

00:00.000 --> 00:09.300 Support for Yale Cancer Center Answers comes from AstraZeneca, working to eliminate cancer as a cause of death. Learn more at astrazeneca-us.com. 00:09.300 --> 00:43.900 Welcome to Yale Cancer Answers with doctors Anees Chagpar and Steven Gore. I am Bruce Barber. Yale Cancer Answers features the latest information on cancer care by welcoming oncologists and specialists who are on the forefront of the battle to fight cancer. This week, it is a conversation about neuro-oncology with Dr. Antonio Omuro. Dr. Omuro is Chief of Neuro-Oncology at the Yale School of Medicine, where he is also the Clinical Program Leader of the Brain Tumor Program, and Dr. Chagpar is a Professor of Surgery at Yale. 00:43.900 --> 00:53.700

Chagpar So, why do not we start off by talking about what exactly is neuro-oncology, how common is brain cancer? Let's start there.

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Omuro Sure. So, neuro-oncology is a subspecialty of neurology or a subspecialty of medical oncology. So, we typically have training that takes place after we finish the residency or fellowship in neurology or oncology, and then you start practicing neuro-oncology as to speak. So, we basically focus on brain tumors and that includes tumors that come from the brain, which we call primary brain tumors. It could also be tumors that come from other parts of the body. In this case then, brain metastasis. We also treat a lot of complications of cancer when it comes to brain and neurologic issues. So, neurologic complications of cancer also falls under our area of interest.

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Chagpar Like what?

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Omuro For example, you can see what we call paraneoplastic diseases, which are neurologic complications from cancer that are not directly related to the cancer. We also deal, again brain metastasis can also be considered a type of complication. We see a lot of inflammatory diseases from cancer treatments; for example, immune checkpoint inhibitors can cause inflammatory diseases of the nervous system. So, there is a lot of types of diseases that are very complicated because they need knowledge, both in neurology and in oncology and that is where we come in.

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Chagpar So, a lot of patients may have heard of chemo brain, is that in your wheelhouse or is that something altogether different?

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Omuro This is something that we also tend to work on. We are seeing that more and more and that is what I think is a good problem to have because back in the day, we were worried about improving survival in cancer, but now, we are

getting patients to survive and now we need to worry about their quality of life and how in this case, the brain is working and how well the brain is working and how they can go back to their normal lives. So, chemo-brain is indeed a problem from many types of chemotherapies and cancer treatments and certainly is an area of intersect across the board.

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Chagpar So, let's start there. I mean, we will get into talking about all of the different kinds of brain tumors as well, but since we are talking about chemo-brain, is this really treatable? I think a lot of people when they are faced with chemotherapy and/or have experienced kind of that memory fog that being kind of not quite as sharp as they once were, really worry about that and wonder like is this reversible, am I ever going to get the cognitive function that I had before, am I ever going to be able to as sharp and memory as good as it was before I had chemo to begin with?

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Omuro Yes, I think that depends a lot on the type of treatment and how intense the chemotherapy was. So, there is a wide range of complications that could go from just minor forgetfulness to actually full-blown dementia. Fortunately, these are very rare and, in most cases,, they do improve over time. So, there is a tendency of the brain to recover, also other parts of the brain start to learn to pick up on functions that were lost. So, I think overall patients tend to improve over-time. And we are trying to understand more and more how this happens and how to prevent and eventually how to treat and there is a lot of research in that area as well.

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Chagpar So, many patients may ask, you know, what can I do, what can I do to keep my brain healthy if I am going to start chemotherapy or if I am going through chemotherapy, what can I do if I have had chemotherapy and I am starting to forget things, like is there a particular diet that I should be doing or is there a certain medicine that I should be taking? I mean, we see ads on TV all the time for vitamins that improve brain health, like should I be doing that?

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Omuro I think the first thing to do is to talk to your oncologist because there are many other causes of brain dysfunction that are linked to cancer treatment that are not necessarily a direct side effect from the cancer. It could be for example a nutritional issue, it could be depression or anxiety, it could be thyroid function issues. So, there are a lot of things that we need to investigate first to determine what is causing that. So, I think that is very important. And then, if we decide that this is from the chemotherapy itself, well I think it is a problem of discussing what are the risks and benefits of the ongoing treatment, and most of the times, we will prefer of course the best and effective treatment to continue. So, what I

would tell patients is to well sit tight and then we will deal with this afterwards because the first thing here is to survive the cancer.

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Chagpar And let's say that they have finished their chemotherapy, they sat tight and they now come to you and they say "okay, it is not my thyroid, I am not depressed aside from the fact that I just went through cancer treatment and I would have preferred not to have cancer to begin with, but I am okay, and we ruled out other kinds of issues, but I still have this kind of fog, this memory lapse," or you know that general chemo brain that people talk about and that certainly is all over social media and websites and so on, and they come to you really asking "I have finished my mainstay of therapy, but I still have this persistent kind of fog, is there other things that I can do, are there medicines that I should be taking, should I see a neuro-oncologist or are there vitamins that I should be taking for brain health, should I alter my diet?" Help me to understand or is this something that you just kind of say, "you know what, give a tincture of time, it will settle out hopefully with time?"

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Omuro I think giving some time is always helpful because there is so much going on at that point in time and many of these things will go away and will improve. But if the problem is persistent and is causing issues in your daily activities, then it is time to consult a specialist. What we typically do is to, of course, investigate other causes and work with what we call a neuropsychologist to perform a very comprehensive what we call neuropsychological testing, which is a lot of questions that take place over several hours to try to understand which functions in your brain are not performing well, and then depending on what we find, we can also #! - use some types of medications and also refer you to a cognitive rehabilitation program and for moderate-to-severe cases, we tend to do that, and there are some good results there. But again, it is difficult to determine if they are working or it could be just time passing by and your brain recovering.

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Chagpar Yeah. But still something for people to think about if they are having symptoms is to go and see a specialist, a neuro-oncologist or somebody who might be able to get you into a cognitive rehab program, kind of training your brain just like you train your body after you might have gone through some physical stress.

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Omuro Absolutely, and I think it comes down to discuss directly with your doctor quality of life issues because we are worried about the cancer treatment itself and the cancer itself and we forget about those things that are actually very important in our day-to-day lives.

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Chagpar Yeah. And it is important to think about the symptoms that you might be having because they may not be just from cancer treatment. I think that people, you know, people who have cancers in other parts of their body need to also think when you start having things like headaches or blurry vision or trouble speaking or difficulty in kind of getting the right words out just like I did for half a second there, you might be, you know, you need to kind of be thinking about talking to your doctor about could this be a cancer that metastasized to the brain because many cancers do go to the brain?

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Omuro Absolutely. That's something that we are seeing more and more in fact. As patients survive longer periods of time, they are exposed to the risk of having a brain metastasis for longer periods of time. So, we are seeing more and more brain metastasis as a growing problem.

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Chagpar And so, if somebody does have a brain metastasis, let's say they had a breast cancer or colon cancer or lung cancer, I guess I have a couple of questions. The first is, why do cancers like to go to the brain and the second is, what can you do about it if it does go to the brain?

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Omuro Right. In the case of metastasis, one of the reasons that we keep researching to try to understand why they are becoming so common is the fact that the brain is protected by what we call the blood brain barrier, which means that chemotherapies and many anti-cancer treatments do not get into the brain well. So, this is because nature is very wise and the brain is protected from toxic things that are in our blood, but in that case, the toxic thing is actually a treatment. And the brain is left behind and that is sometimes how we see more and more metastasis and people with brain metastasis developing even though their primary tumors are well controlled.

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Chagpar But that's the question right? Like, if the brain is protected by the blood brain barrier and we have all been told that, and we get the fact that medicines do not get to the brain because of the blood brain barrier, my question is, so how come the cancer gets into the brain? I mean, the brain is one of the favorite spots for a lot of cancers to go, how come the blood brain barrier cannot keep the toxic thing called cancer out of the brain?

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Omuro You know, unfortunately, tumor cells are also very smart just like nature, they are meant to survive, so these are cells that learn how to insert themselves in between the vascular structures and to reach what we call the brain parenchyma.

So, the cancers have many mechanisms to invade the brain, and unfortunately once they invade, they are protected.

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Chagpar Yeah. And I suppose you know your blood flow does go to your brain and so cancer cells can get lodged there but it would be nice if that blood brain barrier could keep out cancers just like it can keep out some of our drugs?

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Omuro Yeah, it probably does to some extent. Brain metastasis are not as common as many other metastasis.

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Chagpar True enough. So, let us suppose somebody comes to you and they have got a brain metastasis. One of things you had said at the outset is that neuro-oncology really looks at people who have brain tumors whether it started in the brain or it came to the brain from someplace else, so if somebody has a brain metastasis and they present to you, what are kind of things that you can do given the fact that now this cancer is kind of metastasized? You know, as a surgeon, I like cancers that are in a given spot. I do breast cancer as many of our listeners know and love the idea that as a surgeon, I can take that cancer out of the breast and render people cancer free, which I can do most of the time except when it is spread all over the body. So, what can you do as a neuro-oncologist to help that patient with brain metastasis? Is there a way to control that disease, to you know minimize that?

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Omuro Well, there are many aspects to the treatment of brain metastasis. So, the first good news is that the treatments are getting better and better. So, you can start with resection. As a surgeon, you appreciate that especially in the brain, this would be helpful when it is causing compression of brain structures that are vital for functioning. So, that is a way to start if the surgery can be done safely. And then, typically, we also look into what we call radiosurgery techniques on top of taking out the tumor, treat any cells left with some radiation. And of course, that is helpful in limited number of metastasis, but if there is a lot of metastasis, we can use radiation to the whole brain. There are new techniques to do that in a way that you can protect, and then there is also more and more thoughts about how to use better anti-cancer treatments, better chemotherapies to get into the brain or immunotherapy. There are many other options that are helping us to control brain metastasis, especially if they happen in the setting of a patient that has disease control elsewhere.

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Chagpar Okay. Well, we have to take a short break for a medical minute, but right after the break, we will talk a lot more about how to control brain

metastasis with radiation, surgery, and medical oncology as well as treatment of primary brain tumors. Stay tuned.

14:48.300 --> 15:04.800 Medical Minute Support for Yale Cancer Answers comes from AstraZeneca, a global science-led biopharmaceutical business committed to bringing to market innovative oncology medicines that address unmet needs for people living with cancer. More at astrazeneca-us.com. 15:04.800 --> 15:48.500 This is a medical minute about head and neck cancer. Although the percentage of oral and head and neck cancer patients in the United States is only about 5% of all diagnosed cancers, there are challenging side effects associated with these types of cancers and their treatment. Clinical trials are currently underway to test innovative new treatments for head and neck cancers, and in many cases, less radical surgeries are able to preserve nerves, arteries and muscles in the neck, enabling patients to move, speak, breathe and eat normally after surgery. More information is available at YaleCancerCenter.org. You are listening to Connecticut Public Radio. 15:48.500 --> 17:20.200

Chagpar This is Dr. Anees Chagpar and I am joined tonight by my guest, Dr. Antonio Omuro. We are talking about brain tumor treatment and care. And before the break, we were talking about the fact that sometimes people who have cancer in other parts of their body -- breast cancer, lung cancer, colon cancer, you name it cancer, sometimes those cancers can evade the blood brain barrier and end up creating metastasis or little deposits in the brain and you were saying, Dr. Omuro, that there are variety of ways of treating that - whether it is surgery, sometimes we can use targeted radiation with what is called radiosurgery or whole brain radiation if there are many metastases and also using drugs, although the blood brain barrier can sometimes be an issue. Now, you had also mentioned that you treat primary brain tumors, which start in the brain and that neuro-oncology is a branch, a sub-specialization really of medical oncology and neurology, so tell me more about the medical oncology part, both for primary tumors as well as for metastatic tumors, how do we get drugs into the brain to treat these and do we use the same drugs for say a breast cancer that metastasized to the brain as a primary brain cancer?

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Omuro Right. So, in terms of brain metastasis, what we do is to work with the medical oncologist to select the best treatment that could also address the brain metastasis. Of course, again, the main tools to treat these tumors are based on radiation, but sometimes they can benefit from chemotherapy that is a little more penetrant into the brain or some more intensive regimens or the addition of immunotherapy that we are using more and more also to treat brain metastasis.

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Chagpar So, immunotherapy can cross the blood brain barrier?

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Omuro Yes, because one good thing is that immunotherapies basically act on lymphocytes, which is an immune cell and then those lymphocytes can go into the brain. So, the target is in the lymphocytes. So, they can go into the brain and fight the tumor. And in fact, we are seeing more and more that brain metastasis in clinical trials of immunotherapy, they tend to respond at the same rate as the original tumors. So, that is something that is very encouraging because also helps us to direct our new treatments for primary brain tumors, which is a whole new problem that still remains a big unmet clinical need.

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Chagpar Yeah because as we have kind of talked about sometimes on this show, there are some tumors which are more immunogenic, which are more susceptible to immunotherapies and others that are not. So, certainly, if you have a brain metastasis of say a melanoma, which is one that we use a lot of immunotherapy for, that might be an option. How immunogenic or how susceptible to immunotherapy are primary brain tumors?

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Omuro Right. Unfortunately, brain tumors, especially primary brain tumors and in this case the most common one is gliomas or glioblastomas, so these tumors are what we call very cold from an immunologic standpoint. So, they do not have a lot of those mutations that wake up the immune system. So, that is definitely one of the challenges that we are doing. But we are seeing more and more, we are devising ways to spark those tumors that do have some increase in the number of mutations, which would be the best candidates for immunotherapy. So, we are kind of selecting the patients for those treatment. Across the board, it is really not a helpful treatment at this time. I think there are also other issues which have to deal with how the brain tumors evade the immune system that can be different from evading the immune system in the body. The brain has its own ways of dealing with immunologic issues, and that is something that we are trying to understand and we have several clinical trials trying different agents - meaning that these are different agents as compared to agents that are being used to treat cancer in general.

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Chagpar So, tell me more about that. Tell me more about what is new and interesting in terms of clinical trials and where the field of neuro-oncology is going for primary brain cancer? Because I am sure that any of our listeners who are listening, who either have a brain cancer or know somebody who does, I mean that is a very scary diagnosis, and when you think that not a lot of chemotherapy agents kind of pass the blood brain barrier, that these may be in areas that may or may not be resectable given where it is in the brain and nobody really wants to lose a lot of brain tissue and you are dealing with really delicate structures. Where are we in terms of moving the field forward?

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Omuro Right. So, I think brain tumors, primary brain tumors are traditionally seen as very difficult to treat, but I think we are turning the page and there is a lot of reason for hope there. We have so many clinical trials ongoing as we speak and we are trying all sorts of things. So, here at Yale, we are developing new immunotherapies, we are developing nanotechnology to make these drugs get into the brain.

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Chagpar Tell me more about that. What do you mean by nanotechnology?

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Omuro So, one of the issues of course is the blood brain barrier as we just discussed, and we are learning that producing certain types of nanoparticles that could actually carry the drugs into the tumor or into the brain can be a helpful way to improve the efficacy of these drugs.

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Chagpar So, little particles that can kind of sneak in between the little holes in the blood brain barrier carrying their drugs with them and getting through the blood brain barrier to the cancer in the brain?

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Omuro Right, right. This is a very exciting new way of addressing these tumors and dealing with the issues of blood brain barrier. We are also trying other what we call vectors, which means ways of bringing things into the brain to treat the tumors and one of the things that we are using is actually viruses. We have one investigator that actually has been working with all sorts of virus, even Ebola which gets me a little nervous when I talk to him.

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Chagpar Yeah. I am sure it is getting everybody on the audience a little nervous too.

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Omuro Right. But he knows what he is doing and he is discovering certain types of viruses that could be used to attack tumor cells and also wake up the immune system. So, there is a lot of research ongoing that area as well.

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Chagpar So, let's talk a little bit about that. I mean, certainly people have talked about viruses and cancer, but most commonly we talk about viruses causing cancer - we talk about HPV for example or HIV-induced cancer, and here you are really talking about a virus that you are kind of using as I understand it kind of like a Trojan horse to go and attack a cancer. How do you know that that is not going to also cause the disease that the virus is known for, like Ebola for example?

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Omuro Right, right. No, usually these viruses are heavily manipulated to ensure that the properties that they originally had that caused disease are actually mitigated or eliminated. So, that is something very well established and is a very safe procedure, and in fact, we have several types of viruses that are in clinical trials and the safety data of those trials has been very favorable. Now, what we are more interested on is whether they really work and deliver on the task of attacking the tumor cells and awakening the immune system.

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Chagpar And so, do we have data on that?

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Omuro We have very early phase I data and I think that is an ongoing project we have now. I think we are learning how to produce better vectors and more effective because you can imagine that we want these viruses to only go to the tumor cells and that is something that is not so easy to do, but the enormous advancements that we are seeing in the genomics and the understanding of microbiology of these viruses, we are getting to a point where we can get much better vectors to deliver more effective and safe treatment.

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Chagpar And so, if somebody presents with a primary brain tumor to you today, aside from surgery and radiation, what kinds of medicines are they being offered as standard of care and how do you decide between all of these clinical trials that we have talked about whether it is nanoparticles or viruses or other things, what you are going to offer in terms of systemic therapy?

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Omuro Right. So, I think at this point in time, unfortunately the mainstay of treatment is still a treatment that was developed almost 30 years which is basically radiation and chemotherapy - temozolomide. So, I am talking about gliomas. Unfortunately, there is not much in terms of standard of care as to speak, but a lot of patients do choose the clinical trial route in an attempt to get new developments earlier. I think that is the reason why people do enroll in clinical trials. And of course, there is a lot of patients giving their efforts and time to science because they do understand that if they enroll in clinical trial, the clinical trial may not work but at least we will understand more and more about the disease at the very minimum, and again, the clinical trials are getting more and more advanced and smarter, so we tend to enroll patients that are more likely to benefit for a given treatment, so we select the patients from the beginning, and I think nowadays it is very important to have a comprehensive genomic analysis to see if there is any actionable drug that we can address either in a clinical trial or in a so-called off-label use of medications that are out there, and that is something that here at Yale we do routinely, we do a very advanced

whole-exome sequencing in all of the patients and that is a very helpful tool to down the road guide us on choosing clinical trials and matching the patients with the best treatments.

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Chagpar So, really a personalized approach to treating these brain tumors?

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Omuro Yes, that is the way to go. That is very promising, but it also brings a lot of challenges because you can imagine that each of these mutations or abnormalities at the molecular level are relatively rare, so it is hard to run trials when there is so few patients that are alike. So, that becomes a problem with enrollment and selection of patients, but we are getting again better and better and the more we know about these patients, the faster the trials are run.

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Chagpar And so, with all of the clinical trials and with the genomic sequencing and with the personalized medicine and all of that, are we actually getting better in terms of patient survival? Like, what was the 5-year survival of brain tumors, primary brain tumors 30 years ago when you said that we were starting with radiation and temozolomide, and what is their survival now, like have we actually made a dent?

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Omuro So, in fact, if you look trans, overall, the good news is that patients are surviving longer. Even though the treatment is about the same, the way they are delivered is improving and the way we handle complications is improving, there are improvements in surgery and in radiation and also there are some options for when the tumor comes back in spite of the treatment. So, I think we are making progress but still as compared to other cancers, there is a long way to go.

28:55.000 --> Dr. Antonio Omuro is Chief of Neuro-Oncology at the Yale School of Medicine, where he is also the Clinical Program Leader of the Brain Tumor Program. If you have questions, the address is canceranswers@yale.edu and past editions of the program are available in audio and written form at YaleCancer-Center.org. I am Bruce Barber reminding you to tune in each week to learn more about the fight against cancer here on Connecticut Public Radio.