

Yale CANCER CENTER *answers*

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Yale Cancer Center Answers

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Welcome to Yale Cancer Center Answers with doctors 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. Terri Parker. Dr. Terri Parker is an 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 have you been here, and what is it that you do?

Parker I actually recently joined the faculty here at the Yale School of Medicine. Prior to that I was in New Haven doing my fellowship in hematology/oncology through Yale University.

Chagpar Tell us a little bit about what exactly a fellowship is.

Parker It is a good question, as the medical education system can be a little bit confusing, especially when fellows see patients. So, a fellowship is more specialized training that a physician receives in order to specialize in a particular area. So, for example, when you finish your residency, which can be done in general medicine, pediatrics, or surgery, then you can choose to specialize and do additional training. For example, my fellowship was in hematology/oncology and it was a three-year program that I completed.

Chagpar Why did you choose hematology/oncology? What was it about that field that was particularly attractive to you?

Parker When I was in medical school, the first patient I was ever responsible for had acute leukemia and as a medical student, acute leukemia can be a very challenging case, but I enjoyed the challenge and that you got to use everything that you had learned in medical school from your basic histology, to the patient interactions, to really provide good care for patients. And I also enjoyed hematology because you really got to build a relationship with the patient and their families throughout the years.

Chagpar Tell me more about what exactly hematology/oncology is. I mean, I know oncology is the study of cancer, what is a hematologic malignancy?

Parker Hematology has to do with your blood and it is often broken down into benign, so things such as an abnormality in the red blood cells, white blood cells or platelets that are not malignant, or cancer. And then you have your hematological malignancies, which people look at as cancer of the blood so to speak, or of a lymph node.

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- Chagpar Tell me about your practice, if you were to see somebody with a benign hematologic disease, what might that be and how do patients present with those kinds of abnormalities?
- Parker I see a wide variety of hematological disorders. When you look at the benign, some of the things that we commonly see are anemias or a low red blood cell count. These are often discovered incidentally by the patient's primary care physician or family practice doctor when they are doing routine blood work for an annual checkup, and a lot of the time if someone does have anemia, we work them up for nutritional deficiencies, which are very common, and many of our patients have things such as iron deficiency, folic acid deficiency or vitamin B12 deficiency. We also see patients who have abnormalities in white blood cell counts, and that may be due to a viral infection or an abnormality in their platelets that can be associated with other more systemic illnesses.
- Chagpar Tell us a little bit more about disorders with platelets and what exactly a platelet is?
- Parker A platelet is one of your blood components important for clotting your blood. So, if you were to cut yourself, say in the kitchen, cooking, the platelets are what help to stop the bleeding. So, often times we see patients who either have too low of a platelet count, or too high. Someone who has too low of a platelet count, the concern is that if they do cut themselves or suffer an injury, that they would not stop bleeding. So my job as a hematologist when I see these patients, is to try to determine what the cause of the low platelet count is, and sometimes we are successful and sometimes it is what we call immune mediated, which is commonly seen, meaning the patient has developed an antibody that attacks those platelets and clears them from your peripheral blood, and so our job is again to try to differentiate what could the potential cause be, and how we can correct that platelet count back to the normal range.
- Chagpar You mentioned one potential cause is that your body is making antibodies to these platelet, do we know why that would happen?
- Parker A lot of times we see it in patients who have other autoimmune disorders, so for example if someone has a history of autoimmune thyroid problems, or an autoimmune rheumatological disorder such as lupus, but sometimes these can come out of the blue and people say it's idiopathic, meaning we do not know exactly what causes it, but we do see it more associated in clusters with autoimmune disorders.
- Chagpar Are there other reasons why people can get low platelets, or is it mostly because of antibodies attacking these platelets?
- Parker One of the other common areas that we can see a low platelet count is in patients who have liver problems, commonly hepatitis C, as there is a hormone that your liver makes that tells your bone marrow to start producing platelets, and if you have liver damage, you are not producing as much

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as this hormone and there are a few other reasons, but we do often see it in patients with liver disease, whether it is due to hepatitis C which is a virus, or other causes of liver failure.

Chagpar Do patients ever present with platelet counts that are too high?

Parker Yes, we do see platelet counts that are too high and most commonly in two different circumstances. Your platelets are what we call acute phase reactant. Kind of breaking that down, basically if you have an infection or any type of inflammation, your platelets can respond to that and increase, so it is a reactive process. The other type we see is something that is called essential thrombocythemia and that is actually classified as a myeloproliferative neoplasm, considered more of a malignancy, and so my job as a hematologist is to determine if this is something that is a primary bone marrow process, or if it is just reacting to something else that is going on in your body.

Chagpar Tell us more about bone marrow, what is it and how can you figure out whether something is a cancer of a bone marrow or something unrelated?

Parker Everyone has bone marrow, so if you look at your peripheral blood cells, you have your red cells, white cells and platelets, and that's breaking it down very simply, but all of your blood cells are made in your bone marrow. So, you can think of it almost as a factory, is where you are producing these, and so in order to figure out what is wrong with these cells, we go to the place where they are made, which is the bone marrow and we do that by doing what is called a bone marrow biopsy and we usually take it from the back side of your hip, which is where there is a large amount of bone marrow. We look at that bone marrow specimen under a microscope with the aide of our hematopathologist in order to determine what the cells look like, and what the precursor cells look like morphologically, so again this is all done with the help of our hematopathologist. We can do a variety of tests on the bone marrow looking specifically at certain cell markers, morphology of the cell and also cytogenetics, or if there are any genetic abnormalities, and putting all of this information together, depending on what your suspicions were prior to doing the procedure, it can help us make a diagnosis.

Chagpar Tell us a little bit more about bone marrow cancers. What are they, how common are they and how do they present?

Parker If you look at hematological malignancies, and if you are discussing bone marrow cancers, we commonly refer to those as leukemias, or cancers of the blood, and when you compare it with solid tumors, hematological malignancies are much less common than say breast cancer or colon cancer, and with hematological malignancies you can have lymphomas, which more commonly involve your lymph nodes but may also involve your bone marrow, and then the leukemias which only

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involve your bone marrow and then the peripheral blood. Within leukemia, we have acute and chronic types and the most common within these leukemias is actually chronic lymphocytic leukemia.

Chagpar So tell us a little bit about the other type, lymphomas, those occur you said in the lymph nodes as opposed to in the bone marrow. How do they present?

Parker Oftentimes, if patients present with lymphoma, which involve lymph nodes, they may feel a lump or bump, either in their neck region, under the arm or in their groin. So, often these patients will come to their primary care physician saying, I have this growth I noticed when I was shaving, or I noticed it in the shower, and from there you are then worked up for whether or not this could be an infection of a lymph node, and eventually they end up having a biopsy of that tissue that would reveal the abnormal cells.

Chagpar I understand that your primary focus is in something called CLL, is that right?

Parker Currently yes, I do see patients with benign and malignant hematological problems, but one of my interests is chronic lymphocytic leukemia, commonly referred to as CLL and that is also my research interest.

Chagpar What is CLL? What kinds of patients present with it? How do they present? How do they get worked up and then how are they treated?

Parker Most often, we are seeing patients diagnosed with chronic lymphocytic leukemia, or CLL, incidentally. So an individual will have blood work done for a totally unrelated issue or just as part of their routine checkup and in that blood work they find an elevated white blood cell count, and the specific white blood cells that are elevated are called lymphocytes. Oftentimes, these patients have no other symptoms besides an abnormal count. It is usually diagnosed in individuals who are in their 60s or 70s, so later in life, and usually the first time we see the patient is after they have already been discovered to have an abnormal white blood cell count and they are then referred for further evaluation.

Chagpar And then what happens?

Parker Once we see those individuals, our job is to confirm that this is in fact a chronic lymphocytic leukemia. In order to do that, we look at their blood under a microscope to see what the lymphocytes look like. You would expect to see mature appearing lymphocytes and in an increased number. We do a specific test called flow cytometry, which allows us to look at certain cell markers on the lymphocytes to confirm that these are in fact lymphocytes that are involved in the CLL. We also look to see if they have any palpable lymph nodes, meaning do they have any lymph nodes that we can feel on their physical examination. A lot of times, we will be able to feel

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lymph nodes in the neck, under the arms, or in their groin. These individuals can also have an enlarged spleen or enlarged liver, and if we are concerned that they have lymph nodes that we cannot palpate, we will do what is called a CAT scan in order to fully evaluate the chest and their abdomen to determine if they have any lymph nodes that are hiding, so to speak, or that we cannot feel. Sometimes we can make the diagnosis just based on their peripheral blood, sometimes we do have to do a bone marrow, especially for considering treatment in these individuals.

Chagpar And what would that treatment entail?

Parker What is interesting about chronic lymphocytic leukemia is a large majority of our patients do not actually require treatments. CLL is a very heterogeneous disease entity, meaning some patients can go for 10, 20, 30 years without having any symptoms and have very stable blood counts; whereas other patients can progress very quickly. Our job is to initially see the patient and try to determine who is going to progress and who is not.

Chagpar It sounds like some of these patients may or may not need treatment. We are going to take a break for a medical minute, but we will be back and I would like to talk a little bit more about treatments for CLL, some of the novel treatments in terms of trials that are ongoing. Please stay tuned and learn more information about hematologic malignancies and CLL with my guest Dr. Terri Parker.

*Medical
Minute*

It is estimated that nearly 200,000 men in the US will be diagnosed with prostate cancer this year and one in six American men will develop prostate cancer in the course of his lifetime. Fortunately, major advances in the detection and treatment of prostate cancer have dramatically decreased the number of men who die from the disease. Screening for prostate cancer can be performed quickly and easily in a physician's office using two simple tests, a physical exam and a blood test. With screening, early detection and a healthy lifestyle, prostate cancer can be defeated. Clinical trials are currently underway at federally designated comprehensive cancer centers like the one at Yale to test innovative new treatments for prostate cancer. The da Vinci Robotic Surgical System is an option available for patients at Yale that uses three dimensional imaging to enable the surgeon to perform a prostatectomy without the need for a large incision. This has been a medical minute and 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 our guest, Dr. Terri Parker and we are discussing hematologic malignancies. Terri, prior to the break we were talking a little bit about CLL, which is a type of leukemia that you are particularly interested in. You mentioned that patients can go a long time and may not need treatment. Tell us a little bit about how you know whether a patient needs treatment and when that treatment might be initiated?

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- Parker It is very different for each individual patient, so we really need to look at the patient on an individual scale and not categorize everyone into one category. There are certain things that we can look at to help us better predict when and if a patient is going to progress, and a lot of that is through cytogenetic abnormalities, and what that means is do they have any chromosome abnormalities? Do they have an addition or deletion, so not enough or too many copies of a certain chromosome? So that is one of the routine tests that we are doing when we see patients upfront, because that can only give us more information to share with them about how quickly we think they will progress, or if they well at all. That being said, there are outliers to every situation and once we have that information, it still does not change our recommendations or plan for treatment. So if someone has a chromosomal abnormality, for example, a deletion 17, which is loss of the chromosome and the arm at 17, we know that those patients have a higher likelihood of progressing and needing treatment during their disease course, but so far studies have not shown that if we treat those patients upfront, it changes their survival. It would expose them to chemotherapy and maybe the side effects that go along with that, without any benefits. So some of the things that we tell our patients with CLL are that we look at how quickly their white blood cell count is increasing. We call that the doubling time. We would like to see that white blood cell count stay stable over several years. If it is increasing, it goes from 6 to 12 to 24 very quickly and that is a sign that someone might need treatment. Other things we look at are, is the patient symptomatic? So are they having things that we call B symptoms, or fevers? Are they losing weight unintentionally? Are they having night sweats? Are they having very massive swelling of their lymph nodes that causes them to be uncomfortable? Those are some of the clinical things that we work out and tell our patients to look for and that may be cause to treat them.
- Chagpar You mentioned a couple of things that I want to pick up on. One is that you look at the cytogenetics of these cancer cells, and I understand that what you are looking for is a deletion or an addition of a particular chromosome, but does this have implications in terms of family history, so your progeny, whether they are at increased risk of getting the same disease?
- Parker These are what we call acquired mutations, so these individuals acquire them as they age. This is not something that they would pass on to say their children, which we get that question asked a lot because that is a concern of our patients.
- Chagpar So this is something that you are not likely to pass on to the next generation, but it is really a tool for you to look at these cancer cells and help you to decide whether to treat or not treat and perhaps with what particular agent. Is that right?
- Parker It does not necessarily tell us that we are going to treat. It tells us that we may need to treat sooner but not necessarily treat that individual, as again we have not seen any improvement unfortunately if we do treat these patients at the time of diagnosis versus when they become symptomatic.

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- Chagpar Tell us a little bit more about some of the interesting clinical trials that are ongoing. I understand that you are doing some pretty innovative work?
- Parker I was very fortunate when I was a fellow to have had the opportunity to work with several of my mentors, who are now colleagues here at Yale Cancer Center, to write and start a clinical trial from the ground up. Currently the only trial we have open specifically for CLL at Yale is whether or not consolidating, and by consolidating we mean adding additional therapy after the upfront chemotherapy, if that makes a difference. For example, if someone with CLL were to require treatment, the standard treatment currently is something called chemoimmunotherapy, which is the combination of certain chemotherapeutic agents in addition to the immunotherapy rituximab, which is a monoclonal antibody. So that would be considered standard treatment, but we know a lot of these patients who receive treatment may have improvement in their symptoms, but the abnormal cells do not go away, so you may still have a certain percentage of your lymphocytes that are abnormal. Our trial is looking at if we treat these patients with standard care upfront, which is the chemoimmunotherapy in individuals who have stable disease or who achieved a partial response, if we give them an oral medication to try to consolidate that for a year, can we improve upon their initial response?
- Chagpar So this trial is really looking at whether in addition to getting rid of these symptoms, that this additional therapy might get rid of these abnormal cells?
- Parker To decrease them that is the idea so people call this, maintenance therapy, or consolidation therapy. Obviously the challenge in having consolidation or maintenance is you want to find an agent that is well tolerated. You do not want to give your patients more side effects, especially if it is a medication that is going to be taken for a long period of time such as a year in this study.
- Chagpar One other thing that was interesting is that so many patients with CLL will present initially just with an abnormal blood test. They will go to their doctor, they will have their annual exam and then they may be diagnosed with a cancer. What must that feel like for patients?
- Parker It is very stressful for the patient because they are not having any symptoms. Sometimes when you think of a malignancy or a cancer most people think that you are pretty sick, but these patients are going to the store, they are spending time with their families, they are doing everything that they would normally do. So to be told based on just one wellness visit, so to speak, that they have leukemia, can be very devastating and it really requires a good multidisciplinary team with the physician, nurses, and social work to kind of support them and say this is the diagnosis but this is something that you can live with potentially, hence the word chronic. So you really need a lot of patient education and a lot of support for them initially.

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- Chagpar And what must it be like if you are a patient? You feel well, you have just been handed this diagnosis, do you get a lot of patients who say, I know that you are telling me that I may not need therapy right now, I feel great, I do not have any symptoms, but I really want everything possible done. Does that happen?
- Parker It happens a lot actually. It is very hard to have a diagnosis of cancer and not do anything about it. People want to be treated once they hear that word and so again it does take a lot of education to educate them that if we do treat them we may actually be doing more harm, because they would have symptoms from the chemotherapy that sometimes are worse than how they are feeling now. It is good patient education to say, we want to give you the best quality of life that we can, and that may mean very frequent visits to the physician to reassure them that everything is stable and that they do not necessarily have to have treatment right that instance.
- Chagpar It is sounds like you are treating the patient and how they are feeling rather than the diagnosis or the abnormal cell that might be there that may or may not need treatment?
- Parker That is correct, and it can cause a lot of anxiety for patients but I think the big thing is to work with them to come up with a plan that the physician and the patient are comfortable with. Whether that is initially, for example, in the patients who do not need treatment we'll often see them once a month just to make sure that they are not progressing, not developing any worrisome symptoms and that their blood counts are remaining stable, and if everything goes well in those initial few months, we can stretch out that time period to every three months, every six months, and there are even some patients who have had the disease for thirty years, again outliers, and they come once a year. So it really depends on what the patient's comfort level is and the physicians.
- Chagpar I am sure that at least reduces some anxiety, knowing that their physician is always there and that they are going to go back and see their physician and make sure that everything is okay.
- Parker It definitely does, and the one thing that we do stress is just because you have an appointment in three months or six months, that does not mean we cannot see you earlier if you have something that comes up that is worrisome to you. So we take a lot of time to educate our patients on the symptoms that might cause us to consider treatment, again new lymph nodes or lumps and bumps, or fevers, or just not feeling well in general. We encourage them to call and be seen sooner and I think for a lot of patients that reassurance that we are a phone call way definitely helps.
- Chagpar Another thing that you mentioned, that a lot of our guests mention, is this as a multidisciplinary effort. Tell us a little bit more about that and how it works in hematologic malignancies and why it is so important?
- Parker I think one of the main things with hematological malignancies is what you are treating as the blood, is not one specific area, it is the whole person and you definitely need your whole staff to

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help manage these patients because it is complex and we physicians and nurses who are wonderful both in the inpatient and the outpatient setting who really get to know the patients and the patients always have a favorite nurse that they like to go to if they require treatment. We have dieticians who work with the patients to try to keep up their nutritional needs if they are going to chemotherapy. We have social work that helps deal with things such as, how am I going to get to my doctor's appointment, to, how do I tell my family members about this diagnosis?

Chagpar There are really a lot of people who play a very big role in taking care of the whole patient and I think the patients get a better experience with that team. The other piece too that I think you touched upon and I want to circle back to is with CLL the longevity is really long. We talk a lot about survivorship these days in cancer and cancer care. Tell us a little bit more about what survivorship is and how that works.

Parker Oftentimes people think of survivorship as patients who have been diagnosed with any type of malignancy or cancer and once they go into remission, but really survivorship, for example, palliative care, can start when the patient is diagnosed, because it requires following up not just for their malignancy and making sure that they reach goals such as when do I need my next physician visit, but also making sure that their other health maintenance does not fall by the wayside. So just because a patient is diagnosis with CLL, you want to make sure that they are still following up with the remainder of their health maintenance, if it is a female, their mammograms, if it is a male, making sure their prostate health is up-to-date, making sure they get the correct vaccinations. So, it is really coordinating care and making sure they do not miss out on other things because they are so focused on this one diagnosis.

Chagpar It is so interesting that you mentioned palliative care and survivorship beginning at diagnosis, and yet we talk about this being a longtime, you can have patients living with CLL for 20 or 30 years. Many people think about palliative care being end-of- life and yet if it starts at diagnosis it really is not. Tell us a little bit more about palliative care and how that fits in?

Parker I do have an interest in palliative care because I did do a palliative care fellowship prior to my hematology fellowship, and palliative care is more about symptom management, not end-of- life care, which I think people confuse with hospice. We are using palliative care to help with symptom control.

Dr. Terri Parker is an Assistance 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.