

Brain Tumor Clinical Trials

Webcast

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Introduction

Andrew Schorr:

Brain tumors--malignant brain tumors--can sometimes be difficult to treat. Can we do better? Coming up, an expert from Northwestern Memorial Hospital in Chicago explains how clinical trials may help those who may otherwise have limited options. It's all next on Patient Power.

Hello and welcome to Patient Power sponsored by Northwestern Memorial Hospital. I'm Andrew Schorr.

Well, when you think of cancer diagnoses they're all scary. One particularly scary one is if you're diagnosed with a malignant brain tumor, and these are often unfortunately fatal conditions, although certainly I've interviewed people who are living many years. It's variable. What is the exact tumor? Where is it? What medicines are available or surgery to treat it? But obviously we want to do better. And so we talk about clinical trials. Is there research that's going on that's open to you that could potentially help others of course, and could it give you some advantage now?

To help us understand that and what's going on at Northwestern is Dr. Sean Grimm. He's a neurologist. He's also a neuro-oncologist, assistant professor of neurology at Northwestern University's Feinberg's School of Medicine. Dr. Grimm, thank you for being with us.

Dr. Grimm:

Thank you.

Andrew Schorr:

Dr. Grimm, so as I said in the introduction, when someone has a malignant brain tumor unfortunately often--and you've seen the whole range I'm sure of people who are doing surprisingly well, and that's our dream, but it's not always the case--it's a very serious diagnosis, isn't it?

Dr. Grimm:

It is. It really is.

Andrew Schorr:

So where are we now, we have a number of different types--and we're going to talk about brain tumors that start in the brain. Now, we have other cancers that spread

to the brain, and we'll reserve that for a different discussion, but at Northwestern at the brain tumor institute there, you have a lot of research going on to try to help us come up with better approaches, am I right?

Dr. Grimm:

You're correct. We do.

Types of Brain Tumors

Andrew Schorr:

And so that brings us to clinical trials. Now, when we talk about brain tumors give us some of the names and help put it in perspective. I've heard of glioma, but I know there are other types. Just give us the landscape first, if you could.

Dr. Grimm:

Sure. So the tumors we are talking about are what we call primary brain tumors, and as you had mentioned these are tumors that arise within the brain. That is, they don't come from some other area of the body and spread to the brain. The most common primary brain tumor that's malignant is called a glioblastoma. That is a tumor that is thought to arise not from the nerve cells in the brain but from the helper cells called the glial cells, particularly called astrocytes. This is a tumor that's most common in elderly people or people over the age of 60, although any age can be affected by it. It is a tumor that we don't know the cause for it. And it's a tumor that can behave very aggressively, and so we consider it a malignant brain tumor. And it's a tumor that in most cases with our current treatments it's not curative, although we do think that we can delay the time for the tumor to grow and prolong people's lives with treatment.

There are other types of tumors that can be in the class of primary brain tumors. These include what we call gliomas or glial tumors. So as I mentioned glioblastoma is a sort of a member of the broader category called gliomas. Other tumors that are considered gliomas are tumors such as anaplastic astrocytoma, anaplastic oligodendroglioma, and then there are tumors that we consider low-grade tumors where low grade doesn't necessarily mean benign but it means that they behave less aggressively. Those include astrocytoma and oligodendroglioma.

There are other categories of what we call primary brain tumors that we often treat as well, the largest or the most common of which is called meningioma. This is a tumor that actually is not in the brain. It's actually a tumor of the lining of the brain so that even though it's listed under brain tumors it's really a tumor that's outside the brain. And in most cases meningiomas are benign, so they usually can be cured by surgery or radiation, but in rare instances there can be malignant meningiomas that often are treated with additional treatments after surgery and radiation treatment.

Andrew Schorr:

Now, at Northwestern you have an institute, you have a center that's devoted to this.

Dr. Grimm:

Correct. We have a brain tumor institute which is a multidisciplinary center that's made up of neuro-oncologists, neurosurgeons, radiation oncologists and neuropathologists that basically has a mission to treating patients with primary brain tumors.

Understanding Clinical Trials

Andrew Schorr:

Let's get into this discussion of clinical trials. So you want to do better, help people, certainly, if people could be cured or live a longer, better life. So clinical trials are about research. Unfortunately in the US typically not that many people participate. Help us understand the clinical trial activity at Northwestern and why you would recommend that that often be part of the discussion with people who come to see you.

Dr. Grimm:

Sure. So for many of the tumors that we treat, as I mentioned before, there's no cure, and as a result there's a large amount of research being done to look at more effective treatments and hopefully at some point ultimately find a cure for these types of tumors. And because the standard treatment options are limited and not curable, [we] don't cure most patients, it's worth considering enrolling in a clinical trial. And there's really two settings where this occurs. One is where you're newly diagnosed with a brain tumor and you would consider a clinical trial. The other is if you received the standard treatment and the tumor has come back at some point despite that standard treatment.

In either case a clinical trial looks at an investigational agent, could be a drug or a protein, that is thought to have some effectiveness against the tumor. And the reason why it's being looked at in a clinical trial is that it's not known whether or not the drug is effective against the tumor that a patient would have. So because of that and because the options are limited for patients with brain tumors it's worth considering.

Andrew Schorr:

Now, would a major center such as Northwestern typically have more trials than you'd find at just any hospital?

Dr. Grimm:

So typically Northwestern would have more trials available, and one of the reasons for that is that if you look at the incidence of primary brain tumors they're actually fairly rare as compared to other tumors such as lung cancer or breast cancer. As a result many centers don't see that many patients with primary brain tumors so that they just don't see enough patients to have clinical trials specifically for that population. Whereas at Northwestern because we have our primary brain tumor institute we specialize only in treating patients with primary brain tumors. So as a result we have a number of clinical trials that are available.

Andrew Schorr:

Let's talk about the phases of clinical trials because often people don't understand. I

was in a phase 2 clinical trial for leukemia, it was only at a single center. So what's phase 1, what's phase 2, what's phase 3?

Dr. Grimm:

Sure. So phase 1 is a study that is just looking at the safety of a drug and the best schedule of a drug. So this is usually a new agent that's never been tested before in people, and the goal of the study is to treat patients at different doses of the drug and monitor for side effects and find out the best dose and the best schedule to use the drug.

Phase 2 on the other hand is performed after phase 1. So you already have a dose that you know is safe, and the goal of the phase 2 study is to determine whether or not the drug's effective. So this is a study that's looking into whether or not the drug works. Usually this is a relatively small study. Usually it can be performed at just one institution or occasionally it will be done at multiple institutions, but the goal of this study is to look at whether or not the drug seems to be effective.

The goal of a phase 3 study--so basically for a phase 3 study we already suspect the drug works based on the results of the phase 2 study, and what we want to see is whether or not the treatment is better than some standard treatment or better than placebo. This is usually a much larger study. This is a study where patients usually are randomized to receive either the investigational drug versus either some standard drug or in some cases a placebo, and this is usually done at multiple centers just because of the large number of patients that are involved.

Andrew Schorr:

Now, tell me about what kinds of trials are available today when we look at what's going on related to learning more and hopefully curing if we could brain tumors. Of all these different types where is the research going on now? I don't mean specifically yet at a certain site, but just the kinds of research that's going on.

Dr. Grimm:

So there's different types of research going on. One type of research has nothing to do with the treatment, but it's looking at ways of predicting whether or not a tumor will respond to a certain treatment or looking at various what we call biomarkers in the blood to help perhaps monitor how treatment is going for a tumor. So those are sort of more of the diagnostic studies.

Another type of study is what we call a quality-of-life study, and that's looking at areas where--you know, not just a treatment but what are some areas where we can actually improve patients' lives or improve, reduce economics for patients--burden for patients.

The main type of studies you'll see are treatment studies, and these are studies looking at investigational treatment agents, and there are several different types. One is looking at chemotherapy. These are sort of the traditional cancer treatments, and these are drugs that basically work on cells that are dividing rapidly, such as tumor cells which are dividing rapidly.

But in addition to traditional chemotherapy there's quite a bit of work at looking at what we call biologic therapy. These are treatments designed to instead of work broadly on cells that are dividing to work on a specific target that's thought to be important for a cancer cell to grow and continue to spread.

And then a third type of treatment--it's sort of a subcategory of the biologic therapy--is the use of immunotherapy, and that is the use of either vaccines or other drugs to stimulate the immune system to attack a tumor.

Andrew Schorr:

Let's go through that. So, first of all, chemotherapy has been around a long time and it's helped a lot of people, and yet a lot of these chemotherapies that have been helpful that people might receive, infusion or even orally for cancer elsewhere in their body, have not worked in the brain. What makes the brain separate? Why can't drugs that can kill cancer cells or kill cells that are quickly dividing elsewhere in the body, why can't they work on the brain?

Dr. Grimm:

So this has been a particularly challenging area for the treatment of brain tumors, and one of the reasons is there is a physiologic barrier that's known as the blood-brain barrier. And what that means is basically there's a barrier--when a blood or substance enters the bloodstream it is prohibited from entering the brain because of a barrier that exists, and the purpose of this is to protect the brain from any type of toxins in the body. As a result of it, though, often many of the chemotherapies that we use for other cancers don't enter brain tumors in sufficient quantities so that it's one of the areas that limits our ability to treat brain tumors.

Another issue is that in addition to this blood-brain barrier that excludes drugs from entering the brain there is also often these tumors are under a lot of pressure, there's a lot of edema associated with them, and as a result of that again it limits the blood flow directly to the tumor.

Brain Tumor Studies at Northwestern

Andrew Schorr:

Let's talk about Northwestern being a major center for the study of this, and you're right in the thick of it. Give us kind of an overview of the kind of studies you're doing there.

Dr. Grimm:

Sure. So we are doing a number of clinical trials here for patients with primary brain tumors. The majority of them are drug trials although there are some surgical trials as well. The trials that we have available at Northwestern are constantly changing in that as a study opens, patients are enrolled in the study and then within several months or so the trial closes and another study may open. So there's a number of different studies going on.

The majority of studies that we have at Northwestern are for patients with glioblastoma, and the reason for that is that that is the most common malignant primary brain tumor. So we have a number of trials looking at new treatments. We have trials looking at treatments for patients with newly diagnosed glioblastoma. So these include basically trials looking at adding other chemotherapy agents to the standard treatment for glioblastoma. We also have trials looking at adding tumor vaccines to the standard treatment of glioblastoma.

We also have clinical trials available for patients who have already received their initial treatment for their glioblastoma but the tumor [has] come back. And again this is the same in that we have both trials looking at new chemotherapy drugs, trials looking at biologic agents and trials looking at immune therapies such as vaccines.

In addition to glioblastoma, we have trials available for patients with anaplastic astrocytoma, anaplastic oligodendroglioma, astrocytoma, oligodendroglioma and meningioma.

Andrew Schorr:

Lots more to talk about on a very serious subject and with the hope that clinical trials and your participation can make a difference. We'll be back with more with Dr. Sean Grimm, neuro-oncologist at Northwestern Memorial Hospital right after this.

The Clinical Trial Process

Andrew Schorr:

Andrew Schorr from Patient Power back with Dr. Sean Grimm, neuro-oncologist at Northwestern Memorial Hospital as we continue our discussion about clinical trials for malignant brain tumors.

Let's talk about the process. So someone comes to you, they become your patient or they come to you for a second opinion. You know what trials are going on and you through diagnostics learn what this individual patient's situation is. How does the discussion of clinical trials that could be right, how does that happen? Does the patient have to bring it up themselves or how does that happen?

Dr. Grimm:

Sure. So any patient we see at Northwestern as a consultation, whether it's with their primary doctor treating them or whether they are being treated at another institution and they come to see us for a second opinion, we always will discuss in a very comprehensive manner all the treatment options that are available. So we'll begin by discussing the conventional options that are the options that are available as not part of a clinical trial. And then we also discuss the different treatment options that are available in clinical trials, both at Northwestern and at other institutions. Because the neuro-oncology field is a relatively small field we are very close with researchers at other centers as well, so we have a good pulse of what's going on across the country, and we basically would discuss treatments at Northwestern as well as at other institutions.

Andrew Schorr:

So if someone comes to you, it sounds like they can be confident that you're looking at current therapies, investigational therapies at Northwestern and then what might be going on at other institutions to have an interactive discussion with that patient on what might be right for them, knowing that in the clinical trial area there are questions that need to be answered about the therapies, but it can be an educated discussion.

Dr. Grimm:

That is correct. You know, I think one concern patients have when considering a clinical trial is, is there any conflict of interest with the investigator or the doctor that's talking to them about the trial. That is, are they interested in my well-being or are they just interested in enrolling patients on their studies and that's all they care about? And I can tell you, at Northwestern our approach is to consider the patient, and the clinical trials that we have at Northwestern versus another institution are all options. And, as you mentioned, the goal is to have an educated discussion regarding sort of the benefits or negatives of the different options that are available.

Ongoing Research**Andrew Schorr:**

Dr. Grimm, let me go back to the science. As people research cancer they begin to understand that the cancer developed because their immune system failed them and defective cells grew, didn't die, multiplied and start affecting function. And so you mentioned about immunotherapy along the way, and you used the term vaccines, and in some other cancers there's been very promising research on could we train the patient's own immune system to recognize and kill the cancer cells that it missed the first time around. What is your thought about that related to these brain tumors?

Dr. Grimm:

Correct. So I think that is one of the very interesting areas in the treatment of brain tumor, and you're going to see a lot more of that in the coming months and years. And there's sort of two strategies to tackle that problem. One is what we had mentioned, vaccines, which are basically treatments that try to stimulate the immune system to attack the tumor that's there.

The other sort of way to tackle it, and this is what you're seeing in melanoma right now, is that the cancer is thought or tumor is thought to escape the immune system, that it actually has the ability to shut off the immune system from attacking it, and what we're seeing is--coming out now are drugs that are able to bypass this inactivation to keep the immune system able to attack the tumor.

Andrew Schorr:

Right. Yeah, they have like a little sort of a stealth shield or something.

Dr. Grimm:

Correct.

Andrew Schorr:

So some of that relies on understanding almost the biologic subtype of a cancer, even a glioblastoma, whatever it may be, that that particular patient has. So where are we now in testing to try to see is there a certain approach that might be right for that individual that might be different from another patient who has in the broader category the same type of cancer?

Dr. Grimm:

Right. One of goals of cancer therapy is this idea of personalized medicine or personalized treatment, the idea being that just because someone has a type of brain tumor such as glioblastoma there can be different genetic abnormalities in that tumor that may cause it to grow and to continue to divide so that one of the big thrusts in current treatment and research is to try to identify the unique makeup of each tumor and then consider treatments that are relative to that makeup.

It's an area that's very actively involved in research right now for glioblastoma and other malignant brain tumors, but it's an area where we still have a long way to go. I think right now there have been some targets that have been recognized, and patients may come across these. I think some of the targets, or some of the genetic abnormalities that patients will hear about include this issue of MGMT, which is an abbreviation for methylguanine methyltransferase. There's also been a type of receptor called EGFR, or epidermal growth factor receptor, that's being looked at for glioblastoma. I think as time goes by we will also identify others.

Andrew Schorr:

Now, you mentioned a multidisciplinary approach at your institute, and you mentioned surgeons. And sometimes people have surgery or they have other kind of, I guess radiosurgery approaches as well. So is part of the thing you're looking at is what modalities come together when for the most effective result?

Dr. Grimm:

Yes, so whenever we are evaluating a patient and considering what's the next step in treatment, in addition to the different types of drugs and chemotherapies and those types of treatments we also consider surgery and radiation therapies. So it's part of evaluating sort of the optimal treatment for a patient. And some clinical trials will have surgery as part of the clinical trial or perhaps radiation is part of the clinical trial.

Andrew Schorr:

All right. So you have all this on your plate there at Northwestern, your colleagues around the country. It's been a difficult field, and you're trying to do better but certainly--I like to say the statistics sometimes are not meaningful for an individual because they hopefully maybe could do better. People, you hear stories of people beating the odds or their situation is different or they respond better than others do to a certain drug. But overall, how do you feel about you're field? You talk about there being a lot of work to do, but do you have a sense of progress?

Dr. Grimm:

So--I do. I think there's been dramatic progress made in the field of neuro-oncology and that if you just sort of look from a historical perspective we really only had one or

two approved chemotherapy drugs from the 1970s up through the 2000s. So really there was very limited innovation during that time. Since then, or since 2005, we've actually had two treatments that are approved for the treatment of glioblastoma, and in addition to these two treatments there's just been an explosion in the amount of research that is being done in hopes of treating and curing this tumor. So I'm actually very optimistic on where we're headed.

Andrew Schorr:

Now, of course the drug companies can't pour money into everything nor can the tight budget of the federal government, but are you feeling that industry does have an interest in this, or do families and patients need to lobby, or where are we with helping you have the tools for the research, and the funds?

Dr. Grimm:

So I think it's sort of an all-of-the-above answer in that I think that as the federal budget--you know, with the recession and the tough economic times the federal budget for research of cancer and brain tumor treatments is decreasing every year, so I do think industry is picking up a bigger chunk of the cost. And I think at the current time they do have an interest in it particularly because the treatment of brain tumors and other cancers is sort of a new and evolving field so that they have quite a bit of interest to try to develop effective therapies.

But, in addition, I think that because these treatments can be expensive there is a sense from the government to try to limit the number of new therapies because of cost, so I do think that it's important for patients and families to be advocates for the development of effective treatments for their tumors.

Andrew Schorr:

One last question, when we use the word families. You know, a patient says when they develop cancer, "Is there anything I did to bring this on?" Like we worried about using a cell phone, you know, but whatever. Whether genetically, heredity, something they did in their life, close to microwaves or who knows what, power lines, you know, is there anything I did, and is there anything about my family where another family member is likely to get this too. What's your understanding about that now?

Dr. Grimm:

That's a great question. I often get asked that question. First of all, in the vast majority of patients with malignant brain tumors we do not know the underlying cause. The only two known underlying causes are patients who were exposed to radiation; either as treatment for cancer as a child or--or the other is patients with very, very rare genetic syndromes, and these are patients who have multiple different types of cancers. For example, they have colon cancer, and then they also develop a brain tumor and they develop skin cancer. These are patients who have multiple cancers in multiple organ systems. But in the vast majority of cases we do not know the cause.

To date, the whole issue of cell phones has not been resolved, but at least there is no

convincing evidence that cell phones cause brain tumors. That goes also for microwave as well as any other sort of environmental exposure that we're aware of.

And then you asked another good question about hereditary brain tumors and, you know, basically these are not usually inherited, so patient's family members, you know, their siblings or their children, don't need to be screened for brain tumors because these are not typically inherited.

Andrew Schorr:

And we're all on the internet now, and we have wireless in our homes, we have cell phones, wireless, all this kind of stuff, but there's no evidence right now that that's bringing on brain tumors for us?

Dr. Grimm:

Correct. At the present time we have no evidence. I think we'll continue to accumulate evidence as time goes by. It may be that at this point cell phones and wireless haven't been around long enough to cause these tumors, so we will see over time, but at least at the present time there's no convincing evidence.

Andrew Schorr:

All right. As we wrap up, though, this discussion of clinical trials, particularly related to new medicines that may target the specific type of brain tumor that you have, that's a very important discussion I think that people would have. And it would seem like, and I would urge people that you want to sit across from a subspecialist, a neuro-oncologist like Dr. Grimm, but it sounds like the discussion of clinical trials is one that should be part of the discussion, right, Doctor?

Dr. Grimm:

Correct. As I mentioned, because we don't have--our treatments are not curative and not the most effective it's something that definitely needs to be considered.

Andrew Schorr:

Well, I want to thank you for what you and your colleagues do at Northwestern and your brain tumor institute and all the work. And wouldn't it be great if we could have this discussion in a year or two years, or even in two months, but where you could say, "Hey, we made this discovery and this is lengthening lives and wouldn't it be great if it could save lives." But thank you for your dedication. I hope you get there.

Dr. Grimm:

Absolutely. Thank you so much.

Andrew Schorr:

Well, this is what we do on Patient Power is connect you with leading experts like Dr. Grimm, neuro-oncologist from Northwestern and the brain tumor institute there, and hopefully this gives you and your family information and hope. I'm Andrew Schorr. Remember, knowledge can be the best medicine of all.

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