Hello and welcome to the American Brain Tumor Association's webinar series. Thank you for participating in today's free educational webinar. Today's webinar is on "The Role of Genetic Information in Understanding and Treating Low-Grade Glioma." It will be presented by Elizabeth B. Claus, M.D., Ph.D. Please note 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. Claus will answer questions at the end of her presentation. Tomorrow you will receive an email asking you to evaluate the webinar. It is a very brief survey. 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 in a follow-up email message once the webinar is available. Let's pause for a moment so we can begin our webinar recording year.

>> The American Brain Tumor Association is pleased to welcome you back to our webinar series. Our webinar today will discuss "The Role of Genetic Information in Understanding and Treating Low-Grade Glioma." My name is Andrea Garces, program manager at the American Brain Tumor Association. I am delighted to introduce our speaker today: Elizabeth B. Claus M.D., Ph.D. Elizabeth B. Claus M.D., Ph.D. is professor and director of medical research in the Yale University School of Public Health as well as attending neurosurgeon and director of stereotactic radiosurgery within the Department of Neurosurgery at Brigham and Women's Hospital in Boston. She is a member of the board of advisors for the Acoustic Neuroma Association as well as the Central Brain Tumor Registry of the United States (CBRTUS). Dr. Claus's work is focused on cancer and genetic epidemiology with an emphasis on the development of risk models for breast and brain tumors. In addition to her research activities, Dr. Claus trained as a neurosurgeon at Yale-New Haven Hospital and completed a fellowship in neurosurgical oncology at Brigham and Women's Hospital. Her clinical focus is on the treatment of meningioma, glioma, acoustic neuroma and brain metastases. In partnership with national patient brain tumor organizations including the American Brain Tumor Association and the ANA, Dr. Claus is working to develop cost and time-efficient web-based recruitment strategies to be used in the study of brain tumors. Thank you so much for joining us Dr. Claus. You may now begin your presentation.

>> Thank you and good afternoon to everyone. Just listing my disclosures and support here and wanted to thank the American Brain Tumor Association who's helping us to present our work and get a start on our low-grade glioma registry.

>> I thought I would start with a definition. People use the term low-grade or lower-grade glioma in a number of different ways so I want to list what I am using the term as. So low-grade glioma is a generally slow-growing tumor of the brain. It's called a glioma because it arises from glial cells in the brain. Traditionally, and this is an important point that's moving quickly in terms of this field, gliomas have been graded from 1 through 4 based on the World Health Organization histology groups. Although there is some variability, generally Grade I tumors occur primarily in children. They are an entity separate from adult grade 2, 3, and 4 tumors. The tumors I am discussing today are adult grade II tumors and I'm using the term low-grade glioma. These include astrocytomas, oligo-astrocytomas, which are also known as...
mixed gliomas so you might see either of those terms, and oligodendrogliomas. High-grade, which are grade 3 and 4 gliomas, include anaplastic tumors as well as glioblastoma. One piece of information that's important to note and I will discuss a little bit is this past summer there were 2 exciting reports in the New England Journal of Medicine. One led by researchers at UCFS at Mayo, and the second by members of the cancer genome Atlas group or TCGA and their analyses which have been confirmed by other groups suggest that tumor marker and genetic profile data likely are better predictors of outcome prognosis and potentially response to treatment than these traditional WHO histology subgroups. It's quite a big change in terms of how we look at things, how we think about treating patients with low-grade glioma and also the information we give to patients.

>> Some numbers to start which are taken from the Central Brain Tumor Registry of the United States, which does include data from the National Cancer Institute. This is a listing of all brain tumors from 2007 through 2012. It includes both benign and malignant tumors. When you go through the numbers there are approximately 3000 new low-grade glioma, adult low-grade glioma tumors, diagnosed in the United States every year. The mean age when we do statistics on the data set is about 41 years of age. Obviously, the range is from about 20 to 60 years old. Higher rates are seen in males, as well as in whites and that's consistent across countries and data sets.

>> When I am talking about risk factors that relate to glioma, we know that there is not much known in terms of environmental risk factors for glioma and the 2 big ones that have been confirmed across a wide variety of data sets are exposure to ionizing radiation and an inverse association with allergy. Then we look at things that are genetic. As in any cancer, inherited genetic predisposition occurs in a small percent and whether it's breast cancer or brain cancer or colon cancer, we think it's about 5% to 10% of cases have some sort of inherited genetic component. In part, we know this because individuals have a first-degree, and that would be a parent, sibling, or child that have a diagnosis of glioma, those individuals have up to a twofold or twice the risk of a person in the general population. We do know that there rare genetic syndromes that we don't see terribly frequently and they include glioma as one of the potential diagnoses that show up in these families. You may have heard of some of these like Li-Fraumeni, neurofibromatosis 1 and 2 but these are very rare and explain only a small proportion of familial risk of glioma. It's quite rare that we run into these in the general brain tumor clinic. One thing that is interesting and which has been recently discovered over the past six or seven years is there are additional inherited variants associated with risk. I will talk a little bit about those, as well, and whether there is any implication in terms of screening for both individuals and family members.

>> When we talk about genes, it's a complicated topic. We're talking about two types of genes. One is what is called inherited, another term you might see is germline. These are the genes that are passed on from parent to child. When we as investigators attempt to measure something about that, the way we get the information is after a patient consents, we draw blood or gets saliva or we can use a cheek swab, and we are able to get from those materials things that might be related to glioma. There is a second type of gene we talk about and this is in the glioma tumor itself. Another term that is used is somatic or sometimes will people talk about acquired. There are things that are inherited that are in all the cells of your body and then there are things that are in the tumor itself. The findings recently have related to both of those things. But you have to keep straight in your head when we talk about which one. We're now learning that in glioma, both these type of genetic changes are important. Both things in the germline and things that are acquired and in the tumor. We know for some of these tumors, we think that these acquired changes might be related to exposure. For example, to radiation or a lung cancer patient to smoking, so the environment for that can be important as well.

>> When we talk about inherited genes, these are the ones passed on from parent to child, there are some that are quite rare, but generally associated with a very high risk. One that is very famous that I'm sure many patients have heard of, is the breast cancer or BRCA1 and 2 genes. Rare in the general
population but if an individual has the gene they have high risk of breast, ovarian and other cancers. Some of those genes have been found in glioma. In addition, polygenic are genes that are relatively common in the general population, but associated with a much lower risk. Those are the eight that we mentioned and will talk a little bit about.

>> What is the evidence that inherited genes exist for glioma? As I mentioned, and to just look at this column here, when we have done in some of our large epidemiology studies, and I just get the reference here, this is the GLIOGENE or the glioma international case-control study led by Dr. Bondy who is now at Baylor, we have found that in general if an individual has a first-degree family member affected with glioma, then their risk is twice that of the general population. That gives us evidence that there are genes that are inherited that seem to relate to glioma.

>> How do researchers go about looking for these genes? There are a lot of different ways but there are two main ones. One is we try to identify families in which there are multiple individuals diagnosed with a glioma. A second method and these require thousands of people is we look at groups of individuals who have glioma and individuals who do not have glioma and try to compare genes or genetic variants across the two groups.

>> I know probably a number of you have participated in GLIOGENE and just to let people know, this is still ongoing. It’s led by Dr. Melissa Bondy, a professor at Baylor College of Medicine and it’s an international effort to try to identify families that have two or more living members with glioma. We have been able to identify over 500 families so far. We have been able to identify in particular one gene that appears to be associated with both glioma and melanoma. Presenting here just a table of one family. Each line gives a generation of family members. In this particular family or pedigree, you can see they have six individuals with glioma and notice there are few other types of tumors as well. Very rare and very difficult to locate. We hope to make people aware of this study in case they have any interest to help us find these families. I have the website down here as well as the contact individual below.

>> As I mentioned, there have been some genes identified that are rare, but have a high risk of cancer, one of which might be glioma. This POT1 is a new gene identified through the GLIOGENE study and these are some others that have also been associated with glioma risk.

>> What about the more common inherited genes? I mentioned this in terms of looking at groups of people who have glioma and comparing genes in persons without glioma. This requires thousands of study participants. In some of the studies we have organized, we have over 10,000 individuals so as you can imagine, very expensive time-consuming but needed to find the rare genes.

>> In 2009, two groups found evidence of such genes and I have the references listed here. What was amazing, and this does not always happen in epidemiology, is each group independently found evidence for similar genes and others have been able to verify that. That very strongly indicates that these genes are of interest. These are the eight that I have mentioned that we have found so far. These are the formal names and this is what we think they do – and you can see the word unknown is listed a number of times so we obviously have a lot to do in trying to figure out what these genes do or do not do. If you look in the final column, you can see some genes seem to be related to certain types of glioma. For those of you interested in Grade 2 you can see something called TERT. Some other genes are noted to be specifically or more likely to be associated with grade 2. One thing to note here, and I haven’t put numbers in, but it’s important to think about not only is a gene associated with risk, but how great is that risk? You can have genes that are associated, but the risk is not very high. For example, where you see a single + sign, that’s about a 20% to 40% increase in risk. Note that we have a few that have a couple of positive signs. This particular candidate gene has a six-fold increase in risk, in terms of a certain type of glioma. This one here has a twofold increase in risk. That is something as a patient or
physician that you think, well, that seems like a good pretty good increase in risk. Should I or my family member be tested?

>> There is a very nice review of the topic and I listed the reference here regarding whether or not people should be screened in the general population. At least at this point, screening for any of these variants, even those with higher risk, is not recommended for the general population. The thinking behind that is the general risk of these gliomas is about 0.1%. Even if the risk is increased, so now it's 0.6%, that's still quite a low risk. The cost of putting people through MRIs or screening, and we're not even sure how we should screen people, and it's not clear that intervening helps people in terms of their prognosis, at this time there is no recommendation for screening in the general population for any of these variants. The example I have to compare to is the breast cancer gene that we mentioned earlier. In the general population, there's a risk of breast cancer among men and women of about 13% over a lifetime. Individuals that carry the BRCA gene have up to a 65% risk of breast cancer over lifetime. Therefore, screening is suggested and that is in part because there's an intervention that is shown to offer benefit in terms of survival and outcome. So just to compare that to the breast cancer scenario. >> What about other types of genetics that we talked about? Not germline or inherited, but in the tumor itself? What do those tell us and how might we use those to select treatment, to think about outcome and to make general clinical decisions?

>> At this point we're all still learning and it's an imperfect science. It is intriguing and we're starting to get pieces of information. As I mentioned, in the New England Journal of Medicine last summer there was a very exciting article, one by the TCGA group and one by researchers at UCSF and Mayo, and that's the article I have presented here. They had data from a number of large population-based studies and they were able to go back and compare when I have information on histology, on germline genetics, on the tumor, what pieces of information seem to be important? It came down despite some very sophisticated analyses and large numbers of tumors and patients that there were three pieces of information and these three pieces relate to tumor characteristics. A mutation in a gene called IDH, a mutation in a gene called TERT and deletions or missing pieces of arms or parts of 2 chromosomes. Chromosome number 1 and chromosome number 19.

>> What they found was that outcomes, clinical characteristics, what genes look like in the inherited component differed across each of these groups. They came up with names for some of the larger subgroups - so triple positive means they have a finding or mutation in IDH, TERT and they have co-deletions. Triple negative means they don't have any of those changes and then there are some groups in between. The three symbols here relate to three different data sets and the point of that is to show their findings were consistent. They found it in the Mayo group, the UCSF group and the TCGA. That indicates there is probably good evidence what they are seeing is correct. What this shows is that there are certain age onset characteristics of the different groups, the triple positive group seems to be the youngest and the TERT mutation-only group seems to be the oldest.

>> There is a association with outcome and this does not incorporate any clinical information. That's important to know - this is not incorporating any effect of radiation or chemotherapy. This is simply what the tumor shows and how individuals did. The triple positive and TERT IDH mutation group did best. One thing to note and this is true across many studies is that the data are both grade 2 and grade 3. That is one point we want to note and why we're interested in further pursuing grade 2 is because the number of patients is smaller and lumped into higher grade studies. We don't have great information specific to grade 2 tumors in terms of how they respond, what did the prognosis is, so that's an interest in terms of genetic and other factors is focusing on just a grade 2 group to give patients better information about what they can expect with that diagnosis.
>> What are these markers? Essentially the IDH is a metabolic enzyme. If there are mutations it alters the cell’s ability to program itself to divide and to act normally. TERT is another gene and it helps to control whether or not the chromosome continues to enlarge or shorten. That relates to cell death. This is unclear in terms of what gene is associated with it, but we know that loss of this area on chromosome 1 and this area on chromosome 19 is important.

>> The point in this slide which is taken from the New England Journal paper is that grade 2 tumors are always joined with other grade tumors. They are rarely presented separately. It’s difficult to give good information to patients with a grade 2 because they are always mixed in with other groups. You do see however that there are certain characteristics of the lower, which is 2 and 3 groups, that differ from the higher groups. You see there are many more triple positives than if you go to a grade 4. There are many IDH mutation individuals versus grade 4. You see the characteristics of what is seen in the tumor varies quite a bit by grade.

>> I don’t want to spend too much time on this, I’ve given the reference below, but the point is it is important to know both information about tumor genetics as well as inherited genetics, in order to be able to tell patients what sort of outcome and response to treatment you might expect.

>> So tumor tissue testing is ongoing - most of the large neuro-oncology centers, I’m at Brigham Women’s and Dana-Farber but also Mayo, UCSF, M.D. Anderson and Memorial Sloan-Kettering, all of these centers are now starting to add increasing markers or genetic changes to the panels that are tested. I will tell you this changes constantly. I just had a patient who was treated about eight years ago and that tumor was not tested at that time for any of these changes because even over that short period of time we have learned a lot and we know there are things we need to look at. This is just an example that I made up, but it is based on the sort of information that we give to our patients. Looking across different genes, so you can see here this is TERT and this is where it is located and in this tumor there is no change or mutation detected. BRAF particularly for pediatric tumors, but for other tumors as well, is looked at and here is the 1p and 19q. This is the sort of report you would get and that would help a neuro-oncologist decide what sort of treatment and tumor it is, to better tell what the pathology is.

>> Does treatment strategy vary by tumor, genetics and markers? In terms of low-grade glioma, we don’t know a lot about this. We’re gaining some information and there are certainly intriguing findings, but again that’s why we would like to try to gain more information on grade 2 to give patients better information.

>> Surgery at diagnosis? I think in general, the consensus among neurosurgeons is that gross total resection is the goal. It’s obviously important to pick a good neuro-oncology or neurosurgical center that has things like intraoperative MRI and mapping and other key surgical tools to help get the best outcome. There has been no clinical trial looking at extensive resection and outcome. However there is clearly a strong correlation between extensive surgical resection and increased survival. It’s not only important for that, but to get enough tissue to make sure we know what the pathology is, what the grading is – if you get a small piece that might give you one piece of information that may not be a complete picture of what is going on in the tumor. It’s also important if eventual clinical trial entry is to be considered that sufficient material is obtained and stored to allow a patient to be eligible for clinical trials, should that become necessary in the future. One thing that’s quite interesting is there is some new data for higher grade glioma that suggests an association between IDH mutation and benefit from surgery. So that people might benefit more from surgery if they have certain mutations and I listed the reference right here.

>> However, it’s not a clear-cut picture. The reason is, and this is a complicated slide, but tumor marker, which I have a graph for the 1p/19q change as well as for the IDH change, and location are correlated. These are the general areas we talk about in the brain. It turns out that the frontal lobe, which surgically
is a bit safer than some of the other locations, is more likely to show IDH mutation and more likely to show 1p/19q co-deletion. All these factors are correlated and interrelated and hence it’s difficult to know if the survival benefit is due simply to having surgery in a place that is a bit safer or because the markers exist more frequently there. Lots of things we need to continue to look at.

>> Another important question is should patients have a recurrence, whether or not surgery should be undertaken or whether we should assume that the tumor is the same as it was prior to any intervention. Some patients will have had treatment in between initial diagnosis and recurrence, and others will be managed conservatively with serial MRIs. In the past, I would say it was generally not suggested that surgery be redone and there are many factors that go into this like how long the time has been between initial diagnosis and recurrence. We are now considering surgery more frequently and that’s because of information that is presented in this paper, again led by the UCSF group in Science of 2014, which followed a number of patients, admittedly a small number. It followed 23 patients with an initial diagnoses of grade 2 astrocytoma mixed or oligodendroglioma. They looked at the time of recurrence what the tumor looked like. What was interesting was in 43% of the patients, at least half of the mutations that were in the initial tumor were not found in the recurrent tumor. The message there is things can change in terms of mutations from start, and this is a tree diagram showing for all their patients, how they started and what mutations occurred over time, so it may be important to consider whether additional tissue might be needed at time of recurrence. You see this is one patient with initial surgery, recurrence, recurrence and over time the different mutation. Some of which may be treatment-related that occurred over time, but to treat a person at each time point might require an updated piece of information in terms of mutation. At least something to converse with your physician about.

>> Chemotherapy? Most of the clinical trials to date have included the higher grade individuals. Some of you may be aware there is new data out that look at both higher-grade as well as high-risk low-grade patients. And now that survival time or time at start of clinic have increased, PCV, which is a type of chemotherapy has been shown to have added benefit in terms of survival. But we need much more data for low-grade glioma.

>> Radiotherapy? We know even less but there are hints that IDH1 mutant tumors may show increased sensitivity to radiotherapy but we really don’t have much trial data to base that decision upon.

>> That leads me into our goal to get more data for low-grade glioma. As we mentioned, the low-grade glioma patients generally only a convenient subsample and studies of higher grade glioma. Then when you draw results or conclusions from these studies, it will be driven by the much larger number of high-grade glioma. We’ve now formed a consortium and it’s called LOGLIO and it’s UCSF, Yale, Mayo, Brigham and Women's Hospital and a number of other individuals. We met last summer and across all the studies and sites in the United States, we found only 651 low-grade glioma cases that have this sort of data available to allow us to address some of the questions that we brought up. I think that points out that larger numbers of low-grade glioma cases are needed that have all the information. So clinical, tumor, germline, so we can focus separately on these individuals. I think we’re also interested in hearing what sorts of quality of life or symptoms patients are having. How can we get information to patients and make things better for people?

>> We are partnering with this LOGLIO group to create the International Low Grade Glioma Registry. We are trying to use patient organizations and as I mentioned the American Brain Tumor Association has started us on our way by giving us some funds to start development of our web-based registry. We’re also going to create an iPhone app and hopefully eventually for folks that don’t have an iPhone and Android, to make a cost-efficient way so everyone gets access to it means to collect data for low-grade glioma.
We’re hoping that enrollment will start this summer. We are working with a lot of great patient organizations like the American Brain Tumor Association, National Brain Tumor Society, the International Brain Tumor Alliance and other websites. We will have patients enter through internet study websites. We are starting with iPhone and if that goes well we will move into android. We’re asking patients, and this is part of what makes a cost-efficient, to help in terms of the management of the study. We will be asking patients to identify or locate their pathology report and to get that to us. You can mail it, fax it, scan it, whatever way is good for you. You can upload it on your phone or iPad or other device to get it to us. We do that to make sure we have a uniform study group and people we say we’re studying actually have the diagnosis that we think they have.

These are some of the hard-working graduate students and project director and this is us working on getting the online questionnaire up and going.

What are the goals of this study? We want to try specifically for low-grade glioma to get a little better handle on what is the prognostic model. If someone comes to clinic, what is the prognosis, what are the outcomes, can we guide treatment selection better? We want to see if there are genetic variants specific to low-grade glioma. We’d also like to standardize the information that is given to low-grade glioma patients more. One of the things we have noted is especially when people come from an outside location, they have not been given information on prognosis, on issues relating to family planning, so for example if there is a young lady and she wishes to consider having a family, what information do we have on becoming pregnant when you have a diagnosis of glioma? How about talking about driving? Do people know that there are rules generally varying by state about the Department of Motor Vehicles related to driving if you have seizure or any other cognitive disability? We want to look if there are ways we can make things better. Are there associations between physical activity, exercise, diet, quality of life? And we hope to use some of the mechanisms on the iPhone like Research Kit and the Health app to gain information on that. We’re trying to get a feel for what people are willing to do and how much information they are willing to share with us.

We will model the registry after a similar registry we did for Acoustic Neuroma. If anyone is interested in seeing what it will look like the Acoustic Neuroma website is hosting that registry. We hope soon in the summer we will have it up for our low-grade glioma group.

What are the things we will ask people for? We will ask you to confirm your eligibility and that is to get a pathology report and send it to us, so we can make sure the diagnosis is uniform across the group and we are actually looking at what we think we are looking at. We will ask you to give us a saliva specimen. This is the container we would send that out to you. It’s easy to do. It’s not glamorous, but works well. You spit into the well and put the cap on it and send it back to us. You need to allow review of your medical record and this gives us information on different pathology, genetics that might have done on your tumor, what sort of treatment you received, and a little bit of the online questionnaire to give information on family history or risk factors you might have.

This is the kit that we send out. You open it and there is a well where you put the saliva sample and send it back through regular mail.

One thing you can help us with is to tell other patients. You can do it anyway works for you like internet, telephone, groups. It will be internationally available and we hope we can get large enough numbers. Our goal is a couple of thousand, so that’s what we’re hoping to do.

We also need help because one problem is when we do these large studies, sometimes genetic variants can be different for different racial groups. It’s important we get sufficient numbers for different ethnicities and races so we can guide people of all race in terms of what the outcome of prognosis or best treatment choices might be. Sometimes we ask people to help others because as you can see this is a very internet or web-based study and some people might not have access to that. We
usually work through other patients, patient support groups and patient associations to try and get to other groups to make sure everybody gets to join us.

>> We need your input. We are right now just developing the app as well as the questionnaire. We're working with the LOGLIO group and we need to know what information have you had a hard time getting. Is it just treatments, is it understanding the genetic information that you get from your pathology report, things like seizure management, pain management, insurance, driving? What do you want us to ask about and develop information on? We also want to get a feel for how would you be willing or like to receive this information? Do you feel it should always be in person? Are you interested in having internet resources or webinars, Skype, what is most helpful and easy for you to access? When do you want to receive the information? Is at time of diagnosis too confusing, or is it when you feel that's most appropriate? Do you want it always available on the internet, or what would be helpful to you? And also we're trying to get a feel for are you willing to use things like a Fitbit and iPhone? And iPhones, if you put it in your pocket it can measure through GPS where you are and number of steps and your heart rate. We can get a lot of information on patients simply by having people put their phone in their hip pocket and walking around. Are you willing to give us access to that and are you interested in that sort of thing? We would like to look at what is the amount of physical activity that people are willing to undertake and how does that relate to outcome? So glioma@yale.edu, any thoughts or comments you have, we would love to hear or you can call the phone number here 617-732-4092 and I want to thank everyone and take any questions if you have them.

>> Thank you so much Dr. Claus. That was a very informative presentation. Everybody we will now take questions, so as a reminder if you have a question you would like to ask, please type and submit it using the question box in the webinar control panel on the right-hand side of the screen. Dr. Claus there is a question here about contributing. Is it possible to still contribute to your data registry if the diagnosis was from over 20 years ago?

>> Absolutely. That's a great question. In terms of eligibility, it's persons who are 21 years of age and older. You can be diagnosed anytime, anywhere and in fact, it's very helpful for us to have individuals that have variable amounts of follow-up time because that gives us a more complete picture of what's happening for low-grade glioma, so great question.

>> And can you also speak a little bit about rescue therapy in relation to improve genetic understanding?

>> I don't think especially for low-grade glioma we know a lot about that. We're still just looking at what should the initial treatment be. At this point in time I don't think there's much information on it, which again is why we need to get the whole timespan of low-grade glioma.

>> Thank you. There's also a question about prevention of higher grades. Do you have any information about preventative treatments during a stable period of the disease?

>> At present, there are no known preventive treatments. I think one of the things we're trying to do and there's another consortium we're involved with called GLASS, where we will try to collect over time all the samples a patient might have and see if we can predict what genetic changes might occur and that might help us to say if there's any sort of prevention, but at this point we don't know of any.

>> Thank you. For the study as well, are you looking for mixed-grade diagnoses or only grade 2?

>> At this point we're looking at grade 2 only because there is so little study of that group specifically. We are trying to enrich the study for grade 2 lesions so we have a large enough sample size to have enough statistical power to address it for that group.

>> Thank you. Are there associations of any type regarding the molecular markers to outcomes of immunotherapies?
That is still a new field. They are certainly interested in looking at that. There are no trial results at this point. Certainly that is of interest and also looking at any sort of markers within the blood with respect to immune factors. One piece we're looking at for this low grade registry is for individuals that are willing to give blood. There are a number of researchers that want to try to look at what is the patient's immunologic status and how does that affect outcome in response to treatment. That's another big area that people are very interested in.

>> Thank you. Can a low-grade glioma on the thalamus be biopsied?

>> Without seeing the specific case, it would be hard to say. It's certainly possible in general. There are variable thoughts about whether that is a safe thing to do or not. It would depend on the specifics of the case, but certainly in some instances it's possible to do.

>> Thank you so much. What is the standardized counseling given to women with low-grade glioma who want to get pregnant?

>> That is an emerging field. There is some new data that has been looked at by both the M.D. Anderson group as well as Memorial Sloan-Kettering. It's very small numbers because most centers don't have very many women who go on to have a child and have a low-grade glioma. There is antedotal data that it can increase the risk of progression. I think we have all had a few patients where we have seen that. Most of the larger centers now will have you visit specifically with a counselor to go over the risks and benefits of that and to show the data. I do think it's a very important conversation both for males and females to have, to understand what the risks and benefits might be. I know at our center, Dana-Farber, patients receive a separate counseling session to go over that sort of information.

>> Thank you. Do you know if there will be literature available on the registry study that we can provide to participants or health care providers’ patients when it’s available?

>> Absolutely. We will try to be good about providing the materials online, in print and all sorts of ways so people can get access to it. Absolutely.

>> Thank you so much. Would a targeted therapy inhibitor treatment be recommended for patients with IDH1 or 2 mutation?

>> You really have to know the specifics of not only the IDH status but the specifics of other markers. It would certainly be something that a conversation should be had about, but the further details of the pathology and other markers would have to be considered.

>> Thank you. Do you have any information on TERT mutation? If you weren’t tested for that at the time of surgery?

>> The TERT mutation, that has only more recently been tested for, so I know if I were to look back at my patients from five or 10 years ago, we did not test anyone for TERT because it’s only been a fairly recent finding. You certainly could have your materials tested for it. Usually materials are saved at time of surgery, so it certainly possible to go back. Where we are now and I think most big centers now are adding or have already added TERT to the panel of things that are tested for. It would not have been something even a year or two back that most places would have tested for. Things are changing fast.

>> Thank you. With GBM being more prevalent and more aggressive and also getting the bulk of the share of research support, what do you feel is the likelihood of any new therapies for GBMs translating relatively quickly into improved outcomes for low-grade glioma patients?

>> That's a great question. When we look at the genetics of both the germline genetics as well as tumor genetics, although they are quite different, we do see some of the low-grade gliomas are moving to become glioblastoma. One of the things we’re doing is to look in the low-grade gliomas to try and identify because clinically they may not look any different, but based on their genetic makeup to pick out those that are more likely to be high-risk and move on to glioblastoma, so that upfront they might...
be treated more aggressively. Whereas individuals with low-grade that don't have high-risk profiles might be able to spare treatment, or wait a longer time until treatment is given. That's one of the big goals of this group's efforts, is can we tease out at the beginning who needs treatment and who doesn't need treatment, or at what time might they benefit from treatment to spare people that don't need aggressive treatment up front, the side effects of that.

>> Thank you. A question from another health care professional who has had female clients diagnosed shortly post-pregnancy, do you know of any links between the influential hormones on diagnosis?

>> It's a great question. We're trying to think about what is it that might make a glioma move more quickly during a pregnancy. The 2 main thoughts although this is not known at all is obviously hormonal influences, but also whether it's something to do with changes in the immune system, changes in vascularity and whether that also changes the vascular structure in the brain. It's not known and those are the three hypotheses that people are talking about. Obviously, it's something important for us to collect more data on. Each center has a few cases so we're hoping this registry can start to address that and bring attention to the fact that this might be an issue and its data that patients should have up front.

>> Thank you. With regards to low grade glioma treatment options, is there a consensus on how long Temodar should be used for low-grade glioma?

>> I would say in general there is little consensus of anything in low-grade gliomas. If you look at literature you will see frequently it's one of the most controversial areas in terms of neuro-oncology. It's because of that issue that we really want to try to focus specifically on it. There are controversies regarding everything. Surgery, treatment, when, how much. It's a very tough field and needs more information.

>> Thank you. For those who want to participate, but are located outside of the continent, is there any way they may be able to still participate?

>> Absolutely. It's open to everybody.

>> We are hoping the internet, and that's why we partnered with some groups like the IBTA which is based overseas in Europe, we want to make it open to everybody. At worst, people might have to pay some postage to get the sample back to us, but otherwise it's open to everybody.

>> Thank you so much. Is there anything else you would like to add?

>> No. I want to thank everyone for listening today and thanks to the ABTA for supporting us.

>> Thank you so much and thank you everyone for all your questions. We truly appreciate you joining us and thank you once again Dr. Claus for your wonderful webinar presentation. For more information on brain tumors and to help patients and caregivers process the diagnosis, understand a new and difficult vocabulary and access resources to help make informed decisions call the ABTA CareLine at 800-886-2282. Let's pause for a moment to conclude our webinar recording.

>> We invite you all to continue to check back at our website www.abta.org for the ABTA's library of free, on-demand webinars that feature experts addressing a range of brain tumor topics, from treatment options and tumor types to diets and coping with a diagnosis. Our next webinar will be on Caring for the Caregiver on Tuesday, March 22 from 1:00 until 2:00 p.m. Central Time. Caregivers of brain tumor patients face many difficult issues including fatigue, serious role changes, depression and grief related to the trajectory of the disease. But unlike other caregivers of other conditions, they may also deal with sudden and significant neurological and functional changes of their loved one. Join the American Brain Tumor Association's interactive educational webinar to learn more about how caregivers can navigate these rough waters. Vickie Leff, LCSW, clinical social worker, palliative care at Duke...
University hospital will discuss these challenges faced by caregivers and offer immediate and long-term strategies to help them cope and manage all along the brain tumor journey. This session will focus on finding educational, financial and emotional support. Also please join us for partners in treatment and care, the American Brain Tumor Association's one-day educational and networking meeting held in communities across the United States. Patients, families and caregivers are invited to participate free of charge to gather the most up-to-date brain tumor information from leading experts, receive guidance on managing symptoms and to network with each other. To register or for more information please visit www.braintumormeetings.org. This concludes our webinar. Thank you so much for joining us and be sure to complete the evaluation survey you will receive by email tomorrow. You may now disconnect.

>> [Event concluded]