Yale CANCER CENTER answers

WNPR Connecticut Public Radio

Clinical Trials for Breast Cancer

Guest Expert:
Lyndsay Harris, MD

Associate Professor of Medical Oncology
Director, Yale Cancer Center Breast Cancer Program

Yale Cancer Center Answers

is a weekly broadcast on

WNPR Connecticut Public Radio

Sunday Evenings at 6:00 PM

Listen live online at

www.wnpr.org

OR

Listen to archived podcasts at

www.yalecancercenter.org

Welcome to Yale Cancer Center Answers with doctors Ed Chu and Ken Miller. I am Bruce Barber. Dr. Chu is Deputy Director and Chief of Medical Oncology at Yale Cancer Center and Dr. Miller is a medical oncologist specializing in pain and palliative care and he also serves as Director of the Connecticut Challenge Survivorship Clinic. If you would like to join the discussion, you can contact the doctors directly. The address is canceranswers@yale.edu and the phone number is 1-888-234-4YCC. This evening Ed Chu is joined by Lyndsay Harris, Director of the Yale Cancer Center breast cancer program and co-director of the Yale New Haven Breast Center. Dr. Harris is an expert in the treatment of breast cancer and focuses research on identifying the subtypes of the disease.

Chu How common is breast cancer here in the United States?

Harris Breast cancer is extremely common in North America and in fact, is the most common solid tumor in women. The incidence is about 1 in 200,000 per year; although it has been decreasing over the years.

Chu Are there any racial or ethnic differences in terms of the incidence of breast cancer?

Harris Yes, breast cancer is more common in white women, however, in African American women, it is more likely to lead to death so it is a much more serious disease in that group of women.

Chu Actually, in getting ready for the show this evening, I went on the American Cancer Society website and to bring things closer to home, here in the State of Connecticut there will be an estimated 2500 cases of breast cancer diagnosed in the year 2008.

Harris Right.

Chu So it is a pretty significant major public health problem. A very common misconception, Lyndsay, is that if there is no family history of breast cancer then a woman does not have to worry about the possibility that she, or one of her loved ones, may develop breast cancers. Is this fact or fiction?

Harris It is a fiction, in fact, the risk of breast cancer is about one in eight if a woman lives through the age of 85. In fact, the vast majority of women do not have a strong family history; probably at least 80% to 90% of women who are diagnosed with breast cancer do not have a strong family history.

Chu What are some of the other risk factors that one needs to think about?

Harris Breast cancer is most likely related to hormonal exposure in life. We know

2:59 into mp3 file http://www.yalecancercenter.org/podcast/Answers_Aug-31-08.mp3

that certain things like estrogen replacement therapy over a long period of time, or having exposure to estrogen either early on in life with early menstrual cycles, or later with frequent menstrual cycles with a late menopause are all risk factors for breast cancer that suggest hormone exposure is the strongest risk factor. Another interesting fact that has recently been reported in the news is that since the decline of estrogen replacement therapy in the last five years or so, there has been a decline in the incidence of breast cancer, which is quite striking. There was a report in the New England Journal recently indicating that the decrease in hormonal replacement may partially explain the reduction in the incidence of breast cancer.

Chu And what about the role of diet?

Harris Well, it is a complicated question because we do not have really good information on whether fat in the diet is related to breast cancer risk. There is some evidence that fat in the diet is associated with risk, however, it is controversial and not all studies are equivalent or show a similar effect.

Chu There has been very positive news recently that, as you say, the incidence, but in particular mortality of the breast cancer has been dropping. Many folks have attributed that to the focus on early detection screening. Can you tell us a little bit about that?

Harris It is actually equally encouraging that the mortality from breast cancer has started to decline over the last decade, even before this recent observation with the reduction in the incidence over the new cases and that appears to be due to two different things. One is the screening for breast cancer and earlier detection. The second is better therapies for women who are diagnosed with breast cancer and those are mainly systemic therapy such as chemotherapy and hormonal therapy.

Chu We will focus, I guess, on the therapy part later on in the talk, but focusing on this issue of screening early detection, for an average risk women, when should screening for the possibility of breast cancer begin?

Harris The recommendation is that at the age of 40 a woman starts having annual mammograms. There is some controversy, but many agencies recommend starting with the baseline screening mammogram at the age of 35.

Chu And again, these are women who do not have a family history of breast cancer. Say for instance someone has a first-degree relative that had breast cancer in the past, would screening start earlier in that setting?

Harris It depends a little bit on how strong the family history is. A first-degree

6:18 into mp3 file http://www.yalecancercenter.org/podcast/Answers_Aug-31-08.mp3

relative, in other words a sister or mother, who was diagnosed over the age of 50 only slightly increases the risk of developing breast cancer in that person, whereas having a first-degree relative less than 50 increases your risk more substantially for women. With a very strong family history such as someone carrying one of the genetic predispositions, we recommend starting screening 10 years before the first person in the family developed their breast cancer; in other words if that first person in the family was 40, you should start screening at 30.

Chu Great, so these predisposition familial syndromes you just mentioned, could you explain exactly what that is?

Harris There are certain genes that we know predispose women to breast cancer and these are, what we call, dominant change. You only need one of them to be abnormal in order to stromatically increase your risk. The BRCA-1 and BRCA-2 genes are two of them, p53 is another and P10. There are several that have been identified that predispose to breast cancer. Those particular genes give you a risk of somewhere between 20% and 40% likelihood of developing breast cancer in your lifetime, which is much higher than the average women in the population.

Chu An important point to emphasize to our listeners out there is that if in fact one carries one of those genetic mutations that does not necessarily mean they are going to 100% develop breast cancer.

Harris Correct, and in fact there are many options for prevention and screening that are now available to prevent that from happening as well.

Chu One issue that has come up recently is the traditional mammography approach versus using MRI. What are your thoughts on that?

Harris MRI is, on the one hand, a wonderful tool and is very helpful for screening high-risk women; in fact, it has been approved by various insurance companies for screening women with a genetic mutation such as BRCA-1 or BRCA-2, but the use of MRI in women with average risk is at this point not recommended.

Chu How often should women be screened? You mentioned you should typically start at the age of 40, but what are the general recommendations for follow-up screening efforts?

Harris Well, it is controversial and some agencies recommend annual whereas others

9:20 into mp3 file http://www.yalecancercenter.org/podcast/Answers_Aug-31-08.mp3

recommend every other year for a 40-year-old woman. I would say to speak with your surgeon and understand what their particular approach is, because there is some variation depending on the person, but in general we recommend annual screening after the age of 40.

Chu I would imagine the same would hold for a woman who has had a prior history of breast cancer, where they are worried about the risk of breast cancer occurring on the other side, and those women should get annual mammogram screening as well?

Harris Yes, for women who have been diagnosed with breast cancer, annual mammograms are absolutely essential and in some cases, MRIs are used in women who have difficulty with mammograms where they are not that helpful. They are not that sensitive because of the denseness of the breast tissue.

Chu Typically, if a woman has had a screening mammogram and there are some abnormalities seen, what would be the next step that individual should take?

Harris The mammography community is very sophisticated and typically a woman should receive her information from her screening mammogram the same day, this is part of legislation, and if there is any abnormality it should be followed up either with a 6-month mammogram, or if there is a higher degree of suspicion, they would recommend that it be biopsied.

Chu And typically who would do the biopsy?

Harris Radiology departments now do biopsies in the mammographic screening facility with something called a core biopsy used as the most common approach for those areas and they are easy to biopsy using that approach. If the mass is not detected that way but is felt as a lump, then the surgeon will typically do the biopsy.

Chu So, once a diagnosis of cancer has been made, then what is the next step for that woman?

Harris Well, once the diagnosis has been made definitely, there are a number of different things to be considered for a particular woman. The treatment of breast cancer is really multidisciplinary, meaning that there are several different specialties involved in the treatment even at the very beginning. These include the medical oncologist, radiation oncologist, and the surgeon working as a team to decide what the most appropriate approach for that particular patient is.

12:11 into mp3 file http://www.yalecancercenter.org/podcast/Answers_Aug-31-08.mp3

Chu Great, maybe we can pick that up at the other side of the break. At this time, we would like to remind you to e-mail your questions to canceranswers@yale.edu, or call 1-888-234-4YCC. At this time, we are going to take a short break for a medical minute. Please stay tuned to learn more information about the treatment of breast cancer with our special guest expert, Dr. Lyndsay Harris from the Yale Cancer Center.

Over 170,000 Americans will be diagnosed with lung cancer this year and more than 85% of these diagnoses are related to smoking. The important thing to understand is that quitting even after decades of use can significantly reduce your risk of developing lung cancer. Now everyday patients with lung cancer are surviving thanks to increased access to advanced therapies and specialized care. New treatment options are giving lung cancer survivors new hope. Clinical trials are currently underway at federally designated comprehensive cancer centers like the one at Yale to test innovative new treatments for lung cancer and patients enrolled in these trials are given access to medicines not yet approved by the Food and Drug Administration. This has been a medical minute and you will find more information at www.yalecancercenter.org. You are listening to the WNPR Health Forum from Connecticut public radio.

Chu Welcome back to Yale Cancer Center Answers. This is Dr. Ed Chu and I am here in the studio with my close colleague and friend, Dr. Lyndsay Harris, discussing the latest treatment options for women with breast cancer. Before the break we were talking about the multidisciplinary approach to women with breast cancer. For those listeners who did not catch it, if a woman is diagnosed with breast cancer and coming here to our center at Yale, the different disciplines would all be working together to figure out what the best treatment option for that individual patient is.

Harris Right, and the different disciplines that are so essential for helping a woman with the diagnosis of breast cancer are the breast cancer surgeon, the medical oncologist, and the radiation oncologist. These specialties are all experts in their own field and all of these treatments are often offered to a woman with the diagnosis of breast cancer.

Chu Also part of that team is the pathologist, the radiologist and some other folks as well.

Harris Absolutely. The treatment team is those that I mentioned and the team that helps with understanding the type of breast cancer and the extent of the breast cancer which includes the pathologist, radiologist and our genetics counselors. Our genetics program is also integrally involved all the way from the

14:59 into mp3 file http://www.yalecancercenter.org/podcast/Answers_Aug-31-08.mp3

beginning of the diagnosis of breast cancer to help us make the best recommendations for treatment.

Chu On a very simplistic level, we tend to think that breast cancer is just one disease, but what you, and many of your colleagues around the country, have now found is many different diseases within the umbrella of breast cancer.

Harris That is right, Ed. Although we know the most common type of breast cancer is ductal carcinoma, within the ductal type there are multiple different molecular subtypes that behave very differently from one another and it is critical to know those differences when you are beginning to treat a patient in order to offer her the best type of therapy.

Chu So this molecular profile of a tumor really can help pinpoint a treatment that will work as opposed to a treatment that might just provide side effects and toxicities and really have no benefit at all.

Harris Yes. That is exactly right and these molecular subtypes are now recognized and are part of standard of care in order to decide if a woman's tumor has the HER-2 receptor, for example, and she should be receiving herceptin or the estrogen receptor, and she should receive hormonal therapy, and there are new entities that we think are more sensitive to chemotherapy. There are many important features from the pathology that are critical for us to make the best recommendation for treatment.

Chu It really is remarkable, the advances that we have seen in the treatment of breast cancer, because this has happened over the last, say, 4 to 6 years.

Harris Yes. Certainly within my career, I have seen the development of understanding of the molecular biology of breast cancer and now within the last 5 years or so, we have had changes in the way we treat patients based on those molecular features of the breast cancer.

Chu We would like to talk about this concept of individualized, personalized medicine, but there is probably no other disease besides breast cancer that highlights what we can really do if we have a better understanding of what is going on in the tumor itself.

Harris I agree completely and fortunately for women with this diagnosis of breast cancer, scientists have really led the field in terms of understanding the molecular biology of the disease and being able to subdivide the tumors into different types for the benefits of patients specifically.

Chu Your own research has focused on trying to get a better understanding of this

HER-2 new gene protein. Can you tell our listeners what your research has focused on?

Harris The breast cancer subtype that is dominated by the HER-2 gene is something we have been starting for many years in our group, and we and many others have found that this particular type of breast cancer has a worse prognosis without treatment, but given specific therapies, the prognosis is actually just as good as those less aggressive types of breast cancer. We have looked specifically at which therapies are best and in some cases women benefit a lot from therapies such as herceptin or chemotherapies, and in other cases they do not. So, we are focusing our efforts on trying to define which molecular features predict. Who is going to benefit the most from herceptin and who is potentially not going to have this much benefit and maybe should try a different medication.

Chu You are very actively involved in helping to lead our efforts here at the Yale Cancer Center to develop new clinical trials, which incorporate a lot of this state-of-the-art science. Can you tell our listeners out there what some of the interesting trials that you and your group are leading here at Yale are?

Harris Our goal is to take the next step to try to improve on the standard therapies that exist. We do this by adding new drugs to the standard therapy such as herceptin in order to overcome resistance to those drugs. For example, Dr. Abu-Khalaf in our group has a trial with herceptin and rapamycin. There is a recent report from a meeting suggesting that combination is highly active in women who are resistant to herceptin, and we now have this available as part of a clinical trial. In addition, we are looking at new approaches in early stage breast cancer by adding new medications to herceptin or changing the way that we deliver it in order to optimize therapy for HER-2 positive patients.

Chu Not a new drug, but a new drug to breast cancer, is an agent called Avastin which has received a great deal of attention and is standard of care now, but I know that your group also is very interested in incorporating Avastin in some of your clinical trials.

Harris That is right and Gina Chung leads our efforts looking at the activity of Avastin and other angiogenic drugs. This class of drug actually acts not so much by targeting the breast cancer tumor itself, but the surrounding blood vessels that allow it to grow and so there are a number of different drugs now with Avastin being the first one that has been approved that can essentially starve the tumors ability to develop its blood supply and can be added to therapies to improve the outcome. For example, Avastin was just approved by the FDA for women with advanced breast cancer to be used in addition to paclitaxel.

21:37 into mp3 file http://www.yalecancercenter.org/podcast/Answers_Aug-31-08.mp3

Chu It is interesting, as you know my own area of interest is colorectal cancer where Avastin was first approved. This drug is quite remarkable and in addition to inhibiting the tumor blood vessels if you will, it also seems to enhance the normal blood flow delivery of chemotherapy to the tumor which then makes the chemotherapy work that much better. I wonder if that may also be happening in breast cancer?

Harris That is a great point, there are other ways that Avastin is working. We do not entirely understand exactly how it benefits patients but what we are trying to do in our program, and Dr. Chung is leading this effort, is to offer Avastin to early stage patients which would not otherwise be available and to try and determine if the blood flow to the tumor is improving by doing an MRI before and after the dose of Avastin.

Chu All of your research interest is in tying to understand why minority women, particularly African American women, may not have the same level of benefit to treatment as their Caucasian counterparts. Can you tell us a little bit more about that?

Harris The difference between outcomes from breast cancer in African American and white women is really quite striking and has been seen in multiple studies now. The reasons for it are still a bit unclear. It appears that African American women are just as likely to be screened for breast cancer, although some of the studies suggest that the follow-up screening may not be as likely and so that is an area of active research, trying to understand how to improve that. In addition, we know now from our molecular biology studies that tumors that arise in young African American women are likely to be more aggressive. This triple negative, or basal cell type of tumor, is much more common in those women and partially as a result of that, the prognosis may not be as good.

Chu So they are less responsive to the traditional chemotherapy and the newer therapies?

Harris Suffice it to say they are not able to benefit from hormonal therapy or herceptin. It may be that they are more sensitive to chemotherapy, however, it is unclear exactly what subgroup is more sensitive to chemotherapy. That is the area of active research, to determine whether it is simply not receiving adequate therapy that leads to a worse prognosis or whether there are some breast cancers in African American women that are more resistant to therapy.

Chu Your group is also very keen on trying to identify some newer agents that

really have not yet been used in the community. Can you tell us a little bit more about some of the newer agents that your group is working on?

Harris We have as our goal to try and improve the outcomes of women with breast cancer and we know that while there are many active drugs, there are still breast cancers that do not respond to the standard therapies. So for the HER-2 tumors, for example, there are a number of drugs that do appear to work in women who do not benefit from herceptin, or they become resistant. The HDAC inhibitors are one class that is being actively evaluated in our group. In addition, the triple negative breast cancers that do not have either ER or HER-2 appear to be more sensitive to certain types of drugs such as PARP inhibitors. We have a study that combines PARP inhibitor with chemotherapy, which is about to open here at Yale.

Chu What was remarkable about this class of agents was that probably a year ago at last year's ASCA meeting there was a very early preliminary phase I study looking at a PARP inhibitor. It was from Europe and it had unbelievable activity in women who had these BRCA genetic alterations. I guess the thinking would be that for women with breast cancer, these PARP inhibitors really should be quite active, in particular for those who have either BRCA 1 or BRCA 2 mutations.

Harris That is right and in fact, there is a close relationship between this triple-negative type of breast cancer and the BRCA mutations. Women who have BRCA mutation often develop these triple negative basal tumors but there may actually be a type of breast cancer that is not associated with family history that behaves in a very similar way.

Chu Lyndsay if anyone out there would like to get more information about any of the clinical trials that you or your group are doing, do have a number or a website that they can go to?

Harris Yes, the best place is to dial 1-888-234-4YCC or to go on to Yale Cancer Answers website.

Chu The other website would be www.yalecancercenter.org where there is a complete listing of all of the clinical trials and a particular focus on the breast cancer team with you leading the way. We are ending our evening discussion, any last minute words of advice for those out there?

Harris I just want to emphasize that it is an incredibly hopeful time in the treatment of breast cancer and cancer in general. There are so many new developments, new treatments, that are making a huge impact that are improving outcomes

28:22 into mp3 file http://www.yalecancercenter.org/podcast/Answers_Aug-31-08.mp3

for patients. I would remind patients to please seek as much information as you can when you are diagnosed and make sure that you are getting the best therapy that is right for you personally. Seek the resources that are needed and make sure that you have a multidisciplinary team of doctors helping you make decisions about how to be treated for your breast cancer.

Chu That is terrific advice and I want to thank you for joining me this evening on Yale Cancer Centers Answers.

Harris It is a pleasure Ed, thank you so much.

Chu Until next week, this is Dr. Ed Chu from the Yale Cancer Center wishing you a safe and healthy week.

If you have questions, comments, or would like to subscribe to our podcast, go to www.yalecancercenter.org where you will also find transcripts of past broadcasts in written form. Next week, we look at the latest information on skin cancer with Dr. David Leffell. I am Bruce Barber, and you are listening to the WNPR Health Forum from Connecticut Public Radio.