

Dr. Gina Chung, Innovations in Breast Cancer Treatment June 13, 2010 Welcome to Yale Cancer Center Answers with Dr. Ed Chu and Dr. Francine Foss, I am Bruce Barber. Dr. Chu is Deputy Director and Chief of Medical Oncology at Yale Cancer Center and Dr. Foss is a Professor of Medical Oncology and Dermatology specializing in the treatment of lymphomas. If you would like to join the conversation, you can contact the doctors directly. The address is canceranswers@yale.edu and the phone number is 1888-234-4YCC. This evening Ed welcomes Dr. Gina Chung. Dr. Chung is an Assistant Professor of Medical Oncology at Yale Cancer Center specializing in the treatment of breast cancer. Here is Ed Chu. Chu Maybe we can start off by defining what breast cancer is, and then after that can you comment on how common breast cancer is in the general population here in the United States? Chung Breast cancer is one of the most common cancers in American women, it is actually the second most common cancer. As for a definition it's a malignancy, an invasive cancer in the breast tissue. Over 200,000 patients are diagnosed with breast cancer each year in the United States and the incidence is extremely common. Estimates are that about one in eight American women in their lifetime as they live into their 80s will develop breast cancer at some point in their life and that translates to about 12% to 13%. Chu That one in eight chance of developing breast cancer, is that in women who have a family history of breast cancer, or in any women with or without a family history of breast cancer? Chung That's all comers, meaning it's any woman, but of course there are certain risk factors that can put certain women at increased risk. Two of the most obvious risk factors are of course gender and increasing age. The peak incidence of breast cancer for most women is in their 60s. It's typically a cancer that's diagnosed in older or postmenopausal women, but there are other risk factors, some more well established than others. For example, the family history that you alluded to is a very strong risk factor and this can be either more vague, such as a strong family history of breast cancers, or in fact ovarian cancers, in multiple first-degree family members, but it can also be more specific. There are specific genetic tests called BRCA1 and BRCA2 gene mutation testing and these are two breast and ovarian cancer susceptibility genes that can be passed along from family members to family members and can put patients at much higher risk for these and other cancers. Chu If a woman should have a family history of one of these breast cancer genes we typically only think of this occurring on the female side, but does one also have to worry if in fact there is breast cancer on the male side of the family? Chung Absolutely, as I alluded to gender is a strong risk factor, obviously, but we do see patients, rarely, who are male and develop breast cancer. One of the things that we have learned is that it is 3:55 into mp3 file <http://yalecancercenter.org/podcast/jun1310-cancer-answers-chung.mp3> certainly very rare in the common population. This is a red flag that there may be a genetic link, and in addition, mutations, especially the BRCA2 gene, have been particularly associated with male breast cancers. Chu If there should be a family history of one of these breast cancer genes, how much is the increased risk for potentially developing breast cancer or ovarian cancer? Chung I can safely say that it's quite a bit higher than the

average population. Depending on which studies you look at the range is quite broad, but in general, the increased risk for breast cancer is estimated to be in the 50% to 80% lifetime risk. Chu Certainly a high statistic. Chung And that's in comparison to the 12% to 13% I mentioned earlier for the average risk woman. Chu Gina, when you see women who present with breast cancer in your clinic, what percentage of that population will in fact have a genetic cause for their breast cancer as opposed to other causes for them developing breast cancer? Chung That's a good question. I think many people are under the misconception that you won't develop breast cancer unless you have a family history, and in fact that's not true. The majority, probably about 90% or more, of breast cancers that are diagnosed are what we call sporadic. What that means is that there is no obvious gene mutation or a family history of breast cancer. Clearly there are other factors that are involved in those patients breast cancer. Chu What are the typical kinds of questions that you pose to women you see in the clinic to try to get at that underlying risk factor? Chung Well, family history as we mentioned. We certainly ask the patient about first-degree relatives such as mothers, fathers, sisters, brothers, and children, but extended family members are also important. Certainly breast cancers and ovarian cancers are more important, but there are other cancers that probably have a weaker link with the breast cancer susceptibility genes as well. Chu What are some of those other cancers, just for our listeners to be aware of? Chung In addition to breast and ovarian cancers, there are certain other ones. There is what we call family cancer syndromes that are weakly linked. There are some gastric cancers, some melanomas, pancreatic cancers, and other GI cancers, as well as even brain cancers. There are other cancers6:55 into mp3 file <http://yalecancercenter.org/podcast/jun1310-cancer-answers-chung.mp3> that are important to know about, and in addition not only the presence of cancer, but the number of family members with cancers, and very important, the age of onset, when those cancers were diagnosed in those family members. If you are very young and diagnosed with cancer, that's a very important red flag. Chu Are there any dietary, nutritional links for the development of breast cancer? Chung There are many-many studies that have looked at these questions. Unfortunately, it is very-very difficult to pinpoint the cause and effect relationships accurately in these kinds of studies. Certainly things like obesity, high fat diets, even smoking and alcohol and those kinds of things, have been linked, although the precise relationship is unclear and I should add that among other important risk factors is a women's lifetime exposure to estrogen, women who take hormone replacement therapy for example. Other questions we ask are things like age of onset of menstruation, age of menopause, number of pregnancies, and age at the delivery of the first baby for that woman. Those are all important questions as well. Chu What about the role of oral contraceptives, does that come into play at all? Chung We do ask about that and there have been links. The link probably is not as great as with the hormone replacement therapies that women take at an older age. Chu And if there is no family history of breast cancer, do you not test for the presence or absence of those breast cancer associated genes, how do you approach that? Chung

We actually send a good number of patients and refer them to the genetics department for testing, but obviously we don't send everybody because we will get a lot of negatives. In general, again, we look for certain red flags, signals in the patient's history. First of all, the patient's age is very important, so if she is very young, typically under the age of about 45, we refer almost all patients for genetic counseling and possibly testing if she is younger than 45, irrespective of other risk factors. Family history as I outlined earlier is very important. If there is a very suggestive family history, I think that would be an important consideration. Then finally, there are ethnic considerations. The Ashkenazi Jewish women are at a particularly increased risk for hereditary breast cancer and BRCA abnormalities, and so these patients are very commonly referred as well. Chu What about African-American women? Is there an increased or decreased risk for developing breast cancer in that population? Chung What we are learning more and more is that in the African-American population, when they10:26 into mp3 file <http://yalecancercenter.org/podcast/jun1310-cancer-answers-chung.mp3> develop breast cancers it tends to be of a more aggressive subtype, the so called triple negative breast cancer, meaning that the estrogen receptor, progesterone receptor, and HER2/neu protein are all negative on these breast cancers. Now, these types of breast cancers happen to be more common in patients who have BRCA mutations as well. The exact and precise relationship between them is not entirely clear though. Chu Let's switch gears a little bit and talk about screening and early detection for breast cancer because obviously that's critically important. What are the current guidelines, recommendations for screening for breast cancer? Chung To date screening mammograms are still the gold standard. There has been a lot of controversy more recently. Epidemiologically, we know that mammograms are effective and they save lives. From a health policy standpoint, however, there is a lot of controversy as to what age, in particular, screening should be started for the average risk women. Some people advocate screening to start at age 40 and others at age 50. In addition, the interval is in general recommended to be annually, although some people would argue that for the average risk women every other year may be adequate. At this point, the American Cancer Society still recommends annual screening mammogram starting at the age of 40 for all women. In terms of new modalities of screening, the MRI is being used more and more frequently. In carefully selected patients this can be very effective, but in those patients, perhaps with very dense breasts, especially younger patients, those patients who have a strong family history and/or a known BRCA mutation, those are the patients that we typically use screening MRIs. Chu Is it a much more sensitive test? Chung It is, but that's very problematic as well. On the one hand, because it is more sensitive, clearly you can pick up cancers that are missed on mammograms, which is a good thing. On the flip side, because it is so sensitive, you will also pick up a number of other suspicious looking abnormalities that require biopsies which then turn out to be benign. You need to be very careful about who you select and how you interpret the MRIs. Chu For women who may be listening to the show this evening what general recommendations can you give to them

in terms of doing their own self exam to look for the possibility of the presence of a breast mass? Chung The benefit of self breast exams is more unclear, but in general, the guidelines say that women at the age of 20 or thereafter, really after they start menstruating, should start breast self examinations, typically monthly and they recommend after the menstrual cycle.14:13 into mp3 file <http://yalecancercenter.org/podcast/jun1310-cancer-answers-chung.mp3> Chu

If a woman should feel something funny, feel a lump or something like that, what should they then do? Chung First of all they shouldn't feel shy about bringing this to the attention of their clinicians, even if they are very young, even if they don't fall into a high risk category. Suffice it to say the majority of these "abnormalities" do turn out to be benign where it's just normal breast tissue or a cyst or something like that. But I think bringing this to the attention of either your primary care doctor or your gynecologist would be appropriate and they can certainly take it from there. Chu So they typically will then go to their primary internist or OB/GYN physician as you suggest. If they then do a physical exam and feel something suspicious, do a mammogram and identify a calcified mass, which I guess is the typical abnormality seen, what would be the next step in that process? Chung If there is definitely a suspicious or abnormal appearing lesion on the mammogram, the mammographers typically do recommend that the patient have a biopsy of this abnormality. In certain instances this does proceed, but in other instances, and this is probably the recommended way of going about this, a referral to a specialist in breast cancer is made, in particular at this point a breast surgeon would be important. Chu And then presumably they would go to the surgeon, the mass would be biopsied, and a diagnosis of breast cancer would be made at that point, is that correct? Chung Yes. Chu And once that's done, does that then go to you, the medical oncologist, who would then be the next line of defense, if you will? Chung There are many different ways we can do this. The approach that we have here at Yale and that many other places have is that breast cancer is a disease that is treated by numerous physicians, surgeons, medical oncologists, radiation oncologists etc., and thus trying to get all of those different types of physicians involved earlier on in the process rather than later is important. Although the breast surgeon is typically the first breast cancer doctor that sees the patient, once the diagnosis is made, often times the patient then will go see all the other physicians, so that a coordinated approach and treatment plan can be made. Chu Great, maybe we can pick up on that on the other side of the break. At this point we are going to take a short break for a medical minute. Please stay tuned to learn more information about the17:34 into mp3 file <http://yalecancercenter.org/podcast/jun1310-cancer-answers-chung.mp3> treatment of breast cancer with my special guest expert Dr. Gina Chung, Assistant Professor of Medicine and Medical Oncology at Yale Cancer Center. Chu Welcome back to Yale Cancer Center Answers. This is Dr. Ed Chu and I am here in the studio this evening with our guest expert Dr. Gina Chung who joins us today to discuss the treatment approach to breast cancer. Before the break Gina, you were talking to us about the multidisciplinary approach to evaluating and treating patients with breast cancer. For our listeners who

may have missed us on the other side of the break, can you tell us again the physicians that are involved in this multidisciplinary clinic that you have at Yale Cancer Center to see breast cancer patients? Chung The primary treating physicians are the breast surgeon and the medical oncologist who discuss chemotherapies and other medications, and the radiation oncologist, but it is important to remember that it is not those clinicians only, there are a number of other supporting staff as well as other diagnostic departments such as mammography and radiology as well as pathology. All of these clinicians typically confer when they see a new patient with breast cancer and we do have weekly meetings where we review all the data and discuss the best treatment approaches for each individual patient. I think that's important to emphasize. Chu In terms of general treatment approaches, we are not going to get into the nitty-gritty specific details, but for women who have early stage disease that's confined to the breast area, what would be the general treatment recommendations? Chung We try to individualize the treatment for each patient based on what our estimate of their relapse risk is in the ensuing years. There are a number of prognostic factors that we look at in a breast20:55 into mp3 file <http://yalecancercenter.org/podcast/jun1310-cancer-answers-chung.mp3> cancer that can help us make this estimation. These things are stage, for example, which is basically how big the tumor is and whether the lymph nodes are involved, but there are other features, biologic features of the breast cancer itself such as grade and things like how rapidly the breast cancer is growing. There are also three very important protein markers that are checked on every breast cancer. These are the estrogen receptors, the progesterone receptors and the HER2/neu protein, and those are very important markers because they help guide which kinds of drug treatments we would give to the patient. Now, in terms of sequencing of different modalities of treatment, typically and traditionally it has been surgery first whether it be a lumpectomy or a mastectomy, and then this would be followed by what we call adjuvant chemotherapy or hormonal therapy, and then typically radiation would follow. More and more now the preoperative approach is being used, that's giving chemotherapy upfront to shrink the tumor first, and then following it with surgery and radiation, and I think this does have several advantages which we can discuss at another time. So, there are many different approaches. In terms of specific drugs and medication treatments, I mentioned chemotherapy which some people will receive, hormonal therapies like tamoxifen, anti-estrogen pills, and these are given to patient's who are estrogen receptor positive, and an antibody therapy called Herceptin for the patients who are HER2/neu positive. Chu There has been so much talk and discussion in the press about targeted therapy. And breast cancer is sort of the poster child for targeted therapy in the era of personalized, individualized medicine and as you say, this antibody Herceptin, is really one of the first true examples of targeted therapy. Chung Yes, absolutely and it's really an exciting time for us in the oncology field. For example, Herceptin as you noted is a very important treatment for patient's who have this HER2/neu product on their breast cancer, which represents about 20% to 30 % of women who develop breast cancer, it's highly effective. It

is most effective when delivered in combination with chemotherapy. It is approved for use in patient's with metastatic breast cancer in combination with chemotherapy, but more recently it's now approved for women with early stage breast cancer in combination with chemotherapy whose breast cancer expresses the HER2/neu protein and in several large studies it has been shown to reduce the risk of relapse by about 50%, which is huge. Chu It is pretty significant. What other targeted therapies are you now using in your everyday clinical practice? Chung The other one is called bevacizumab, or Avastin, and this is a very interesting drug. It is also an antibody based therapy and its target is angiogenesis, the process of new blood vessel growth that tumors in particular seem to have. Its specific protein target is something called vascular endothelial growth factor, or VEGF. It is now approved for use, again in metastatic breast cancer25:06 into mp3 file <http://yalecancercenter.org/podcast/jun1310-cancer-answers-chung.mp3> patients in combination with chemotherapy, and the studies have also shown a benefit when you combine it with chemotherapy as opposed to giving the same chemotherapy alone. It is not yet approved for patients with early stage breast cancer, but there are many-many studies ongoing looking at its effectiveness and safety. Chu As you mentioned earlier Gina, when you are thinking about using hormonal therapy such as tamoxifen, you look at the estrogen receptor and progesterone receptor and if we are thinking about using that antibody Herceptin, you look at the HER2/neu status, are there markers that can identify which patients might benefit from this Avastin therapy? Chung Great question, and the subject of intense research. Unfortunately, to date, there are no good reliable markers for Avastin effectiveness similar to chemotherapy. I guess one could argue, is Avastin truly a targeted therapy? My guess is it probably is, but we haven't identified it. Notably, many people have tried to measure VEGF levels of course and correlate that with Avastin effectiveness and that really has not proven to be a reliable predictor. Chu You have been very actively involved in trying to develop new agents and new approaches to treat women with breast cancer, perhaps you can tell our listeners a little bit about the interesting studies that you have ongoing? Chung At the Cancer Center we have a number of clinical trials currently open and in development and our approach is that we try to make available to all women with breast cancer of different stages and different subtypes a variety of different clinical trials that may be beneficial to them. For example, the Avastin drug that we mentioned is incorporated into a number of our clinical trials currently both in the metastatic settings as well as in the early stage setting. They are incorporated with more novel agents whether it be chemotherapy or other targeted agents and we are looking at effectiveness, meaning is it better than standard of care, and also safety issues as well. Chu In the last couple of years there has been a great buzz about classic compounds called PARP inhibitors, I am just curious what your thoughts are on that class of drugs. Is your group at Yale Cancer Center involved in any of those clinical studies? Chung Yeah, these have generated a lot of excitement and in particular for a specific subtype of breast cancer. The studies to date have predominantly enrolled patients who have known BRCA mutations and strong

family histories, as well as patients who are predominantly what we call triple negative, and these are patients with breast cancers who do not have expression of ER, PR and HER2/neu. This subtype of breast cancer, in particular, seems to be a more aggressive form of breast cancer; it's more rapidly growing and in general confers a poor prognosis. The PARP inhibitors are drugs that take advantage of the knowledge we have about the biology of BRCA29:07 into mp3 file <http://yalecancercenter.org/podcast/jun1310-cancer-answers-chung.mp3> genes and their functions in the cells and so the PARP inhibitors have been studied extensively in early phase clinical trials and are rapidly moving up in the hierarchy of clinical trials. Particularly in patients in combination with chemotherapy, some of the early studies have shown extraordinary results that generated, as I mentioned, early enthusiasm. We do have a PARP inhibitor plus a chemotherapy called irinotecan, study. Unfortunately, it did complete its enrollment and recently closed, although we are looking to open a follow-up study in the near future. Chu In the last few seconds that we have Gina, if someone out there listening is interested in learning more about the types of clinical trials that your group is doing at Yale Cancer Center, how can they get more information? Chung We are readily accessible and I would recommend going to yalecancercenter.org and there is quite a bit of information on that website. Chu Gina, it's been great having you on Yale Cancer Center Answers, we look forward to having you on a future show and hearing more about the really interesting clinical trials that your group at Yale Cancer Center is doing. Until next week, this is Dr. Ed Chu from Yale Cancer Center wishing you a safe and healthy week. If you have questions or would like to share your comments, visit yalecancercenter.org, where you can also subscribe to our podcast and find written transcripts of past programs. I am Bruce Barber and you are listening to the WNPR Health Forum on the Connecticut Public Broadcasting Network.