

Yale CANCER
CENTER

answers

WNPR Connecticut Public Radio



Hosts

Anees Chagpar MD

Associate Professor of
Surgical Oncology

Francine Foss MD

Professor of Medical
Oncology

Advances in the Treatment of Lymphomas

Guest Expert:

Daniel Persky, MD

*Assistant Professor of Medicine
(Hematology), Yale School of Medicine*

Yale Cancer Center Answers

is a weekly broadcast on

WNPR Connecticut Public Radio

Sunday Evenings at 6:00 PM

Listen live online at

OR

Listen to archived podcasts at

Welcome to Yale Cancer Center Answers with Dr. Francine Foss and Anees Chagpar. Dr. Foss is a Professor of Medical Oncology and Dermatology, specializing in the treatment of lymphomas. Dr. Chagpar is Associate Professor of Surgical Oncology and Director of the Breast Center at Smilow Cancer Hospital at Yale-New Haven. 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 1-888-234-4YCC. This week, Dr. Chagpar welcomes Dr. Daniel Persky. Dr. Persky is Assistant Professor of Hematology at Yale School of Medicine. Here is Anees Chagpar.

Chagpar Let's start off by having you tell us a little bit about yourself, how long you have been here at Yale and what you do here?

Persky Thank you. I came to Yale not so long ago. I started August 1, 2012 and I came from the University of Arizona where I was focused on treating lymphomas. The University of Arizona is actually an old program that has been doing interesting lymphoma research since the 1970s. Before that I finished my fellowship in medical oncology and hematology at Memorial Sloan-Kettering Cancer Center so in a way it is actually coming back for me.

Chagpar Tell us a little bit more about lymphomas. It is certainly something that we have all heard a little bit about, but I do not know that we completely understand what a lymphoma is?

Persky I am glad that you have heard about lymphomas because a lot of people have not. It is not one of the most common cancers, it is not as common for example as breast cancer or colon cancer, but it is fairly common. This year the American Cancer Society estimates that about 79,000 Americans are going to be diagnosed with one type of lymphoma and the word lymphoma really means a cancer of lymphocytes and lymphocytes are a type of white blood cell that fights infections.

Chagpar So, as a breast cancer doctor, I can tell you that when you present with a lump in your breast or bloody nipple discharge or you get a mammogram that has an abnormality, that is a sign of breast cancer. What are the signs of lymphoma?

Persky Often there are no specific signs of lymphoma, but the most common way that people notice that there is something wrong with them is they notice an enlarged lymph node somewhere on the surface. For men, for example, it is really common to notice a lump in their neck while they are shaving and people can notice lumps under their arms or in their groins and these lumps if they are cancerous would usually persist and typically they would not be painful. That being said, the majority of the lumps that people have in those areas are usually due to infections, but the key thing is to pay attention to are the lumps that do not go away or that grow. Other symptoms of lymphoma could be fevers, drenching night sweats where you have to change bed sheets or clothing,

3:14into mp3 file <http://valecancercenter.org/podcasts/2012%201028%20YCC%20Answers%20-%20Dr%20Persky%20copy.mp3>

unexplained weight loss, but unfortunately, those signs are kind of nonspecific, a lot of different diseases can cause them.

Chagpar If I have any of those symptoms, should I go and talk to my doctor?

Persky Yes, the best idea would be if you have those symptoms to talk to your primary care doctor first and the doctor should examine you and go from there, for example, if there is a lymph node that the doctor feels on the exam, the doctor should think about lymphoma as being one of the explanations in addition to infections and other possible explanations as well and the doctor can take the workup further.

Chagpar What would that workup entail? If they were worried about lymphoma, what would happen next?

Persky The doctor would probably do some blood tests just to check some basic things, blood counts, organ function labs, but often enough lymphoma does not impact those much and often they come back normal. Often the doctor then would go and ask for a radiology scan, so a CAT scan for example is the most common approach, and that would often pick up an enlarged lymph node or several enlarged lymph nodes inside the body where you cannot feel them and then the main way you diagnose lymphoma really is to do a biopsy and typically we ask for a lymph node to be removed and then that lymph node is sent to our pathology colleagues, specifically our hematopathology colleagues, those are pathologists, doctors who specialize in examining tissue and making diagnoses on them who specialize specifically in the tissues of blood and blood cells.

Chagpar Let's say they take a lymph node out and they send it to this special pathologist who looks at it and says its lymphoma, are there different kinds of lymphoma?

Persky Absolutely, there are over 60 kinds of lymphoma and everytime the classification of lymphomas gets revised there are more and more types of lymphomas because there are more specific molecular tests that tell us that what we thought was one lymphoma in reality turns out be three or four.

Chagpar Are the treatments for these different lymphomas different? What happens after I am told I have a certain type of lymphoma?

Persky There is a general approach to treatment. Lymphomas after all are cancers of lymphocytes and lymphocytes being blood cells, travel, so the main way to treat lymphomas is with drugs which go throughout your body and kill the lymphoma cells wherever they are. Drugs can be traditional chemotherapy drugs, or they can be newer drugs, a lot of which are pills which do not work by the traditional means that chemotherapy drugs have worked. They may target a particular part of the

6:27 into mp3 file <http://yalecancercenter.org/podcasts/2012%201028%20YCC%20Answers%20-%20Dr%20Persky%20copy.mp3>

lymphoma or even a particular pathway which triggers the lymphoma cells to grow. That being said, we also enlist the help of our radiation oncologists who often administer radiation therapy after chemotherapy if the disease is located in one area, but the primary treatment is usually with chemotherapy. The regimens, however, are widely different for different kinds of lymphoma.

Chagpar What is the prognosis after treatment for lymphoma? Do people do pretty well? Or does it depend on the type of lymphoma?

Persky It absolutely depends on the type of lymphoma that the person has. On average, lymphomas may be cured about 50% of the time, but that differs from let's say Hodgkin's lymphoma which could be cured about 85% of the time to some rare subtypes of T-cell lymphomas which are cured only 5% of the time and all the other lymphomas are in between.

Chagpar Tell us a little bit more about who gets lymphoma, is this primarily a disease of older people or younger people? Is it more common in men or women? Are there are any racial distributions that we should know about?

Persky Again, it depends on the type of the lymphoma, but in general, lymphoma is a disease of people who are little bit older, so on average people get diagnosed when they are in their mid 60s. That being said, there are some specific types of lymphoma, for example Hodgkin's lymphoma, that are diagnosed in much younger patients, typically in their late 20s or late 30s. In terms of gender, lymphomas are a little bit more common in men than women, but that again depends on specific subtypes of lymphoma. Follicular lymphoma, for example, which is a relatively common type of lymphoma is somewhat more common in women, and mantle cell lymphoma, which is a bit more rare, is three times as common in men than women and we do not know exactly why. In terms of race, usually lymphomas are thought to be higher occurring in whites, but again, that depends on some lymphoma subtypes as well. In terms of other things that should be mentioned, we do not know why most of the lymphomas are there, we know there are certain things that are risk factors for developing lymphomas. Usually, they have to do with dysregulation of the immune system, so people whose immune system is not great such as people who have HIV or people who are on immunosuppressive drugs because they had an organ transplant, they are at high risk of lymphoma. People who have autoimmune conditions such as rheumatoid arthritis or systemic lupus are at high risk and there are specific lymphomas that even have certain co-relations with infections such as H. pylori, the bacteria that causes stomach ulcers and a particular type of lymphoma called marginal zone lymphoma of the stomach, but overall most people do not have any specific risk factors which makes it harder for us to pick it up and means that there is not any specific screening strategy that we can have.

9:58 into mp3 file <http://valecancercenter.org/podcasts/2012%201028%20YCC%20Answers%20-%20Dr%20Persky%20copy.mp3>

- Chagpar As with many cancers, there is a lot of exciting research that goes on that helps us move the field forward. Tell us a little bit about some of the advances that are happening in lymphoma research?
- Persky There are lots of new drugs that are being tested. I think there is a general revolution in how quickly the drugs can be designed. I wish that the revolution of how quickly we can test could keep up with that, but the speed with which we can test the drugs is getting better, but the way that we test the treatment is also changing. When we are realizing that one lymphoma is in fact actually three or four in the molecular level, we cannot approach it with the same kind of treatment. So, the drugs are starting to target specific pathways and therefore specific subtypes or subsets of lymphoma. That brings with it its own challenges in how you design clinical trials. Now we are starting to see newer designs of clinical trials where we start to do molecular testing and we try to target the new treatments to that specific molecular signature of lymphoma. Those trials are getting started, they are fairly new and they are also studying another cancer sub types as well and there are a lot of interesting drugs that we are testing such as drugs which target certain pathways, I do not know if you want me mention certain pathways, it can get pretty technical, but for example some lymphomas tend to be addicted to signal links through one of the surface molecules that ordinarily would be used to just signal growth and activation, called B-cell receptors, and there are several drugs targeting many parts of that pathway. One drug is ibrutinib that is thought to be very important in the sub type of diffuse large B-cell lymphoma which is the most common lymphoma diagnosed in people in the United States.
- Chagpar It sounds like a lot of the work in lymphoma, like in a lot of cancers is really towards this whole concept of personalized medicine, figuring out the genomic signature of that particular cancer and then targeting your therapy, is that right?
- Persky Yes absolutely, I think we are all moving toward the same goals. It is sometimes harder to move toward the goals depending on how common the diseases are and one of the problems in lymphoma is that we have a lot of different types of lymphoma, including some very rare lymphomas where studying them becomes very difficult because you just do not have enough patients to make any conclusion in the trial. In those kinds of lymphomas, it is very important to collaborate with investigators not only around the country, but sometimes around the world.
- Chagpar That is fantastic and is that the type of work that you are going to be engaged in here at Yale?
- Persky Absolutely, I am privileged enough to work with Dr. Francine Foss who is a world expert in T-cell lymphomas and she already participates and leads many of the trials that are part of the T-cell lymphoma consortium. I participate in a cooperative group that does trials in lymphoma called

13:27 into mp3 file <http://yalecancercenter.org/podcasts/2012%201028%20YCC%20Answers%20-%20Dr%20Persky%20copy.mp3>

SWAG, which used to stand for Southwestern Oncology Group, and there I developed some of the trials for diffuse large B-cell lymphoma where more than 100 centers around the country share these trials and can enroll in the trials and share their experience.

Chagpar We are going to take a break right now for medical minute, but please stay tuned to learn more information about lymphoma with my guest Dr. Daniel Persky.

*Medical
Minute*

Breast cancer is the most common cancer in women. In Connecticut alone approximately 3000 women will be diagnosed with breast cancer this year, but there is new hope, earlier detection, non-invasive treatments, and novel therapies provide more options for patients to fight breast cancer. Women should schedule a baseline mammogram beginning at age 40 or earlier if they have risk factors associated with the disease. With screening, early detection and a healthy lifestyle, breast cancer can be defeated. Clinical trials are currently underway at federally designated comprehensive cancer centers such as Yale Cancer Center to make innovative new treatments available to patients. A potential breakthrough in treating chemotherapy resistant breast cancer is now being studied at Yale combining BSI-101 a PARP inhibitor with the chemotherapy drug irinotecan. This has been a medical minute brought to you as a public service by the Yale Cancer Center. More information is available at yalecancercenter.org. You are listening to the WNPR Health Forum on the Connecticut Public Broadcasting Network.

Chagpar Welcome back to Yale Cancer Center Answers. This is Dr. Anees Chagpar, and I am joined today by my guest Dr. Daniel Persky and we are talking about lymphoma. Dr. Persky, before the break you described lymphoma as a cancer of lymphocytes. How is that different from leukemia?

Persky That is an excellent question Anees. Leukemia usually implies that the cancer is in the blood and in the bone marrow, but lymphoma can also go there. So, leukemias can also come from lymphocytes and some of the lymphocytic leukemias are known as either acute lymphocytic or lymphoblastic leukemia, or ALL and chronic lymphocytic leukemia or CLL, and they have parallel lymphomas meaning that in the cases of leukemias and lymphomas that come from lymphocytes, they are in effect two sides of the same illness. For CLL, its lymphoma counterpart is called small lymphatic lymphoma and they should really be treated as one disease. We only differentiate between the two with an arbitrary rule where we say that if there are more than 5,000 abnormal lymphocytes, meaning malignant lymphocytes, in the blood we call it CLL. If it is less than that we call it SLL meaning lymphoma distortion. That being said, if the cancer starts in the blood stream it often goes to the lymph nodes and vice versa. Similarly for acute lymphoblastic leukemia, it can often start in the lymph nodes as well and then go to the bone marrow in the blood. There, an arbitrary line in the

16:51 into mp3 file <http://yalecancercenter.org/podcasts/2012%201028%20YCC%20Answers%20-%20Dr%20Persky%20copy.mp3>

sand that we draw as the amount of malignant lymphocytes that we find in the bone marrow. If there more than 25% of them present in the bone marrow space than we call that leukemia, if it is less than that, it is a lymphoma.

Chagpar It is sounds like the two are really part and parcel of the same process. Is that right?

Persky Yes, and that is why the treatments for them are very similar.

Chagpar The other kind of cancer that we think about in lymph nodes is when cancer starts in another part of the body and goes to lymph nodes. Breast cancer will sometimes go to lymph nodes, but that is not a lymphoma or leukemia. How does that work?

Persky You may actually be in a better position to answer the question of how it works in breast cancer, but clearly for a breast cancer that comes from a breast cell to go a lymph node, the cancer must have acquired a new ability that let it go there. On the other side, for a lymphoma to go from let's say a lymph node in the neck to a lymph node in the groin area, that takes almost no new ability because the cancer comes from the lymphocyte, the cell that travels. Consequently, when we do staging, our staging probably is less important than the staging in breast cancer and some of the other solid cancers, meaning that a lot of times, probably the majority of the time, most lymphomas get diagnosed at the advanced stage, stages 3 or 4, but it does not mean that they are not curable. A lot of them can still be cured.

Chagpar Wow, so it sounds like as opposed to breast cancer where the cancer starts in the breast, in a lymphoma or a leukemia it starts in the lymph nodes, or in the blood cells. It is interesting to me that so many leukemias and lymphomas can be cured even at an advanced stage. Can you tell us a little bit more about what that therapy involves, what are the side effects that a patient can expect from these drugs that we talked about prior to the break?

Persky We are fortune enough in lymphomas and some leukemias that we have had treatments that work and can cure patients for quite a while. The first trials of chemotherapy drugs such as nitrogen mustard started in the 1940s at Yale, and in the 1960s Dr. Vincent DeVita who is also a Yale faculty member, was at that time a member of the NCI, the National Cancer Institute in Bethesda, Maryland, and came up with one of the first drug regimens where several drugs were combined, and he showed that this combination can actually result in a significant number of patients with Hodgkin's lymphoma being cured. A lot of these drugs that we use are still old chemotherapy drugs, which work extremely well for some diseases, and it is very hard to know why in lymphoma and some leukemias we have had this success, but obviously we are very happy to offer patients those drugs and like with a lot of typical chemotherapy drugs, some side effects may include drops in the blood

20:16 into mp3 file <http://yalecancercenter.org/podcasts/2012%201028%20YCC%20Answers%20-%20Dr%20Persky%20copy.mp3>

counts, which would predispose patients to high risk of infections, bleeding, or tiredness if they develop anemia, a drop in their red blood cell counts. With some chemotherapy drugs, patients lose their hair, but with some they don't. There have been a lot of developments in supportive care in the last 10 to 20 years, so that the patients do not experience nearly as much nausea and vomiting as they used to in the past, and now there are growth factors to support some of the white blood cell counts and often the red blood cell counts, which decrease the risk of infections and decrease the need for transfusions.

Chagpar Tell me a little bit more about some of the newer therapies that are being developed. Are they more effective or do they simply reduce toxicity, or a bit of both?

Persky They can do different things, and just because they are more targeted, does not necessarily mean they do not have side effects. It is true that a lot more of them are given in the pill form as opposed to through the veins, but again a lot of the new drugs are also given through the veins. On average, I would say they result in fewer side effects, but the key with a lot of the newer drugs is to find how exactly to pair them up and which patients to use them in. With use in the right group of patients with the right kind of lymphomas, they can be extremely effective. Side effects of a lot of the drugs could actually be allergy-like infusion reactions, which is of more of a typical reaction for some of the drugs called monoclonal antibodies. The most common of which is rituximab, a drug that has been approved for certain types of lymphomas since 1997.

Chagpar With a lot of the cancers that we talk about on this show, we always talk about a multidisciplinary approach. Today, we have talked a lot about drug therapy. How do the other disciplines play a role in lymphoma treatment, or do they?

Persky They absolutely do. I believe that medicine is a team sport. You cannot do well without your colleagues and first off it is very important to have a good hematopathologist with whom you work, because they are the ones who make the diagnosis and we are fortunate to work with outstanding hematopathologists here at Yale. We also work together with radiation oncologists who administer radiation, we work with surgeons who help us perform biopsies, also interventional radiologists who use imaging such as CAT scans and ultrasounds to guide needle biopsies in places where lymph nodes are harder to reach and where surgery is really not possible. We work with a lot of scientists and Yale again is very fortunate to have a very large group of excellent basic scientists who do more basic work on not only cancers, but sometimes on lymphocytes and how they develop and what could go wrong in the process of lymphocyte development, and let us not forget the radiologists who do a lot of the imaging and they can actually help us administer some of the drugs, and also of course our nurses, nurse practitioners, physician assistants, nursing assistants, and all the people that you need to make the treatment successful.

23:54 into mp3 file <http://yalecancercenter.org/podcasts/2012%201028%20YCC%20Answers%20-%20Dr%20Persky%20copy.mp3>

Chagpar So it really is a multidisciplinary effort. Tell us a little bit more about some of the newer things that we may hear about, but we're not really sure what they are, things like what is radioimmunobiology, or immunotherapy? What is that?

Persky That is an interesting concept. Radioimmunotherapy is a type of drug therapy that is given to some lymphoma patients, particularly with slow growing lymphomas such as follicular lymphoma and what it is, is a monoclonal antibody much like rituxan or rituximab that is coupled to a small radioactive particle, so when the antibody binds the lymphoma cell, not only does it kill that lymphoma cell, but the small radioactive particle also kills the lymphoma cells in the surrounding radius of that radioactive particle, and there are two drugs on the market right now that can do this that are approved for use, particularly in follicular lymphomas, although they are found to be effective in some other types of lymphomas as well. One is called ibritumomab tiuxetan, you have to bear with me because their generic names are fairly complicated. The brand name was called Zevalin and there is also iodine tositumomab, which is known as the Bexxar regimen, and we actually get help administering them from nuclear medicine, which is part of radiology. They are actually fairly easy to give in the sense that people come, they will have a test dose, and then a week later, they get a therapeutic dose, and then we just watch them, and common side effects are a slow drop in the blood counts, which can be monitored, but generally those drugs are fairly well-tolerated. The issue is that a lot of the oncologists who practice especially in the community, sometimes have difficulty getting those drugs, because you have to work together with the nuclear medicine specialist to administer them because they involve radioactive particles. So that is again a place where a multidisciplinary approach is crucial.

Chagpar It sounds like there are a lot of really interesting therapies that you can administer with your multidisciplinary team, and I guess another advantage of being in a tertiary academic center like you are at Yale is clinical trials. Do you participate in clinical trials, and can you tell us a little bit about clinical trials and some of the exciting ones that you have?

Persky Absolutely, clinical trials are very important because they are a way to advance our treatment. Without it we often do not know on an individual basis whether the treatment that we gave the patient before really worked well, or do we think the patient would have done well by him or herself. So only with clinical trials do we actually learn how to improve therapy compared to what we have done in the past, and all the clinical trials are monitored closely by different federal agencies and there are, at this time, three basic phases of clinical trials, and perhaps you have discussed it on previous shows, but typically phase one clinical trials just test if the drug is safe and a person discovers a safe dose in phase two trials, which tend to be a larger look at whether there is a signal of effectiveness, they will look at response rates, and phase three clinical trials typically look at how this new drug or drug combinations compares to the standard of care and they are the ones

27:59 into mp3 file <http://yalecancercenter.org/podcasts/2012%201028%20YCC%20Answers%20-%20Dr%20Persky%20copy.mp3>

that are typically used to get approval from the FDA. So, we definitely participate in clinical trials and we consider it an important part of what we can offer our patients. As I mentioned before, I participate in clinical trials within the corporative group SWAG, but we also participate in clinical trials that we initiate at Yale, for example, and clinical trials of different drugs that are provided to us by pharmaceutical companies. Some of the exciting trials that we are doing here, for example, are for diffuse large B-cell lymphomas, where a standard treatment is R-CHOP. We are trying to improve that treatment by using a drug that we think can improve some of the body's own ability to detect it immunologically. The drug is called vorinostat and it is approved but for different kinds of cutaneous T-cell lymphomas. We also use new imaging modalities such as PET scans to direct therapy further and we are doing it both for Hodgkin's lymphoma and diffuse large B-cell lymphoma and finally we have some of these new and exciting drugs that address some of the important molecular pathways in lymphoma, for example, a drug that target PI3-kinase and we have other drugs that target interesting neurologic targets.

Dr. Daniel Persky is Assistant Professor of Hematology at Yale School of Medicine. If you have questions or would like to add your comments, visit YaleCancerCenter.org, where you can also get the podcast and find written transcripts of past programs. You are listening to the WNPR Health Forum on the Connecticut Public Broadcasting Network.