

Dr. Jennifer Choi, Skin Related Side Effects of Treatment June 20, 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. Jennifer Choi. Dr. Choi is an Assistant Professor of Dermatology at Yale School of Medicine and will lead the Oncodermatology Clinic at Smilow Cancer Hospital. Here is Ed Chu.

Chu Jennifer, before we get into the nitty gritty discussion on skin care for cancer patients, let's start off by having you give a little background for our listeners on how you became interested in the speciality of dermatology.

Choi When I was a medical student I was very interested in medicine in general and when I was trying to decide what field to go into my father, who was a psychiatrist, actually suggested that I look into the field because he had always seen it as a good field where you can combine both medical knowledge and also use your hands with surgery and procedures. So when I did my medical rotation, for me it was one of those moments where automatically I felt that this was the field that I fell in love with. It's a very unique combination of both medical knowledge as well as procedures, in addition to the fact that it's very integrated in medicine in general. On the skin you can see signs of things that are happening systematically, in addition to, in oncodermatology, there are a lot of skin side effects from treatments that need to be addressed.

Chu My good friend Dr. Edelson, who is chair of dermatology and the former director of Yale Cancer Center, always reminded me that the skin is clearly the most important organ in the body as it is the largest organ in the body.

Choi That's correct too, yes.

Chu It's interesting, so then how did you get interested in bringing together the specialty of dermatology, which again is the study of skin diseases, and cancer care?

Choi For me it happened while I was a resident. When you are resident you are on the consult service and we very frequently got consultation from the oncology clinic, and a lot of times they would ask to see patients on the same day because these issues are very urgent and they cannot wait one to three months for a dermatology outpatient appointment, and so at that time I recognized the need to have a dermatology service that is dedicated to these oncology patients so that they can be seen right away, there can be good

2:56 into mp3 file <http://yalecancercenter.org/podcast/jun2010-cancer-answers-choi.mp3> follow-up, and there can be very close communication between us as well as the primary oncologist and the oncology surgeons. That need is definitely there and I have recognized that without such a service sometimes oncologists will try to manage it themselves or try to get them into somewhere but they have to pull a lot of strings and so with something like this, we can provide a much needed service to these oncology patients.

Chu Is this what the Oncodermatology Clinic is going to be focusing on then?

Choi Yes, correct. It actually has two purposes; one is to serve patients with skin cancer, obviously including melanoma, a lot of basal cell cancers and a lot of squamous cell carcinomas. This clinic will also serve to provide very vigorous skin cancer screening

as well as care and detection and treatment of pre-cancers and cancers. The other aspect that we are talking about is skin care in terms of any skin issues that occur within any patient with cancer. Chu Great! And where will this clinic be located? Choi The clinic will be located in Smilow on the 8th floor, which is the same floor as the melanoma unit. As of right now, it is going to be starting in the next couple of months. Currently we are at the 2 Church Street office at the Yale Dermatology Associate office. I see patients there currently and will until it opens in Smilow. Chu Terrific. There are two different aspects that we'll be focusing on during the show, one will be skin care in cancer patients and then a more detailed discussion about skin cancer. Let's start off by talking about skin care in cancer patients. I guess the first question I would ask you is, are there particular cancers for which skin problems seem to be particularly important and relevant? Choi Yes, skin issues in cancer patients occur mostly due to treatment, so chemotherapy and radiation most of the time, and the skin issues that we see are related to the treatment that is chosen based on the cancer, so for example, in lung cancer, colorectal, breast, and head and neck they use a lot of EGFR inhibitors, EGFR stands for epidermal growth factor receptor, and so the inhibitors that are directed against that target, we see a lot of skin reactions. For example, one of the most common that we see is papulopustular eruption where it starts off as redness and then within the next week they then develop red papule and pustule that looks like acne. It's 5:39 into mp3 file <http://yalecancercenter.org/podcast/jun2010-cancer-answers-choi.mp3> commonly affects the face, the chest, the back and the scalp, and when these patients are on these medications 45 to 100% of them may actually develop some degree of this rash. When we talk about other medications such as multikinase inhibitors, one of the most common that we see in up to 60% of patients, they will develop some type of hand-foot syndrome where they develop red patches that are very painful and can be swollen and can really start to impact activities of daily living on the hands and feet, and so a lot of the skin reactions are based on the treatment that is chosen. Chu That's interesting because as you know, my area of specialty is colorectal cancer and we do use these anti EGFR antibodies quite frequently, Erbitux, and Vectibix, and it's interesting because there has been a pretty strong correlation between the development of this acne like skin rash and eventual response to the therapy. Choi Right. Chu Can you explain how that happens? Choi In some studies they have shown, like you mentioned, that the incidence and the severity of the skin rash is correlated with better outcome, and we are not exactly sure exactly why that happens right now, but it is a very significant observation, and so in that sense, it's almost in a way a good thing if you see a severe rash, but at the same time, it may be so severe that it can actually limit how long or the dosing that you can use. So the answer is we are not exactly sure what that mechanism is, perhaps it's because it's an indicator that it is actually targeting that EGFR receptor and in that sense it's exhibiting on the skin. Chu If someone should develop the skin rash that in some cases can be quite painful, what are your usual treatment recommendations? Choi Treatment recommendations usually are a combination of different things. One of

them includes just a cool compress, the second part then will include perhaps a combination of either topical and oral antibiotics as well as topical and oral anti-inflammatory such as corticosteroids, and so usually that combination will work very effectively. There have been a few case reports where we used different types of medication including oral retinoids, when used at low dose can also help to clear the rash, but as of yet there are actually very few clinical trials that are randomized control trials looking at these treatments, so there is a need for that.8:35 into mp3 file <http://yalecancercenter.org/podcast/jun2010-cancer-answers-choi.mp3> Chu

Do you ever think about perhaps prophylacting patients with either oral or topical antibiotics to try to prevent the rash from occurring?Choi That's actually a very important part of this field right now. There have been three case studies so far where they looked at tetracycline, minocycline and doxycycline use preemptively and the most recent was this step trial where they took patients who were being treated with Vectibix and they started them on doxycycline 100 mg, twice a day, 24 hours prior to the start of Vectibix, and they compared it to the patients who were put on doxycycline as reactive therapy, meaning they started it once the rash started, and they actually found that at week six, there was more than a 50% reduction in the incidence of more severe rash. So that is definitely something that we are considering doing more of. It's interesting that you say that because we are starting a new small clinical trial where I want to actually compare the use of low dose isotretinoin versus doxycycline as preemptive therapy, so we can actually look at them head to head.Chu This would be in patients who are receiving anti EGFR therapy?Choi CorrectChu So that would be the antibodies or small molecules?Choi Yes, that's right.Chu As you mentioned, one of the side effects from chemotherapy is this development of hand-foot syndrome which can affect the palms, and the soles of the feet. What is your general approach when you have someone who presents with that kind of skin reaction?Choi This can be a very painful process and indeed affects somebody's quality of life when they do develop it. This skin reaction, like we are talking about, usually occurs later on in treatment, so usually around weeks 2-4 so that's something also to understand, that it may not happen right away and in some patients it happens even 2-10 months after starting treatment. We can actually talk about two things, one is prevention and then two is treatment, so when it comes to prevention there are a few things that definitely are helpful. We talk about using emollients, gentle emollients to moisturize the skin on a daily basis, basically to try to prevent it from drying out which can then make it more susceptible. We also talk about some measures such as avoiding tight-fitting or ill-fitting shoes or clothing, anything that is restrictive tends to make this occur. Other things like avoiding direct sun11:24 into mp3 file <http://yalecancercenter.org/podcast/jun2010-cancer-answers-choi.mp3>exposure and also avoiding direct extreme temperatures such as very hot or very cold are important. When you do use emollients, wear socks or gloves at night to help increase the moisturization. When it comes to treatment, there have been a couple reports that suggest that cold compresses or localized hypothermia, meaning some people will actually take ice packs and put them on their wrists and ankles, around their hands and feet, even during

administration of the medicine, or while they are taking it and that seems to help. There are some case reports saying that oral vitamin B6, known as pyridoxine and sometimes oral vitamin E, have been shown to work in a few cases, so there again needs to be a lot more studies in a very controlled way to see what the real benefit is, but at least the reports are out there that that helps. Chu I know a drug that currently is associated with hand-foot syndrome is Xeloda, which is used for colorectal cancer, other GI cancers, and breast cancer and I think an important piece of advice that we always like to give patients is if they begin to notice any redness or tenderness of their palms or soles or their feet, they need to stop taking the medicines, call either the nurse or the physician and then be seen to see exactly how severe that skin reaction is. Choi That's a very good point and it's great that you bring that up because part of the treatment, if it becomes severe, is to actually reduce the dose or sometimes increase the length between administrations, so a lot of times that ends of having to be part of the treatment. Chu To emphasize that point, I know a lot of patients do not like to let us know that they are experiencing that because I think they are fearful that we will stop the treatment or reduce the dose and they are concerned that it might harm them in some way. Choi That's a very good point, and one thing I do want to emphasize to the listeners is that it is important to talk with your oncologist regarding possible skin reaction even in advance of starting the treatment, so that you are aware of what might happen because sometimes things seem a lot worse if they are not expected and then two, definitely let your oncologist know right away as soon as something happens because if you let it go it can just continue to get worse and at that time it can actually become harder to treat. Chu We are here with Dr. Jennifer Choi from the Department of Dermatology. At this point, we are going to take a short break for a medical minute. Please stay tuned to learn more information about the approach to patients14:14 into mp3 file <http://yalecancercenter.org/podcast/jun2010-cancer-answers-choi.mp3> with skin issues and the skin care of cancer patients with our special guest expert Dr. Jennifer Choi. Chu Welcome back to Yale Cancer Center Answers. This is Dr. Ed Chu and I am joined by my guest Dr. Jennifer Choi, Assistant Professor of Dermatology and Jennifer will be leading the effort in the new Yale Oncodermatology Clinic at the Smilow Cancer Hospital. Jennifer, we have been talking about some of the different skin issues that are associated with the treatment of various cancers, and one of the other side effects that can be a significant problem is this radiation dermatitis. Can you describe for our listeners what that is and how you typically approach that problem? Choi Radiation dermatitis is definitely a very prevalent problem. As you know, radiation is used in a number of patients and in conjunction with chemotherapy and surgery, and in those patients almost all will develop some degree of dermatitis. Dermatitis, essentially, is characterized by skin that becomes pink or red and that can also become inflamed and is often times associated with scaling or crusting. The associated symptoms can be pain, sometimes when it is very severe even erosions or blisters, and in addition it can also sometimes become itchy. In most patients this will occur anywhere from 20-25 grey in terms of cumulative dose and usually that ends up occurring in the range of anywhere from the 3rd to the 5th

week of treatment. Some of the measures that we take in order to prevent it are difficult in this field because there have been hundreds of reports and17:26 into mp3 file <http://yalecancercenter.org/podcast/jun2010-cancer-answers-choi.mp3> literature out there regarding what is the best in terms of prevention and treatment, and yet there is actually not one single thing that has come out in terms of the top or standard of care. Some things, however, that have been shown to help include gentle emollients and avoiding any perfumes or dyes or any harsh chemicals. In addition, they found that sometimes the use of low dose corticosteroids, even at the start of treatment, may help to prevent the development of severe reactions. There have been a number of reports on other things such as aloe vera and things like that, but that has not yet been shown to be very helpful in terms of concrete evidence.Chu Do you typically recommend waiting until there is evidence of skin damage or would you start at the time radiation therapy is initiated?Choi Based on my review and given that there is still not a standard of care, my preference is actually to use a low dose topical steroid even at the start of treatment, because I do think that it may help to prevent severe reactions and if you are using this steroid for only about 8 weeks, for example, the risk of causing skin atrophy or thinning is actually very minimal, so for that reason I do think it would be beneficial.Chu I have noticed for a number of treatments there can be associated nail changes, nail issues, which can be pretty significant and pretty painful to some patients. What are your thoughts as to how you treat these patients?Choi Patients, for example, who are on EGFR inhibitors can develop several things, one is something called paronychia where there is inflammation around the nail folds and along the sides of the nails and this can be very inflamed, very painful, and sometimes it can be associated with bacterial infections. Some other changes include painful fissures, which are cracks in the skin along the nail folds. Another change can also be the formation of something called pyogenic granulomas, and what that is, is basically overgrowth of granulation tissue, and those can actively bleed and be very painful. The management of these is usually a combination again of either topical or oral antibiotics and also sometimes topical or oral corticosteroids, and some of the same measures that we used before in terms of just gentle cleansing, and gentle emollients, things like that.Chu One other issue that as oncologists we do not always pay careful attention to is that a number of cancer drugs that we give to our patients can increase what is called photosensitivity, which in some patients can be a pretty serious issue.Choi Photosensitivity means that because of the medication that you are on your20:33 into mp3 file <http://yalecancercenter.org/podcast/jun2010-cancer-answers-choi.mp3> skin can be much more sensitive to the sun, and when it's more sensitive to the sun, it can develop brisker burn reaction even from regular sun exposure. You can develop pink and very red and sensitive skin. One of the most important things that we do for patients on chemotherapy is basically counsel them against sun exposure, and there are numerous things that you can do, one example is seeking shade when you are outside. We definitely don't want to tell people don't go outside at all because that's effecting your quality of life, but when you are outside definitely use a good sun screen with at least SPF 30 and SPF means

sun protection factor, which is an indicator of protection against UVB rays, which brings up the important point that sun screen should also contain something that protects you against UVA rays, and the UVA rays can be protected against using either chemical sun screens, which absorb the UVA rays and then disperse them as heat, and those include things like Parsol 1789, which goes by the term avobenzone and other things like mexoryl. Most importantly, the physical blockers are very good, including the zinc oxide and titanium dioxide, since that literally blocks out the sun and deflects the sun's rays. They are not a white paste that goes on your nose anymore, they are micronized, so when you put them on they can actually still absorb. Some examples for the listeners include things like Blue Lizard or SolBar and these are just some examples of ones that contain physical blockers as well. Chu Why don't we switch over and talk a little bit about skin cancer if that is okay? Choi Yes. Chu Obviously skin cancer is a serious problem. Maybe you could first define for our listeners out there the different types of skin cancer. Choi The different types include basal cell carcinomas, squamous cell carcinomas and melanoma. Basal cell carcinomas are by far the most common types of skin cancer. These occur from chronic sun exposure over the years, usually we think from the UVB rays, but as well as the UVA rays. These are cancers that occur usually in the upper part of the skin and sometimes into the dermal part of the skin, but in general these have very low rates of ever metastasizing, and so we consider these as very manageable and if you surgically take them out they are considered cured. Squamous cell carcinomas are also another type of skin cancer that are also very common and these are also associated with chronic sun exposure. They do have a slightly higher rate of possible spread to other parts, but usually only if its been there for a long time or its grown to the point where somebody has not really brought it to somebody else's attention, but these do have a slightly higher risk. The next type of skin cancer is melanoma, and there are an estimated 70,000 new cases per year. These are the types where if you detect them early it can literally save your life, in the fact that if the prognosis of melanoma is directly related to what we call the Breslow depth, which is how deep the melanoma is when measured from the dermal epidermal layer, the top layer of the skin, if they are very deep they have a higher risk of recurring and spreading to other parts of the body. Chu Therefore, for basal cell and squamous cell, as you say, sun exposure is obviously a major risk factor. Are there any other preexisting skin conditions that predispose individuals to develop these forms of skin cancer? Choi Predisposing skin conditions include some of the risk factors for basal cell and squamous cell for people with fair skin, if you have light or blond hair, or if you have grey, blue or green eyes, those are all risk factors for it. You do not have the natural melanin to protect you, so you are at increased risk of developing damage from the UV rays. Chu What are the recommendations for preventing the basal and squamous cell skin cancers? Choi The recommendations are basically some of what we talked about earlier in terms of sun screen use on a daily basis, and we should also talk in terms of how often and how much you should apply. You should be reapplying every 2-3 hours at least and

anytime you sweat a lot or you go swimming, you should reapply as soon as you come out of the pool, for example, or come out of the water. In addition, it's recommended that one adult should use one ounce per application, sometimes people are not putting on that much and they actually should be putting on about the size of shot glass to cover your entire body surface. We should talk about clothing, in general you want to wear hats, baseball caps will protect sun from the forehead and the nose, but it is really not doing much for your ears and neck, a broad brimmed hat helps a lot in addition to wearing clothing like light, thin, long sleeved shirts and pants. There is this product out there that called Sun Guard where you can actually put it in your wash and soak your clothes for about 50 minutes and you wash it out and it actually puts SPF 30 into your clothing and it does not affect the dye, it does not affect the color, and it lasts through 20 washings. That's something you can get at your local stores. Chu Looking at catalogues, it seems that there are a lot of clothes that actually say they have SPF protection, so presumably that stuff is already in those clothes is that right?27:14 into mp3 file <http://yalecancercenter.org/podcast/jun2010-cancer-answers-choi.mp3>

Choi Yes, and clothes that are marketed as that, the SPF is in there and does not wash out so those are permanent SPF clothes, that's also a very good option. Chu If one should develop say basal and squamous skin cancers, are those individuals at high risk for developing the more aggressive form of skin cancer, melanoma, or is there not really any relationship? Choi There is not a direct relationship, so for example, people can develop even 50 basal cell skin cancers in their life and still never get a melanoma, so it actually is not directly related, however, if you do have a lot of basal cell or squamous cells, that is an indication that you have received a lot of UV exposure over time and so that in itself is a risk factor for developing melanoma, so there is that relation there definitely. Chu In the last 45 seconds that we have Jennifer, can you remind our listeners what the Yale Oncodermatology Clinic is, and where it's going to be located within the next couple of months? Choi The Yale Oncodermatology clinic is a specialized clinic that is designed to serve patients with any type of cancer and to help manage any of their skin issues. Right now it is at the 2 Church street office, Yale Dermatology Associates, where you can be referred by your oncologist and soon it will be on the 8th floor of Smilow Cancer Hospital where again we will be seeing patients referred by their oncologists and if there are any issues you can always call and we can help set it up for you. Chu I have to say, this is really a tremendous service that you are providing because unfortunately I think we as medical oncologists are very poorly trained at dealing with these skin issues, which really are so important for quality of life for many patients. Choi Great, thank you. Chu We look forward to having you come back on a future show and tell us how your Oncodermatology Clinic is doing. Choi Fantastic, thank you. Chu You have been listening to Yale Cancer Center Answers and I would like to29:23 into mp3 file <http://yalecancercenter.org/podcast/jun2010-cancer-answers-choi.mp3> thank our guest this evening Dr. Jennifer Choi from the Department of Dermatology for joining us. Until next time, I am 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.