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00:00:00.076 --> 00:00:21.730 Announcer Funding for Yale Cancer Answers is provided by Smilow Cancer Hospital. Welcome to Yale Cancer Answers with the director of the Yale Cancer Center, Doctor Eric Winer. Yale Cancer Answers features conversations with oncologists and specialists who are on the forefront of the battle to fight cancer. Here's Doctor Winer.

00:00:21.807 --> 00:00:55.769 Eric Winer Today we're going to talk about pancreatic cancer. We're actually going to talk about both adenocarcinoma of the pancreas. And we're going to talk about neuroendocrine tumors that arise in the pancreas. Joining us is Doctor Pamela Kunz who is a professor of medicine at the Yale School of Medicine and director of the center for Gastrointestinal Cancers at Smilow of Cancer Hospital and chief of the Division of GI Medical Oncology within the Cancer Center.

00:00:55.846 --> 00:01:16.884 Eric Winer As you can imagine, Pam is an expert in GI malignancies, and she herself particularly focuses on these neuroendocrine tumors. We have some advances related to other types of pancreatic cancer, and we want to touch on that first. So first Pam, welcome to Yale Cancer Answers. Thank you so much for for joining me.

00:01:17.000 --> 00:01:18.884 Pamela Kunz Hi, Eric. My pleasure. Thanks.

00:01:19.076 --> 00:01:45.884 Eric Winer This year for the first time in a long time, people and doctors who care for people with pancreatic cancer literally stood up and cheered. And tell us a little bit about what that's about and maybe a little bit about what the what the feeling was in the room when these data were presented.

00:01:46.115 --> 00:02:14.192 Pamela Kunz Yeah, sure. Happy to. This is a big deal. So what Eric is referencing is our annual American Society of Clinical Oncology annual meeting that takes place in Chicago every year. And this is the meeting where the big news comes out about new clinical trials and new advances in oncology. And there are sessions called plenary sessions, where really the I would say the biggest news gets presented.

00:02:14.192 --> 00:02:43.384 Pamela Kunz And it's often kept pretty secret up until right around that time. And so there was a big clinical trial for pancreatic adenocarcinoma that took patients, and half of them got a new medicine that will talk about it's called...I even have a hard time saying it Eric, daraxonrasib, and so if our listeners think that these are hard to say, oncologists even have a hard time saying them.

00:02:43.384 --> 00:03:11.038 Pamela Kunz And it took half the patients who got daraxonrasib and half the patients got regular chemotherapy and the punchline and I can get into the details if you're interested, but the daraxonrasib did better than standard chemotherapy. And this medication is something called a RAS inhibitor. And over 90% of patients with pancreatic adenocarcinoma have a mutation in Kras.

00:03:11.115 --> 00:03:37.576 Pamela Kunz And this was once upon a time thought to be meaning we couldn't target this mutation. And so this was a big deal. And what Eric just mentioned is this presentation by Doctor Brian Wolfson, who's a medical oncologist at Dana-Farber, got a standing ovation from thousands of oncologists. And this does not happen routinely at big scientific meetings. So a huge deal in the GI and college community.

00:03:37.615 --> 00:04:01.115 Eric Winer KRas which is mutated in pancreatic cancer, is a driver of pancreatic cancer. So the mutation itself leads to the ability of the cancer to grow unchecked and really is very much related to the whole lethality of pancreatic cancer.

00:04:01.153 --> 00:04:34.230 Pamela Kunz That's it. That's exactly right. It's something called an oncogene. And in this particular instance, the mutation turns that on. It's sort of like a constant green light. And it is mutated in several other cancers. And I think that this is really just the beginning of being able to target that particular mutation. And so patients had a doubling of their overall survival from about seven months to a little over 13 months.

00:04:34.230 --> 00:05:03.346 Pamela Kunz And this is really a big deal. And I'm really hopeful. I think many, many of us who treat GI cancers and pancreatic adenocarcinoma in particular, have been really waiting for a big breakthrough like this. I think that this will immediately, hopefully help our patients, and I'm really excited to see the direction that future trials will take, incorporating this both in pancreatic adenocarcinoma and other cancers.

00:05:03.346 --> 00:05:28.269 Eric Winer Yeah. And of course, going from 7 to 13 months doesn't mean that everyone lives seven months with with chemotherapy and everyone lives 13 months with the ras inhibitor. That's that's just the median. And so there are people who unfortunately don't do as well, but there are also half of the people who do better than that, some much, much better than that.

00:05:28.346 --> 00:05:57.730 Eric Winer So it's really important, you know, this whole idea of mutations turning certain pathways on and off is a little confusing. It's confusing for patients, is also confusing for doctors because, for example, there's another gene called p53 and it's loss of p53. That's important. And that makes a cell susceptible to become a variety of different cancers.

00:05:57.807 --> 00:06:27.269 Pamela Kunz Yeah. That's right. And I think that this is a really nice example of just broadly the direction oncology has gone in the last decade, where I'm sure our listeners have heard of personalized medicine or personalized oncology. And it's a way of nowadays, we will test the genetics of the cancer and determine if there are genes that are mutated or changed and ones that maybe have changes that are susceptible to certain medications.

00:06:27.269 --> 00:06:41.615 Pamela Kunz And I think lung cancer is really a wonderful example of this. They've certainly taken advantage of this in pancre-

atic cancer to date, had no targeted therapies available. And so this is really the first targeted therapy in pancreatic cancer.

00:06:41.807 --> 00:07:12.846 Eric Winer No, it's it's really great. And it so happens that it's a targeted therapy that is applicable to a large number of patients with with pancreatic cancer. You know, this also brings up the topic of the difference between somatic and germline mutations. Germline mutations arise in all of the cells in someone's body. You're born with a germline mutation, such as a mutation for BRCA one or BRCA two, where there's a very high risk.

00:07:13.000 --> 00:07:36.615 Eric Winer If you have that mutation of developing breast cancer or ovarian cancer, or actually with BRCA two pancreatic cancer over the course of your lifetime. The Kras is instead a somatic mutation, meaning it's found in the genome of the cancer itself, but not in the genome of the rest of the person. Is that correct?

00:07:36.653 --> 00:07:59.461 Pamela Kunz That's that's exactly right. And I think that can be very confusing. I absolutely try to make that distinction when talking with patients about genetics. It's sort of the genetics of those cells in your whole body. There are passed from parent to child, and then they're the genetics of the cells of the cancer. And absolutely we try to it's very routine to test both of those for the germline mutations.

00:07:59.461 --> 00:08:11.423 Pamela Kunz There's certain indications. But pancreatic adenocarcinoma is one of those that we test all patients for the germline mutations. And now we will also be testing routinely for the somatic mutations.

00:08:11.461 --> 00:08:37.346 Eric Winer I often say to patients that all cancers are associated with the change in genes, but not all cancers are inherited. And it's the minority that are truly inherited, although there may be a predisposition. But for a cancer to be a cancer, it's genetic. Makeup is different from the surrounding cells. So what do you think the next step will be?

00:08:37.346 --> 00:08:57.615 Eric Winer Because of course, you know, everyone stood up and cheered and there was a doubling of overall survival. But we're still talking about a median survival from the beginning of this second line therapy of 13 months. So we got to do more. And what do you think? What do you think will be next?

00:08:57.730 --> 00:09:17.461 Pamela Kunz Well, that's a great question. You know, I would say that just to talk a little bit about the process of drug development, we often will test new drugs in later lines of therapy in patients who have metastatic cancers. Once they are proven to be both safe and effective, we often start moving it up earlier in lines of therapy.

00:09:17.461 --> 00:09:40.153 Pamela Kunz So I would hope to see clinical trials looking at can we use this in the first line, or can we be using it pre-operative in patients who have locally advanced disease or disease. So I would expect to

see trials that are looking at it in different lines of therapy we want to use. And this has happened in the past for several of our other therapies.

00:09:40.192 --> 00:09:46.807 Pamela Kunz So I think that and then the other question will be, can we combine it with other therapies to make it more effective?

00:09:46.884 --> 00:10:26.846 Eric Winer Yeah. No, I think that that's likely to happen. And of course, within the world of drug development, you can be sure that there are scientists and drug companies that are trying to come up with a better Kras inhibitor. That's one that is both more effective and works for longer, and also potentially Kras inhibitors that are less toxic. So tell us a little bit about the side effects, because unfortunately targeted therapies, which you think are just going after the target and not going after anything else, still sometimes have plenty of side effects.

00:10:26.884 --> 00:10:52.615 Pamela Kunz Yeah, absolutely. So the most common side effects with daraxonrasib. So this particular drug that was studied in pancreatic cancer were rash and mouth sores. Now those were the most common. However these types of medications will have several other side effects, often like fatigue sometimes lowering of blood counts. But in this particular case again rash was the most common.

00:10:52.615 --> 00:11:20.884 Pamela Kunz And you know, I want to just mention that I think sometimes several of our side effects are often not visible to the outside world. And I think that sometimes when we have side effects that are more visible, that can often be very hard for our patients. So rashes can be tricky to manage. We, like many institutions, have partnerships with a dermato-oncology expert, and these are really critical partnerships and helping to manage some of these side effects.

00:11:21.000 --> 00:11:28.576 Eric Winer You know, I think some people hear rash and they figure, oh, rash, I can deal with a rash. It's not such a big deal. But rashes can really make you miserable.

00:11:28.615 --> 00:11:29.307 Pamela Kunz Exactly.

00:11:29.346 --> 00:11:44.269 Eric Winer Yeah. Is it your sense that people were able to continue with their usual activities, that those who worked could keep working, that those who were who had other activities they were pursuing could pursue them?

00:11:44.384 --> 00:12:15.115 Pamela Kunz Yes, yes, that is my understanding. We were I did not in participate in the trial myself, but I think in both hearing the results and sort of reading through some of the details, that's my understanding. So there were very few patients who discontinued the medication based on side effects. And I think that's a really important takeaway. The large majority of patients, in fact, more patients on the daraxonrasib actually continued the full course of treatment compared to even chemotherapy.

00:12:15.115 --> 00:12:27.615 Pamela Kunz And so it's pretty routine in cancer treatments that we have to perhaps modify treatments based on side effects. But actually the daraxonrasib had very few discontinuation and dose changes.

00:12:27.692 --> 00:12:31.192 Eric Winer And is there going to be an easier name at some point?

00:12:31.269 --> 00:12:32.769 Pamela Kunz I hope so.

00:12:32.846 --> 00:12:36.115 Eric Winer They haven't they haven't released it yet though. Is that correct?

00:12:36.153 --> 00:12:48.038 Pamela Kunz Not. Yes. I have not heard of that yet. And actually, Eric, it might be worth just mentioning. I think we get asked all the time, how can I get access to this, this and you. Maybe we're going to ask about that, but I'll just.

00:12:48.076 --> 00:12:48.807 Speaker 4 I was about to ask.

00:12:48.846 --> 00:13:13.076 Pamela Kunz Okay. All right. Perfect. So it is complicated. So in the period of time where we wait for the FDA to make a decision, sometimes companies will offer something called an expanded access program. This is happening with the particular company that is offering this, but it is through officially. It's almost like a clinical trial, but it is a much easier.

00:13:13.076 --> 00:13:24.769 Pamela Kunz So that is something that actually I've just heard from the director of our GI clinical research team, Doctor Michael Cecchini, that we actually hope to have that open the next couple of weeks.

00:13:24.807 --> 00:13:54.615 Eric Winer That's great. And presumably this will get fast tracked at the FDA and it'll be approved quite soon. But it's important with something this remarkable, that it became available to patients even before the FDA approves it. All right. Well, we're going to have to take a just brief break. And when we come back, we will talk just a little bit more about this new finding and then move on and talk about neuroendocrine tumors.

00:13:54.653 --> 00:14:05.230 Eric Winer Again, I'm with my guest, doctor Pamela Kunz, director of GI cancers at Smilow Cancer Hospital and Yale School of Medicine.

00:14:05.307 --> 00:14:25.230 Announcer Funding for Yale Cancer Answers comes from Smilow Cancer Hospital, where the early onset cancer program provides care and support for patients from 18 to 45 years old. Their mission is to reduce the burden of cancer and improve patients quality of life. Smilow-CancerHospital.org.

00:14:25.307 --> 00:14:47.192 Announcer Genetic testing can be useful for people with certain types of cancer that seem to run in their families. Genetic counseling is a process that includes collecting a detailed personal and family history, a risk assessment, and a discussion of genetic testing options. Only about 5

to 10% of all cancers are inherited, and genetic testing is not recommended for everyone.

00:14:47.307 --> 00:15:20.269 Announcer Individuals who have a personal and or family history that includes cancer at unusually early ages. Multiple relatives on the same side of the family with the same cancer. More than one diagnosis of cancer in the same individual. Rare cancers or family history of a known altered cancer predisposing gene could be candidates for genetic testing. Resources for genetic counseling and testing are available at federally designated comprehensive cancer center, such as Yale Cancer Center and Smilow Cancer Hospital.

00:15:20.307 --> 00:15:27.000 Announcer More information is available at YaleCancerCenter.org. You're listening to Connecticut Public Radio.

00:15:27.076 --> 00:16:12.653 Eric Winer Welcome back to the second half of Yale Cancer Answers. I'm Eric Winer and I'm here with my guest, doctor Pamela Kunz, who is a GI oncologist and directs our GI oncology program. We've been talking about this new drug recently demonstrated to be far better than than chemotherapy and which will be available in the next few weeks on through expanded access and then will be commercially available, probably within, I would imagine, several months before we move on to another topic, let me just ask you, what's your sense or what's been your experience with patient reactions to this finding?

00:16:12.769 --> 00:16:39.461 Pamela Kunz I think there's a lot of enthusiasm. You know, this is a space where we have not had a lot of wins and we haven't had wins in a long time. Eric. And I think that it's really through the advances of clinical trials and the importance of patients participating in clinical trials that have really led us to this and just broad enthusiasm.

00:16:39.461 --> 00:17:02.807 Pamela Kunz I think a lot of hope, which is, you know, really important for all of us, both patients and physicians. I think patients are really eager to try to get the medicine for themselves or family or friends, and we're really working hard on that. And I believe, I think, as we've said earlier, that this will become available through an expanded access program and hopefully soon through the FDA.

00:17:02.807 --> 00:17:23.807 Pamela Kunz But lots of enthusiasm and hope, and I, I know, Eric, you and I have talked about this before, but as even I've just finished my clinic today and as I'm talking with patients about even days that are difficult, I really want to try to balance, you know, hope and reality. And I think what keeps me going are the advances in clinical trials.

00:17:24.038 --> 00:17:52.384 Eric Winer At the risk of getting up on my soapbox, I just want to point out that drugs like this come from years of research, years of research that start in basic science laboratories eventually are picked up, sometimes by the pharmaceutical industry, sometimes by other researchers in academia, and ultimately become drugs that are tested in human beings like

this one.

00:17:52.423 --> 00:18:41.192 Eric Winer And it's why federal grants to support cancer research are so very critical. And without research, we don't make progress. And at this moment in our country's history, where there seems to be some anti-science sentiment, I think it's so important to recognize the importance of science and the importance of funding for science. So let's move on and talk about what you actually specialize in, which are neuroendocrine tumors which arise in many different parts of the body and even outside of the GI tract, but are most commonly seen somewhere in the abdomen, if I'm correct.

00:18:41.230 --> 00:18:42.115 Pamela Kunz That's right.

00:18:42.153 --> 00:18:44.576 Eric Winer Why don't you tell us a little bit about these tumors?

00:18:44.769 --> 00:19:12.000 Pamela Kunz Sure. Well, I'm happy to maybe put it in the context of a pancreatic tumor, too. So. So we were just talking about pancreatic adenocarcinoma, and that is really over 90% of all pancreatic tumors. About 5 to 10% of pancreatic tumors are other kinds of cancer. And we can tell that based on what the cells look like under the microscope, some of those are neuroendocrine tumors.

00:19:12.192 --> 00:19:37.461 Pamela Kunz They get their name neuroendocrine because some of them, about 30 to 40% of them, can secrete funny hormones that can cause symptoms in and of themselves. The pancreas is comprised of really two main cell types and exocrine cell and an endocrine cell. And so the exocrine cells are where the pancreatic adenocarcinoma is derived and the endocrine cells are where the neuroendocrine tumors are derived.

00:19:37.461 --> 00:19:46.653 Eric Winer And can I just ask you those exocrine cells are the cells that produce enzymes that help us digest food.

00:19:46.692 --> 00:20:11.038 Pamela Kunz That's right. Yeah. And so I think, you know, hopefully our listeners, it's one really nice example of even within an organ we have different cancer types. And therefore we have to tailor our treatments very differently based on that cancer type. And that's why one size does not fit all for all cancers. They're very unique and have very different kind of genetic changes and therefore respond differently to treatment.

00:20:11.038 --> 00:20:36.076 Pamela Kunz So so neuroendocrine tumors, as Eric said, can originate in almost any part of the body. But the pancreas and the small intestine are the two most common places, the less common cancers. So there are fewer people that are expert in this. And we have a great program here at Yale. It's very multidisciplinary. It requires input from medical oncologists and surgeons and endocrinologists.

00:20:36.076 --> 00:21:01.230 Pamela Kunz And maybe I'll give an example of a relatively new area of therapy, Eric, if I can in it's it's not so new anymore, but there's a sort of idea or a field called Serrano. And it's really combining

this idea that you can target sort of a certain receptor on the surface of a cell, you can image it and you can treat the same receptor.

00:21:01.230 --> 00:21:30.500 Pamela Kunz And we now have treatments in that space for neuroendocrine tumors and also prostate cancer. And so by being able to treat what you can see with a special type of Pet scan, that really helps us target the therapy. And so for neuroendocrine tumors that therapy is called lutetium doda Tate or Luna. And it's a form of IV radiation that targets a receptor on the surface of the cell called a receptor.

00:21:30.538 --> 00:22:00.038 Pamela Kunz Think of it like a flag. And that flag or receptor. When treated with radiation, it sort of treats those cells very directly. So it's targeted radiation. And that therapy, the the treatment course is for doses. And that therapy has really been a game changer in neuroendocrine tumors. And then it kind of went beyond that. And there's an approved therapy called lutetium psma or victor for prostate cancer.

00:22:00.038 --> 00:22:17.884 Pamela Kunz And there are sort of new and improved versions of that that are being studied in clinical trials with different radioisotopes and different kind of protein compounds. So this has been a really exciting field, and one that we've been contributing to in clinical trials.

00:22:17.884 --> 00:22:22.884 Eric Winer And how often are those four doses given over what period of time.

00:22:22.884 --> 00:22:44.807 Pamela Kunz So each dose is given. It's sort of every two months for four doses. So it takes about eight months to give a full treatment course. It's actually very well tolerated in terms of side effects. I will often describe to patients that this particular treatment kind of hits the sweet spot, where it's one of our most effective treatments, but it's also one of our best tolerated treatments.

00:22:44.807 --> 00:22:48.076 Eric Winer And do patients become radioactive?

00:22:48.153 --> 00:23:14.423 Pamela Kunz That's it. So the short answer is yes. It's actually a very low dose of radiation. It is cleared through the kidneys and into the urine. And so we give patients special precautions, really mostly around toileting and bathroom use for three days following the infusion, where they have to do special precautions and can't sleep with a partner for three days, have to use.

00:23:14.423 --> 00:23:27.192 Pamela Kunz We recommend that they use a private bathroom for three days. But again, it is mostly us being extra conservative with those precautions and it poses very little risk to families and to the general public.

00:23:27.269 --> 00:23:36.230 Eric Winer So is this a little bit like an antibody drug conjugate, which is an antibody linked to a little bit of chemotherapy?

00:23:36.269 --> 00:23:37.192 Pamela Kunz It is.

00:23:37.230 --> 00:23:40.307 Eric Winer In this case it's linked to a little bit of radiation.

00:23:40.307 --> 00:24:06.730 Pamela Kunz That's exactly right. And so this is another really nice example of personalized or precision oncology, where we are using a target that we know that patient has unlike. So some of the antibody drug conjugates which maybe target a genetic mutation a kind of a known antibody. This is targeting something that we can image with a special Pet scan called the gallium 68 Pet scan.

00:24:06.730 --> 00:24:17.769 Pamela Kunz And but yeah, broadly these are all targeting unique markers on the surface of the cancer cell, which allows us to be very tailored for that patient.

00:24:17.884 --> 00:24:29.730 Eric Winer Now these neuroendocrine pancreatic cancer do differ from adenocarcinoma of the pancreas in that typically they're associated with a much longer survival.

00:24:29.807 --> 00:24:55.692 Pamela Kunz That's exactly right. So it's still often for patients especially if they have metastatic disease this may end their life sooner. But on average patients with a metastatic pancreatic or consumer may live 5 to 8 years. And so it is definitely longer. We still have work to do to make that even longer than it is, but this tends to be a much slower growing cancer.

00:24:55.692 --> 00:25:21.076 Pamela Kunz And when diagnosed, we will tell patients we anticipate that they will have years to live. And it's really a matter of kind of sequencing several therapies together to hopefully help control the cancer. And Eric, I know that, you know, several cancers, even breast cancer, were starting to think about how can we make cancers chronic and how can we turn them into more of a chronic disease that we can control.

00:25:21.076 --> 00:25:28.692 Pamela Kunz And I think that the field of neurotic and tumors is we've been trying to talk about it in those terms for a long time.

00:25:28.730 --> 00:25:53.000 Eric Winer One of the nice things, being a doctor, taking care of patients who have these cancers, that that really do become chronic problems as you get to know patients very well over the course of many years, sometimes decades. And that's the case with neuroendocrine tumors as well. You have patients who live with this for really decades.

00:25:53.076 --> 00:26:12.807 Pamela Kunz That's absolutely right. Even with metastatic disease, you know, it's honestly such a gift. I it is a real treat to be able to kind of be on a journey with a patient for several years and, you know, be with them when they have grandchildren born and kids get married, and we get to know them and they get to know us.

00:26:12.807 --> 00:26:17.038 Pamela Kunz And that is really, I think, incredibly rewarding.

00:26:17.038 --> 00:26:17.807 What about.

00:26:17.807 --> 00:26:24.500 Eric Winer Drug trials for patients with neuroendocrine tumors? What are the what are the new treatments that you're most excited about?

00:26:24.538 --> 00:26:51.115 Pamela Kunz Yeah. So you mentioned antibody drug conjugates. So we have a perfect target for consumers this somatostatin receptor. So finally we're looking at other ways of targeting it. So we have something that's called a non peptide drug conjugate. So it's a small molecule linked with a small dose of chemotherapy that targets the somatostatin receptor. So we have that trial open and it's in early phases.

00:26:51.115 --> 00:27:20.000 Pamela Kunz So it's a phase one trial which means we're testing safety and doses before it goes into a phase two trial that Im excited about. I'm also really excited about kind of newer ways to either improve delivery of these radio ligand therapies. This is that radiation that I just talked about, the Luna Thera. So there are new radioisotopes that deliver the radiation in slightly different ways.

00:27:20.038 --> 00:27:44.346 Pamela Kunz There are also slightly different compounds that may actually make them safer. Right now there's a lot of exposure to the kidneys. And so patients have to receive a four hour kind of hydrogen special hydration of amino acids to flush their kidneys. And there are newer compounds being developed that may allow us to avoid that. So that is a really hot space right now.

00:27:44.384 --> 00:27:47.653 Pamela Kunz So lots of really cool trials that are happening.

00:27:47.653 --> 00:28:19.423 Eric Winer Well, you know, this all sounds very promising. And for diseases that used to be uniformly fatal and associated with the short survival, it seems like we're making progress. And that that very much is, I think, going to be true of of standard pancreatic adenocarcinoma. I don't know what standard means, but typical pancreatic adenocarcinoma. And we're also excited about what has transpired there.

00:28:19.423 --> 00:28:38.500 Eric Winer So Pam, thank you so much for joining me tonight. It's been a true pleasure to our listeners. I've been speaking with Doctor Pamela Kunz, professor of medicine at Yale School of Medicine, who directs our GI oncology program. See you all next week.

00:28:38.538 --> 00:28:57.769 Announcer If you have questions. The addresses CancerAnswers@Yale.edu and past editions of the program are available in audio and written form at Yale CancerCenter org. We hope you'll join us next time to learn more about the fight against cancer. Funding for Yale Cancer Answers is provided by Smilow Cancer Hospital.