American Brain Tumor Association Webinar

Beyond the Standard of Care: The Role of Clinical Trials

>>Welcome to the American Brain Tumor Association's Free Educational Webinar Series. Thank you for participating in today's webinar. Today's Webinar is on Beyond the Standard of Care: The Role of Clinical Trials. The webinar will be presented by Ryan Merrell, MD and Julian Bailes, MD. Please note that all lines during our webinar today are muted. If you have a question you would like to ask, type and submit it using the "Question" box in the control panel on the right-hand side of your screen. Dr. Merrell and Dr. Bailes will answer questions at the end of their presentation. In the next few days, you will receive an email asking you to take a brief survey to evaluate the webinar. Please take a few minutes to share your feedback, which is important to us as we plan for future webinars. Today's webinar is being recorded- the recording will post to the ABTA's website on the Anytime Learning page shortly. Registered participants will receive the webinar recording link in a follow-up email message once it is available. My name is Antoinette Tiu, Program Manager here at the American Brain Tumor Association. I'm delighted to introduce our speakers today, Dr. Ryan Merrell and Dr. Julian Bailes. Doctor Merrell is an attending Neurologist and medical direct of Neuro-Oncology at NorthShore University Health System in Evanston, Illinois. He is a Clinical Assistant Professor at the University of Chicago. He received his medical degree from the University of Alabama, School of Medicine in Birmingham, Alabama and completed his residency in Neurology at Mayo Clinic, Rochester. He then completed a Fellowship in Neuro-Oncology at Massachusetts General Hospital Cancer Center/Dana-Farber Cancer Institute. His primary interests are treatments of primary brain tumors and meningioma. Dr. Julian Bailes is a nationally-recognized Chicago neurosurgeon, with special emphasis on brain tumors and the impact of brain injury on brain function. Dr. Bailes and the NorthShore Neurological Institute team are among the first in the country to use emerging technology to treat brain tumors, including Visualase MRI Laser-Guided Therapy and NICO BrainPath. NorthShore Neurological Institute has become the first in the state and only a handful in the country to utilize Synaptive Servo, a robotic technology that improves access, precision and visualization.

>>Good afternoon this is Dr. Ryan Merrell and I would like to thank the ABTA for inviting us. It's an honor to be here today. These are just some disclosures. I have had some consulting work with the Abbvie Company. Other than that I have no disclosures. So just an overview of what I will be talking about today. I will be talking about what is a clinical trial and what are the phases and different types of clinical trials and why or why not would you want to do a clinical trial and where and how do you find a clinical trial that is right for you and how do you qualify so with the eligibility, different types of clinical trials and then as a bridge to what Dr. Julian Bailes will be speaking about what is the connection between clinical trials and different types of novel brain tumor surgery.

>>So some of the key terms I will be using, a clinical trial is a study designed to test a new treatment that has been previously shown to have benefit in brain tumor models. Now this could be a model such as a mouse model or it could be an early phase of the trial that was tested first in humans but something that has scientific merit and safety in order to be tested in a brain tumor patient. The phases of the clinical trial these range from 1-3. Basically 1 being the earliest phase and 3 being the final phase needed to achieve FDA approval for a drug or treatment.

Inclusion and exclusion criteria are the parameters needed to enroll in a trial, a checklist of what you need and what you can't have in order to do a clinical trial. When we use the term placebo this is misleading because I think most patients think of like a sugar pill, but that is not the case because it would not be ethical to give a patient a sugar pill or sham treatment so usually a placebo is going to actually be a drug that you have received if you are randomized for that arm of the trial.

>>So what are clinical trials? Our goal as neuro-oncologists is to find better treatments for tumors and we have to find these for all different kinds of brain tumors and spine tumors and one of the questions we often ask is am I going to be a guinea pig. I think when people think of clinical trials they think of a study where we might just be trying to test out a treatment and see how a patient would react to that, but that is not the case. Because all of these trials are very well thought out and years go into the design of these trials and we're really trying to find as quickly and safely as possible better treatments for these tumors. If you participate in these trials, the vast majority are going to be emphasizing a treatment that will add benefit to the standard treatment that you would be receiving. It's important to know that all research is conducted under strict safety guidelines so in the United States we have very strict criteria for the safety testing of these treatments and all of us are subject to institutional review boards which really are designed to make sure that we provide safe treatments and we are completely abiding by the rules that we need to follow. These trials are conducted with multiple sites so we call that consortia. We have anywhere from 20 to 50 different institutions in the United States and often times even in Europe participating in the same trials. And all the current standard treatment originally had to be tested in the context of the clinical trial for the drug Temozolomide which is widely used in treating brain tumors it originally had a go through the same testing that we are talking about for these clinical trials. So trials can be in different stages. The example I will use often in this talk is glioblastoma. It's one of the more common tumors that we conduct clinical trials for. If you have a glioblastoma you may be new in your diagnosis and that would be a time when you could have the possibility of doing a clinical trial or if the tumor goes back at some stage then you could be a candidate and trials are designed for these different stages of treatment. So what exactly are the three stages of clinical trials? Phase 1 is a dose finding study and it’s testing the safety of a drug. It's very different than phase 2 and phase 3. Many times, a drug that is new and has a lot of promise, it's important to know what are the side effects that will be experienced that may not have been elucidated through a mouse model and you know so in that sense phase 1 study is a good study to participate in because it is a promising drug and often times it is more than just finding the right dosage. It may be that that drug is really impactful and it may have a great benefit from participating in a phase 1 study. The other thing is they have looser criteria, so the eligibility is easier to enroll in a Phase 1 study. Phase 2 is basically you have the dose established and you are testing it out. Often these are randomized within the placebo arm and phase 3 is really the final stage where a drug is passed enough benefit in the phase 2 to go into phase 3 and then hopefully would show enough benefit to be FDA approved so we have randomized placebo trials and we have open label trials and this means that all of the patients will get the study drug no matter what. There is no mystery as to whether you may be on the placebo arm. When we talk about double-blind, which is another term you may see in all that means is the investigators, the doctors, and the patients don't know whether or not the patient is receiving the study drug or the placebo arm.

>>So glioblastoma newly diagnosed trials are adding on treatments to the standard treatment. This is a question we often get. We are going to give radiation and Temozolomide no matter what and then we are going to add on potentially another drug to that treatment. As I said, there is no such thing as a placebo. There is no sugar pill in our trial. One question we often are asked is, are these covered by insurance? Whoever sponsors the study, whether it be a consortia of multiple institutions, like the National Cancer Institute or a pharmaceutical company,

much of that cost will be covered through that mechanism. All the standard of care things like MRI scans and doctor visits will be covered by insurance. There always is a possibility that there could be an out-of-pocket expense and that's something we have to inform our patients about. For the most part these are covered by insurance.

>>So what are the pros and cons of doing a clinical trial? Well obviously, if you have a treatment that adds benefit to the standard treatment, that is a big deal and that is what we are all looking for in this field is better treatment. You will receive more care so there will be more visits than the standard care you would normally get. And you can think of it as altruistic in the sense that you are contributing to science and you are participating with a number of other patient and adding knowledge to the field. Now, the more care can also be a con because you will also be required to come to the doctor more often and if you don't live close to the doctor, you may be required to travel more. This is especially true for out-of-state travel which we will talk about later. What about side effects? All these have potential side effects and some of them can be unpleasant. And then the unpredictability. So even if we have a sense of what are the common side effects for the treatment there will always be something unpredictable and potentially life-threatening that can occur as a result. Where you find clinical trials? Talking with your neuro-oncologists or medical oncologists, it's important because that person can guide you in terms of knowledge of what's available in your city and region so I think that is the best starting point. The ABTA has a great tool called ABTA TrialConnect which I will display for you in an upcoming slide which helps you to search clinical trials. ClinicalTrials.gov is a long-standing website that has a pretty good search engine. I recommend that site but I will show you there is some difficulty navigating that. Whether to stay in town or travel out-of-state is a common question I get. You know, I think for the most part I recommend that you stay close to your home because for many patients, there are institutions nearby where you can have access to good clinical trials without having to travel out-of-state. And the thing about it is if you were to do a clinical trial in your hometown, or do a clinical trial 500 miles away, no one can really say that their trial is better than another person. So that is one of the things we often discuss with patients but it's a situation where there is a clinical trial that one of my patients really wants to do 500 miles away, I will do everything I can to support them in being connected to that trial. Here is an example of the ABTA TrialConnect website. You type in some search terms and there is a list which I wasn't able to display and what I did is I typed in glioblastoma and a number of other terms like newly diagnosed, and then it gives me this nice menu to look at of all the different trials that are available and I can search by location and I can put another types of criteria. This is a nice tool. In contrast to the other website which is a good website this is a little bit cumbersome because as you can see I put in the term glioblastoma and I have 1147 studies. Who could possibly navigate all of these? If you do some refining, I put in glioblastoma vaccine I get down to 74. So you can refine your searches. I think these are two good site. There are other sites out there and I think this is a helpful tool for patients.

>>So what does it mean by eligibility criteria? These are some of the main things that trials will look at. Age: unfortunately some of the trials will cut off by age so many say you have to be younger than 70 and sometimes 75 so that can be an important thing to look at. Performance status: what is your level of fitness? So how neurologically well are you? If you have the inability to walk for example that is a significant impairment that may disqualify you from doing certain types of clinical trials. The number of previous treatments: when you're looking at a recurrent trial for glioblastoma for example many say you can only have two prior treatments to enroll. So that is important to look at. Surgery: becoming increasingly important especially in some of the immunotherapy trials. If you have a recurrent glioblastoma for example, some of these trials will say that you have to have an 80% or more ability to remove the tumor at that time and so for some patients that is impractical because they may have a tumor that isn't able to be operated on to that extent. Molecular markers: these are increasingly important and these are things you

can test for in the tumor and some of these tests are required in order to enroll in certain types of clinical trials and I will tell you about that an upcoming slide.

>>So no one knows what the best trial is. That is important. The location of the trial can really influenced your decision on which one to do whether it is in your own town or far away. Some patients really don't like the idea of being randomized to a placebo so that is an important consideration so looking for open label as I mentioned earlier. The side effects of the treatment. Let's say it comes down between a decision of two or three trials on your looking at these and don't know and no one knows which one is better, maybe one of the trials has an unpleasant side effect that you don't want to have the possibility of experiencing. That certainly can influence your decision about which trial to choose. And then the schedule of the trial. How often are the visits? Are they every two weeks or every month or every other month? That is important consideration for traveling. And then whether or not to do surgery. Some patients can be very wary of undergoing a second surgery or undergoing a surgery that could possibly give them a deficit. That is an important thing to think about. As two different types of broad categories of clinical trials I would like to talk about our targeted therapies and immunotherapies. In no way does this represent the entire field but these are two kind of big categories and certainly the latest and greatest of what is going on right now.

>>So what our targeted therapies? This is a cartoon that represents growth pathways in a brain tumor. Let's just say it's glioblastoma. These are pathways on the surface of the tumor cell that need to be activated in order to drive growth of the tumor. Much of the research over the past 10 or 20 years has focused on how do you interrupt these pathways in order to slow the growth or stop the growth of the tumor. Many trials have been done over the past 10 to 15 years looking at all of these different mechanisms of slowing growth. A couple of them that I mentioned here are for example vascular endothelial growth factor, and these are some of the angiogenesis inhibitors such as Avastin. Epidermal growth factor receptor continues to be an important pathway because this pathway depicted on the slide is a pathway that is often overexpressed in glioblastoma and so there has been great effort to try to target it. What about immunotherapies? It's very different in terms of what we're doing here. We are trying to engineer the immune system to attack the tumor. We have known for a long time that in brain tumors much like other tumors in the body there is a derangement of the immune system. That is one of the ways these tumors grow is that our own immune system is not able to fight them off. Many of these are delivered through a vaccine which is somewhat of a misleading term because I think when we think of vaccines we think of getting a shot for shingles. You know, the whole idea here is that you are trying to trigger the immune system to attack the tumor. And there are many different ways of approaching this. So this is a cartoon that demonstrates how the immune system becomes deranged. Normally we have a population of lymphocytes which are serving for foreign invaders including tumor cells. And the smart tumor will actually send signals out that will down regulate this process and put it into this T-regulator mode. And there are many recent breakthroughs that have looked at how you turn off the signals so you can turn back on the normal lymphocyte response. So what are some very broad categories of these different types of immunotherapies? We have peptide based vaccines (rindopepimut), dendritic cell vaccines (ICT-107), tumor lysate vaccine (DC Vax) were you actually take the tumor and you expose the broken down tumor. CAR T-cell another interesting pathway where you engineer lymphocytes to respond to molecules on the surface of the tumor. Viral vectors (polio, measles) and then viral gene therapies (Toca, adenovirus) which I will talk about in an upcoming slide. So there are different types of clinical trials and there are different categories of tumors. In high-grade glioma, there are several types of ongoing trials. So we have dendritic cell vaccines like ICT-107 and we have checkmate inhibitors like nivolumab and we have heat shock protein inhibitors. We have other types of checkpoint inhibitors that target this PD1/PDL-1 pathway which you may have heard of and we have ABT-414 which is an EGR targeted and Toca 5 is a viral gene engineered

therapy. And then in other types of tumors like low-grade glioma there has been emphasis on clinical trials for these. The most representative is one called AG120 which I will talk to you about an upcoming slide and then a recent trial using an mTOR inhibitor, Everolimus, which is a way of targeting one of those pathways that I showed you earlier. What about meningioma that is traditionally had the least amount of clinical trials but there are some that can be very aggressive? There is no defined tumor therapy for meningioma. There is a clinical trial currently for an alliance consortium that's targeting the smoothened/AKT Inhibitors pathway that is open through that consortium.

>>So just to give an example of a few clinical trials ABT-414 is a targeted therapy that interacts with the EGFR receptor and it actually introduces a toxin after this antibody bonds to the binds to this receptor. This is a cartoon which shows you how this works so this antibody binds and releases a toxin and then ultimately that interacts with the DNA of the tumor to lead the death of the tumor cell. The Toca 511 and Toca FC are part of the Toca 5 trial in recurrent high-grade glioma including oligodendroglioma and astrocytoma. This is an interesting treatment that actually delivers a retro-virus which will cleave a drug given orally into a potent anticancer drug like 5-FU. This is been around for a long time. The whole idea here is that if you give 5-FU intravenously it won't get into the brain and this is a way of circumventing the blood brain barrier by giving a prodrug which is called the Toca FC which will become eventually become 5-FU by this gene that is delivered at the time of surgery. This is an example of the trial that requires surgery in order to participate because the viral vector is actually introduced at the time of the surgery. The AG120 trial which I mentioned earlier this is for tumors that have mutation of IDH1 and it seeing much more so in a lower grade glioma. We know this is a deranged metabolic pathway so if you have a mutation ordinarily with the Krebs cycle which some of you may know about from biochemistry this leads to a downstream product called 2HG which normally is not produced by the Krebs cycle. This drug actually interferes with this mutation and ultimately that will decrease growth of the tumor cells. So it's very interesting thing that we have learned as a result of uncovering this IDH1 mutation which is the most recent molecular mutation that has become known.

>>So now I would like to introduce Dr. Julian Bailes, who will talk more about novel neurosurgical techniques and this is important nowadays because of the link between surgery and clinical trials and we work together closely here at Northshore University Health System. He is a wonderful colleague and I am happy to have him with me here today.

>>Thank you Dr. Ryan Merrell. I will tell you a little bit about what we do from the surgery perspective for brain tumors ordinarily. Neuro-oncology treatment on the trials you heard about go hand-in-hand with the first step in most people's treatment which is to take the tumor out analyze it in the lab and find out what tissue type it is in great it is and how we approach it to standard treatments or emerging drug treatments as you have heard a lot about today. I have no disclosures or anything else to report related to this presentation. So the concept of minimally invasive brain surgery is really taken off in the last two years and you will see a lot of it has to do with the new instruments we haven't technologies that we bring to bear at the point of disease of the tumor. And also, a big part of surgery has always been and remains today maximum removal of the tumor because that is consistently been shown to be one of the best prognostic factors you can have so certainly we want to be safe enough in the process by removing more tumor allows a better diagnostic accuracy and sampling all the tissue that you can find for the neuropathologist to look at and it is needed now for molecular studies, really looking at some of the more genetic traits, which gives us insight to tumor treatment. Maximal surgical treatment is a requirement for entry into many clinical trials. For example, some trials with new and emerging treatments require 80% to 90% removal of the tumors for maximum debulking or reduction of the amount of cells that are there. New and emerging novel neurosurgical techniques allow for maximum surgical removal and often with less harm to the

patient because they are focused. I will mention later that laser, inserting a laser fiber to a plate will destroy the tumor and it's a new technology that we have here at North Shore University Health System and we are very excited about the potential for that. Now this is not me operating. This is our forefathers in neurosurgery.

>>They were doing the best we could with the tools of that time however they worked through larger openings and that big problem was getting light into a surgical incision or an opening and through the skull into the brain and not only light, but magnification. So there have been a lot of advances, just in our lifetime that has transitioned us from what you see in the bottom right picture to what we have today. This is sort of how the operating room now looks. It's full of technology and replete with high-tech capabilities and bringing many new instrumentation and techniques to bear at the point of the surgery.

>>You know it is said by neuroscientists that our brain contains over 100 billion neurons or nerve cells, probably five times that many supporting cells astrocytes and if you take all the connecting fibers and you see the major pathways here that we have to avoid and navigate around, that if you put all of these connecting fibers together it would equal 100,000 miles. It wouldn't go from the East Coast to the US in the West Coast it would be about 30 times that distance. That is a lot packed in and this is the most complicated structure on the face of the earth and one that we are privileged to try to help patients as they deal with the different legions or problems within the brain but these are the areas that we have to be aware of. These are the major fiber pathways that are taking motor, sensory, visual, speech, hearing, and other key components of brain function so this is a big part of what we think about and do. Here is an example of a malignant brain tumor and one that comes to the surface. You can see in this case it is sort of the bottom right be a regular white enhancing lesion there. It has challenges in terms of its geometry, irregular shape, and blood supply.

>>Here is another one it's a major fiber bundle between the two halves of the brain. It's deep and also very irregular and very vascular. These are some of the challenging lesions that we take on. One of the new technologies that I have been very enthusiastic about and have had a lot of experience with is the Nico six pillars approach and what this does is it shows you new ways that we look at taking out tumors based on this technology. It involves fiber tracking and knowing where those tracks are and it involves navigation, which is like a GPS system so we have cameras on the ceiling in the operating room and we know where we are as we coursed through the brain and special optics like magnification and light and you see in the bottom left this is a dime sized port or tube that in her blue part is removed and it is placed in a navigated manner of avoiding major areas of concern and placing it into the tumor. The middle bottom picture is the new instruments that we have to resect or remove tumors now. As you can see here, this is called a myriad. It’s one of the many devices that we have to take out tumors. I am often asked by patients, how are you going to get that out? And of course in the bottom right we have great hope and there is promise for after removing the tissue to really analyze it and one day hopefully we will be able to do more with the analysis of what we removed. This is the six pillars.

>>Here is a picture of me operating and you can see on the top left, there is this fiber tracking and the green fibers that control motor control on the left side. You see the white tumor and you see how those fiber tracks are thin and displaced laterally. So our approach here would be between the two halves of the brain, right in here. And that would be a safe approach knowing that the fibers are displaced to the outside. Here is how we operate. You see the optics and the magnification and here is an intraoperative ultrasound as we go through and here's the lesion on the brain and here is how we look on our monitor sort of in our surgical cockpit.

>>This is an artist drawing showing that port that to that we can place in there. We place it in the natural holes of the brain. And then we don't have to remove part of the brain and we can go through the natural folds and get the deep lesions inside. The brain is the last organ in the

human body to be conquered and we are working on the inside aspect of it. On the right you see sort of the surgeon's view, the white matter of the brain here and this is the whole where that bad tumor was resected and we save all that tissue for further analysis and diagnosis. Here is another example here showing how we look at a tumor and how we also can analyze the different fiber tracks around it. That diagram I showed you with all the important fiber tracks, this is how we overlaid this to help us do surgery deep in the brain safely.

>>Another example here, this is showing not only the tumor but the motor pathways in the century pathways and here is the speech pathways with the tumor. This is called the arcuate fasciculus and here is the motor fibers coming down that helps us with something called functional MRI where we can analyze different parts and functions of the brain are an overlay that all in our surgical planning.

>>Here is an example of a meningioma and here is one deep in the brain inside the cavity, the ventricle. And the tube was placed in here and you can see postoperatively after the tumor has been removed.

>>So we have published our first 20 cases that we have done using this technique and you see we have a small commitment here at NorthShore to not only do patient care but also the academic side and trying to really understand what we are seeing and what makes a difference for patients.

>>Here is another tumor where the patient has it in the back of the brain causing visual problems and then once that was removed, as you can see it here it's displacing its visual fibers which are here and then after the tumors are removed those fibers then get restored.

>>Another example, here is the normal fiber pathways. You don't see them because they are thinned out and visualize well by the tumor. There is the port, which tube placed in. We operated through there. The tumor has now been removed and you see the restoration of those fibers controlling vision so they were preserved in his vision recovered and that is an example of minimally invasive through a small opening, and the scalp and a small opening maybe a half-dollar size and the skull and placing this tube in to work through a very small channel using the natural folds of the brain.

>>We have other technologies. There is a fluorescent dye. This dye is injected and it turns yellow and fluorescent and emits fluorescent that we can see under a special filter that we use under our optics and the big issue for us is as we get to the peripheral edge of the tumor, it's a safe area to resect. We worry about if there is still cancer cells left behind that maybe we can't see under a white light. So this fluorescent emerging technology, there are two types, and this is the one we use here, to look at the emission by cancer or tumor cells of this fluorescence and then normal cells don't take up this dye.

>>Schematically here again, is that tube, and we have on the surface is one thing. Deeper in the brain we go through the natural folds, the lesion is then removed and the tumor is removed and as we have already started in the Toca 5 study, you can then began to look at injecting certain therapies. We think this is currently available and emerging technology that again delivers the minimally invasive and safe approach.

>>This is the laser system. This is laser brain surgery called laser tumor obliteration and this is the system we use. This is really intriguing. It's an adjunct or extra treatment that we use for some tumor if it is indicated and that is the fiber is placed stereotactically in a very small open and about a quarter of an inch and the scalp and you will see the surgeon at the Council and in the MRI scan this lesion is targeted. There is the fiber going into the tumor and then once everything is in position, we turn on the laser and you can see it and you can see the outline of the tumor here in the heat map is what we follow to see that the tumor is destroyed. This is another very exciting minimally invasive technique and is usually a one day overnight stay in the hospital and that little catheter is taken out and one stitch put in and the patient goes home the

next day. It's really remarkable and a miracle surgery in a way that we can do certain things sometimes through very minimal approaches.

>>So I will stop there. I think we may have some time for discussion or questions and answers. I hope that I impressed you as much as Dr. Ryan Merrell did about the advances in chemotherapy and the resulting clinical trials. We are working very hard on our side to do a good job, to get the tissue out, to make the diagnosis, but also to do this safely in aggressive surgical removal to allow the patient to do much better by getting the bulk of the tumor out and that sets it up for the subsequent treatment with chemotherapy or focused or general radiation. Thank you for your attention.

>>AT: Thank you both to Dr. Merrell and Dr. Bailes for your presentation. Right now they will take questions. If you have a question you would like to ask, type and submit it using the question box in the webinar control panel on the right hand-side of your screen. We will do a brief Q&A session. I do have a question here. Phase 4 of the trial wasn't mentioned. Can you please explain what the Phase 4 is?

>>RM: Yes this is Dr. Merrell. Phase 4 is often not discussed in neuro-oncology but it has been recently brought into the discussion arena. Basically that would be once a drug is approved or a treatment is approved, how you further expand upon that and modify it in terms of the dosing in the schedule of the treatment. Right now we are really lacking in FDA approved treatment. As of last count if you include devices we have a total of five FDA approved treatments or devices. So as we make further progress in the field, there will be more of a need for Phase 4.

>>AT: Thank you. I think you mentioned this a little bit in your presentation but could you go over what type of questions should a patient or participant ask when considering a clinical trial?

>>RM: Sure. This is Dr. Merrell. I think it is important to ask what the treatment is all about. So one of the things that I didn't mention is that we have literature that we give to all of our patients about the clinical trials and that is called a consent form. That is written in language that is not overly medical so that anyone can read and understand the nature of the clinical trial. So we prefer actually that patients will take that home with them and read it and then come back to sit down with us again and asked specific questions that they may have it typically generates a number of questions about what is the schedule of the treatment. Is this a pill form of treatment or is it intravenous form or how long will I be required to be there for the treatment. What exactly are the side effects and what are the ones that are the most commonly expected to experience. One of the things about the consent form is it will often with percentages of side effects. So let's say a particular side effect maybe seeing them roughly 20% of the patients versus another one that may be very rare and you know all of the side effects have to be listed just like they would be for aspirin or any other prescription drug that you may take so we tried to make it understandable so that patients know what to expect like what is the most common side effect. As I mentioned in my presentation, where is the trial taking place. A lot of these trials open and close which is another important thing to know and is the trial currently active. If it is not active, when will it be expected to open again? Those are a few other things that I didn't have in my presentation.

>>AT: Thank you. Also, this kind of goes along with this last question. What kind of rights to the patients have during a clinical trial and are they allowed to leave the trial if they should desire to do so?

>>RM: Yes. So that is a very important question, and we try to emphasize that whenever we talk about clinical trials. There is absolutely no obligation to stay in a clinical trial at any point in time. We prefer that patients to do, but there are all sorts of reasons why you may want to drop out of the clinical trial. Often, the most common reason would be that maybe there is an unpleasant side effect that is just too much to handle. But there is absolutely no requirement to stay on a clinical trial at any point in time.

>>AT: This is a question on the surgery for the injecting of a fluorescent dye, is that a better option instead of an MRI to see if a tumor has returned?

>>JB: Well the fluorescent dye is an inter-operative during the surgery adjunct or extra treatment that we sometimes use. We often don't need it but in certain cases when we think that it is in a safe area where additional tissue can be removed, we use the dye to see if there are any tumor cells hiding and what it looks like opposed to normal brain tissue. If it is not an area that we can take a little bit more out, we would not use it or if it is already obvious what we are dealing with. It is for hidden cells. It's an inter-operative drug we inject, and it is different than MRI which is imaging studies done pre and post op.

>>AT: Great. Thank you. Do you know if any of the minimally invasive surgeries techniques have been used on patients with Vestibular Schwannoma?

>>JB: In the sense that minimal exposure and minimal incisions and minimal access, yes they have. But not the tube going through the small port or tube that I showed. That would not be used Vestibular Schwannoma. You wouldn't need it in that area.

>>AT: Thank you. Do you need approval of your surgeon or oncologist to participate in a clinical trial?

>>RM: I have to clarify that question but if the question is: if some of our patients will be referred from outside institutions. They may have had their original surgery by their hometown or local neurosurgeon. Then they may be interested in the clinical trial at our institution. So what we typically do is we like to have a good team approach so even if someone is not a part of our own institution, say the outside neurosurgeon, we will have a discussion with them to make sure they would understand the nature of our clinical trial and if they feel like it's compelling enough for their patient. Is important that they are agreeable to that. Ultimately, it's the patient's decision to participate in that trial. But I think we like to have all of the teams involved in that decision so everyone is in agreement that this is the right thing for the patient.

>>AT: Thank you Dr. Merrell. I have time for one more question. If I were using a standard care of treatment should I be concerned that it would disqualify me from participating in a clinical trial?

>>RM: That is a good question. The simple answer is no. If you are just using glioblastoma again as an example. The standard treatment is to have fractionated radiation that takes place over six-week time with the daily Temozolomide and then that would be followed by additional monthly cycles of Temozolomide. That is the standard treatment and in fact if at some point down the line the tumor grows, then the patient in that situation would be very eligible for a clinical trial. Some of the things that can be problematic is if the standard treatment is deviated from. So let's say for example a patient had some experimental treatment or even an approved treatment that was done at the time of the original surgery. A good example would be Gliadel wafers which is an FDA approved treatment, but these wafers are actually often excluded or they exclude patients from participating in clinical trials. Another example is let's say a patient had not completed the full six-week course of radiation. That may be a way of disqualifying the patient. But generally speaking, if you are just having standard treatment, you are very much eligible for clinical trials down the road.

>>AT: Thank you. Well that is all the time we have for today for the question-and-answer so I want to thank you all again for joining us and thank you again to Dr. Merrell and Dr. Bailes. Besides our free educational webinars, ABTA has a variety of programs available to help connect patients and caregivers with information and resources to help support them in their brain tumor journey, as well as publications and resources for health care professionals. For more information visit ABTA's website at www.abta.org or call the ABTA CareLine, which is staffed by caring professionals, at 800-886-2282.

>>We invite you all to continue to check back at our website, www.abta.org for ABTA's Anytime Learning page, a library of free on-demand webinars that feature renowned experts addressing a wide range of brain tumor topics from treatment options and tumor types, to quality of life and symptom management. Our next webinar will be on Laser Interstitial Thermal Therapy (LITT): An emerging therapy for brain tumors on Tuesday, January 17, from 1:00 pm - 2:00 pm CST.

>>A brain lesion is caused by injured tissue or disease in the brain, such as a brain tumor. For some patients with brain lesions, surgical methods and medicines may not be enough as an effective treatment. Laser interstitial thermal therapy (LITT) is a new emerging therapy that uses heat to treat brain lesions. This new technology has already been used in more than 3,000 patients in the U.S. and Canada. Learn more about LITT in the ABTA's free educational webinar presented by Paul J. Camarata, MD, University of Kansas Medical Center, who will discuss how the emerging procedure works, when it may be an appropriate choice for patients, and what results one can expect after LITT. This webinar is sponsored by Monteris Medical. To register please visit our website www.abta.org, click on Brain Tumor Information and then Upcoming Webinars.

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