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Event Started: 7/15/2014 6:00:00 PM

Please stand by for real time captions. Welcome everyone and thank you for joining American brain tumor Association webinar series thank you for purchasing today start free webinar. Our webinar will address pediatric low-grade glioma presented by Dr. Peter Manley please note all lines during the webinar I did. If you have a question you'd like to ask please type submitted using the question box and the webinar control panel on the right hand side of your screen. Dr. Manley will answer as many questions as possible at the end of the presentation. Tomorrow, you will receive an invitation to complete a free feedback survey. Please do take a few minutes to complete the survey and send it back to us. We are planning our 2015 webinar schedule and we really, really rely on your feedback to help us plan our future webinar schedule. We are recording today's webinar that will post to the a PTE website in our anytime learning section. You also receive the webinar Lincoln the follow-up e-mail message once the webinar is available. We are going to pause for a moment and I'm going to start recording the session.

>> The American brain tumor Association is pleased to welcome you back to our webinar series. Our webinar today will discuss pediatric low-grade glioma. My name is Jillann Demes per program senior management at the American -- I'm delighted to introduce our speaker Dr. Peter Manley. Peter Manley is the director of pediatric rain tumor survivorship clinic at Dana Farber Boston children's Cancer and blood disorder clinic has research include long-term effects of treatment on brain tumor patients with specifically and fatigue sleep and obesity. Thank you so much for joining us Dr. Manley you may now begin your presentation.

>> Take you very much Jillann. I appreciate having the opportunity to speak to you today. I done my name is Peter Manley and IMF does Dana-Farber Boston children's Center for Cancer and blood disorders. I am going to talk to you today about low-grade gliomas. We're going to talk about diagnosis and advances in treatment and outcomes. I look forward to hearing your questions after I am done with my talk. I made it a little bit on the short side because I know there'd be a lot of questions and feel free to ask anything. Just to go over before we give any talks we want to disclose if we have any relationships with any pharmaceutical companies. I have some trial support from a company called Dan au fait and other than that there are no conflicts. We're going to do today is we're going to look at how as parents and caregivers we evaluate treatment options for treating low-grade gliomas and that would include surgery, chemotherapy cut targeted agents and radiation. Then also understand long-term outcome of low-grade glioma and knowing this can this influence our choice of how we would choose therapy. And what the outcome would be based on the choices we make.

>> Just a brief overview of brain tumors in general. Brain tumors have an incidence of about three and 100,000 children work this pediatric can. At have gone up slightly and that is probably most likely to improve diagnostic imaging that we utilize now. We to diagnose children who have had head trauma and we find a brain tumor that is a low-grade glioma and usually those children to very well. They still get categorized as a brain tumor and so the numbers have increased slightly. And most common time we see this is usually under the age of 10. Boys maybe a little bit higher than girls and there is no racial predominant in terms of who gets a brain tumor it's equally distributed across all ethnicities.

>> If you look at the different types of pediatric cancers that we have the most common is leukemia. Not far behind in spring tumors. Brain tumors are what we call the most common solid tumor in children's and there are about 12,000 12,500 new cases of pediatric cancers per year in we see about 3 to 4000 in the United States per year.

>> At our center, we are one of the larger centers in the United States and we see about 100 through 120 cases a year. It may not seem like a lot but pediatric cancer compared to adult cancer is much less common. If we break it down even further and look at all of the different types of rain tumor is that there are you can see that low-grade glioma or low-grade astrocytoma are the most common brain tumor in pediatrics. It is a good thing because most children with low-grade glioma do quite well. Whereas the adults try to have these -- have these high grade one or more common the adult population.

>> When we talk about low-grade gliomas what are we talking about? Sometimes you hear all go back between low-grade glioma and low-grade astrocytoma. The glioma is the cell of emerging and or prices from and within a glioma there are different types of cell types. We see here there are a glial cell called and astrocytes and this is the most common type that we see and astrocytoma. We divide these into multiple grades. Low-grade can be a great one or pilocytic and a grade to can be a Ferber Larry were diffuse inter-filled in -- infiltrating astrocytoma. You also see a pie low mix 08 astrocytoma and sometimes we cannot classify it as pilocytic or for blurry soldiers the low-grade glioma.

>> If you get a tumor from and only go to enter glioma this is much less common and is less common in pediatrics and occur more in adult. And astrocytoma or low-grade is determined by how we were we find it. If it's a me I had sent that should say hypo-final Mike glioma. We will also if it's in the back part of the brain we will cauda posterior will loss of pilocytic to -- pilocytic astrocytoma and sometimes it's called the tech to glioma. There is a wide variety of types of tumors that all are classified as low-grade glioma and as we learn more about low-grade tumors we can separate them even further.

>> Oddly diagnose them? We are still using technology that has been around for a while and looking at these tumors under a microscope. When the tumor is removed from the brain we take it and freeze it and we also fix it into wax and take small slices and tenet with different material that help us diagnose a low-grade glioma. This is what we have been using for the last hundred or a few hundred years. I will show you that removing a little bit further beyond the microscope and we are learning more about these tumors on a molecular level and we'll talk about that a little bit later.

>> As I said before, there's a lot of different grading of low-grade gliomas that range from grade ones which are very slow growing to only grade -- PXA which can be a little bit more fast-growing and they all fit into act similarly in long-term outcome.

>> In addition, low-grade gliomas can occur anywhere in the brain and they can look a lot different depending on where they are. So this is a low-grade glioma in the back part of the brain called the posterior fossa and this is the most common were received low-grade tumors this is a posterior fossa juvenile pilocytic astrocytoma or a grade 1. This is a hypothalamic optic pathway tumor when you can see this looks a lot worse than this tumor here. This can cause more symptoms with regards to vision loss and endocrine function and these patients will usually present with balance issues and headaches. So even though they are classified under the same category as low-grade astrocytoma they can look completely different. Depending on where they occur they can also be more difficult to take out. This tumor here from liturgical standpoint might be a little bit easier to remove than this tumor here because it is attached to be optic nerve and pituitary gland and there can be a lot more morbidity from the surgery.

>> This is what a tumor looks like under the microscope here it is not very cellular and if you go to a higher magnification here if you have a very aggressive tumor all of the cells are packed together in the cell is this little dark blue dots and you can see thousands of these next to each other if it wasn't aggressive tumor this is what a low-grade astrocytoma looks like. Pattern is how they smeared across the side as to how it looks like.

>> Rosenthal fiber just in case people are wondering is if you have had a tumor for a long time these form and are much more indicative of a both slow-growing process fast-growing process.

>> Oddly diagnose pediatric brain tumors? The first thing we use as a or MRI some people have a CT scanner Scan and these are not great at looking at tumor tissue. They are really good at looking for hydrocephalus or increased pressure in the brain and spinal fluid is not draining properly it looks for blood, bones, fractures cause sometimes you can see tissue injury in that respect. And MRI really gives us the best definition of a tumor and word is. Also a CT scan you cannot see the back part of the brain very well because the build up skiers that area. Within MRI it does not. The nice thing about an MRI is that there is no radiation associated with it with the Scan there is. We are trying to avoid as much radiation in children as possible and so we limit the number of CT scans and x-rays as possible in order an MRI is a magnetic field in a big magnet. Again the bone does not obscure the posterior fossa.

>> So how do we treat brain tumors? We usually use a multimodal approach. Sometimes we you surgery depending on the location, radiation we have used in the past although I will explain a little bit later while we are trying to get away from that and chemotherapy as well. Chemotherapy can include these molecular targeted hairpiece and they are usually systemic treatments and when we talk about chemotherapy we talk about systemic therapy where he we either take something orally or you get something injected into your bloodstream and that will go all over and cover every area of the cerebral spinal I'm sorry the CNS accessibly of the brain and the spine.

>> So what have we done in terms of neurosurgical advances? There is a lot that has been improved in neurosurgical techniques. When you were in the operating rooms they can look and see where's your tumor is and when a dissecting microscope there something called a Tron which basically can liquefy a tumor and you do not need such a large incision to remove it, usually they do not take out tissue and a big chunk it'll take out enough tissue to get a diagnosis or for price Balaji and a lot of times they will liquefy with an ultrasonic aspirator. Also we have an MR operating suite mostly what that means in the second, also there is MRN CT guided biopsies. Sometimes when it child has a large tumor we do not feel can be taken out completely but we want to get tissue the neurosurgeon utilizes a computer-aided guidance system that they use from an MRI that has been done with the patient and in the operating room that MRI is loaded into a computer system and they can tell exactly where their biopsy will go and that way they can maximize the effective for the biopsy will go in getting the appropriate tissue to get the type gnosis.

>> This is what I was talking about in terms of the matter operative Omar. This is among having surgery on a brain tumor you can see here that this goal is open and this just to show what is going on this is the neurosurgeon's finger. What this allows the surgeon to do is once they remove this tumor they can have the child go back into the MRI scan while under industry shut and under surgery to the skull remains open and a do an MRI scan to make sure all of the tumor, if the goal is to remove all of the tumor that all of the tumor has been removed. Right here say they left a small amount behind so they left a little bit behind prior to doing this the child would go back upstairs, be woken up Cotter skull would be closed cost it would be sutured and they would go for an MRI 24 hours after the surgery and if there was a little bit left 100 sometimes the surgeon would have to have them go through an additional surgery. Which means or in Ossetia cost you have to have your

skull opened up again, for this allows the surgeon to see if they removed as much tumor as they feel as possible and sometimes allows them to go back without having to wake up and go back to the ICU and do another MRI scan this the benefit of children to allow a maximal surgical reception without significant issues going back to the operating room a second or even third time.

>> In addition, we can to computer imaging where we can see where the nerves are and where the tumor is and elation to the nurse and the screen part here is the tumor the blue is the ventricles that's where spinal fluid is, the red obviously our blood levels, yellow is the nerves that run through this area of the brain. The surgeon can see where the nerves are running through this part of the brain and see whether or not they would be able to take this completely. Sometimes the tumor world push nerves aside it can be resected and in if it's profusely infiltrating sometimes the only respect some tissues. For low-grade gliomas yes you can if you can get a maximal reception that is possible but because children do well who do not want significant morbidity from surgery so our surgeons now if they cannot take it out completely without causing significant damage to the child we do not recommend that that is done. This imaging can sometimes help guide the surgeon where the tumor is a location to some very delicate structures within the brain.

>> So what happens in zero surgery? Obviously we feel the experience of the neurosurgeon is very important there are excellent neurosurgeons all over the country, pediatric neurosurgeons who specialize in cancer and oncologic surgery and that is something that we always want the best surgeon possible to operate on a child. We are not saying we have the best surgeons here, like I said there are great surgeons all over the United States you do want to know how many times a surgeon has operated on a patient with a low-grade glioma. Obviously location of the lesion is very important as I showed you before cost is it in a delicate were de-structure of the brain we do not necessarily want the whole to removed is there other therapies that can shrink the tumor. We obviously would talk with the surgeon about the degree of reception that will take and the age of the patient is very important, young children in the surgeon does not have a lot of space to work so we do not want a young child to undergo a major resection if we think it is going to cause a lot of rapidity. We also want to know how they are prior to surgery if they have significant issues are to surgery there that as a result of the tumor we do not want to make them worse. In addition cost the patient is completely functional hard to going to the operating room we obviously want them to come back completely functional after going through the operating room. We do not want to cause more problems are there.

>> So radiation therapy and I will talk a little bit more about this as we move forward, this is actually used to be the gold standard for the treatment of low-grade gliomas. We do know it is effective and we know what works well on treating low-grade glioma Scott however there significant issues that are associated with long-term consequences of radiation. We are getting radiation to a developing brain can cause neurocognitive dysfunctions. That's how you think how you remember things, how you process your language, their younger you are the more risk you are for having neurocognitive deficits if you get radiation. We tried to in all brain tumors we try to avoid any radiation under the age of three years but in low-grade gliomas if we can avoid radiation completely we do. I can also cause secondary malignancies and so if you get radiation 10 years later you are risk for other types of tumors such as a high-grade glioma called glioblastoma or another type called and I Gianna. All patients who received radiation to lots of areas with what vessels the midline structure of the brain there at risk first analysis of those vessel the neck can cause a stroke. That also happens much later and also if you have other issues as obesity and high cholesterol that puts you at higher risk. In the right behind the nerve of your eyes there's a gland called the pituitary gland in of packets radiation you can have hormone deficiencies such as thyroid deficiency cut growth deficiency, difficulty going through puberty and the nice thing is if you do of Homeland issues we can replace everything that

the pituitary does that does require lifelong replacement and the patient will beyond medication for their entire life. If we ever radiate the spine that's what gives you most of your tropical or chest growth when you get older and if you radiate the spine you will have a shorter trunk and longer legs.

>> Again will we do before we discuss radiation is how old are they, where is the tumor, will be exposed if you get radiation, what is the dose of radiation going to beat a child?

>> Other types of treatment we do we talked about watching cost of someone has a gross total resection or near total resection for the tumors completely removed or there's a small amount left we sometimes recommend observation year if you have a tumor removed completely that is the standard of care you would just have the tumor watched with frequent MRI scans for the first year. Radiation we just discussed and chemotherapy is the next thing that we will talk about. There is these are kind of the older regimens than Christine and carboplatin Dr. Packer from Washington DC DC hospital published on this in 1993. Looked at children who receive that this therapy and there's a group in San Francisco who utilized this medicine called TPCV it's for medicines together and other regimens as multi-carboplatin and than Christine Astin, my sins that others others that have been used in low-grade glioma and some newer drugs like Avastin.

>> The height of these children do? If you look at -- how do these children do? -- And event free survival these are patients who received carboplatin and TCP regimen a and regimen B is TC and regimen B is TCP and these are for children with a Canonsburg -- cancer predisposition syndrome with an increased risk at low-grade glioma and if you give them regimen be there at a higher risk -- I know looks like there is a big difference between A and B but statistically there really is not. Essentially these two regimens were be deemed equivalent. Regimen B did a little bit better but not significantly different in that respect there is a difference if you didn't have that and then if you did. What is assuming by event free survival? This means children who had this drug whether or not they recurred. It does not mean that they've died it just means they recurred. Most shall drink they recurred have a 50-50 chance that they would recur for three years from the start of therapy. Why is that important to us? We also know if you get chemotherapy you still have a very good chance of survival and the overall survival of these children is 90+ percent. Remember 50% do not require additional treatment and that is a good thing. These children can still respond even if they recurred three years later and even sometimes the exact same regimen or it might switch to a different regimen such as they had TCVP or if they had not received -- or with some of the newer therapy which I will get to see Ken then they receive that treatment as well.

>> Where the future directions? We talked about the fact that we look at these tumors under a microscope in our going deeper than looking at them under a microscope. We are looking at the DNA. Once we look at the DNA we can learn about the abnormality within the tumor cells and then we can think of medications that can potentially help these children based on their molecular signature and what it is. Tumors can look very similar under migrants scope and but from a Mike molecular level they can look different. In the federal low-grade noumena might have completely different molecular abnormalities that would require greater different treatment. Locally this is what we call a heat map and it looks at the abnormality within a tumor. These are chromosomes, when you see the little red spot that's where the abnormality is and you can see here there is not a lot of red. There's not a lot of blue that means there's an abnormality. This by rate here is what any abnormalities that we see in a gene called BRAF it's a fairly quiet genome in terms of all of the mutations and in low-grade glioma space show you what ovarian cancer looks like with all of the mutations you can see there is a much bigger difference between low-grade glioma and ovarian cancer. Probably tumor like this that has all these abnormalities from genome you do not know which is the thing that is driving the tumor to grow. With 30,000 after abilities and one little needle in a haystack is what's causing the tumor to grow. Luckily we found out this is what as part of a driving

force behind tumor growth. This is the pathway that people who have low-grade glioma in pediatrics should become very familiar with. There's a lot of medications that are being targeted to the pathway. So this is what we call the grass raff pathway if you have neurofibromatosis. It turns off this protein here called RAS the cable low-grade without NF you can have an abnormality in this protein called RAF for this gene called RAF these are the other signals that go down to this target NTOR which tells the cell to keep growing. If this pathway is always on is going to tell the cell to keep growing and growing and that's what develops into a tumor.

>> These are just where the PRAF is an this is the mutation and there's also a mutation. So I will just talk briefly about BRAF so you can understand this better and what happens. This is a protein called RA the rest which activated this below its NEK normally when it is not active it's a single entity. What happens is when it activates it is appears up with something. So appears up with itself so now it's a double opt in and it activates MEK and if this is single it doesn't work and in patients who have ganglioglioma or grade to they have a mutation called the V 600 E called the V 600 EE Tatian which makes this protein active very active and it does not need to double up to be very active. Patients who have a duplication they always have the to RAF together so there also constituent Leon and this is what we see in juvenile polycystic settlements and this is what we see the low-grade glioma and again glioma and astrocytoma and so come back to this a little bit because this will influence what kind of treatment we went to give them.

>> So right now they're two studies going on in of these two pathways. One is to breath in it and there's another drug that targets specifically this V 600 E mutation and currently their studies going on here and in other centers in a phase 1 trial in pediatrics and also in adult population they are utilizing the Strug as well. This works in patients who have this V 600 E mutation. The problem is some people always ask is does it even matter if I know what the status is of my child's tumor? Cannot we just give this medication? The problem with that is if we do not know what your molecular statuses and we block or take a the 600 and someone who has it duplication costs Arredondo and it keeps happening, if we just block one spot rate here this actually speeds up even further. The drug the 600 drug does not always block every single duplication and so this can then cause the tumor to start to grow. So there was a case where they used treatment using a drug called to ref and had without knowing the status of the tumor and the had to shut it down early because the tumors grew. If we give someone of the 600 E drug and the patient has unknown duplication and not a mutation dear tumor could grow significantly were much faster than they had previously. That's why we can only give to patients who have this.

>> That's why we then go to open a trial that inhibits one downstream from RAF. It's happening here is the accelerator is right here that's causing the tumor to grow and were putting a big bridge right here. So this is accelerator and this is more of it breaking it. It cannot move past this spot rate here down this pathway to then cause the tumor to grow. In patients with a duplication we utilize the NEK drug first before we even think of using this. There's a thought of combining them for even potentially could you use this for a the 600 E. Yes you could but if you have a duplication we do not want to give the Strug. That's very important. Will never give the Strug to someone unless we know their molecular status. So if your child did not have a biopsy you cannot find this out. We would not utilize the medication.

>> Now going to talk about an area rehear, so basically people are thinking well if this is where the abnormality is that one only block it right at the very bottom before it allows the signal to tell whether or not the tumor should grow or to stop growing. So this is a drug that inhibits that NTOR inhibition in this patient have an abnormality above that tubular sclerosis may develop brain tumors and we give them in I'm sure inhibitor and their tumor shrinks them and if we stop bickers back and we give again the contrary we also tried this inhibitor on patients without tubular Sbarro system we have seen

effects in children with neurofibromatosis and progressive low-grade glioma. This was another option. The nice thing about these medications is that they are all world. You can take them by mouth, or they have turned them into a liquid formulation it. In younger.

>> So what is next. So you can see there is multiple places to target and there can be feedbacks into pathway of can you block both pathways and we can locker with trying to block RAS we try to block RAF we can block MEK and we can block and letter TOR we can block this protein as well to rent any feedback and the king at this complex here. There are a lot of new treatments coming out for patients with low-grade glioma that this pathway is selectively involved in. That's looking very bright Eric we have seen these in response from these patients and these treatments.

>> So the other thing people always ask is how is my child going to do? If you get on the Internet rate after child is diagnosed with low-grade glioma have a lot of parents who come and see me in are very disturbed because they type in low-grade glioma. Adults get low-grade gliomas to in the outcome as much different in pediatrics than adults. Unfortunately copied type in low-grade glioma usually see a lot of adult ETA. Here at Dana-Farber we undertook a project where we decided to look at all the low-grade gliomas that were diagnosed in the United States. There is a program called the surveillance at the Tao mythology and results in a gives us a snapshot around the US and that gets put into a database that's maintained by the National Institutes of Health. We looked at this database from 1973 through 2008. So 35 years of diagnosis I looked at the age, race, religion was, whether not you had radiation, when you were diagnosed, whether not you had a biopsy gross total resection or subtotal resection, and what grade tumor. Only looking at low-grade gliomas which agreed to and less. We found 4000 patients. This was a very busy slide about where was. But equal for boys and girls. I'm and was up pilocytic astrocytoma and the most common place was the top of the brain or in the cerebellum and private. There given to the majority of patients with subtotal resection or gross total with some receiving even know resection. And about 80% actually did not have radiation and 736 did. You can see out of this there were 10% steps. From pediatric low-grade gliomas. Which is actually good. The prolific the same kind of survival curve and we look at pediatric low-grade gliomas and we did a search for patients above 19 years of age we can see the outcomes are patients who have Patrick low-grade glioma versus adult leader low-grade glioma. Is very important to recognize that these are two different entities. Even though they may look the same under a microscope molecularly they are different. So these tumors and adults unfortunately usually transform and become something more aggressive were pediatrics they usually do not. The majority of deaths usually unfortunately they do occur occurring the beginning. And then if we took all low-grade gliomas and compared to adults we can see there's a much bigger difference about 88% in pediatrics and term of survival in adult it's about 25% and if we only focus on the grade 1 grade 2 it's even better. 90+ percent to write compared to the adults which is much less and also in the 40% range.

>> Then we took all of the different types of tumors that were listed and here's a pilocytic bodices a grade 1 astrocytoma inheres the survival rate is well over 90% and the grade twos are still very [Captioner experiencing technical difficulties]THE GOAL OF CHEMOTHERAPY IS TO GET PATIENTS AND THEIR 20S WE FEEL BIOLOGY WILL TAKE CARE OF THE REST IF YOU DISSECTED COMPLETELY IF OFTEN CURATIVE RADIATION IS EFFECTIVE IN -- you have to do the -- chemotherapy is less defective and we know patients patients have a lot mortality and that they should reach adulthood and patients who receive radiation again have an increased mark Talladega and we have to think about what drugs we are choosing. Hopefully as patients or as we learn more about the molecular status of patients we can use targeted treatments that will minimize the effects of chemotherapy. Those drugs are fairly new and we are learning more about the man we

do have a long history of the drugs with carboplatin and most drugs and treatments right now have worked towards the targeted therapies.

>> When a child is diagnosed with a recurrence or progression we want to get to a medical center that specializes in pediatrics and that has a good understanding of pediatric low-grade site, never feel bad about getting a second opinion. Were one of the larger centers in the country and patients come here and ask for second opinions and that is fine. You need to know what is best for your child. Treatment usually provided locally but sometimes expertise is needed from an outside institution minimize pain us but anyone else. That might have a little more expertise in that area. I will close by saying thank you very much for allowing me to give this talk to you and if you do have heard you need additional information we do have a couple of websites that the brain tumor website at Dana-Farber and those are the websites forte that's is give a lot of our information and that have if you have any questions you can contact us directly with a lot of information with a variety of different brain tumors. With that I will say thank you and I hope this was educational for you and I look forward to hearing your questions.

>> Wonderful, thank you so much Dr. Manley that was amazing. As we talked about earlier you are correct questions are flooding and thank you for being so much time. We will get right into it. First question. I read online for PMA and the outcome is not great -- what is your experience of children surviving that type of tumor?

>> So PMA. For GPA?

>> Dave wrote PMA.

>> I am not on hundred per cent sure by PMA. We can come back to it.

>> If they could specify that.

>> If they could specify that they will read another question she right now. Next one is, do you perform MRIs on pediatric patients and what software do you use for FMR I and their own navigational system?

>> We use brain lab for Nero navigational systems and I'm not a radiologist I'm not 100% sure on the software we only used FMR I that will benefit a surgical resection or where if we are close to an area that we are concerning for damage during a surgical procedure for radiation. FMR I is not that helpful in terms of diagnosis we do not usually is a poor diagnosis. We do you think if we feel we are near an area that could be damaged in a surgical procedure.

>> Perfect work can you talk about proton radiation in regards to Ella Gigi low-grade glioma.

>> Proton radiation is a little bit different. What proton radiation is in comparison to standard radiation which we refer to as per protons protons have a mask and there is no exit dose. When you're getting someone radiation you are passing it through the had and if your photon radiation he make sure that the beam all focus on the area of the tumor but then no separate beams will come out. Stone someone who has a posterior will follow some mass if they have photon radiation they will get some exposure to the front part of their brain and eyes and throat and depending on where the tumor is protons prevent that exit dose. However they still carry all of the same toxicity of that radiation that standard radiation does. There is no difference between a photon and proton excess decreasing the exposure to other parts of the brain. But you're still at risk for secondary malignancies and if you still radiate areas that are near vessels are still at risk for strokes and if you radiate parts of the cortex your risk for cognitive deficit. The hope is that with protons you will have less exposure.

So, we still consider it radiation in we do not usually recommend protons or photons for a low-grade glioma unless absolutely necessary.

>> Great. The other woman on the webinar clarified by PMA she meant high low mix alloyed?

>> Title mix allied great title mix alloyed tumors usually occur in younger children and they are hypothalamic region and they are a fairly new entity and that they just have just been described 10+ years ago. Is feeling is that the outcome may be our little bit worse than all juvenile pilocytic for grade 1. Because of their location are usually not as easy to respect because they're in the team at Sixers of the brain they can be associated with more morbidity in terms of surgery and treatment. But we tie have treated number of kids with pilocytic astrocytoma and they have all survived. So I think has a fairly new described entity we still need a little more time but if you can or if you remember my slide here. I'm sorry. This is like here even in the astrocytoma not otherwise specified which might be some of those tumors were glioma not otherwise specified you can still see that these did well. So the lowest rubies of their still 75+ percent. If they were not diagnosed as high low mix alloyed back in the 80s and 90s they might be under glioma not otherwise specified so you could still see all of these tumors still the patients do well. And usually as children if it does cause problems it causes problems in the very beginning.

>> What about longtime server April you have tell me out here again. To be a very astrocytoma.

>> February astrocytoma: right here so there's still long-term outcomes of 400+ months of 80%. They still do quite well. So the pilocytic to the best in the fibrillary do the worst. We just looked at fibrillary astrocytomas only and found that if we break it down just a fibrillary astrocytomas this slide stills holds fairly true that if you did not have radiation you did a little better and that was independent of whether you had it removed completely are not. The survival rate is still well and 80% and it still held true long-term to if you got into your 20s your chance of dying from a fiscal area great to the astrocytoma went down. So you did very well.

>> Good. This is interesting because most of the phone calls I get about side effects are for radiation. Someone is asking that they have heard that perhaps chemotherapy might cause me to side effects. Should we be worried about how chemo might cause the late side effect into adulthood?

>> Yes there are risks associated with chemotherapy. We talked about that there be called TC TV and there's two drugs once called procarbazine and one is CCNU and there in the family of ocular drugs with another drug other people may have heard of -- it's a small where there is a risk associated with secondary tumors and secondary cancers usually leukemia associated with it. Is lower than radiation the and it still present tenant if you develop secondary leukemia it is 100%. So there are there is that risk and procarbazine invoice can cause infertility. So there is that risk as well. So we know it's effective but we also tend to stay away from that because some of the newer drugs that are coming out will lean more towards those such as -- invest in and Christine in -- does not have any long-term significance and there's risks with hearing loss the the dose is very low in we usually do not see hearing loss associated with those agents.

>> Okay. What treatments are used to used to increase the percentage of survival if the patient had radiation and what is the percentage of survival probability after the 23rd birthday if they did take radiation?

>> So we have to look at that little more in depth I don't have a perfect answer for you there. If you look at this here the survival within radiation after 20 years from diagnosis so if you are two or three at that age it still 70%. You still do fairly well compared to the adults which will be way down in this

range in the 30% range. Once you've radiation there's really nothing you can do to improve or make any differences unfortunately when it's done it's done. But you need to be aware of any changes in physical exam or symptoms that could be associated with a secondary tumor. The most common type of tumor meningioma growth early slowly in the also tend to start growing 10 years after radiations given. Usually do not see those tumors are you going to do because of your risk first drug use want to be as healthy as possible and decrease any other comorbidity anyone have a low-cholesterol carload what pressure, you do not weren't totally of a sedentary life and overweight those put you at risk for stroke and at their own writing if you have that to patient who already had an increased risk of stroke that can cause problems in these urges for maintaining a healthy lifestyle.

>> You must've redheaded the questions, someone asked about diet and nutrition. So good job. [Laughter] to set one off.

>> Someone is actually on the web and are from NDS and that she shows you how important these are for people who can come from anywhere anywhere anytime anyplace. They're talking about their younger brother is diagnosed with ADI GP and is showing that response to radiation and chemotherapy, wanting to know any advanced treatment protocol that they might explore. Now being that they are in India not knowing what is over there is what protocol should they look to come here? Were should they stay there and what could they ask over there? Any comments that?

>> AG IPG is a lot different today low grade glioma. Unfortunately it's a very aggressive tumor in children that involves the brainstem and the best treatment there getting now is radiation. We are doing says look at molecular targets for PA IgG but right now there is not a great treatment for these tumors except for radiation. You could go anywhere in the United States or Europe that all of the things that were using to treat the tumor our experimental. Nothing right now has been effective at treating the D IPG so you can just keep posting if you want to send us your information were happy to take a look. Really there's no great therapy in the United States or Europe or Canada to curate.

>> Thank you for answering that. I'm sure that means the world to them. Just to be able to reach out and get an answer.

>> Dissipation who test positive for be our AF mutation have a better outcome of the patient who does not have the mutation?

>> That's a good question. Returned to figure that out right now. We still think that patients who have mutations still do well but we are just getting all of that information together and that information would not be in that database so we are doing it as a collaboration with other centers around the US and looking at their outcomes and their treatments. The one thing just now is pilocytic astrocytomas have the duplication and diffuse astrocytomas and gangly oh gliomas tend to have the the raft mutation and the nice thing is are separated out snore similar to the scrap here where the pilocytic tend to do a little better and we also have not treated those mutations with specific drugs so the jury will still be automatic. I still think overall everyone does quite well.

>> Good news. C here. We have time for maybe one or two more. What are some new treatments being used to treat PLO GG and what are the side effects associated with these treatments?

>> Most of these drugs I was talking about these Mac and have the terrorist for BRAF inhibitors our new drugs are being used to treat pediatric low-grade gliomas and you to at least get pretty inhibitor you 600 he you need to know your status that we will not treat you unless we know you have the mutation itself. The side effects, so far have been fairly minimal and some the side effects associated with the BRAF Barash can cause renal dysfunction and that a short-term father is concern if you're on some of these medicines for long-term you can cause cardiac issues and these

are more from adult data and the Mac inhibitor. The hitter can also cause skin cancers. The interesting thing is if we combine the the ref inhibitor with Michael inhibitor we decrease the chance of skin cancer and a lot of that if you stop drug the symptoms go away. We are still learning about these medications because they not have not been around a long time Mike some of the other ones I cannot tell you if you're on it for four 510 years bracket had a five years ago how would you do because pediatrics we are just starting to test.

>> Okay I will fit one more question in here. Someone's child has to total receptions one John at age years old and one a couple weeks ago. What is the chance that it will recur again even with to total receptions?

>> The chances are low if they had a total grocery section. The fact that they're older now sometimes puts the risk even lower. The nice thing again is the likelihood is that if it grows back it will grow back locally and again it will usually does not transform into something more aggressive. The chances are quite low have had to guess the percentage of being less than 20% chance of coming back and even if it does come back surgery would still potentially be another option and the likelihood of a transforming into something more aggressive is very low.

>> That's a good answer 10 done. That is all of the time for the questions that we have today thank you so much Dr. Manley and everyone for answering her asking a lot of really good questions and I'm sorry we did not get to everything. For more information on immunotherapy another brain tumor related topics we of healthcare professionals here that can provide you with support or help you navigate our site to help you answer the rest of your questions. You can give us a call at one 808 eight answer the rest of your questions. You can give us a call at 1-800-886-2282. We will pause for a moment and we are going to and our recording. Then we will share some housekeeping details.

>> We invite you all to join us back further brain tumor related topics in webinar series and Wednesday and Wednesday, August 6, 2014 from 2 PM to 3 PM we are going to have a webinar on demystifying palliative care and join Michael Chan M.D. assistant professor of radiology and ecology on the comprehensive cancer center at Wake Forest Baptist Center.

>> He explains palliative care and what includes and members of the care team and what you can expect by adding this treatment mortality to your care. Then on Wednesday Wednesday, August 13 from 1 PM to 2 PM as well living well with and beyond brain tumors drain Elizabeth Sherwood nurse, MS from University of North Carolina survivorship in integrative medicine program and the oncology for webinar on living well with and well beyond brain tumor. -- Multiple challenges and stressors for patients and caregivers so Mrs. Sherwood will discover helpful strategies for approaching wellness and teach skills for living mindfully with a brain tumor diagnosis. Lastly, but most importantly we invite you to our patient and family conference providing in pursuing answers Eric advances in research treatment and care coming up on July 25 and 26th at the Renaissance show Chicago O'Hare suites Hotel. The program highlights include brain tumor specific breakout sessions symptom management can't integrative medicine, ketogenic diet information legal and financial matters and strategies for successful caregiving. Do not miss out because it is coming up quickly on July 25 and 26th. Registration closes on July 20 then you can register on-site as available. Please visit www.brain tumor conference artwork or call us at 800 886 as available. Please visit www.brain tumor conference artwork or call us at 800-886-2286. This concludes our webinar wiki for joining us and please remember to fill out the survey that you will get tomorrow. You may now all disconnect. Thank you. [event concluded]