

Yale CANCER CENTER *answers*

WNPR Connecticut Public Radio



Hosts

Anees Chagpar MD

*Associate Professor of
Surgical Oncology*

Susan Higgins MD

*Professor of Therapeutic
Radiology, Obstetrics,
Gynecology, and
Reproductive Sciences*

Steven Gore MD

*Director of Hematologic
Malignancies*

Clinical Trials and Research

Guest Expert: Debra Brandt, MD

*Medical Director, Smilow Cancer Hospital Care Center
at Torrington*

Yale Cancer Center Answers is a
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Welcome to Yale Cancer Center Answers with your hosts doctors Anees Chagpar, Susan Higgins and Steven Gore. Dr. Chagpar is Associate Professor of Surgical Oncology and Director of the Breast Center at Smilow Cancer Hospital. Dr. Higgins is Professor of Therapeutic Radiology and of Obstetrics, Gynecology and Reproductive Sciences and Dr. Gore is Director of Hematological Malignancies at Smilow and an expert in Myelodysplastic Syndromes. Yale Cancer Center Answers features weekly conversations about the research diagnosis and treatment of cancer and if you would like to join the conversation, you can submit questions and comments to canceranswers@yale.edu or you can leave a voicemail message at 888-234-4YCC. This week it is a conversation about the importance of clinical research with Dr. Debra Brandt. Dr. Brandt is a Clinician in Medical Oncology and Medical Director of the Smilow Cancer Hospital Care Center at Torrington. Here is Dr. Steven Gore.

Gore Debra, certainly one of the things that attracted me to come to Yale 2 years ago was what I think is a pretty unique structure with our care centers, but perhaps many of our audience do not really know how that works, so could you tell us about the Cancer Care Center structure as it interfaces with you at Torrington?

Brandt We were a private practice, 5 oncologists covering all of Litchfield County up until approximately 3 years ago and with all of the changes in medicine, we wanted to look at a different way of practice that we could sustain care in the communities and Yale offered us an opportunity to become part of the Smilow Care System and we jumped on that opportunity and what that has meant is that we can still practice and give care to patients in the community at home, close to home. It allows us to have access to more and different clinical trials than we were able to have access to before. It allows us to have an incredible comradery and ability to reach out to experts on a very easy basis, calling into tumor boards, participating in tumor boards, e-mailing each other, calling attendings and physicians that are on the main campus and saying, hey I have this difficult case, can I run it past you, can we share care for that patient and it has been just a wonderful blending of care allowing us to reach out to the academic center and bring a lot of the academic center to the community.

Gore I totally agree with you. I think that in many places which have developed networks, often it seems that the satellites have the brand stamped on them of whatever they are affiliated with but it does not seem to be as integrated a system as has been developed here. I feel like you guys are co-faculty with us and totally integrated colleagues. I do not really feel like there is any kind of 2-tier practice or 2-tier structure.

Brandt I agree. It has been really nice, and that was one of my fears, how are we going to integrate, how are we going to all get along, what access would we have, would we need to send patients out more often to get different levels of care, and I think quite the opposite has happened, I think it has been a really collegial system the way that it works; actually, earlier this morning, I was down

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teaching the first year medical students and running a workshop that is being done 4 days in a row which has been really a wonderful experience for me because I love to teach and that is one of the opportunities I did not have a lot of in the community and I am hoping that we continue to grow that. I had some nurse practitioners students come up and shadow me and work with me and do some of their clinic time there. I am optimistic, I do not know if the medical students will make it, but some of the fellows to come up, and that has been great. That was an opportunity that we did not have.

Gore Although for you to organize yourself to come down to New Haven as one of our geographically more distant care centers is a little bit of a challenge, Torrington is about an hour away.

Brandt It takes about an hour and 10 minutes to get between the office and here, so it takes a little bit of orchestration for sure.

Gore You are probably more organized than I am.

Brandt Well, this was a nice class because it was 8 o'clock in the morning so I could come here first and luckily I have good colleagues and we can share rounding at the office. The other benefit, and I think one of the ways that Yale has done a great job integrating us, is that I have 2 new physicians that have joined me and my particular practice has gone through a lot of transitions with physician retirements. And we have gained new and exciting and very educated young physicians but they each get to spend one full day a week in New Haven working on their focus of interest, participating in person in tumor boards. I get to Skype into tumor boards a lot which is great and everybody can see my face and I can see the pathology slides and I can be part of the conversation but it is nicer to be here in person.

Gore There is nothing like FaceTime, right. Debra do you have a particular disease area, I think of you as a wonderful general oncologist. Is there one area that you most love?

Brandt I am part of the breast cancer tumor working group, and so I do call into more of those meetings and I would say that my own particular interest is everything but it would be hematology and hematologic malignancies and probably breast cancer for a solid tumor.

Gore One of the things which has been really wonderful for our patient's downtown in New Haven, is the ability to share care. For some of our treatments that we have for leukemia, for the audiences benefit, have months and months of therapy, sometimes intensive, requiring hospitalization and sometimes not and with Debra, some of these patients are on clinical trials, have some of the

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care actually delivered in Torrington which I think has made it really workable in a way that it would have been very difficult for the patients who live far away to be down in New Haven as often as would be required otherwise.

Brandt I think it has been fantastic, particularly for those patients who need high intensive treatment, so if they have been hospitalized in New Haven for a block of time and they can leave, but they still need aggressive counts and hydration support and maybe IV antibiotics, we can do that locally in the office so they do not have to drive quite as far to continue their care and we can share care and we have shared patients on clinical trials before which has been wonderful.

Gore And another thing which attracted me to this place as a place to do research is the opportunity to have clinical trials which really are I think uniquely optimally delivered in the community, so for some of the diseases that I treat which are more chronic blood disorders, the therapies are kind of chronic, if they are on a clinical trial or it would require them to be in New Haven to get their medicine, injections, for example, they just probably would not do it, but those trials can be delivered really conveniently to patients in the care centers.

Brandt I think the ability to do clinical trials and to get that kind of care out to the community is incredibly important. I think what we all try to do when we take care of our patients is make the cancer, or the hematologic issue that they are living with, a part of their life, not the only part of their life and if we can make the time that they have to spend traveling or in the office much more convenient, then it is much better for them and their families. Maybe it allows them to work, maybe allows them to just spend time with their families and doing things that they enjoy rather than focusing 100% of their time on their medical care, and so I hope we can do that by working together and I think we do it as often as possible.

Gore One of the frustrations that I have heard from community physicians in general is that enrolling a patient on a research trial requires a lot of time, both in terms of educating the patient and screening the patient and getting consent from the patient and doing a lot of extra stuff that you might not do in your daily care and how does that affect your work flow and ultimately I suppose revenue stream because you cannot keep billing for that research time?

Brandt I would even go back a step further, before you open a trial you need to be educated on the trial as the physician but not just the physician, the staff and your office needs to be educated. You need to be sure that you have the resources to provide that care, so we need to be sure we can get the medication from the pharmacy and that we have the appropriate pharmacy to mix it if the clinical trial requires lab draws, do we have the right equipment, can we transport the labs to wherever it needs to go in a timely fashion, do we have the appropriate radiologic evaluations available to us

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to do that? So even before the trial opens, it takes an enormous amount of time and effort to be prepared to do it, but it is absolutely worth it. So that time is worth it, the time that it takes to enroll the patient, it definitely takes time to explain to a patient why they would want to do something slightly different than standard of care, so a patient has to trust you, understand their disease, understand that the clinical research is being done to improve care, hopefully for the patient themselves, but definitely for care in the future. Some clinical trials give everybody the same treatment, some clinical trials randomize patients to different treatment, so you may get standard of care treatment alone or standard of care treatment plus something new or some combination thereof and that takes a lot of explaining, understanding the cancer that you have, what the treatments would be, what the side effects would be, that is a lot to understand just when you are describing standard of care, you then have to explain why going on a clinical trial is potentially beneficial and what unique side effects and extra tests might be needed, that all takes time, but it is absolutely worth it because the only way we are able to make advances in care and make treatments better, hopefully make them easier to tolerate, lead to more cures, lead to better quality of life is if we do those clinical trials. I could not be a community oncologist unless I was also doing clinical research, which I do not think I could because I love taking care of patients, I love the experience that I have being a caregiver and a caretaker for these people but so many of our treatments are lacking, so much of our understanding and our knowledge base is still in its infancy and I feel like when I put a patient on a trial, I am helping us move forward for the next, hopefully that patient is going to have benefit, that is of course what I hope, but going forward, that the next person who walks in with the same disease the next day, the next year, the next month will have better treatment options, a better chance of overall survival, a better quality of life while they are going through the treatments and it makes me want to go to work every day and it makes me feel that I am part of this bigger picture of cancer care. When you work in the community, you sometimes feel very distant from that. Being part of it really helps, but putting somebody on a clinical trial makes me feel like I am doing something for the world, for the larger community because hopefully the research will get translated not only into cancer care but maybe some other care of other diseases as well as we go forward. You asked me what my specialty is or my unique focus, my unique focus has been clinical trials. When I did my fellowship here at Yale and I chose to go out to the community 15 years ago, I said I will come here if you let me do clinical trials and the group that hired me said absolutely and they let me begin the clinical trial program there.

Gore We are going to take a short break for a medical minute. Please stay tuned to learn more information about clinical research with Dr. Debra Brandt.

Medical

Minute This year over 200,000 Americans will be diagnosed with lung cancer. More than 85% of lung cancer diagnoses are related to smoking and quitting even after decades of use can significantly

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reduce your risk of developing lung cancer. Clinical trials are currently underway at federally designated comprehensive cancer centers, such as, Yale Cancer Center and at Smilow Cancer Hospital at Yale-New Haven to test innovative new treatments for lung cancer. Advances are being made by utilizing targeted therapies and immunotherapies. The BATTLE-2 Trial at Yale aims to learn if a drug or combination of drugs based on personal biomarkers can help to control non-small cell lung cancer. This has been a medical minute brought to you as a public service by Yale Cancer Center and Smilow Cancer Hospital at Yale-New Haven. More information is available at yalecancercenter.org. You are listening to WNPR, Connecticut's Public Media Source for news and ideas.

Gore Welcome back to Yale Cancer Center Answers. This is Dr. Steven Gore and I am talking with our guest tonight, Dr. Debra Brandt about clinical research. Debra, you gave a great summary about why participating in clinical research was meaningful to you, and also how important it is in the larger sets and before the break and I was thinking as you were speaking about it, I have been in the business for...

Brandt Longer than you want to admit to.

Gore No, I just cannot even count, since 1990 for sure, that is when I finished my fellowship, so how many years is that, 26, and early on in my career, I had faith that things might be changing because they seemed like they were all the same, and then I look back at 25 years and some of the diseases that you and I treat, just remarkable things have happened. Even in the last 5 years and all of that really is due to clinical research and to people being willing to enroll on the clinical trials, which is sometimes pretty scary stuff.

Brandt I agree, the changes in cancer care and hematologic care in the last 15-25 year have been enormous.

Gore 15 for you, right?

Brandt Yeah, now look at molecular markers. We know about more and more targets and markers on different cancer cells which started in breast and prostate when we were playing with the hormones and knowing that some of those diseases were hormone mediated and we could do that and it has just blossomed into a multitude of molecular markers in many diseases and coming up with more and more treatments that actually target the abnormalities that are in the cancer cells and if we did not do clinical research, we would never have known that those markers existed. We would never have known that we needed to target them. We would not have figured out that certain

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medications target certain markers or certain cancers differently. What we used to think was one cancer we know now is 5 or 6 different cancers under the same big heading, so adenocarcinomas of lung for example, we thought they were all the same, well we now know some of them have a molecular marker called ALK, granted that is a small percentage, 3% or 4% but there is a medication now that targets that abnormality.

Gore Specifically for those?

Brandt Specifically for those and that is true for many more diseases. In leukemia and in the chronic myelogenous leukemia subgroup, we have known about the genetic abnormality but we have more and more medications that are able to target that abnormality in slightly different ways and patients are living decades with that particular disease where when I first graduated 4 years was the average survivor.

Gore 3.5, yeah.

Brandt And that is all because patients have been willing to give of themselves to try to get better and to try to get that new medicine that is going to help them, but even when they sometimes knew that was not going to be the case, they were willing to participate to help the next generation.

Gore Is it harder for the patient to get treated on a clinical trial from the patient's point of view?

Brandt No I do not think so, I actually think often it is easier, you have more eyes watching you. I do not know if it is harder or easier. It is probably the same, but I believe there is more benefit, in addition to the physician watching and the treatment nurses who watch all of our patients and help the physicians care for them, you have an extra staff of research personnel who are focused on making sure that we follow what is required of the protocol to every detail so that when we are putting somebody through this treatment, we are gathering the data appropriately so that data is really useful, so if the patient needs CAT scans or x-rays every 6 weeks or every 8 weeks, we are making sure that we are following them closely; drug modifications if you need to go up 10% or down 25% you are being watched very closely to make sure that you follow that to the tee.

Gore So in some ways the care is more routinized.

Brandt Absolutely, because there are more people looking in at the patient's care to make sure that it is being followed.

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Gore And the protocol is vetted by committees or large numbers of people to establish what the right care is for those patients or at least in terms of the clinical trials.

Brandt Clinical trials, before they come to the clinic, are vetted by lots of different committees. Not only does somebody write the clinical trial, but then in each institution, there is something called an institutional review board that looks at the protocol to make sure that it is scientifically sound, that you are actually going to get some useful information at the end of the clinical trial and that it is safe to the best of our ability to know that it is safe for the patient and that there are safety measures for the patients for their personal protection but also for their medical protection as well and so all of those things are looked at before the trials come to the clinic whether that is in the academic center here in New Haven or out at the multiple care centers.

Gore Patients often express the feeling of being guinea pigs, at least that is my experience, how do you answer that?

Brandt Well a guinea pig does not have a choice in what we do to it, a human being reads the informed consent, has the opportunity to ask questions, knows exactly what they are getting into, the informed consent document very clearly outlines what treatments you might be getting, so you are not a guinea pig, you know exactly what you are getting into and most of the time, we know a lot about the medications or the combinations before, there is a lot of information before my patient would go on this, so there are different phases of clinical trials and I will describe them for people who are listening. When a new medication or a new combination of medications is coming from the lab to the first patient and we do not really know the toxicities or we are worried about the combination toxicities, that would be a phase I trial. Those trials are done almost exclusively in academic institutions or large institutions and everybody who goes on those trials knows that they are one of the very first human beings to receive this medication and the goal of that trial is to say yes, does the drug work, but what is the toxicity of the drug. Once the phase I trials are complete and we feel like we know what dose of the drug or combination of drugs is safe and how to give it safely, now we say, what we thought these drugs or this drug is going to be useful in a particular disease and then we move on to phase 2. We look at usually somewhere between 30 and 60 patients in a phase 2 trial and we say, we are going to take 60 people with the same disease and we are going to give all 60 people this medication and we are going to get an idea from that trial how well this drug works and some phase 2 trials can be done in the community very safely and some cannot, and if it can be done safely in the community, those are trials we love to have in the care centers and then the next phase of trials is phase 3 and then they say, we have this new drug but we want to know how this new drug compares to standard of care and so we are going to randomize patients, everybody is going to get a treatment, everybody is going to know what treatment they

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are getting, but people are going to be randomized to get standard of care versus the experimental arm. So nobody is a guinea pig ever, I do not like that description, everybody is a human, everybody is treated as a human being but depending on what phase trial they are in, it will depend on what the goal of the treatment is but that is very clearly outlined and the patient is very aware of why they are participating.

Gore Do you find that most of the patients for whom you think the clinical trial is appropriate, and who are potentially eligible for a particular trial, in general are happy to go on with the trial or is there push back, does it depend on the kind of trial?

Brandt I think it depends on a lot of different things. What I have found is that patients who have had their cancer for a long time and their cancer has progressed on prior treatment are more open to looking for new drugs, I think they are more understanding of the disease process and the process of treatment and the knowledge base that exists for their cancer, and so they are willing to go on clinical trials later in their disease. I find it much more challenging when patients are coming in with a new diagnosis to discuss with them participation in a clinical trial. I think that is when patients have much more fear that maybe I am doing it for my benefit rather than for their benefit, why would I not give them standard of care, what is the trade off and I think a lot of it is it takes them a long time, some time, maybe not a long time, everybody is different, but understanding the role and just their disease process, for some people, it is concerning, first line. It is a little harder first line.

Gore One thing that I find when I am discussing clinical trials early in their disease process is that more often than not, the clinical trials become the standard of care for the frontline therapy that is lacking in some way and the response rate is not as high as we would like or the response does not last as long as we would like and if it were not for the clinical trial, I would present this as the best treatment and give details about it that the patient may or may not really want to know about what particularly the outcomes are. They just want to know if there is a treatment that you recommend, but when you are talking about the clinical trial you kind of have to be a little bit in your face that well with the standard of care, only 30% of people respond or only 50% of people respond and in some ways, I kind of feel I have conflict even though I think it is the right thing to do that I am almost giving them sometimes more information than they would otherwise necessarily want. Do you have any experiences like that?

Brandt I agree, patients really have to trust us and trust the system to be willing to participate in a clinical trial and they have to have a real clear understanding of why we are doing it and that is not easy ever, and I think it is particularly challenging when you are first faced with your diagnosis.

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Gore Right, because they just want to know that they have got something that is treatable and hopefully it will go away.

Brandt And they want to believe that they are in the percentage that is going to get the best benefit whether that is cure or long term outcome, we often do not know that.

Gore Do you ever have clinical trials where both arms get a standard of care and one gets the study drug on top of it, but the other gets a placebo and in that case they do not really know?

Brandt A lot of the cancer clinical trials are set up that way, so it is standard of care plus a placebo, placebo meaning you are getting water, sugar or something that is inactive or standard of care plus the agent that we are trying to test. Most people can follow that line of reasoning, it takes a little bit of explanation but people get that they are still getting active treatment.

Gore They are still getting the basic care that you would give them otherwise.

Brandt I have not ever participated in a clinical trial for a cancer patient where they either get placebo alone so they are getting nothing versus an active drug, that does not really exist in oncology. That may exist in other diseases, but those are not really the clinical trials that we participate in.

Gore I think they do in Europe actually, sometimes where a drug that has not yet been approved in Europe sometimes people are offered placebo, I think that it would be a tough sell to my patients I think.

Brandt It would be very difficult.

Gore But I do find personally that sometimes when there is a placebo involved even in some type of standard care, it makes people a little bit as you said, it requires a little bit more explanation to get them on board and not feel that somehow this is not right and why cannot I choose to get the experimental drug.

Brandt Right, and that is part of the discussion. The experimental drug is still experimental.

Gore Yeah, we do not know if it is going to work.

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Brandt It may actually be negative. We really do not know. How many times have you been surprised by outcomes over the last 25 or 26 years. I was so convinced that the one arm of the trial was going to be better than the other arm and the results came out and I am like oh, I was wrong.

Gore Some of my biggest efforts as a researcher eventually came to national trials and the thing that I had spent 10 years developing turned out not to be any better than what we had before.

Brandt Right, so what we think we know and what we really know are often incongruent, they do not go together, so we really do need to do these trials.

Dr. Debra Brandt is a Clinician in Medical Oncology and Medical Director of the Smilow Cancer Hospital Care Center at Torrington. We invite you to share your questions and comments, you can send them to canceranswers@yale.edu or you can leave a voicemail message at 888-234-4YCC and as an additional resource, archived programs are available in both audio and written form at yalecancercenter.org. I am Bruce Barber hoping you will join us again next Sunday evening at 6:00 for another edition of Yale Cancer Center Answers here on WNPR, Connecticut's Public Media Source for news and ideas.