00;00;00;01 - 00;00;31;11 WNPR Funding for Yale Cancer Answers is provided by Smilow Cancer Hospital. Welcome to Yale Cancer Answers. The director of the Yale Cancer Center, Dr. Eric Winer. Yale Cancer Answers features conversations with oncologists and specialists who are on the forefront of the battle to fight cancer. Here's Dr. Winer.

Dr. Winer Tonight, we're going to be delving into the world of brain and to some extent, spinal cord tumors.

00;00;32;10 - 00;01;03;08 Dr. Winer These are not super common cancers. They're not like breast cancer or lung cancer or colon cancer, which you hear about on a daily basis. But they're very important cancers, both because they can threaten people's lives and because oftentimes they cause a great deal of disability. Tonight, we are joined by Dr. Sylvia Kurz, who is a leading expert in neuropsychology.

00;01;03;23 - 00;01;31;22 Dr. Winer She is the interim chief of neuropsychology at the Yale Cancer Center. She's been with us at Yale for just a little more than a year and has an interesting journey to us that I will be asking her about in just a little bit. So, Sylvia, thanks so much for being here with us with us tonight.

Dr. Kurz Thank you very much for having me.

00;01;31;23 - 00;02;07;05 Dr. Winer I want to start by just asking you, what made you want to go into the area of neuro-oncology, focusing largely on brain tumors, both in terms of the clinical care and potentially research and new treatments in this area. What got you interested in something? Was there something that sparked you early on?

Dr. Kurz Yes. So when I went to medical school, I really just loved the brain.

00;02;07;05 - 00;02;33;27 Dr. Kurz And I'm one of those neurologists who likes to localize and, you know, pinpoint where the problem is sitting. And I like doing medical school. So, you know, I have like a PhDs and my Ph.D. is in multiple sclerosis or neuro immunology, which, you know, was a way of me getting interested in immunology at large. And then, you know, my life path kind of brought me to the U.S. for training purposes.

00;02;34;21 - 00;03;03;14 Dr. Kurz So I matched for neurology residency. And during my intern year, which is the first year of training, you know, all neurology residents do like a full year of internal medicine training. And just by chance, I happened to be on quite a few of the rotations on the cancer wards, and it just loved that kind of work. I mean, of course it's saying it's grave illnesses and of course these are very sick patients.

00;03;03;14 - 00;03;31;18 Dr. Kurz But what I liked one was the collaborative team approach that kind of goes into this, right? Like we're working together with surgeons, radiation oncologist, palliative care nurse, a lot of, you know,

specialty approach. And as an end to it, just like the connection that you have with your patients.

Dr. Winer Let me just ask you if I can just jump in for a sec.

00;03;31;29 - 00;03;54;07 Dr. Winer What made you come to the U.S.? So you grew up and you went to medical school and did your PhD in Germany. What what brought you here?

Dr. Kurz Like, the short answer is my husband.

Dr. Winer Okay, that's totally fair.

Dr. Kurz Well, so, you know, the person I was dating when I was in medical school, he wanted to train in the U.S. because he was talking about how great the medical training is.

00;03;55;13 - 00;04;16;19 Dr. Kurz So, you know, he very early on during our relationship, already had kind of gone through the U.S. family steps and a match process. So he landed in Cleveland, Ohio. So we had a long distance relationship. He was in Cleveland.

Dr. WinerSo Midwest. And where were you?

Dr. Kurz I was in Germany.

Dr. Winer You were in Germany. And then when you came to the U.S., where were you?

00;04;17;03 - 00;04;36;05 Dr. Kurz I was also in Cleveland. So I you know, I wanted to spend time with him. So I spend a lot of my rotations during as a medical student in Cleveland. And then ultimately, you know, you have to make a decision. Either he comes back or I come here. So I matched for residency in Cleveland, too. So, you know, I was going to get into this later.

00;04;36;15 - 00;05;06;16 Dr. Winer Well, we'll just touch on it now. Oftentimes in the U.S., where we're a bit biased against people who do clinical training outside of the U.S. and we feel very strongly, often, not always, that people have to do their clinical training in the U.S. if they're going to practice medicine in the U.S.. You had sort of the opposite experience.

00;05;06;17 - 00;05;33;25 Dr. Winer You came here from Germany, you did your training here. And then during COVID, I'd find yourself needing to go back to Germany for complicated reasons. And you found yourself in Germany. And my understanding is they sort of looked down on you because you had had training in the U.S. and you didn't have German training. Is that an accurate way of putting this?

00;05;34;05 - 00;06;01;29 Dr. Kurz That kind of is true. Yeah, it was a little. I will say I had great training in the United States and I have a high regards for the system or how training is done here in the U.S.. But, yes, I found myself in this position that I was fully trained like, you know, ten plus years experience.

And I came back home and it kind of looked at me as I wasn't fully grown up yet.

00;06;02;00 - 00;06;37;28 Dr. Winer Fortunately for us, you came back here. So let's talk about brain tumors. I think people hear the term brain tumor and it strikes fear in most of us. But there is some variability in brain tumors and there are some very worrisome brain tumors. And some brain tumors often called glioblastomas that are hard to treat.

00;06;37;29 - 00;07;13;03 Dr. Winer And very often times end up with someone losing their life to the tumor after oftentimes after some period of time. But then there are also brain tumors that are much easier to treat or much more responsive to treatment. So we start off talking about what some of those are.

Dr. Kurz Yes, there I mean, overall, like we recognize there are about like 500 different types of tumors inside the head.

00;07;13;07 - 00;07;38;00 Unknown So there's a lot of variability. And as you say there, like, you know, these very aggressive tumors often referred to as glioblastoma, that large. And then there's some others that some of them may be equally aggressive but treatable, like one one, I would think of his primary CNS lymphoma, where we have like about a two third chance of achieving complete remission and even curing patients.

00;07;39;02 - 00;08;07;25 Dr. Kurz These tumors or these lymphomas are even more rare. And then the TB, I'm sorry, but they are very treatable. They do require intensive chemotherapy treatments. But yeah, so that that is a treatable type of brain cancer. These are lymphomas similar to lymphomas that arise in people's lymph nodes and in other parts of their body, but they're isolated to the brain.

00;08;08;09 - 00;08;35;22 I'm sure they're a little different when presenting in the brain. And interestingly, it's very rare for them to spread outside of the brain. That is correct. So the biologically or like how two cells look under a microscope, these lymphomas are similar to lymphoma that happen in the body, but there seems to be something special about them. How they kind of find their niche in the central nervous system and how they grow there better than elsewhere.

00;08;35;22 - 00;09;02;09 Dr. Kurz So that makes them different from these body lymphomas. And for that reason, think these lymphomas are staying within the central nervous system and don't like to go outside or, you know, spread to the body. There are, though, also secondary CNS lymphomas. So these are the kind of lymphoma that affect the body first and then spread to the brain as a metastases.

00;09;03;00 - 00;09;33;05 Dr. Winer Got it. And what about meningioma? Tell us about what these are.

Dr. Kurz Yes. So these are tumors that arise from skin like layers that are

covering our brains and that we call the meninges, that we are calling the meninges. And there are many Germans that think that these are actually the most common intracranial tumors overall. They're not technically brain tumors because they come off of those meninges.

00;09;34;15 - 00;10;01;18 Dr. Kurz And we do think of most of them as benign tumors that may need to be resected and then are watched. Some of them can be more aggressive and do require repeat resections, may require radiation. And these are the ones where we try and work on finding better treatments. And then and I realized that we're not coming close to the 500 different types of tumors you talked about.

00;10;02;07 - 00;10;41;02 Dr. Winer But then I suspect there are very few neuropsychologists who have seen all 500 either. But then there's a group of brain tumors that are very clearly malignant, involve the primary tissue in the brain. They're not part of the recovering layer of the brain, oftentimes referred to as astrocytoma, but they're not always so aggressive, either acting or looking. And sometimes times those are even curable.

00;10;41;02 - 00;11;08;28 Dr. Winer Is that correct?

Dr. Kurz That is correct. So there are there's a group of tumors called astrocytoma. And like a cousin of those tumors already all down to gliomas. And that they say that one more time, because I will confess that I had to practice saying that word about ten times before I could have it come off my tongue. Yes, the two cousins are astrocytoma and oligo gliomas.

00;11;09;09 - 00;11;41;08 Dr. Kurz Yes, they are both like what we put most often. They're both low grade gliomas. So we recognized grade 1 to 3 and four tumors. And these low grade gliomas are grade one and two, Category two, grade one tumors and astrocytoma, for instance, Felicity astrocytoma or grade one tumors that can be cured by resection alone. Or if you cannot resect them completely, you don't need to be treating them as aggressively.

00;11;41;08 - 00;12;16;04 Dr. Winer I think there it becomes more of a question, you know, how aggressive do you want to be and how high is the price tag of whatever treatment you would consider? in terms of toxicities, of course.

Dr. Kurz Yes. So, you know, when we talk about chemotherapy or radiation, it's all associated with toxicity and these low grade gliomas, the majority of those happen in younger individuals like in their twenties and thirties.

00;12;16;17 - 00;12;48;20 Dr. Kurz So we want to be very mindful about how what we can do, what we must do to preserve quality of life and keep them up, keep these patients in the active workforce so they have a normal work life, normal family life. And sometimes that means we will postpone treatments. And compared to the tumors that we're going to talk about when we come back from the break, which are the Glioblastomas or the GBM is, which are typically grade four astrocytoma.

00;12;48;20 - 00;13;19;05 Dr. Winer So they're the most aggressive ones. How common are these grade one and two cancers?

Dr. Kurz I there are ten times more rare but ten times more rare. So if you hear about somebody with a brain tumor, unfortunately more commonly it is something that is more aggressive than these lower grade cancers. That's true. I think the likelihood of having a more aggressive type of tumor is high.

00;13;20;16 - 00;13;51;01 Dr. Winer So we're going to take a break. We will be back in just a minute. And will pursue our conversation about brain tumors. We'll talk about glioblastomas. We'll also talk about some recent research findings for some of these lower grade tumors as well.

WNPR Funding for Yale cancer answers comes from Smilow Cancer Hospital, where a multidisciplinary team of physicians employs state of the art diagnosis methods for patients with sarcoma and other bone cancers.

00;13;51;15 - 00;14;18;01 WNPR Smilow Cancer Hospital dot org. The American Cancer Society estimates that over 200,000 cases of melanoma will be diagnosed in the United States this year, with over a thousand patients in Connecticut alone. While melanoma accounts for only about 1% of skin cancer cases, it causes the most skin cancer deaths. But when detected early, it is easily treated and highly curable.

00;14;18;16 - 00;14;43;04 WNPR Clinical trials are currently underway at federally designated comprehensive cancer centers such as Yale Cancer Center and at Smilow Cancer Hospital to test innovative new treatments for melanoma. The goal of the specialized programs of Research Excellence in Skin Cancer Grant is to better understand the biology of skin cancer with a focus on discovering targets that will lead to improved diagnosis and treatment.

00;14;43;20 - 00;15;33;19 WNPR More information is available at Yale Cancer Center dot org. You're listening to Connecticut Public Radio. This is Dr. Eric Weiner here returning for the second half of Yale cancer answers. And I'm joined by my guest, Dr. Sylvia Kurz, who is a neuropsychologist. And our conversation tonight is about brain tumors. Before we talk about Glioblastomas, you want to talk for a minute about a recent and by recent, I mean within the last two years, a recent clinical trial and new treatment that was developed largely for patients who have lower grade brain tumors.

00;15;34;00 - 00;15;59;01 Dr. Winer this is a new targeted therapy that when given, seems to delay the time until a cancer gets worse. This is the idea for the H one inhibitor, correct?

00;15;59;02 - 00;16;27;28 Dr. Kurz The reason why I kind of said that is that it's like one of the big things that differentiate a resident from predecessor. H inhibitor studied covers both. And by covering our by addressing both the H one and the H to the group of patients that can be treated is a little bit larger because you have one drug for, you know, tumors that have an H1 or an H2 mutation.

00;16;28;10 - 00;17;00;18 Dr. Winer So this was a, you know, a very exciting finding because it was a large randomized trial. It was at our big annual cancer meeting on the plenary session very specifically because in the area of brain tumors, the progress has been somewhat less dramatic than in other areas. And tell us about what this drug does in both maybe very briefly about what it does mechanistically, but also what it can do for patients.

00;17;01;04 - 00;17;44;13 Dr. Kurz Yes. So Aida staining for eyes with citrate Dehydrogenase is like a hallmark molecular marker that these low grade gliomas, to have low grade gliomas are either India astrotech trauma category or the Allgood and glioma category and were a sit in app or the brand name is more Inigo targets this mutation with in the cell idea are this The enzyme is always present in all body cells, but in these tumor cells it is changed which kind of keeps the motor going of these tumor cells.

00;17;44;23 - 00;18;10;09 Dr. Kurz So it's a little bit of like, you know, you have like a lot of effort on the gas pedal within those tumor cells. So on the one hand, it keeps the tumor cells growing and going and driving tumor growth from that perspective. On the other hand, it forces these tumors in a slower growth pattern. So it's like a slow motion type effect.

00;18;11;09 - 00;18;42;11 Dr. Kurz Now, VeriSign, it kind of addresses that mutation and makes those tumors go even slower or may even stop them from growing overall. So that's like the mechanism how this drug works. Now, why the so-called Indigo trial was so successful or it was such a breakthrough in our field, is that these tumors, the low grade glioma, is like the great twos pre predominantly affect young individuals in their twenties and thirties.

00;18;43;09 - 00;19;14;25 Dr. Kurz And so far until the publication of this trial, the best available treatment for those patients was due respect or remove as much possible surgically and then either watch and wait until something happens or if something grows, then go in and do chemotherapy and radiation. The consequence of treating with radiation and chemotherapy meant toxicity for those young individuals.

00;19;14;25 - 00;19;46;06 Dr. Kurz And that has often to do with neurocognitive side effects. So with more acid, an EP being successful and a study, it was demonstrated that this medication, which is a once a daily pill, the growth of these tumors can either be halted or slowed down to the extent that patients much later require more aggressive treatment. So from a quality of life perspective, does really means the world for those young patients.

00;19;47;06 - 00;20;18;20 Dr. Kurz And I think one of the things that patients in this situation and many of the people we take care of have to keep in mind is that if we have treatments that delay problems, who knows what we're going to have that's better in the future. You know, now it's an idea one and two inhibitor in three years. It may be something entirely different or it may be a better idea.

00;20;18;25 - 00;21;16;17 Dr. Kurz One and two inhibitor. But the the key fact is that, you know, we we need to have treatments that will allow people to continue to do well and to be there when the next breakthrough comes through, because the breakthroughs are coming really fast and furious. I want to I want to talk now about Glioblastomas. And it was now over 30 years ago that I was a fellow and I met on some Saturday morning and neurosurgery resident who had been up, I thought, at least for five consecutive days, because she looked like she was about ready to kill over and was more than a little frustrated with everything in the world.

00;21;17;03 - 00;21;52;20 Dr. Kurz And she spent about 10 minutes talking to me about how terrible brain tumors were. And what I've been struck by over these past 30 years is that we may not have a lot of new treatments, but we're doing a lot better in terms of helping people live somewhat longer than they did once upon a time, and that we're much more sensitive than we ever were to the issues that people face and their families face when they have brain tumors.

00;21;52;21 - 00;22;28;08 Dr. Winer So tell us a little bit about the treatment of Glioblastomas and what where you think that treatment has come over these years.

Dr. Kurz Yes, of course. Recognizing that, you know, remember 30 years ago. I can imagine. Yes. So glioblastomas are an aggressive form of brain cancer and they do require aggressive treatments there. There's no question about that. I think maybe 30 years ago, the treatment looked like biopsy just to make a diagnosis.

00;22;29;15 - 00;23;04;27 Dr. Kurz Resection was difficult and scary because you could give the patient more symptoms and then you would maybe do radiation and that was it. And life expectancy after that was maybe a year, if you were lucky. I do think we've come a long way since then. Today, treatment would consist of like removing as much as safely possible of this tumor, which means improvement of any neurological symptoms for the patients to feel better.

00;23;05;01 - 00;23;38;26 Dr. Kurz It improves quality of life after surgery and kind of takes away mass effect, gives space for the brain to re expand for any tumor to kind of grow back into and also minimizes the radiation field, the area of the brain that will subsequently get radiation. In 2005, so 20 years ago, we also had one positive clinical trial. So we have one chemotherapy agent that drives or improves survival for this tumor.

00;23;39;10 - 00;24;03;10 Dr. Kurz And then I think not to be, you know, neglected, they could manage over to past 20 or 30 years just that we care for these patients much better. I think there's much more detail-oriented care going into this. We're recognizing symptoms. We can deal with symptoms in a better way than we were 20 years ago or 30 years ago.

00;24;04;11 - 00;24;33;28 Dr. Kurz We are seeing patients more often. There is much more of a multi-disciplinary, symptom-oriented approach there. And I

think we also do a better job talking to patients and their families about what to expect and how we can help them be supported in their daily life. And. Has genetic profiling been of value in these high grade tumors? Certainly something that we do more and more.

00;24;34;11 - 00;25;22;08 Dr. Winer But are we at a point where this is helpful as a matter of standard of care?

Dr. KurzI think the honest answer to that is we're continue to be hopeful that some of these targeted agents may be like a solution for a majority of these glioblastoma patients. We're not there yet, but I think the sequencing and like all this work out that has gone into sequencing, understanding the molecular underpinnings of these tumors over the past decades really helped us understand better the biology of these tumors and helped us to kind of carve out some subsets of these glioblastomas that actually can be helped by targeted therapies.

00;25;22;21 - 00;25;50;21 Dr. Kurz One success story in that area is that a subset like a minority of glioblastoma, does have a mutation that also is commonly seen in skin cancer. The BRAF v 600 mutation, and there have been a few clinical trials over the past five years that have shown that for glioblastoma patients whose tumors have that mutation, targeted therapy with a BRAF MEK inhibition combo can actually be very useful.

00;25;51;28 - 00;26;23;02 Dr. Winer So I think that's like a you know, it doesn't benefit the whole group of all glioblastoma patients as of yet, but it demonstrates that targeted therapies could be useful, at least for some group subgroups of patients. And there are always outliers, people who just do far better than you ever expect, sometimes for reasons that we can pinpoint, sometimes for reasons that we just don't understand very well.

00;26;24;02 - 00;26;55;29 Dr. Kurz That is correct. Yes, I, I have one patient here in Connecticut who was diagnosed with glioblastoma 15 years ago, and she's alive and doing well. And we don't know how and what she did to make this happen. Sure.

Dr. Winer So this brings me to the topic of how you talk to patients and the importance of this conversation is when somebody is facing such a difficult diagnosis.

00;26;56;16 - 00;27;22;24 Dr. Winer And of course, it's with a mix of being honest and realistic, but also being hopeful because there's a place for that. And maybe you could just share your thoughts.

Dr. Kurz Yeah, I you know, these are always difficult conversations to have. And I think the same key features that you just mentioned, I tried to kind of take them serious, right? 00;27;22;24 - 00;27;46;01 We want to be honest, realistic, but we do not want to ever give up hope. And I do tell patients that during that first conversation, you know, we do have treatments. Yes. We have to kind of

go through aggressive treatments and we want to do those treatments because we want you to get the best chance of being one of those outlier patients.

00;27;46;13 - 00;28;11;03 Dr. Winer There's always something that can be done and we try to focus on the very first, next best step and make a decision about that and try to not get discouraged about the big picture. And what if when and how. What's your hope for the future for glioblastoma?

Dr. Kurz That I think, will depend on combinatorial treatment approaches currently and oncology.

00;28;11;03 - 00;28;40;01 Dr. Kurz We all talk about either chemo, traditional chemotherapy or targeted therapy, such as the BRAF MEK inhibition combination that I mentioned or the other world is like immunotherapy, is that we haven't mentioned as of yet. But I think that for glioblastoma it may require a combination of a few of those things in the future.

00;28;40;14 - 00;28;59;01 WNPR Dr. Silvia Kurz is an associate professor of neurology at the Yale School of Medicine. If you have questions, email them to yalecanceranswers.org and past editions of the program are available in audio and written form at YaleCancerCenter.org. We hope you'll join us next time to learn more about the fight against cancer funding for Yale Cancer answers as provided by Smilow Cancer Hospital.