American Brain Tumor Association Webinar

Advances in GBM Treatments, including Tumor Treatment Fields

>> Welcome to the American Brain Tumor Association webinar series. Thank you for participating in today's free educational webinar. Today's webinar is on Advancements in GBM Treatment, including Tumor Treatment Fields. This webinar is funded in part by NovoCure. The webinar will be presented by Richard a Peterson MD. Please note that all lines during our webinar today are muted. If you have a question you want to ask type and submit using the question box in the control panel on the right-hand side of your screen. Dr. Peterson will answer questions at the end of the presentation. Tomorrow you will receive an email asking you to take a brief survey to evaluate the webinar. Please take a few minutes to share your comments. Your feedback is important to us as we plan for future webinars. Today's webinar is being recorded. The recording will post to the ABTA website shortly. Registered participants will receive the webinar link and a follow-up email message once the webinar is available. Let's pause for a moment so we can begin the webinar recording.

>> The American Brain Tumor Association is pleased to welcome you back to our webinar series. Our webinar today will discuss advancements in GBM Treatment including Tumor Treatment Fields. The webinar is funded in part by NovoCure. My name is Antoinette Tiu program manager here at the American Brain Tumor Association. I'm delighted to introduce our speaker today Dr. Richard Peterson. Dr. Peterson is the Neuro-Oncologist who has been practicing in Minneapolis-St. Paul after completing a fellowship at the University of Washington in Seattle. Dr. Peterson is very active in clinical research. He is involved in developing new treatments for brain tumors as well as projects aimed at improving the comprehensive care of brain tumor patients. He reviews clinical trials for brain tumors on a local level as well as nationally with his involvement with the Brain Malignancy Steering Committee at the National Cancer Institute. Dr. Peterson has spoken for ABTA on numerous occasions including our Minneapolis Partners in Treatment and Care Meetings. Thank you for joining us, Dr. Peterson. You may now begin your presentation.

>> Thank you. It is my pleasure to be here today and to be able to talk about this exciting topic I think that now more than ever in the past there are reasons to be very excited. And it's great to be able to present today and talk about what's going on. Just in terms of disclosures to say that I am not being paid to do this and I don't have any major stocks or consulting roles. I do have some research that I am doing here locally that is funded by the company that I work with. This is to say that I am not being paid and there is no endorsement that is being done by me or ABTA. Thank you to ABTA for the opportunity.

Thank you for all of the patients and families and friends and caregivers that are involved in taking care of what I consider a special patient population, and I am happy to be able to discuss about the investments that are happening in the world of glass dome and how these will help us provide better treatments and prognosis and how can we do these things in a way that minimize the side effects that we see especially in our world where we talk about the brain and I take this very seriously. I am always saying what how do we protect the brain? Is obviously important for all of us. We need to talk about updated therapies and updated devices.

>> The agenda as I laid it out in terms of therapies. The buzzword is immunotherapy to the third degree. Last year at the site for neuro-oncology which is our major neuro-oncology meeting every year, the main topic was immunotherapy. If you look at another major meeting that happened this year called ASCO the American Society of Clinical Oncology again immunotherapy was a major topic we will be talking about this and what it means. It's an exciting topic. It can be complicated. I have slides that hopefully I will be able to break down in a way that makes sense and in a way that helps illustrate why there is so much excitement. We need to talk about devices and tumor treatment fields. Most commonly known as the opportune device we need to talk about advances and also with radiation.

>>I always like to start does start these talks by saying this is where we are. This is the background. How frequent are brain tumors? In the United States the frequency, the quoted rate is 21.42 cases per 100,000 people. I want to compare this to other things. I usually use breast cancer. By way of comparison breast cancer has 124.6 cases per 100,000 people. When you talk about primary malignant brain tumor, especially glioblastoma, which is the most common primary brain tumor it's a ratio of 18 to 1. The mortality for tumors, like glioblastoma, is roughly 60%. There is a disproportionate number of patients who passed away compared to other types of tumors. Even though it's less common. There is no denying we need better treatment. I know this audience would agree with that.

>> Immunotherapy. There is a long history and there is a slide that will show you this. If we asked the question why does our immune system not eradicate cancer cells? The immune system is supposed to take care of things that are not supposed to be in our body. We have had over the years a number of questions about how this is possible and how it happens. In their last 10 to 15 years is when we have been able to learn more about this and take advantage of it. At a basic level immunotherapy refers to any treatment that is designed to induce or amplify an immune response to treat disease. So here is the slide looking at the history of immunotherapy in the setting of cancer. We can go all the way back to 1863 where there is a description of immune cells and tumors by a famous physician for cow. - - Virchow And there's a huge gap almost 60 years were not much has happened. We start talking about different types of cells in the blood stream and immune cells and you start talking about bone marrow transplants and you move forward to the 1990s where you start learning more about different types of T cells. Eventually you have vaccines and initial medicines that are being FDA approved in the late 2000. This timeline ends in 2010. I will say that since then in the last five years there has been an even greater explosion of data in the numbers of types of treatments FDA proofer tumor types pick immunotherapy.

There are different types. You can look at monoclonal antibodies and these are designed to target specific parts of a cell. Ideally, something that is unique to a glioblastoma that is different from other cells in the body. Vaccines which can be made from a patient's tumor or for example from common components were common proteins or fragments that are found in a tumor type. You can modify viruses, or you can target specific aspects of the immune response itself. We start getting into a little bit of an alphabet soup. We talk about things like PD1, T cells, dendritic cells and we will talk about this more.

>> The main players I will focus on are dendritic cells, B and T cells and antibodies. You see in this slide and this is the complicated version of what can happen with different immune cells. Dendritic cells, T cells, B cells. I want to break this down into a simplified version. That is what this is. If we think about dendritic cells sometimes we refer to them as the commanding officer the general. Things like that. The dendritic cell essentially helps direct what the T cells are going to go after. In simplified terms a dendritic cell can eat a bacteria but in this case we say it could eat or be responding to a cancer cell. Then what happens is the dendritic cell learns that parts of the cancer cell can be expressed and that teaches the T cell to recognize that part of the cancer cell so it becomes activated.

>> This slide represents a similar representation thinking about this cell in what's called an antigen presenting cell and an antigen is something that is foreign and not supposed to be there. You have a dendritic cell that is showing this abnormal protein. This abnormal thing that is not supposed to be there. You again are educating the T cell which then can lead to developing other types of T cells especially what are called cytotoxic T cells which can attack cancer cells and kill them. It can also get the B cells to produce antibodies that also can target that abnormality, those features of cancer cells appear. One of the things we think about is that the B and T cells are soldiers of the immune system. We asked the fundamental question how do tumor cells hide from these cells that are circulating throughout our body?

>> We move to the concept of checkpoints. The T cells especially if we have T cells if you imagine are patrolling through the body and looking for things that are not supposed to be there. You want to make sure the T cells know what your normal cells look like because you don't want them going after your normal cells. There are these receptors and this is where we get into some alphabet soup. There are receptors on the T cells called PD1 that will recognize the other receptors that are called PD L 1. If a cell expresses the PD-L-one they essentially shield themselves so they make themselves invisible to the circulating T cells. If you can block that process, then you can allow the T cells to recognize the cancer cells and attacked the cancer cell and destroy it.

>> The other thing about the checkpoint is there are two phases in what I refer to as the priming phase and the effector phase. The priming phase essentially is using this pathway called CTLA-4 numb such that if that is activated then you are blocking the T cell from being able to recognize what it is supposed to go after. If you block that, then you allow the T cell to become activated and then once you remove the shielding if you will from the cancer cell it's not only primed but then it realizes and sees what is not supposed to be there and can attack the cancer cells. These are agents that are used for lung cancer and melanoma. Not all tumors are known to respond to these treatments. For example not all tumors necessarily have a significant level of PD1 NPD L-1 to take advantage of this system.

>> Fortunately, we know that brain tumors such as glioblastoma do utilize this system. Again this is a way of looking at how this works. I will tell you the number of medicines that are going to work on this pathway are probably going to continue to grow. There are at least two or three that are FDA approved now but more are being developed and are in the pipeline. Again if we think about a cancer cell over here and then a patient's T cells then if that tumor cells shows that PD L-1 then the T cell thinks it's normal it's supposed to be there. If you block it, then you activate the T cells so it recognizes the cancer cell and can go after it.

>> These agents have already been or are starting to enter their way into clinical trials for brain tumors. This is a very exciting line of treatment. It is coming to our neck of the woods. It's hard to imagine that it is the tip of the iceberg. That what I have been talking about is just this one portion of how immunotherapy can go after a tumor cell. They have vaccines and viruses you have engineered T cells. Obviously you have chemotherapy that is doing all of this or you have other agents that can take advantage of antibodies.

>> If we look at the combination of an antibody and a drug together, a form of using part of the immune system antibody and then making that a targeted treatment. Then you lead to this category called antibody drug conjugate. The idea here for example is if glioblastoma and you have this thing called EGFR which is epidermal growth factor the R stands for receptor. 30 to 40% of glioblastoma have an abundance of EGFR. We can take advantage of that. We can create an antibody that targets and will attach to the EGFR and attached to that anybody is a drug called MMAF. Trust me, it's easier than saying the full long name. Which then inhibits the cell from being able to divide and replicate. Whenever a cell cannot divide and replicate when it is supposed to, it leads to what's called Apoptosis or programmed cell death. You're using a feature of the cancer cells to create an antibody that is specific to that that can then deliver a targeted treatment that kills the tumor cells. The data on this is promising and this is in clinical trials for newly diagnosed glioblastoma. If we move on and think about viruses how can we use viruses to treat brain tumors like glioblastoma. What's nice about a virus at least in this setting is that a virus is like a parasite. There's no symbiotic relationship. A virus takes advantage of the cell of the hosts and uses it for its purposes to create more virus if you will. If you can modify a virus so it goes after cancer cells then you can essentially infect cancer cells and kill them, but you can also use that cell to create more virus and induce more of an immune response to eventually lead to the death of more cancer cells. And ideally you want to modify the virus so it targets cancer cells and does not affect normal cells. As I said a virus lives to replicate itself using other cells. There is no symbiotic relationship. We can modify the genetic material of the virus so that it uses cancer cells as a replication center. If we can modify viruses that can lead to insertion of new genetic information in the tumor cells. We can essentially change the message or the instructions of what that cell does on a genetic level. Then we asked the question “what would we want to tell that cell to do” and my favorite responses let's tell it to die and I think that's what we would like to see. Again this is another way of looking at this and thinking about this that if you take a virus and this is a common representation of a virus but the virus gets into a tumor cell and gets into the nucleus where the genetic material is. The DNA. It causes a response where you produce more virus and then what happens is that you can infect other neighboring glioma cells. There is a way of using the cancer cell in a positive way.

>> Here is another way of thinking about it and this is essentially thinking about gene therapy if you will. You can take for example an adenovirus and you neuter it essentially you take out parts of the normal DNA and insert something else into it. You don't want to be infectious and cause the bad things but you give it and you give it some other instructions the virus gets into the cancel cell does cancer cell and you insert the new material so then you can give that cancer cell new instructions. And instructions would be for the cell to undergo Apoptosis, cell death. You are telling the cancer cell is time to be done and time to undergo programmed cell death. Do not pass go or collect $200 and continue to make more cells and do bad things. There are a number of different viruses out there that can be used. I'm sure you've heard about many of them and they all have different properties. Some of them rather have a natural affinity for cancer cells. Some of them can survive longer like the measles virus and they are amenable to being modified like the adenovirus. There are an incredibly quickly growing number of studies with different viruses targets therapeutic effects. I did a quick look this morning to make sure I had the most up-to-date information. I went on clinical trials.gov to look for what are the open clinical trials for glioblastoma. There were 234 results. I would say close to a third of those trials are for some sort of immunotherapy. Five years ago that was a dream. Here we are in a day and age where we are seeing a vast number of our clinical trials are in this line of treatment which is incredibly exciting. If we get back to the idea of vaccines, the idea here is that we're not trying to prevent some disease. Like measles, mumps, rubella. We are trying to create a response in the immune system directing an attack on cancer cells. There are different types of vaccines. Some of these can be made from an individual's own tumor. Some can be made from parts of cancer cells that are common to that particular cancer type. If you look at glioblastoma you can take parts of those cells that are common to most glioblastoma. There are pros and cons to each approach. Let's talk about the dendritic cell vaccine. Again the dendritic cell is the general or part of the immune system that tells the T cells what to do. What would happen here is a patient with a glioblastoma would go through a free says. You would collect stem cells and cells from the blood and you would then identify these precursor cells and give them growth factors to get them turn into dendritic cells. And you expose the immature dendritic cell to properties or proteins of cancer cells. So as this dendritic cell is becoming mature and learning its role in the immune system as becomes mature it knows these are the things that we will tell the T cells to go after.

>> The idea here is that with the dendritic cell vaccine that you get a person's self and you induce them into dendritic cells. You then expose them to the things you want them to go after and then give them back to a patient. You can also create a vaccine from a person's own tumor. You create an breakdown glioblastoma cells and give them back to a patient in the form of a vaccine. There is also called heat shock protein vaccines which play a significant role in the immune response and they play a role in the way that helps to activate the dendritic cells and T cells. You can use a tumor from a patient that has been removed and create a heat shock protein vaccine that given back to the patient really helps to activate the immune response and target glioblastoma cells. There are multiple trials that are open or opening and looking at different vaccines. Whether it's a dendritic cell vaccine or otherwise.

>> What's next? This is all incredibly fascinating and very exciting. Again this is only the tip of the iceberg. As of 2015 we see there are approvals of medicines for the PD1, PDL one and the CTLA-4 the check point inhibitors. But we want to look at what we can do in terms of combination therapy. We also have this other thing called CAR-T that I will tell you about. Looking at vaccines.

>> As of course this is the picture my son wanted me to show talking about CAR-T cell therapy. I showed this slide before and down here is where we see the CAR-T and the CAR stands for [Indiscernible] antigen receptors what does that mean? It means that we are engineering B cells with specified receptors. So we can target tumor cells without needing a dendritic cell. We skip that part of it and go straight to engineering T cells that will go after the targets we want them to go after. Like many things CAR-T have undergone generations and evolution so again my son helped me pick these out but we think about the first-generation. The first kind of car you get to the second generation and we see updated newer cars vintage 1960s, 1970s. And then third-generation we get to something like this car which has more potential if we look at all of these things listed it tells us that these are the different ways that these T cells can bind cancer cells and create an immune response. Immunotherapy covers multiple types of therapy. The potential here is incredible. The basic idea of being able to unleash our immune system to be able to target cancer types. This is a much more personalized mode of therapy. Again using a person's immune system in a way that is beneficial. Ideally we want this to have less impact on the normal cells because we are targeting cancer cells specifically. We are seeing dramatic and long lasting responses from this treatment. Do we see problems? Yes. We see a higher incidence of things like rash and diarrhea. We may see more problems with liver as well as some endocrine function we normally don't see with some of our traditional treatments affecting the thyroid, pituitary and adrenal glands. Sometimes we see affects on the lung. Another thing that we have to keep in mind when we use this line of therapy is that responses can take a bit longer. We don't necessarily see them take affect as quickly as some of our more traditional lines of treatment. We have to be patient with these things. We don't want to abandon treatment too early. We want to make sure if we see there are some inflammation or swelling when we look at an MRI that we don't have a major knee-jerk reaction and say oh my gosh there is swelling because of tumor growth. It can be because of inflammation from the immune response. We have to write that out a little bit. And make sure that we are not abandoning treatment too early. I would like to shift to talking about devices. That boils down to a couple of things.

>>Mostly looking at what's called Optune or what is called Novo TTF the idea of using treatment fields. The idea here is that the cancer cell as it is wanting to do it wants to divide and replicate and wants to make more copies of itself. As a cancer cell goes through that process, the DNA separates and you start to get to a phase where you start to see the genetic material is starting to progress towards both sides of the two cells that are to be. If you expose this to an electrical field, what you get is a positive charge on one end and a negative charge on another. What happens with that? Opposites attract. The two has cannot separate. As we have seen before, when a cell is supposed to divide and replicate and it cannot it dies. That process again is called Apoptosis. I left this slide in. I am sure many people will appreciate this. This was the version of NovoTTF that was later called Optune that we have come to know and love but just as of a few weeks ago we learned about the FDA approval of the newest version which I think everyone agrees is an improvement. It is smaller. It is later it is easier to use. I've seen this in person with patients and it is a significant improvement. All of this. We could say it looks great. It's later it's easier to use but all of that doesn't really matter unless it is effective. This is the data that came from the study that led to its approval in use for newly diagnosed glioblastoma. We had previously used NovoTTF for recurrent glioblastoma that the clinical trial that was done looking at using Optune in the upfront setting.

When patients are first diagnosed with glioblastoma. We see using the tumor treatment fields plus temozolomide after someone has done radiation and today the standard of cars to do six years of combined radiation and temozolomide. We take a four-week break and resume treatment patient would not be using the tumor treatment fields during radiation because we couldn't have that on the scalp during radiation treatment. This started when we restart the temozolomide, those 28 day cycles. Days one through five, the days out of the 28 day cycle. We see there's a benefit versus just starting [Indiscernible] backed by itself. This graph shows progression free survival. How long does it take before glioblastoma comes back? We see there's a significant separation here that you are talking about at least three months and we look at the tail here and we see that no matter what time point you see there is a significant difference between the number of patients that are that have gone without progression and without the tumor coming back compared to using temozolomide by itself. We over - - we look at here at overall survivor not just how long it took to come back but overall survival. We see there's a significant difference between the two. We are seeing that on average if we look at 50% on average we are getting out beyond 18-20 months for overall survival. Is that good enough? No. It's not. It is certainly progress. When I started doing this over 10 years ago, we would frequently say the average life expectancy was close to 12 or 14 months. We are moving in on doubling not. There is progress here. Are we where we want to be, no. This is significant progress. Based on this data the clinical trial ended early. Last fall and October FDA approved the use of the Optune device for the initial treatment of glioblastoma.

>> We previously saw efficacy in recurrent wheel blast Oma and when it came back. But then now we have an indication for using it with newly diagnosed glioblastoma. I believe that there was recently an update on what are called the NCC and guidelines. They are national guidelines physicians use as - - essentially to say what is the standard of care and what are the things that we has physicians should do in the treatment of our patients. And so the use of Optune has a more prominent place in those guidelines. What is nice about this is that you are not taking a pill. You are not taking a shot. It's not IV. You don't have typical chemotherapy side effects. The thing we have to worry about is doesn't irritate the skin? Which is why typically we want to switch out the treatment arrays every 3-40 is to make sure we don't have that skin irritation. To also make sure that hair is cut short enough that the treatment array can adhere to the scalp. Appearance is an issue for some patients. I have told the story many times. I think when I first saw initial data for tumor treatment fields at conferences going back eight or nine years, I also thought that looks really hokey. Here we are we have clear data and the data are strong and you can ignore those things. In my mind if we don't offer this treatment than we are doing a disservice. We are withholding something that patients can benefit from. If appearance is an issue then appearance is an issue. I am not going to force anyone to use it but I am going to encourage people to use it. Another nice thing about Optune is regardless of someone's MGMT status it works. We talk about MGMT status because we know that if someone has what is called MGMT promoter revelation that they are more likely to respond to temozolomide which is the most common chemotherapy we use. If someone does not have that methylation and I'm sure many of you have heard that term. Methylation of the MGMT. Without the methylation there is a decreased chance that someone would respond to temozolomide. Optune works regardless of that. We see more and more this is incorporated into daily practices. Let me transition to advances in surgery.

>> As it stands, we think about surgery and how to proceed. Based on what is the size of the tumor and the location. Can we only do a biopsy or take out a certain portion. We always want to take out as much as possible because it has a bearing on the prognosis and treatment. We also know surgery is not a cure. Tumor is left behind. There are many analogies used here. These tumors have fingers or tentacles or it's like looking for grains of sand on a beach. You can't see all of them. At the end of the day what we talk about with surgery is we want to get a maximum safe reception. We want to get out as much as possible without causing harm. If one of our patients comes out of surgery with more neurological problems than going in. We have done that person no favors. The extent of resection or the amount of tumor that comes out matters. The threshold we commonly use is 70%. If we can get 70% out then that is to a person's benefit.

>> This is the problem we face. We see an MRI and we see this abnormality that looks like a glioblastoma. We see this is after someone gets contrasted it lights up. We look over here and we see all of the swelling and edema. We don't know where the tumor ends and where normal brain begins. Out in all of this swelling there are going to be some glioblastoma cells. How can we do a better job of identifying the tumor cells? As it turns out, there's a chemical called 5 ALA. It's called five MNU Nola Levick acid. It's that part of red blood cells that carries oxygen. So it turns out that there are certain parts of the body that where you can identify five ALA the liver kidney skin but also malignant brain tumors will take this up. What you can do is you can take this precursor this amino acid usually three hours before anesthesia. Because the body cannot metabolize all of that it accumulates in certain parts of the body like malignant brain tumors. You can identify this by fluorescence. This is what it looks like. We look at this picture during surgery. You can see some areas that clearly look abnormal and clearly look like a tumor. Again we don't know where the tumor ends and where normal tissue begins. We don't see there is some sort of order were fine line that surrounds this to tell us where the border is. If someone takes 5-ALA and you use fluorescence you can get a better sense of where is the tumor and where is there not tumor. You can even see here that the edges become mixed. This is more vague. You can get a better idea of where to try to take the tumor out.

>> What is the benefit of this? You can potentially improve survival in prognosis by taking out tumor that it's not obvious on MRI. There is less tumor fries to treat with radiation and chemotherapy. You can potentially reduce neurologic impairment from tumor invasion. What is the downside? By taking too much tissue, by being too aggressive and causing neurologic arm. You can have accumulation in liver, kidneys, the skin can be sensitive to light. Not every patient will be a candidate for using this. Some tumors are too deep in the brain and are only a minimal to doing a biopsy. In a larger resection or surgery will not be possible. When a patient has a tumor where more aggressive surgery is an option, this could help maximize removal. 5-ALA has been available in Europe for a while. We are hoping to have it here in United States sometime soon. I don't know when but I know that it is coming. There is also a way of doing minimally invasive surgery. Using what's called laser a glacier. The idea is that you are heeding the tumor from within to spare the surrounding brain tissue. Because it's less invasive you can potentially access some deeper tumors or tumors that would not be amenable to an open resection.

>>The idea here is you insert the catheter into the tumor and then you heat it up in a uniform way. There is some potential damage to surrounding teacher - - tissue. It can lead to inflammation due to necrotic tissue. Some patients have had such inflammation and edema they have required surgery as a result. The potential here is pretty broad spread. Or widespread and very broad. It can be used for primary tumors such as gliomas and tumors that are on the surface of the brain but also thinking about brain metastases. There are some trials of a limited. There is widespread use but there is another interesting tool in our toolbox that can be used. The last thing I want to talk about is the idea of radiation and what is new. We are thinking about different types of radiation and what we may be exposed to from working on our computers and we think about cell phones and microwaves and we start getting into what's called ionizing radiation or radiation that can actually do damage to cells. And what is nonionizing. You start getting into ultraviolet's because we can get sunburn and skin damage from the x-rays and gamma rays. Our current use of radiation in treating cancers is in the spectrum of x-rays and also gamma rays. Targets can be large or small treatments can be done in a number of different ways. Over days and weeks. Sometimes we hear different terms external beam radiation, IMRT, gamma knife, cybernetic. At the end of the day the overriding goal of this is to cause maximum damage to the tumor but minimal damage to the surrounding normal brain tissue. Where do protons fit in this? What is the big deal about protons? This is another form of ionizing radiation. Which has the potential to deliver a peek dose of radiation with less harm to the surrounding tissue. Let me show you what I mean. If we use with photons or x-rays, then as the dose of the radiation ramps up, you then are essentially treating tissues that are before the tissue. The tumor. You are ramping up the dose and there is exposure to the skin in shallower tissues before you get to the tumor in the brain. Then you also have the tissue beyond the brain that could be exposed. The idea here is if you use protons that the ramp up is different. That you get to your dose and the treatment area and a much more precise fashion, and then afterwards the falloff is much deeper. Theoretically the idea is you minimize the amount of tissue that is exposed and treated before the tumor and after the tumor. The surrounding normal brain tissue. So we say maximum affect less harm what is not to like?

>>To give you an idea of what these things look like. This is a proton beam generator. It is huge. It takes a lot of space and land to do this. This is what looks to treating physicians and patients. This is the debate. Theoretically potentially on paper it looks good. So far hasn't been any real clear-cut data to show it is any better. There was a large trial looking at prostate cancer comparing them. These are large expensive. They are expensive to build you need a lot of land and capital. Treatment with protons can be expensive sometimes it can be double that of photons that are currently available. You have a combination of high expense and not much data show that it is better which creates controversy. There is a clinical trial that is looking at treatment for newly diagnosed glioblastoma looking at the idea of protons versus photons. And in the brain we want to be very careful and minimize the surrounding normal brain tumor or brain tissue is much as possible. This is a very important question that we can answer it comes to glioblastoma. Theoretically if it works you would think more centers will adopt it. Eventually technology improves just like anything else spear technology improves and cost will get better. We have to factor in the cost of side effects and complications. The current treatments create more harm to the surrounding brain tissue then what is the cost of that?

>> In summary, this has been a whirlwind tour of immunotherapy talking about the potential of immunotherapy in the examples of different types and what is currently out there and coming down the road. An update on tumor treatment fields and the Optune device showing you the new version which is a definite upgrade looking at the data and why this is used. Looking at the things that are coming down the road to make surgery more effective. Radiation other devices such as using what's called LA TT the laser interstitial treatment heeding the tumor from inside. ABTA offers a service called TrialConnect which helps to connect brain tumor patients to appropriate clinical trials based on the tumor type and treatment which is fabulous. I was on a panel discussion recently talking about how difficult it can be to sort through even the trials on clinical trials.gov and how to navigate through that. But how do you know what is a good clinical trial and what you are eligible for. This is a valuable service. Thanks to everyone for your involvement for your attention and thanks to ABTA for all the good work that they do and the opportunity to talk about all of these exciting things that are happening.

>> Thank you and I would be happy to take any questions at this time.

>> Thank you, Dr. Peterson. Dr. Peterson will now take questions. If you have a question you would like to ask, please type and submitted using the question box in the webinar control panel on the right-hand side of your screen. Again we will go and take questions.

>>We do have a question submitted. His immunotherapy used in combination with standard of care treatment? Or in place of it?

>>Actually, both. Mostly it is used in combination with. Really at the end of the day that is the question you want to answer. If we add something to standard of care is it better than our current standard of care. If we look at for example if we look at patients with newly diagnosed glioblastoma who do not have that MGMT methylation and so that is the group of patients where we have where we think is temozolomide going to help them as much as if that promoter was methylated. There are now some clinical trials where we start to look at should we use something else in place of temozolomide in that patient group. We are starting to see that approach as well.

>> Thank you. Another question is I know you mentioned a few of the promising immunotherapies that were approved. Do you know when some of the other ones are going to be coming closer to FDA approval status and if so which ones?

>> You have a couple of the PD1/PDL one medicines that are being used in a number of cancer types. We first saw these gaining FDA approval that we now see these medicines are proving to be beneficial in types of lung cancer. I believe we will start seeing approval for these medicines. Renal cell cancer potentially breast cancer. The top of my head I am not sure which ones are necessarily close to gaining FDA approval for all of these different indications. The clinical trials for Leo blast Oma - - glioblastoma are just beginning with a lot of these therapies. We know that some of the vaccines have been in advanced stage phase 3 studies.

Some of them have not shown to be as effective as we had thought or hoped. There are a number of treatments that are also currently in phase 3 studies that are fast tracked so for example, there is a dendritic cell vaccine that is used for newly diagnosed glioblastoma that if it shows promise early enough in the clinical trial that you would actually stop the trial and they would go immediately for FDA approval. You would not even finish the clinical trial if the interim analysis is positive enough. There are a number of immunotherapies that are in phase 3 trials that show promise and could end up going to FDA approval. Within even the next couple of years.

>> Thanks Dr. Peterson. We have another question do you recommend the use of Optune if the patient cannot wear it for the recommended time frame of 75%?

>> Generally not - that's the threshold. 75% of the time is what's felt to be the minimum effective time. I know in a number of patients including my patients as they will bank time so they will try to use it more than 75% of the time and if they are going on a trip or they have an event they won't wear it for as long on a particular day. To go below the 75% is really below the level of where it has been shown to be effective. If I have a patient who for one reason or the other is not able to have the device turned on and powered on and working at for at least 75% of the time then we usually talk about stopping it.

>> Another follow-up question regarding Optune. There is someone who wanted clarification. They were told how long would they be able to use Optune would be first 6-9 months or would you recommend it for the rest of their life?

>> I would break it down into two scenarios. Number one the setting where someone is newly diagnosed. The clinical trial that was done that led to its approval the way it was set up was that patients would use Optune for 18 months or until the second progression. And what does that mean? It means that first progression the tumor would show its growing and it is coming back and it's growing. We already know that Optune is approved for that setting. You would consider continuing the Optune and if possible consider clinical trial or adding another treatment. If you see then it starts to grow again second recurrence than you would stop the Optune. At that point you would be saying and you would be saying that it would make sense to continue. 18 months until second progression. In a setting where someone uses it for recurrent glioblastoma let's say they have never used it for the initial treatment. Then we continue it until we see it's not working. Remember whatever that timeframe is it is indefinite.

>> Thank you very much. We do have another question. Are there therapies being targeted for tumors with tumors that have the ID H1 mutation?

>> Yes. The answer is yes.

>> Thank you. Good. There's a vaccine used that Duke is studying on patients with GBM. Do you have any information on that you could share with the attendees?

>> I would assume because there are so many different vaccines but I would assume that they are talking about the polio vaccine because that has been in the news. It's been on 60 minutes. Obviously very promising. I believe it is the data that has been shown on that were from a phase 1 study. So a dose finding and safety study. The phase 2 study I believe will be opening soon. It is very promising. As with a lot of other immunotherapies. You have seen some very dramatic responses. But not everyone has responded. I think if we take a step back and look at all of these immunotherapies, that we still have to look at trying to identify the differences in glioblastoma from person-to-person and trying to figure out which of these elegant highly targeted, very advanced treatments will work for each person. We know not all glioblastoma's are the same. They vary from person-to-person. The polio vaccine is one of many of these immunotherapies out there that shows promise. It is not going to be for every person because they have to have surgery. Depending on where the tumor is in the brain some patients may or may not be eligible for the treatment.

>> Thank you, Dr. Peterson. We have time for one more question. For any inoperable GDM's are there any other alternative forms of treatment?

>> That is definitely a group of patients that we want to pay special attention to. In that situation we want to try to do at least a biopsy and get at least a good portion of tissue to be able to look at all of the different molecular studies and look at MGMT and ID H and other things coming down the road. To be able to know if someone is going to be eligible for one treatment or another one clinical trial or another. I would say that whether someone has a tumor that can only be biopsy or can have a larger reception that I think as we move forward it will be less and less about how much was taken out and it will be more and more about what are the features of that particular glioblastoma. I know personally I have had patients who only had a biopsy and had a lot of tumor and I would have thought that the person may not do very well just at the onset but have done phenomenally and had a fabulous response to treatment. And then you see the opposite of that also. I think it gets down to not - - how much of the tumor was taken away or taken out but what is the exact nature on a molecular DNA level of each tumor and try to pick the best possible treatment for each person. I think that's where the future is and that's where it is all moving not just with glioblastoma but all of oncology is looking at all of these different factors and looking at what do all of these mutations mean and how do we take advantage of them. What do we know about what these tumors do on a molecular level? It is highly varied and the size of the tumor and how much is taken out is something that we still pay attention to what I think as we move forward that will become less and less important.

>> Thank you again, Dr. Peterson. That is all the time we have for today. Thank you everyone for joining us and thank you again, Dr. Peterson, for your wonderful presentation, and taking time out to answer all of these questions. Another ABTA program is available to connect patients and caregivers with resources to support them in the brain tumor journey is the ABTA CareLine. You can call 1-800 -886-2282 let's pause for a moment to conclude the recording. We invite you all to continue to check back at our website www.abta.org for the Anytime Learning page, a library of free on-demand webinars that feature experts from around the country addressing a wide range of brain tumor topics from treatment options and tumor types to quality of life and system management.

>>Also please join us for Partners in Treatment and Care meeting, the ABTA one day program. Patients families and caregivers are invited to participate free of charge to gather the most up-to-date information from leading experts and network with each other. The next Partners in Treatment and Care Meeting will be held on Saturday, October 15 at the Galt House Hotel in Louisville, Kentucky. If you would like more information or to register please email info@ABTA.org. This concludes our webinar.

>>Thank you again for joining us and be sure to complete the evaluation survey you received by email tomorrow. You may now disconnect. [Event Concluded]