Chisholm and I am the director of education and research at the [Bladder Cancer Advocacy Network](#). On behalf of BCAN and the [World Bladder Cancer Patient Coalition](#), we're glad to have you join us for this discussion of bladder cancer, BCG and COVID-19 treatment and vaccine update for patients and their families. I'm joined today by two international experts in bladder cancer. I'd like to welcome [Dr. Ashish Kamat](#). He's an endowed professor of neurologic oncology and cancer research at the university of Texas, MD Anderson cancer center in Houston, Texas. So welcome Dr. Kamat.

Dr. Kamat:

Thank you. My pleasure to be here.

BCAN | Stephanie Chisolm:

And from Ireland. I'd like to welcome [Dr. Paul Hegarty](#). He is a urologist in Ireland where he delivers service for genital malignancies in the Misericordia University Hospital in Dublin. He also delivers cancer and reconstructive care at the mater private hospitals in Cork and Dublin.

We know that there's a lot of chatter on the internet, and [instillation of BCG into the bladder](#) has long been used for non-invasive basis bladder cancer. And the strain that's been approved in the United States is the Tice strain. A lot of folks have heard the buzz and the news about this vaccine that you are developing and going to be implementing in clinical trials.

BCAN | Stephanie Chisolm:

Can you explain very briefly for the viewers on this program, how BCG for the bladder cancer treatments, that's usually given typically over six weeks, is being impacted by COVID-19 medical distancing issues both in the US and the EU respectively. Are you seeing any differences? Is it more of a regional thing? Are you telling patients it's okay to skip doses because it's better for them not to come in contact with the potential for COVID-19? What do you think?

Dr. Kamat:

As our viewers and listeners probably know we, as part of the Bladder Cancer Advocacy Network, got together early. Thank you, Stephanie, for putting that together. To put out some [guidelines](#) that are on the website for patients and providers to look at. And furthermore, there've been refinements of those guidelines for bladder cancer patients and there's a guideline out in Europe and neurology, that was online in the latter part of last week. Essentially, to answer your question, as far as BCG for bladder cancer is concerned, we are strongly recommending that patients that have high risk bladder cancer, so T1 high-grade CIS of the bladder do not skip any induction therapy with BCG and they do not skip any of the first three weeks of the maintenance there.

Dr. Kamat:

Once they're past that first initial six plus three, they have to weigh the risk of COVID-19 infection with the continued risk of going to the hospital and BCG. And that can in many instances be safely delayed by one, two, three, even four months.

But the initial part, the induction and the first booster course are something that patients that have high risk bladder cancer should clearly discuss with their urologist. And if they don't have access to it at their center, they should potentially seek referral to centers that can accommodate them. Because T1 high-grade bladder cancer, high risk bladder cancer, it really doesn't wait. You can't wait for two, three, four months before treating it effectively.

Dr. Kamat:

And that's what's been recommended in the US and Europe. Paul, what about your place? What's going on there?

Dr. Hegarty:

Exact same [for] high-risk disease. You still give the six and the three of the maintenance after that, then it's individualized. We often individualize it for patients in any case. And so some patients have a bit of inflammation or side effects or symptoms and may have a different or have reduced dosage on the subsequent maintenance doses. And so we've been doing this for years and got a feel for it, but it's not always fully protocol driven. The first six plus three is where you get the maxim benefit to immunotherapy to the bladder.

BCAN | Stephanie Chisolm:

So in the United States, we are only allowed to use the Tice BCG for treatment. Are there other options available in the EU? Doctor Hegarty, [do you have] a different strain of BCG because we know there's a global shortage of the Tice BCG?

Dr. Hegarty:

There is unfortunately [a shortage of Tice BCG], and urologists have been contending with that for a number of years now recently. Now we have a different brand called MEDAC, which is intravesical BCG used in Ireland. It comes in a pre-pack, which can actually be made up on the spot. It doesn't require a separate pharmacist to do it. And so the urologist can do it on the day [of treatment] having placed the catheter, then they follow through. And so that is what we are using and there's been a shortage even of this, but it hasn't reached the level of patients been denied anything.

BCAN | Stephanie Chisolm: Okay.

Dr. Kamat:

There's a shortage of BCG globally when it comes to the bladder cancer formulation. As you know worked with folks are all over the world. Even in Japan where the Tokyo Strain is used and of course they're helping us in the United States with the [SWOG study with the Tokyo Strain](#), MEDACs is a great company and their IVM, the Dutch Strain that Paul just mentioned, that clearly works. But there's a global shortage of BCG for bladder cancer use because it's so effective. Unfortunately we have so many patients that the production of BCG globally has not been able to keep pace with the requirement and demands for BCG, especially since many manufacturers in the US [such as] Sanofi went off the market.

Dr. Kamat:

So manufacturers are going off the market with BCG rather than coming into the market. And that's a whole other ball game and has to do with reimbursement and things like that. So that's clearly not what we want to necessarily talk about. But there is a global shortage of BCG and that's why we need more BCG globally.

BCAN | Stephanie Chisolm:

Absolutely. And I know we have spoken to Merck who is the primary manufacturer of the Tice strain of BCG, and they are at full capacity and have basically told us that they will continue to ensure that the bladder cancer community gets what they are able to produce, because that is most important. I did get a bunch of questions through our [Inspire online community](#) and others, where a lot of patients and their families. [They] are either worried that because they might have this immune reaction with BCG, that they're either at greater risk of developing or suffering from COVID-19. Or they also hear about this vaccine and they're thinking that they are now going to be immune and not at risk because they've had BCG. And your study about the vaccine is looking at is it actually going to help reduce the risks of COVID-19.

BCAN | Stephanie Chisolm:

So they're thinking that they've had this BCG. Can you talk a little bit about the [BCG] installation, and obviously patients are aware that they have precautions they have to take when they void the BCG at home? They have to clean the area and the toilet and make sure that there's no BCG around so that anyone who might be immune compromised is not at any additional risk. What's the story? Is BCG a benefit or a risk or neutral because it is put [directly] into the bladder rather than a systemic BCG that you might get with a vaccine.

Dr. Kamat:

So, there was a lot of questions in there and let me address a few and then I'll have Paul address a few as well. First off the whole correlation between BCG and COVID-19 protection. Let me start that and then Paul, I'll have you talk about the actual study. So the way that came about essentially as Mihai Netea in the Netherlands and other groups around the world that have done TB and BCG studies for tuberculosis for decades have shown that tuberculosis vaccination not only protects people, and this is infants and children, but also elderly against tuberculosis, but also protects them against secondary infections.

Dr. Kamat:

So there's a lower rate of infections with pneumonia, influenza, staph aureus, and in well done studies, randomized studies, small but still randomized. They've shown that BCG vaccination will protect these folks against vaccination or challenge with viruses such as yellow fever. So that's data that's been known for a while in the TB world. Then the COVID-19 came about, of course the pandemic, and we were thinking of the BCG and all of that. One of the things that popped up as we were thinking about the protective effects of TB vaccination against other viruses does it help against COVID-19? And there's a trial that was being developed in the US and we call it the BADAS study, the **BCG As Defense Against SARS-CoV-2**. It's called the BRAVE study in Australia. And in the Netherlands, it is a study, but it doesn't have an acronym.

Dr. Kamat:

When we were thinking of this, one of the things that myself and [Dr. DiNardo](#) at Baylor College of Medicine were thinking, well, could we look at the global response of BCG versus COVID-19. And I've known Paul Hegarty for years. He's a good friend of mine. We trained together. I had the pleasure of having something to do with him being a urologic oncologist as well. And I thought of no better person to reach out to because he has access to all these databases and I literally just asked him, I said, "Paul, would you be able to look at this and give us some scientific information based on the recurrence patterns?" And he was able to turn this out in literally 24 - 48 hours. Paul let me turn it over to you so you can educate our viewers on what you found and the updated results as well.

With the full caveat of course, that this is still in press, so we don't want to violate the terms and confidentiality information and give too much away, but, but Paul can give you the higher-level information.

Dr. Hegarty:

What we looked at, in the public arena, there is data available as to which countries have high level of compulsory BCG immunization at birth and which countries do not. And straight away we saw that the countries in Europe that were being hit hardest by COVID-19 seemed to carry negatively with whether they had BCG [immunization] or not. So the countries that did not have BCG [compulsory immunization] or had not had BCG for a long time seemed to have a much worse outcomes with regard to [COVID-19 cases] there. So that was the initial overall view.

Dr. Hegarty:

Then we took the data of 178 countries and territories and correlated those that have BCG [immunization], yes or no. And there was a few unknown. There's about 21 countries that don't have a BCG program. And when we looked at the incidents of COVID and the mortality, the death rate of the COVID it was far higher in those countries and of those who got the disease or we call the case fatality rate, is the number of deaths divided by the total number diagnosed.

Dr. Hegarty:

It was twice as high in the countries that did not have a BCG program. And we were quite flabbergasted with that. We decided to look more detail out of that where we actually look to countries, neighboring countries, ones with BCG [immunization] and ones without, which are very similar health economics, lifestyle, life expectancy, smoking, other health parameters, other ways of measuring people's health. And again, we saw between three and 10 times higher death rate in those countries. And so we didn't find any country that jarred that or did the opposite. And so it was very consistent and we were very surprised at that.

Dr. Hegarty:

We have to be careful that, this is what we call it [epidemiological study](#) or an ecological study. And that means it's telling us about whole country and it doesn't necessarily translate to an individual's risk. And so we can't definitely say that without examining this hypothesis in greater detail. And that's where Dr. Kamat's trial is going to hopefully give us the answers to that and hopefully soon.

BCAN | Stephanie Chisolm:

Okay.

Dr. Kamat:

And then the second part of the question that you raised, and I've had several patients and others ask, is what about BCG that's given within the bladder? Does that protect people against COVID-19? From a mechanistic standpoint, I could say that there is no reason mechanistically and biologically that intradermal vaccination or an exposure to intravesical therapy would have different effects as far as being protective against a re-challenge with viruses. Clearly as Dr. Hegarty mentioned, this is something that we hypothesized that it needs to be studied. It's not something that I would recommend going out and just assuming that because you've had BCG instillation in the bladder, you're immune. So *don't drop your mask and don't stop washing your hands* and then don't do things like that. We still need to be responsible stewards of this fight against the COVID-19 pandemic.

BCAN | Stephanie Chisolm:

I know that there are different registries that are popping up or different sites around the country that are contributing to a [cancer and COVID registry](#). Are they tracking, do you know, for whether or not they've had different types of treatment like BCG, so that they could see if in fact this is a phenomenon that it's helping or hurting or neutral?

Dr. Kamat:

Obviously now that the BCG data has become so well-known and then as it's got the attention of not just the US but international press, these databases are including BCG as a variable. So yes, absolutely we will have sufficient data on BCG with regards to not just bladder but all different cancers and we're clearly in patients that have bladder cancer. But these are registries that are reported by practitioners of patients who are COVID-19 positive. They're not registries that are capturing COVID-19 negative individuals because clearly that's in the hundreds of millions as far as population is concerned.

Dr. Kamat:

I do think that the survey questionnaire that you incorporated as part of the registration for this meeting will actually help inform our bladder cancer community of patients and providers a lot as to what it shows. I'd be interested to see what our registration from this webinars suggests.

BCAN | Stephanie Chisolm:

We'll be sharing the results of what the 87 people that signed up have contributed thus far. And absolutely, I'm sure there may be some ways that, or some ideas that pop out that you want to know more about. We'll be happy to push that out so people can respond. Because I think again, if they're not going to be reporting any people that are COVID negative to this registry, you won't find out if people who on BCG are ultimately COVID negative. It'll be very interesting to see as they begin to mine that data and they begin to have more and more patients entered into it.

BCAN | Stephanie Chisolm:

If somebody who's listening has gone through COVID in any way or they know that their COVID positive, they can't sign themselves up for the registry, can they? They have to have their doctor do it, correct?

Dr. Kamat:

For the actual cancer registry? Yes. That is correct.

BCAN | Stephanie Chisolm:

As far as the idea of looking and understanding about the vaccine, you've decided to do the trial in healthcare providers. Can you talk a little bit about that. How you're going to be doing this trial? I think patients might know enough about scientific trials from high school, that they know a little bit about how trials might progress. We've certainly tried to explain it as an organization to everyone, but what's the structure of this trial going to look like and how long is it going to be before they have any kind of data that they could use?

Dr. Kamat:

Let me actually answer that in a little bit broader term because I'm sure our viewers are very in tune with what's going on, not just in the US but globally. Based on some of these epidemiological studies, including the one that Dr. Hegarty led. There has been a push from several governments across the globe and several groups even here in the US to suggest that we should take BCG vaccine and vaccinate everybody at risk. Older individuals, nursing home residents, law enforcement and people in the food industry and get them out there so they could start working again. And that's because of clearly a specific COVID-19 vaccine is likely going to be nine 12 plus months down the road.

Dr. Kamat:

And we all recognize that COVID-19, there's likely going to be a seasonal thing and we'll come back in winter. And combined with the flu, it's going to be, potentially [overrun] the US system, just like the Spanish flu did in 1918 when it came back with a vengeance in the cold season. So people are saying, well, if BCG vaccination protects against influenza and there's anecdotal evidence that people have less flu with the BCG and now they're suggesting it protects against, COVID-19. So you just roll it out to everybody. And we think that that should be phase two, if at all.

Dr. Kamat:

In phase one, we believe that we have to answer this question in a rigorous manner. And the only way to do that is to have a randomized study randomized half the population to placebo half to the intervention, in this case, BCG vaccination. And we don't want to put our community and patients at risk because we don't know what the result will be. So we're targeting healthcare workers who have high risk of exposure to the COVID-9 infections just from being day in and day out in COVID-19 units taking care of patients. And half the healthcare workers they'll know that they potentially could get placebo. We're keeping this initial phase relatively small. It's only about 300 healthcare workers at each institution.

Dr. Kamat:

So roughly about 1200 to 1500 in the US and we're going through the FDA regulatory bodies, everything to do it in a strict controlled manner. The results should be out pretty relatively quickly because we will see effects within three, four or five weeks maybe six weeks. Clearly we're planning for the next phase of the reintroduction of the pandemic if it happens to protect people there. I just want to caution everyone, and I know there are countries and organizations that are rolling out BCG [vaccination] without the umbrella of a trial for everybody that wants to get vaccinated. Personally, I think that, that would be too premature. Paul, what do you think?

Dr. Hegarty:

I agree. We just don't know and there is this window that we have now for getting useful information. Healthcare workers are the ideal target in that they're generally young and healthy. So that's what we use in the phase one trial is when we check it on healthy individuals. And secondly, because they have a high rate of infection in my country in Ireland 27% of all cases are in health care workers.

And so because we hopefully get the answer quickly in that regard. It'd be premature to run ahead. We also don't know to what extent it protects people. If it protects at all and does it protect well, does it protect partially because we want to know to what extent we can start lifting some of the draconian limitations we have to people now.

Dr. Hegarty:

We want to know how good this really is and giving it in a blanket way like this would not be measurable if we want to get the maximum information to help countries get back on their feet, both medically and economically. And we need to know really what's the margin of benefit if at all to this.

BCAN | Stephanie Chisolm:

I did have a question about why was the Tice strain was selected for the vaccine if there are other strains out there or is the Tice strain only being used in the United States? And why is that? Because that's the strain that our patients use for bladder cancer.

Dr. Kamat:

Correct. Globally, countries are able to use whichever BCG is approved in that country for either a vaccination or for other purposes. Here in the US we don't have BCG that's produced for TB vaccination because the incidence of tuberculosis is so low in the United States, and the only BCG that's FDA approved is Tice BCG. So the FDA gave us an IND [[Investigational New Drug Applications](#)] exemption to use that formulation in the US essentially. But in other parts of the world, they're using BCG from their local sources. The Serum Institute of India, for example, that produces most of the BCG in the world is more than happy to provide BCG even free of cost for the study in the United States. But it's not something that we can say yes to because it's not approved here and it has to go to the usual FDA regulatory process.

BCAN | Stephanie Chisolm:

Okay. And yes, they're looking at BCG and other strains in other clinical trials, but those are not even near completion yet to see if that's effective. The SWOG trial.

Dr. Kamat:

Again, having worked with BCG for close to two decades and having talked to people that are essentially worked in BCG for 50 plus years, we don't really believe that there's any true difference between the different strains of BCG. And if the difference exists, it's so minor that it's not worth not being able to use those strains. But again, clearly we have to follow the rules that we have and if the rules state we have to do a study to get any strain into US and then we have to do it. And that's where the SWOG study comes in.

BCAN | Stephanie Chisolm:

In the supply chain, what would one dose of BCG that would be used for one patient with bladder cancer do in a vaccine? How many people might be vaccinated with that single dose?

Dr. Kamat:

So this was a very important consideration because as you know I've been a strong supporter and champion of our bladder cancer community and that is primarily what I do. I'm not an infectious disease doctor, I'm a urologic oncologist. It was very heartening for me when speaking to the TB experts and looking at the dose calculations that would be one vial of BCG that is used to treat a patient with bladder cancer. We could potentially vaccinate 500 healthcare workers. So it's one vial versus two, four or 500 people. And I'll tell you there's some logistics and how quickly can you inject, et cetera, et cetera. So even with a little bit of error built into it, up to 300 people, once you get the system going, it could be vaccinated with one vial.

Dr. Kamat:

Early on with the six feet, this new [social distancing] thing and the fact that a lot of people will be driving through these centers to get their vaccine and not actually walking up to people like they would for a flu shot. And that number might be lower. But to answer your question from a pure CFU colony forming unit calculation, it's one vial can vaccinate [up to] 500 healthcare workers.

BCAN | Stephanie Chisolm:

That's a lot of people that could be protected down the road with just the one vial. And is the fact that some [bladder cancer] patients are being deferred [medical distancing, delayed] in some locations going to allow it not to necessarily impact the supply for bladder cancer treatments?

Dr. Kamat:

To be honest with you again, we don't want our bladder cancer patients *not* to have access to BCG if they need it for the higher grade, higher risk bladder cancers. As you know there are a lot of centers in the US today and many of my collaborators on the study, that don't have a single vial of BCG so they can't give it to bladder cancer patients anyways. So that's a problem that's ongoing. The supply chain and we and I know you and others have reached out to Merck to see if they could help with the supply chain of BCG and for some reason they haven't been again, I don't know the reason, but the answer has been essentially no, they're not able to help with this study.

Dr. Kamat:

What the sites that have BCG and are enrolling in the study are doing, is making sure that we don't sacrifice the ability of patients who truly need BCG for that initial induction just for the trial. And fortunately, as I mentioned, a lot of the guidelines are suggesting that even regardless of the trial, patients who are on maintenance therapy should probably not be getting maintenance therapy because of the risk of COVID-19 just coming to the hospital. So that does open up the supply. And as I mentioned, one vial - so if one patient doesn't get one maintenance therapy, 500 people could be vaccinated.

Dr. Kamat:

And patients of mine that I've talked to, and I'm sure that you've talked too Paul, and others, they've all told me, "Hey, Dr. Kamat if one vial can help 500 healthcare workers so that they can then be ready to help us when we come back and actually need help, feel free to take my vial away." No, again, I'm not saying that this is what we're doing, but it's been very heartening to hear that from my own patients.

Dr. Hegarty:

I agree. We're not at the level of rationing that we have to make those difficult decisions at all. Thank God. And so, we have enough for it. I'm really pleased with people's response in general, the generosity of spirit of everybody that they're just want to get it done. I don't think it's a real issue and it's great that the ratio is so large with regard to how many people can get it. Once we have the information, we have a few months while we're getting these data together for the various countries and regulatory systems to sort out the BCG question. And so maybe in the long-term this would actually be helpful. So the BCG is less of an issue with supply chain going forward for everybody.

Dr. Kamat:

That's a great point that Paul you just made, because data speaks for itself. And I suspect that once we have the positive results from the study, and I say positive because I do believe [in] the mechanism, but once we have results from this study, if it's positive, that will put pressure on the supply chain to produce and provide more BCG. And then hopefully we will not have this shortage issue both for bladder cancer and for vaccination if that's something we decide to roll out to everybody. Because like I said, there's plenty of BCG in the world. It just doesn't get to certain places because of rules, regulations, which again, I'm not saying we should circumvent, but we do have to sometimes recognize that no benefit can outweigh certain bureaucratic red tape.

BCAN | Stephanie Chisolm:

Well if I could take a couple of questions from the participants that are on this call, so understanding BCG does not protect against COVID. If a bladder cancer patient were to get COVID-19, would this make BCG less effective as a treatment against bladder cancer? Do you have any idea, any speculation on that?

Dr. Kamat:

Well, bottom line, no. Unless someone is acutely sick with a viral infection, at which point we wouldn't be treating them with any intravesical therapy anyways. But if somebody has symptomatic flu, we do delay BCG therapy. But if someone had COVID-19 infection and recovered from it, then there is no reason why BCG should be less effective.

Dr. Hegarty:

Absolutely. I agree.

BCAN | Stephanie Chisolm:

Understanding that approximately 40% of patients undergoing six months of induction of intravesical BCG become PPD skin test positive. Is that correct? Are there any studies that are looking at that as far as are patients becoming tuberculosis immune because of this, because of the inductions that they've had once they've completed dose? Is that a real benefit?

Dr. Kamat:

It's interesting that somebody brought up PPD. PPD is such an old test to detect prior exposure to TB, tuberculosis. And yes, it does cross react a little bit with the BCG that's used to treat patients with bladder cancer. And not to use it for vaccination, but it's a very nonspecific test. And most TB experts will say that people should not be using PPD. Again, there are centers that still use PPD as a test. But there's other tests, the [IGRA test](#), which is much more precise and it's inexpensive to do.

Dr. Kamat:

Short answer, if a particular center or an employee is still using PPD, by all means you can use it if the person ends up being positive either because of BCG put in the bladder or because of BCG vaccination. And again, I was vaccinated at birth or an infant in India, you can clarify that with an IGRA test so easily that that hypothetical situation should not really defer anybody from getting BCG for their bladder cancer or for this study.

BCAN | Stephanie Chisolm:

Anything to add Dr. Hegarty?

Dr. Hegarty:

As long as the person is well then that's always been a premise with regard intravesical BCG. If a patient was unwell coming into it, it would have been deferred anyway. And so this changes nothing in that respect. And the fact that PPD becomes positive in the skin is a sign ... that their T-cells are responding to it. I don't think it necessarily predicts a better outcome or worse outcome, but it's just a sign that it's getting into the system. And what's interesting is that it's not having an effective just in the bladder and that's what will help us in our studies in the mechanism of how it works. That affects not just the bladder area, but also perhaps throughout the whole immune system. That's the whole argument.

Dr. Hegarty:

If it were just an infected locally, then an injection under the skin should only protect your skin area. So the fact that it generalizes is probably the beneficial mechanisms of most of BCG.

BCAN | Stephanie Chisolm:

Well, that leads me very well into the next question. How is it that BCG vaccination is safe, even though it's systemic in your body? Whereas it's considered very dangerous for a bladder cancer patients. If BCG instillation gets into their bloodstream because their [TURBT](#) hasn't healed necessarily before they have that [BCG]. Why do you have to wait? Why is this such a big deal? And yet they're saying that it's going to be beneficial if you put it into your bloodstream.

Dr. Kamat:

So let me clarify there. TB vaccination when it's given the way we're doing it for the study against COVID it's not intravascular, it's not systemic. It's [intra-dermal](#). It's just underneath the skin. What they small puncture right underneath the surface of the skin. And that's the way that it's been given to billions and billions of babies across the world and with minimal adverse events. In fact, in Africa when it's given to millions of babies of HIV positive mothers in the acute setting, the mothers don't get infected with BCG nor do the babies. So it's a very, very safe when it's given in that manner and it's given right underneath the skin.

Dr. Kamat:

Also, you have to remember that the dose of BCG that's put in the bladder is 500 times that dose and the bladder has blood vessels and we've potentially done biopsies and resected the tumor. So there's a raw vascular surface. If I took a BCG and injected a directly intravascularly into a subject, that would be fatal. And people tried BCG, for melanoma and leukemia and lung cancer back in the 1920s, 30s and 40s. It worked really well against the cancer, but it caused a severe infection because they were putting it directly into the bloodstream. So for the trial, it does not go into the bloodstream. It's only put underneath the skin. There's data that it's very safe from millions, if not billions of subjects. And the dose is much smaller than what we use for bladder cancer.

BCAN | Stephanie Chisolm: Okay. Very good point. Dr Hegarty?

Dr. Hegarty:

It's a question about why would we give BCG, which has some live TB effectively in it? It's a very weakened amount of it. The idea is to expose the person to a small amount of it. If we were to give a high load of this bacterium into the system, then that would be dangerous. And that's why we have very strict criteria on giving it into the bladder that we wait for the person to have settled down after the resection. And if the catheter passes in and they're bleeding, or they've a sign of an infection it gets suspended for that week and they don't get it again until they've settled. That's why we have these criteria.

BCAN | Stephanie Chisolm:

Dr. Kamat, you mentioned that you as a baby in India were vaccinated with BCG. I remember, well I have a scar that shows that I also got the TB vaccine when I was young as a young child. I don't necessarily remember it, but there are a lot of older Americans that also might've been given this vaccine back in the day. Are they protected or is there a period of time that it's helpful and then after a while it just doesn't do much of anything. Maybe you need a booster, like some other vaccines. What do you think about that?

Dr. Kamat:

Unfortunately, all of the above. There are some people in whom the effect of TB vaccination last five years, some in whom it could last 45, 50 years. There's no way to know that other than doing testing for immune cells, et cetera, that we talked about. Just because you have the scar from the TB vaccination at birth does not mean that you can essentially either not need a revaccination. So we're not using that as an exclusion criteria for anybody on the study. Even those that were vaccinated with BCG so long as it's not just within the last year or two years, we'll still be able to get a booster of vaccination shot, number one.

Dr. Kamat:

Number two, the study that Dr. Hegarty did, actually looked at populations that are vaccinated at birth, not just adults. So looking at those correlative studies and Paul, if you want to listen to that a little bit more, there is clearly some protective effect, but we can't say it's for everybody. And as you mentioned Paul, it's population-based, it's not individual because the individual protection could be five years, four years. It's variable.

Dr. Hegarty:

Actually it's protection against TB is thought to be 20 years at least that's more recent data supports that. But there's so many other potential benefits to it that we don't know which effect wears off, or if it wears off at all. We don't know where the death rates lower because less kids got it and then didn't pass it on to their seniors. Or is it something that somebody got eight years ago still affecting them and it may well be that. So we just don't know. And maybe when we have different arms of the trials from different countries don't want done in the country where there's little or no BCG and then done it also in a country where there's a high rate of BCG, but it would have been given to a healthcare worker 30 or 40 years earlier than that will hopefully answer those questions also.

BCAN | Stephanie Chisolm:

This is all really important. So, given that it takes a long time to develop and grow BCG, it's not a simple thing. Do you know what is being done either locally in the United States or globally to help increase [the production]? You mentioned that the Indian supplier seems to have plenty of other strains of BCG. Will those be able to be used [for the vaccine] elsewhere? Do you think that there's any chance that these other strains could get approval down the road for this vaccine so that it does not tap into the supply of Tice BCG?

Dr. Kamat:

The Serum Institute of India has two strains. One is the Russian Strain that has been used in many parts of the world for BCG vaccination. And they also have a recombinant BCG that they have worked on for bladder cancer patients. And again, this is data that was going to be presented at the EAU. But because we didn't have the meeting, of course in Amsterdam, it wasn't presented, but that was developed for patients with bladder cancer who have a recurrent tumor after regular BCG, Tice BCG as a salvage therapy because it's supposed to be stronger, better, faster, et cetera. And again, that's something that they were working on trying to get approved in the US.

Dr. Kamat:

They have been supplying BCG for similar trials across the globe. And like I said, there are many countries where you can apply to the regulatory bodies and say we have a shortage of drug, we have supply of drug, it's not really different. And they do quality control and then they get that approved. Here in the US we have that mechanism as well, but it's a lot longer and more rigorous. So far we're not using any strain other than Tice in the US.

BCAN | Stephanie Chisolm:

The main last question I wanted to just get into going back to bladder cancer as far as if BCG is not available, can you just talk a little bit about some of the alternatives that might be used in intravesical therapy for populations that would benefit from being treated the way that BCG is going to treat them?

Are there other options that can be tapped into? That's a big concern for our community. Chemo or anything else?

Dr. Kamat:

Paul, do you want to say what's been done in Europe? And then I could speak to US.

Dr. Hegarty:

First of all, there's Mitomycin C, which is commonly used and then there's a different way of delivering it, which is called [electromotive](#) where they put a pad on the abdomen and on the tummy. And then they help to drive the mitomycin deeper into the tissue. Those are the two main ways in Europe. But I know that you're involved a lot more trials of other versions and combinations. Maybe you can tell me about the other ones.

Dr. Kamat:

In patients who can't get BCG for whatever reason, whether decided on by their urologist or they just don't want or can't get BCG, there are other options fortunately. They're not as good as BCG because BCG is an immunotherapy, and immunotherapy works only well for bladder cancer. We sometimes forget that BCG is the oldest most effective immunotherapy for cancer because we see a lot of press about the latest drug with IOs and they only have a 20% success rate, whereas BCG has a 60 -70% success rate when used appropriately.

Dr. Kamat:

Fortunately, we have options that also have a 40 - 50 even as high as 60% success rate in some situations, that can be used. And again, as Paul mentioned, that's mitomycin either electromotive or heated. There's combination chemotherapy with mitomycin and gemcitabine. Luckily our patients have a lot of options. Even though they may not be as good as BCG, they're clearly very effective and I would not recommend no treatment. I would recommend some treatment for bladder cancer always. If a patient can't get BCG because of supply chain issues in their country, wherever it is. I'm sure they are having discussions with their urologist about an alternative treatment rather than no treatment.

Dr. Hegarty: I agree.

BCAN | Stephanie Chisolm:

Very helpful answer. One of our participants is using [Dr. Kamat's BCG treatment schedule](#) that we've put out through BCAN and this person is getting their BCG treatment number 19, 20 and 21 in July if it's available. Do you think by then it would be safe to go in and get that in a smaller practice environment rather than coming to a big, large academic hospital that might still be in the throes of COVID-19 treatment?

Dr. Kamat:

First of all, I do want to give a shout out to a BCAN, Stephanie and your group for putting that on the website so people can use it. It was very frustrating for me because I get patients from all over the country and the world, and I would recommend that they get BCG certain way. But clearly we can't have them all staying in Houston to get the BCG. So they would go back to where they reside. When I saw them back in three, four, six months, or even a year just for an annual checkup, I would find that the BCG schedule was all over the place. It wasn't anybody's fault. It was just the way that had happened.

Dr. Kamat:

So we came up with the schedule one of my lead nurses here at MD Anderson, Prasanth Abraham, myself and my team, we came up with this and we use it for our patients. It's almost like a little Starbucks card. We can take it and get stamped when you get your BCG. Stephanie, you were very kind enough to recognize the importance of the community. Now I see a lot of patients have never seen me come see me for the first time carrying that with them. So it really helps.

Dr. Kamat:

Sorry to go about the long way, but I do want to thank you for doing that. But short answer to that question, if you're already on 19, 20, 21 and you've been free of disease for that long. I would only go and get the instillation of BCG if it's safe from a COVID-19 perspective. And absolutely going to any facility where you have qualified individuals. BCG is done so regularly and so routinely in the urologic community, that it can be honestly done safely in most centers that offer it.

BCAN | Stephanie Chisolm:

How far is the trial now? I know you mentioned that it was getting up and running, and that it would probably be about six weeks before things really start to show any data. Can you talk about the fact that it has different names in different countries? Is that the same trial?

Dr. Kamat:

I did see one of those questions and it is ironic. Initially, we physicians called it the BACTRIL B-A-C-T-I-R trial and it was very scientifically named. When we were talking amongst ourselves and my son was overhearing some of my conversations as I was talking with some of the patients who said, "Well, we need a more powerful name." And that's where the *BADAS acronym* came from. It actually came from recommendations from some patients and kids of the investigators that we need a "bad therapy to fix this bad problem". So it's BCG as Defense against SARS-Covid-19. That's the US acronym for the study. All the acronyms have been dropped.

Dr. Kamat:

As far as where it is. Again our regulatory process in the US takes longer than many countries and I think that's a good plus. I have to commend the FDA that they were so quick with granting us a IND exemption and many [IRB](#) have moved with this at a rapid pace. Just to give our audience some idea. Normally trials take anywhere from nine months to 18 months to get up and running. This trial should be up and running next week, which would be in less than five weeks from the idea to implementation, but it's not up and running yet. We don't have anybody enrolled yet. Nobody's received it, but it should be up and going pretty soon.

Dr. Kamat:

And obviously once it gets going, Stephanie, that's what I was saying will be roughly six weeks from the time that we first start that we should have data.

BCAN | Stephanie Chisolm:

So, because certain communities have large outbreaks of COVID-19, are you targeting some of the communities where it's not quite as prevalent to see if it has a preventative effect at all? Or are you suggesting that you can still offer some benefit to the health care community even in places where they probably already been exposed and just might not have come down with the virus yet?

Dr. Kamat:

You are asking a great question and that goes deep into what are we doing as far as testing prior to enrollment, collecting specimens, doing retroactive analysis? All of this will actually be answered once we have the results of this interim look. But we're not restricting communities or healthcare workers or doctors or facilities just based on the prevalence. I know what you're saying. It would obviously be better to get this trial only in the areas that have a very high prevalence of COVID-19, but I'm sure you saw the study out of California that came out a couple of days ago. Where they tested everybody in that city. I think it was LA actually, and they found that 3.9% roughly had evidence that they'd been infected, which was clearly much higher than people ever thought.

Nobody knows the actual incidents or prevalence of COVID-19 infection and to restrict groups from participating just because we think it's not good for them, I really don't think that's fair or ethical.

BCAN | Stephanie Chisolm:

Well this has been incredibly informative. I think we're at the end of our questions. Do you have any last comments that you would like to make for the group about BCG in bladder cancer, BCG as a vaccine preventing and hopefully reducing the risk of very serious complications from COVID-19 anything else?

Dr. Kamat: Paul I'll let you go.

Dr. Hegarty:

First of all BCG has been well proven in its benefit in bladder cancer and it's great that BCAN are supporting this and allowing a vehicle for patients to discuss and raise their anxieties or concerns. BCG clearly is beneficial in bladder cancer. It may well be and hopefully the trials will answer the second question. I think it's great that BCAN is supportive of our processes and I'm very pleased to help.

BCAN | Stephanie Chisolm: Thank you so much. We really appreciate that.

Dr. Kamat:

In closing again, I do want to again echo what Paul said. Thank you for a BCAN for bringing this to the forefront because I know my patients have questions for me about BCG the trial and things like that, and just produce a platform that's really helpful for patients. Once it's out there, in an enduring fashion, they could access it anytime. I do also want to rule out the fact that people do ask me and I saw a question pop up, "How come urologists are leading the fight against COVID-19?" Clearly urologist have the most experience with BCG in the United States. My collaborators and in fact people that brought the idea to me, Andrew DiNardo from Baylor College of Medicine, Jeff Cirillo, from Texas A&M, Megan Martin from Harvard.

Dr. Kamat:

These are excellent, infectious disease specialists and researchers in the TB field. But when they were faced with this problem, they recognize that, BCG is not used in the US other than by urologist and urologic oncologist. And so that's where I got involved in. They approach me, Mihai Netea from the Netherlands approach me as well. And then of course I reached out to Paul because of the access to the databases. So that's how urologist got involved. It's clearly up to everybody that can help our patients and the whole COVID-19 community to do whatever we can. I think it's great that everybody's chipping in and being part of this fight against the COVID-19 pandemic.

BCAN | Stephanie Chisolm: I have one more question. Somebody asked, could you again say slowly, what did B-A-D-A-S study stands for? They are probably taking notes.

Dr. Kamat:

So B for BCG, A for As, D for Defense, A for Against and S for SARS-CoV-2 to BCG as defense against SARS-CoV-2.

BCAN | Stephanie Chisolm:

I do want to let everybody know that we will be making a transcription of today's program and we will post it along with the video recording of today's program on our website, bcan.org and on behalf of the bladder cancer community, Bladder Cancer Advocacy Network and the World Bladder Cancer Patient Coalition for which we are a member, I thank you both very much and I do express my deep gratitude for you coming on and doing this program. We'll be sharing that information people submitted with our experts and if they have any follow-up questions, they will reach out to us and we will reach out to you to see if you might want to participate in whatever informational gathering studies they might be working on about BCG, bladder cancer and COVID-19.