00;00;00;02 - 00;00;27;27 Funding for Yale Cancer Answers is provided by Smilow Cancer Hospital. Welcome to Yale Cancer Answers with 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.

00;00;28;24 - 00;01;08;24 Dr. Winer I just spent the last week in Chicago at the American Society of Clinical Oncology. This is the largest oncology meeting anywhere in the world. There are over 50,000 members of ASCO. Again, the American Society of Clinical Oncology, and there were about 40,000 people at the annual meeting. To put it simply, it's a bit of a zoo, but it's a zoo where there are all sorts of exciting scientific findings presented new treatments.

00;01;09;07 - 00;01;51;10 And while many years ago it was common for us to go to the meeting and hear one new finding across all of cancer in 2025, where generally there is expecting to hear two or three or four new treatment approaches in virtually every type of cancer. Joining us in our show tonight to help explain what ASCO is and to then talk about clinical trials in cancer is Dr. Ian Krop, Chief Clinical Research Officer at the Yale Cancer Center and director of the YCC Clinical Trials Office.

00;01;51;21 - 00;02;28;19 I might add Dr. Krop is also a world renowned breast cancer medical oncologist, and welcome to Yale Cancer Answers. Dr. Krop Thank you, Eric. Thanks for having me. It's a pleasure.

Dr. Winer First, I just want to start by congratulating you on receiving the G.A. Bernard Donna breast Cancer Award at ASCO. This is the highest breast cancer award given at ASCO, and it acknowledges your contributions to breast cancer research over the course of the past couple of decades. 00;02;30;04 - 00;03;02;17 Do you mind just sharing with us what this means to you personally and professionally?

Dr. Krop Sure. You know, I was incredibly honored to receive such an important award. I also was was surprised to be going be honest. But you know, what's particularly nice about this specific award is that it not only recognizes the research that I've done over the past couple of decades is, as you've said, trying to develop new treatments for breast cancer.

00;03;03;07 - 00;03;40;00 Unknown But it's also an award for mentorship because Dr. Bonadonna, was known for his absolute commitment to mentorship. So when I got the award and I gave a lecture to the audience, it gave me the opportunity to highlight all of the incredible work that the faculty who I've mentored over the years have accomplished. And it was very rewarding to be able to acknowledge all of the people who've done so much work over the years and who will represent the next generation of oncologists and investigators.

00;03;40;18 - 00;04;22;27 Unknown And just for a little history, Dr. Bonadonna was Italian. He did spend many years at Memorial Sloan-Kettering. But in 1976, just 50 years ago or thereabouts, he returned to Italy, where he led a med-

ical oncology program at the Institute Tomori in in Milano and was intimately involved in developing some of the first treatments for breast cancer and some of the initial treatments for lymphoma as well, and really had a very long and productive career. 00;04;23;27 - 00;04;53;10 He ultimately died about a decade ago. And so I think an award in his honor really means something.

Dr. Winer So why is the annual ASCO meeting such an important, important event for the whole oncology community and what impact does it have on both patients and clinical care? And I should mention that more than ever before, there were many patients presence at ASCO. 00;04;53;10 - 00;05;34;23 Many patients and patient advocates there throughout the whole meeting.

Dr. Krop Yeah. So I mean, I think as you said, I mean, the most important aspect of ASCO or ASCO meeting is that it brings all of us together. It brings the researchers, the practicing oncologists, the patients together, and we share the results from the latest clinical trials. And, you know, I think it because oncology research is now a global enterprise, that there really is top notch research and trials going on all across the world.

00;05;35;03 - 00;06;10;20 It makes it that much more important than ASCO is is a is an international event. And, you know, I think the other reason that the meeting is important is that there's a substantial amount of education as part of it. Many of us give lectures about how to use the latest approved drugs because, you know, it doesn't matter if all the treatments, you know, the greatest treatments in the world are developed, if the oncologists and nurses who are giving these drugs in the in our clinics don't know how to use them.

00;06;10;20 - 00;06;38;25 Unknown So I think it's a way ASCO is a way to share all of the the most cutting edge research. And it allows us to talk about how we move forward. And it allows us to disseminate the information to everybody so that we can all use it to help our patients directly. And at least within breast cancer. Maybe you could share some of the most important findings.

00;06;39;04 - 00;07;05;03 And I'm going to ask you to start first with the the two studies that looked at antibody drug conjugates. And I'm going to ask you just a little bit more about what these antibody drug conjugates are, ADCs are, and what their role will be in cancer treatment in the years ahead. But first, let's talk about the actual studies.

00;07;05;23 - 00;07;36;23 Yeah, So, you know, I think what we're seeing in in year after year at ASCO and in all of the oncology conferences is a move away from kind of old fashioned chemotherapy, which were drugs that were were effective at killing fast growing cancer cells, but they weren't specific for cancer cells. So the chemotherapy also damaged, fast growing normal cells.

00;07;36;23 - 00;08;11;12 And that is why chemotherapy causes all the side effects that we all think about with chemotherapy, nausea, hair loss and immune suppression. But we've been able to gradually move away from chemotherapy towards what we call targeted therapy, meaning therapies that are specific for

something that's within the cancer cell itself. And so if it just blocks or damages that target, it's much more likely to be specific for the cancer cell and cause less side effects.

00;08;12;19 - 00;08;35;07 And in fact, to give you a sense of how much our field has moved away from chemotherapy, less than 5% of drugs that have been approved in oncology over the last 25 years actually have been chemo therapy. The other 95% are what we call these targeted therapies. So it's really been a sea change since Doctor Barnard on it was working.

00;08;36;22 - 00;09;00;21 So one of the ways we've made drugs more targeted and we there's hundreds of different types of targeted therapies, but one that I think is has been one of the more impactful in breast cancer is the one you just mentioned what's called an antibody drug conjugate. And it's actually kind of a clever way to take a non targeted therapy that is chemotherapy and make it more targeted.

00;09;00;21 - 00;09;32;06 And the way you do that is you take advantage of something called an antibody, which is basically a synthetic protein that's very specific. For just one thing, you can make an antibody against almost anything, but if you make an antibody that's specific for something that's on the surface of a cancer cell and only on the surface of a cancer cell, and you if you inject that antibody into a person, it's going to that antibody is going to go through the bloodstream, find all the cancer cells and stick to it.

00;09;33;18 - 00;09;58;10 And so with that tool, it was realized that what if we take our chemotherapy drugs and actually attach them to these antibodies so now when we inject it into a person, the antibody goes and finds the cancer cell, but now it's bringing with it the chemotherapy. And because the chemotherapy is attached to the antibody, it's not able to float around and damage normal cells.

00;09;58;17 - 00;10;24;21 So it's an antibody drug conjugate. It's basically a way to start to to give chemotherapy in a targeted way. I people call these smart bombs or cruise missiles or something like that. But essentially it's a way to to give the chemotherapy in this targeted fashion. And and this was kind of first developed in breast cancer. It's now being these ADCs are being used in many type of cancers.

00;10;25;20 - 00;10;53;17 But we continue to develop new and better ones in breast cancer. And so two of the ADCs were tested and in very large clinical trials and the results were released at ASCO. This this week. And one was in a type of breast cancer called HER2 positive breast cancer and HER2, it's called HER2 positive because it expresses a lot of a protein called her two on the surface.

00;10;53;17 - 00;11;37;29 So this HER2 turns out can be a very good target for one of these ADCs. And we showed or it was shown at ASCO this year that when you use one of these ADCs against her to pretty early in the development

of patients cancers, then when they first have cancer that spread it was remarkably effective and that even though HER2 positive disease is one of the most aggressive kinds of breast cancer, when you when patients were treated with this ADC, it led to control of their disease.

00;11;37;29 - 00;12;01;06 On average for over three and a half for about three and a half years. So they got this one drug, they stayed on the drug and their cancer basically went into remission for, again, on average almost three and a half years, which is dramatically longer than we've seen it with with any other drug in any other situation in breast cancer.

00;12;01;06 - 00;12;31;26 So that was that was quite striking and shows how far that field has come. There was another trial you had mentioned there you were referring to that's actually looking at triple negative breast cancer, which is a cancer that we had no targeted therapies up until pretty recently. And we and in a study that was presented using an antibody drug conjugate along with another kind of target therapy, an immune therapy, which we can talk about because I think it's also quite interesting.

00;12;32;03 - 00;13;00;12 It's a way to stimulate a person's own immune system to target the cancer that that combination also was markedly more effective than kind of the previous conventional chemotherapy approaches to triple negative breast cancer. So a lot going on with with ADCs. But, you know, there were there was progress seen in in other areas of breast cancer. There were some really, I think, exciting work in some other cancers that we could talk about.

00;13;00;12 - 00;13;39;11 But it was a very good ASCO this year. And there was one study that took a somewhat different approach. It was a study where women who had hormone receptor positive breast cancer and where hormonal or endocrine therapy tends to be the most important treatment. And rather than waiting for the patient to show signs that the treatment was no longer working, they used a special blood test looking at circulating tumor DNA, which is something that we have been doing increasingly.

00;13;39;22 - 00;14;22;19 And they looked for markers of resistance in that tumor DNA. They then made a switch based on not any clinical findings that the patient was not doing as well, but based on changes in in the blood test. And that too, showed promise, although that's a situation where maybe we're not ready to to adopted full scale yet. Yeah, no, I would agree and I think we're going to you know, I think we as a as a field are going to have to think about exactly how and when we should use this approach.

00;14;22;19 - 00;14;59;17 But I think the very fact that you know, as we we move towards targeted therapies, we used to have to biopsy a cancer every time we wanted to look at what targets are existing in the cancer. And these targets can change over time, as you suggested, as the cancer becomes resistant to one drug, new targets can appear. But so with this new technology where we can actually just from a blood test, look at the DNA just coming from the cancer cells and see when a new mutation which can become a target is developing.

00;14;59;28 - 00;15;29;03 It's really an, you know, I think should be a better experience for patients because we won't have to do these biopsies as much and we can just do a simple blood test. And as you're kind of alluding to exactly when we change therapies as these targets kind of evolve and the cancer changes over time, I think we're going to have to, you know, work on to make sure we're doing it in an optimal way.

00;15;29;03 - 00;15;59;04 But it's really an exciting technology that we can now use, I think. And in many situations to again, to kind of optimize therapy for our patients in real time.

Dr. Winer All right. Well, we're going to have to take a quick break. We will be back in just a minute. And I will continue my conversation with Dr. Ian Krop about new research findings, mostly in breast cancer, but in other areas as well.

00;15;59;22 - 00;16;34;13 (radio) Funding for Yale cancer answers comes from Smilow Cancer Hospital, where their survivorship clinic serves as a resource to support cancer survivors, providing patients and families with information on cancer prevention. Wellness research on survivorship Smilow Cancer Hospital Dawg There are many obstacles to face when quitting smoking, as smoking involves the potent drug nicotine. Quitting smoking is a very important lifestyle change, especially for patients undergoing cancer treatment as it's been shown to positively impact response to treatment.

00;16;34;21 - 00;17;01;22 Decrease the likelihood that patients will develop second malignancies and increase rates of survival. Tobacco treatment programs are currently being offered at federally designated comprehensive cancer centers such as Yale Cancer Center and its Smilow Cancer Hospital. All treatment components are evidence based and patients are treated with FDA approved first line medications, as well as smoking cessation counseling that stresses appropriate coping skills. 00;17;02;09 - 00;17;36;10 More information is available at Yale Cancer Center DOT org. You're listening to Connecticut Public Radio.

Dr. Winer Welcome back to this edition of Yale Cancer Answers. I'm Eric Winer and I'm joined tonight by Dr. Ian Krop, director of the Clinical Trials Office and chief clinical research officer at Yale Cancer Center. For those just tuning in, we've been discussing key highlights and takeaways from the American Society of Clinical Oncology annual meeting held just over the past five or six days in Chicago.

00;17;36;22 - 00;18;11;22 This is the largest oncology conference in the world. Before we move on to talk about some studies in other cancers, I and I just want to ask you how it is and maybe why it is that sometimes we hear a presentation and we scratch our heads and we say, hmm, this is sort of interesting, but maybe it's not ready for primetime yet.

00;18;13;03 - 00;18;40;03 And what are the differences between those kinds of presentations in presentations where you know that on Monday morning you're

going to go home and you're going to use that new therapy right away? Yeah, I think that's an interesting question. And it and I'm sure it's stimulated by several of the trials that we did see the results from this at this ASCO meeting.

00;18;40;20 - 00;19;11;00 And I think they happen more when you have when if you have a trial, as you can imagine. So some trials are just here's a new drug and we're going to compare it against the old and older drug and that new drug is identified in the trial as being much more effective than the older drug and it has less toxicity or the same amount of toxicity, meaning side effects as the older drug.

00;19;12;02 - 00;19;43;25 So it's you know, it's a clear it's a clear win for patients. It's more effective. Doesn't seem like it makes more side effects. So, you know, we're we all go home and start using it. You know, as soon as the FDA approves it. And that's clear cut. And there's a lot of trials that are like that. But sometimes as a drug has been, you know, once it's been approved, we then start trying to figure out, okay, exactly when the best time is to use it.

00;19;43;26 - 00;20;14;08 And in the trials get a little bit more complicated because it's not comparing a new drug to an old drug, It's comparing a new drug, you know, to be used in this particular situation or compare it to using a slightly different situation. And then things can get a little bit murky because even if it looks in the trial to be a little bit better in the new situation, it may not in the long run really be any different.

00;20;14;08 - 00;20;41;07 If you wait that long enough, it may find that actually it it all kind of comes out in the wash that they they're being the same. And and you know when we do a trial typically we we report the results after a relatively short time and you don't have the at least in the initial report, you don't really know what's going to happen in the long run if patients, you know, maybe actually used it in a different situation.

00;20;41;07 - 00;21;23;23 But then switched later on to to another drug. So, you know, the bottom line is sometimes when you're really trying to finally hone exactly how to use a drug, it can be a little more ambiguous than the more straightforward, hey, is this a good drug or not? And I think, you know, as our field gets more sophisticated, as we have more drugs available to us, we do sometimes get trials where the results, how they impact what we do in the clinic the next, you know, when we get back to our our our institutions, it's a little less clear.

00;21;24;07 - 00;21;58;21 Yeah. And I do want to make it clear that when we hear results that either lead to an unequivocal improvement in how long someone lives or lead to a dramatic difference in quality of life, those are the kinds of studies where I think there's relatively little argument and we just move forward. And Monday morning it's essentially moving forward and it's more in these ones where we're just scratching our head a little bit and it's important to have those presentations.

00;21;59;03 - 00;22;40;25 It's important to begin to ask the next set of questions, but we just may not be quite ready. And as you said, sometimes turns out to be better and sometimes it's it's not the case. Well, I want to move on and talk about a very different kind of research, finding this one in colon cancer. And not only was the research study presented at ASCO, but it also was a manuscript that appeared in the New England Journal of Medicine, and it looked at a different kind of intervention.

00;22;41;10 - 00;23;10;18 Won't you tell us about that a little bit more? Yeah. So, I mean, certainly if you look at all the trials that are reported at ASCO, most of them are about drugs. And, you know, that makes sense because there are so many new drugs being developed at any one time. But there's also a movement to try to, you know, as we made progress in cancer treatments, there's also a movement to really focus on the patients experience more holistically.

00;23;11;03 - 00;23;38;10 And so there is interest in in looking at supportive care. You know, are there medications or other interventions that can help reduce the side effects of therapies or improve quality of life? And they're kind of somewhat along those lines. Was that was a study, the study you mentioned, which was looking at patients with which with relatively high risk colon cancer, these are patients who had their colon cancer surgery.

00;23;38;10 - 00;24;21;02 They've had the cancer removed. They got some chemotherapy afterwards to try to minimize the chance that the cancer could recur. And what they did was they randomized the people, about 900 patients, to either kind of standard approaches where patients were were given some education about, you know, what's a healthy lifestyle to to do. But the other patients, the other half of the trial patients were given an exercise intervention where they were given a trainer and education about how to exercise.

00;24;21;02 - 00;25;03;11 And they met with the trainer, I think once a week or actually three years to ask the question of whether something as simple as regular exercise can actually impact the patient's chance that that their colon cancer could recur. And what they found was that those patients who were who were on the exercise program had about 30% lower chance of their cancer recurring and about a 40% improvement in their overall survival.

00;25;03;25 - 00;25;36;29 With this exercise program, which, you know, I think was is really remarkable. I certainly congratulate the the the investigator who did this, this ambitious and and, you know, really definitive trial because the results are so clear and so good for for for for patients. And we've you know, we've had a number of pieces of data to suggest that exercise could be beneficial in patients with cancer.

00;25;36;29 - 00;26;04;09 Obviously, it's good for, you know, overall health and cardiovascular health and quality of life. But to show that it actually prevents recurrence of cancer is really exciting. And I think that now we need to go back and try to understand exactly how that happened. What is the mechanism by

which the cancer recurrence is were reduced so that we can, you know, try to continue to tweak that?

00;26;04;09 - 00;26;43;07 But, you know, I think it's just an incredible result and, you know, it's going to change. I think the way we think of these kinds of interventions going forward and of course, are far less expensive treatment approach than some of our new drugs, since it's it is less costly to hire and a coach or an exercise physiologist or whoever exactly it is than it is to spend tens of thousands of dollars on a new agent.

00;26;43;19 - 00;27;06;14 Yeah. And although although there were more muscle pain and muscle strains in the people who got the exercise, I noticed that. Yes. Which of course, those of us who are those of us as we get older, are noticing that when we do our own exercise as well. So I guess there's no completely free lunch. So as I often say to people, science moves forward.

00;27;06;16 - 00;27;45;28 We see results from experiments in the laboratory, but nothing gets into a patient without a big step. And that big step is clinical trials. How do clinical trials play a role in advancing cancer treatment? Yeah, I mean, I think you just you just said it. You know, nothing goes right from the lab to the patient for for obvious reasons, not only because we need to make sure that a drug is is is safe in patients.

00;27;45;28 - 00;28;12;03 And that's not just safety, you know, when you get the drug, but, you know, six months later and a year later, five years later. So we need to know what's safe and we need to prove that it's really effective because there's unfortunately lots of drugs that look great in curing mice from cancer. But when we when we test them in patients, the results aren't as aren't as good.

00;28;12;03 - 00;28;40;05 So, you know, it's so important that that we test these drugs thoroughly to prove both that they are both safe and effective. And, you know, I think we would certainly be doing patients a disservice if we tried to, you know, cut back on those kinds of I'm doing the trials. Dr. Ian Krop is the chief clinical officer at the Yale Cancer Center.

00;28;40;18 - 00;28;58;28 If you have questions, the address addresses cancer answers at Yale Dot edu and past editions of the program are available in audio and written form at Yale Cancer Center Talk. 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.