Highlighting Clinical Trials | Muscle Invasive Bladder Cancer

Part II: Current MIBC Clinical Trials

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BCAN Patient WEBINAR SERIES

Presented by:

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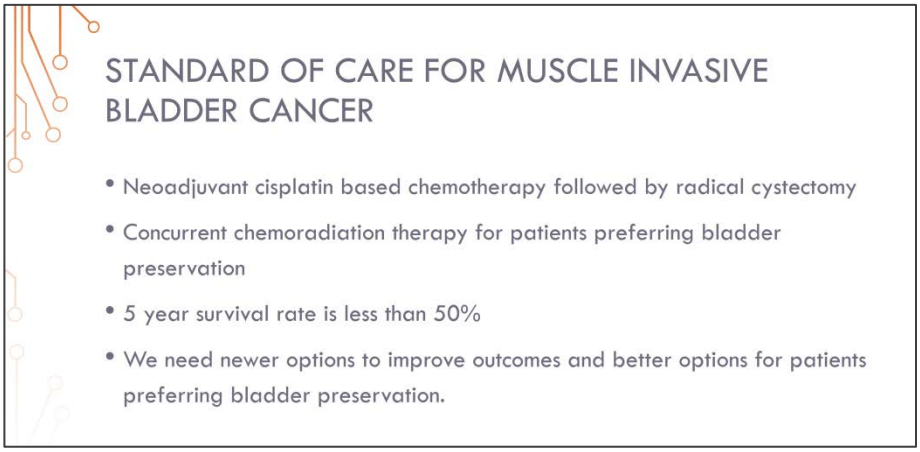
Dr. Singh: I would like to thank the Bladder Cancer Advocacy Network for organizing this webinar to help educate our patients and caregivers regarding bladder cancer and advancements in the field occurring in the form of clinical trials.

I'm sure the audience is fascinated by seeing what Dr. Black had talked about how we change the cure of bladder cancer patients by investigating new surgical techniques and, in fact, nutritional supplements. I have so many patients in my clinic who ask for a variety of supplements that they want to take to help their cancer treatment.



We, as scientists, we want to explore each supplement which we want to prescribe in a clinical trial to prove that it truly works and just don't take them based on anecdotal reports of my family member or my friend's friend took this and their cancer went away.

Everything which we practice in our clinics, when we treat patients with cancer, is based on hard data based on these clinical trials. You saw that Dr. Black assured that even extending the lymph nodes from deep pelvis to just another level up in the pelvis, it is based on hundreds of patients enrolled on the trial, and then they'll figure it out over many years after following these patients to see if it truly makes a difference in survival.

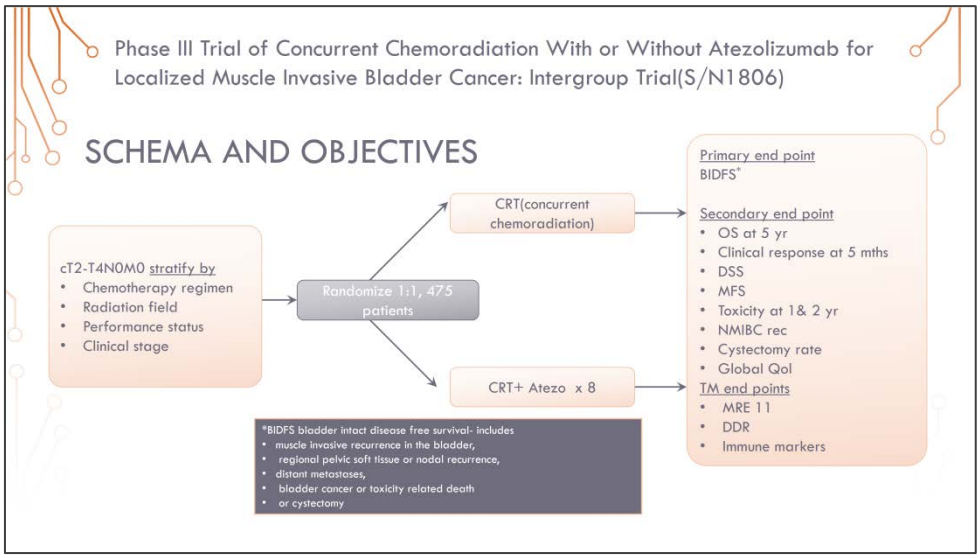
It is not based on what a surgeon or a physician feel about a patient, it is every decision we take is based on these clinical trials. That's the main idea or driving force behind BCAN's initiative to tell patients that they should look for trials for their treatment, how critical they are in advancing this field.

My presentation is going to give you a glimpse on the medical side of the treatment of this disease, what new medications or combinations we're investigating to better control the cancer, or even possibly achieve long-term remission or cure.

As Dr. Black mentioned regarding the treatment of bladder cancer, the standard of care is chemotherapy and then having your bladder removed. But in many patients, it may not be possible. Patients may not be a good candidate for surgery, or a patient may just refused to have their bladder removed.

In situations like this, or in a very select group of patients, strategies like combining chemotherapy and radiation maybe an option. We know from our experience in the past of treating patients with chemo and radiation and/or even surgery, the long-term outcomes still are not very good. We have around 50% of patients who will die after five years of their definitive treatment. The trials that I'm going to show you are focusing on improving the long-term outcomes of chemo radiation or, in fact, bladder surgery itself.

This is one such trial, which is opening this fall, which is investigating chemo radiation combined with immunotherapy. The drug name of the immunotherapy is atezolizumab. This drug is already approved for treatment of bladder cancer. What we're trying to do is we are adding this to chemo radiation to see if it improves the outcome of chemo radiation alone.



The idea behind combining immunotherapy with chemo radiation is that when the chemo radiation is in process of killing the cancer, our immune system will take the cue from the immunotherapy and may then eliminate any residue of cancer which is left behind, or even eliminate any cancer which has spread out of the bladder, and then prevent it from recurring in the future.

This study will enroll over 450 patients. Half of the patients will get the standard treatment, which is chemo radiation. Half of the patients will get chemo radiation and immunotherapy. It's a randomization

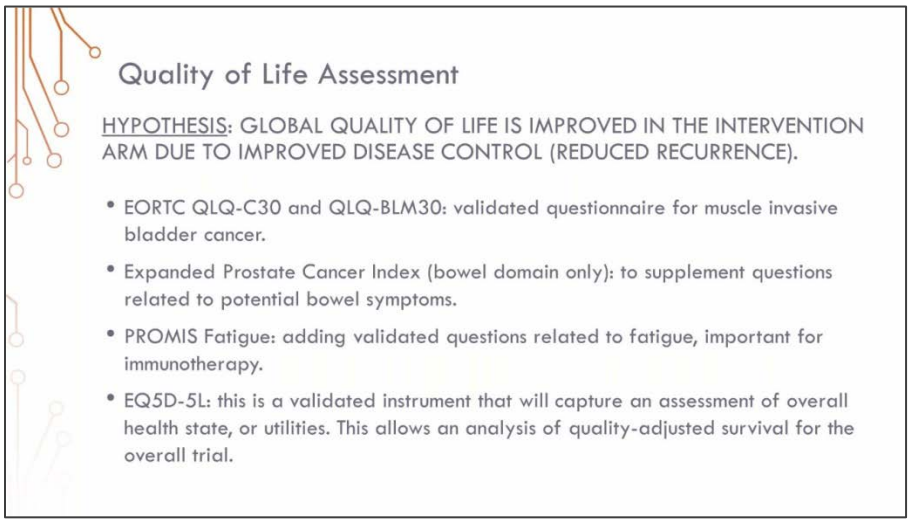
process, so it's a flip of a coin. Somebody who wants to go on this trial thinking that they want to go on immunotherapy, which is not a choice. It is decided by a computer, but not a human. Then Rick is going to address these concerns with you in his presentation.

Then we will follow patients to see that at three years and five years, how many of the patients are alive and they are able to maintain their bladder function? Because this is critical that the idea is patients are able to maintain their bladder and be cancer-free.

The endpoint we are looking at is what we have written as BIDFS, or what we call as bladder intact, disease-free survival. This is a technical term. I know you can get confused with it, but essentially looking at how many patients are able to keep their bladder and be cancer-free at three and five years.

Then we'll be looking at how many patients are live at five years and among other endpoints, including how many patients have metastasis or toxicity at one or two years, and cystectomy, or some patients may end up getting their bladder removed even after chemo radiation. How many patients are those?

Then we also look at variety of what we call in technical term translational endpoints, which are essentially looking at tests which can help us later on predict which group did better, or somehow identify which treatment modality maybe better for what group of patients. We just don't look at giving the medicine and if it works or not, we look at a lot of other things, what we call as translational endpoints in our clinical trials.



As I was saying, in addition to clinical endpoints, we also look at quality of life endpoints, which is how is the treatment going to affect the quality of life of the patient? It is based on validated questionnaires that we have experienced with in patients who have muscle invasive bladder cancer.

Then we look at the component of fatigue coming from the treatment and also overall health state of patients. There would be a set of questionnaires which we'll be giving to all the patients going on to this trial. We'll assess it after one year and see what the difference is in the quality of life of patients who received immunotherapy versus those who received chemo radiation alone.

This kind of data tells us what's the burden of the treatment we are adding to the patient's quality of life. Is it worth doing this or if it is justifiable that the chemotherapy or the treatment we are doing is helping the patient? Are we adding too much toxicity? Many patients ask me if the immunotherapy is so good, why do we have to do a clinical trial? Why can't we just add immunotherapy to the treatment mix?

The answer is that we need to test whether we are adding any additional toxicity to the treatment. What if the toxicity is so high that even if we see the incremental benefit, it may not be justifiable? Or there may not be any additional benefit. What if the chemotherapy and radiation therapy nulls the efficacy of the immunotherapy? These are questions which are answered through these clinical trials

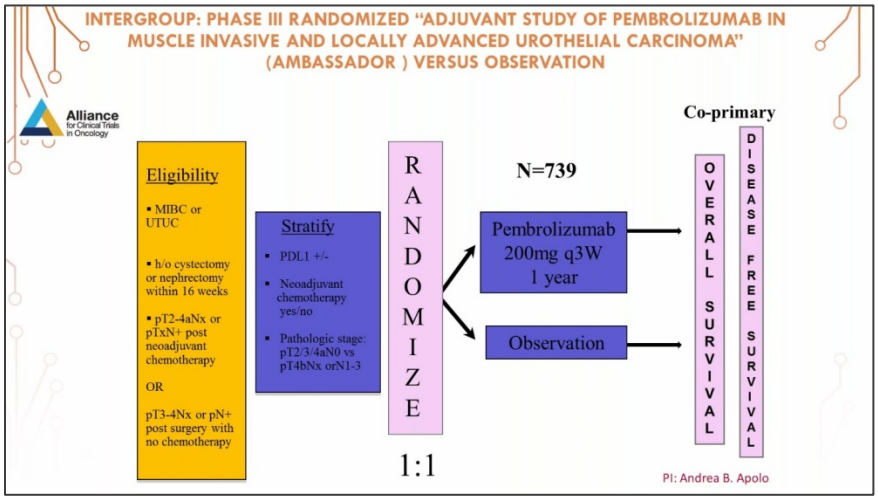
In fact, I would just like to spend a minute talking about the immunotherapy. I know immunotherapy is the rage right now because it's getting a lot of media attention and a lot of high profile people like Jimmy Carter getting immunotherapy and having his cancer going away.

Basically, the drugs which we are referring to as immunotherapy are also called as immune checkpoint inhibitors. These drugs, how they work, as I try to explain to my patients, is that if you're trying to catch a flight in the airport, you have to go to the TSC and show your ID. The TSA may say, "Well, this is not a valid ID, so you can't take the flight," like the Arizona license will not be a valid ID next year, so I may have to have another form of ID next year. They may say, "You don't have the right ID."

Similarly, our immune system goes around and checks proteins on every cell in our body every day. If the cell doesn't have the right ID, the immune cell will kill that cell. Bacteria or viruses will not have the right ID.

Whereas cancer cells are our own and they carry the same IDs, and so the immune system ignores them and they let the cancer cells grow in our body. But if somehow we are able to cover these IDs by giving medications like these, then the next time around the immune cell will go to the cancer cell, they'll not be able to see the right ID. Then they may choose to kill the cancer cell.

That's the idea of these immune checkpoint inhibitors which are now being used in nearly every possible cancer, including hematological malignancies and solid tumors. But the caveat is that not everybody responds to these drugs, or not all cancers respond to these drugs.



This is another trial, as I said before, when patients get their bladder removed for bladder cancer. Many of them will have their cancer recur after a year or two years or three years. Then these patients will eventually die from their disease because metastatic bladder cancer is still incurable.

We want to see if we can prevent the patients who we know are at very high risk for recurrence after bladder removal, especially, as Dr. Black said, patients who have residual disease at the time of radical cystectomy. They're technically high-risk, and we may some time offer them chemotherapy.

But if they had chemotherapy before, and even then they have residual disease at the time of radical cystectomy, that patient is at a very high risk for their cancer coming back. We don't have any treatment options to prevent that from happening.

This trial, which is run by Dr. Apolo, NCI, through Alliance Clinical Trials Network, is investigating a kissing cousin of the other immunotherapy drug, which I talked about. It's called pembrolizumab. It works with the same mechanisms.

It is being given to over 700 patients. The patients will be randomized to either receiving the medication or not receiving the medication. They'll be followed to see which group lives longer and if it truly affects the long-term outcomes of the patient

If this trial shows benefit, then patients will have access to this drug to reduce the chance of the cancer coming back and possibly even cured even if they are high-risk. I'll end my presentation here, but my goal was to give you a sense of how we are advancing the field of bladder cancer treatment in making the treatments better and also trying to see if we can add on to the other treatments like surgery and radiation in advanced disease.

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