



Hematology

American Society of Hematology (ASH) Meeting 2016: Highlights

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Welcome to Yale Cancer Center Answers with doctors Anees Chagpar, Susan Higgins and Steven Gore. I am Bruce Barber. If you would like to join the conversation, you can contact the doctors directly. The address is canceranswers@yale.edu and if you are interested in listening to past editions, all of the shows are posted on the Yale Cancer Center website at yalecancercenter.org. This week Dr. Steven Gore will be speaking with Dr. Scott Huntington. Dr. Gore is Director of Hematological Malignancies at Smilow Cancer Hospital and an expert on myelodysplastic syndromes. Dr. Huntington is an Assistant Professor of Medicine at Yale School of Medicine and he joins Dr. Gore for a conversation about hematological malignances.

Gore Scott, you treat lymphoma. What is lymphoma?

Huntington Lymphoma is actually the most common blood cancer. Blood cancer as a whole is actually relatively rare, so about 10% of all cancers are blood cancers and lymphomas make up the majority in terms of numbers. But lymphoma represents a disease arising from the lymph nodes and in total, there are almost 60 different types of lymphoma, so it is a rather basket diagnosis and we are learning more each and every year about subdivision within lymphomas and how we actually recognize patients have different lymphomas and need different treatment, so it is really a fascinating field that is moving dramatically to improve patient outcomes and diagnosis.

Gore Does lymphoma include Hodgkin's disease, is that a lymphoma?

Huntington Yes, you can parse lymphomas in a number of different ways. One is Hodgkin's lymphoma versus non-Hodgkin's lymphoma. Non-Hodgkin's lymphoma is more common and that is typically a disease of aging whereas Hodgkin's lymphoma has 2 distributions, one in the early phase where people are typically in late adolescence and late adulthood and then again closer to their 60s. That is about 8500 cases in the United States each year in terms of Hodgkin's lymphoma. Non-Hodgkin's lymphoma is much more common. We are talking about closer to 70,000 to 80,000 cases in the United States each year.

Gore Wow, so 70 or 80,000 and there are 60 types or so?

Huntington Yeah, and although I am a specialist in lymphoma, each day is very different in clinic where I have different ages and certainly different histologies and diagnoses that really keep my day varied in the clinic.

Gore And you organize your days that way, like today is my lymphoma day and tomorrow is my that kind of lymphoma day.

Huntington Not quite yet, but certainly we could get there.

Gore It seems really complicated to have to keep track of that many different diseases. We train in oncology and there are a lot of different cancers and I cannot keep track of all those and now here you are theoretically treating one kind of cancer but it is really so many.

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- Huntington I think as we learn more about cancers in general we are further sub-classifying lots of cancers in a personalized medicine approach to treating patients. In terms of lymphoma, although there are 60 different types, in my mind how I classify things are whether they are aggressive and whether they are more indolent or slow growing, so even though we have 60, we can further classify those patients in terms of presentation, how patients present with these illnesses and also how we might be able to treat them based on whether these are aggressive diseases or more indolent.
- Gore Why is it important to differentiate between those that are more aggressive and those that are more slow growing or indolent as you put it?
- Huntington That is a really good question, and in terms of aggressive lymphomas, what makes them aggressive is that typically these cause patients symptoms over weeks to months, so the patients present to their provider with say fever or chills or night sweats or rapidly enlarging lumps or lymph nodes and when a diagnosis is made that typically would show a histology where the cells are replicating and this is an aggressive disease. Conversely, a more indolent processes typically progresses over months to years and typically the patients are asymptomatic when they are diagnosed and so the patient may present to their primary doctor and have routine blood work or a routine exam and have a slightly abnormal finding which could lead to the diagnosis. In aggressive versus indolent, it not only clinically has an importance but actually in terms of treatment as well. Aggressive lymphomas are actually quite sensitive to our treatment, so if we give chemotherapy, we are hoping that we are actually going to cure the majority of patients with aggressive lymphomas whereas patients that have the more indolent process, we actually may just observe these patients over time because they may either never become symptomatic or they may be able to live quite well with their disease for a number of years before needing treatment and so although there are 60 sub-classifications of lymphoma, we can really focus on whether they are aggressive and require more intensive treatment, versus the more indolent that could really be potentially watched and surveyed very closely.
- Gore It seems to me if I were a patient and I found a lump or my doctor found a lump and you told me it was cancer but we are just going to watch it, I am not sure I would really go for that, I would want that thing out of there? Why can't you just go in there and cut it out or blast it out?
- Huntington An indolent process or indolent lymphoma can really be varied in itself whether it is more extensive, whether the patient has only one location or multiple locations and if it is only one location, sometimes surgery or blasting it with radiation as you may say, can actually lead to a very good outcome, but if lymphoma in the indolent process is more on the systemic side that patients have multiple regions, what we found over time that if we give treatment right away, patients can certainly have side effects from the treatment and what we find over time is that the indolent lymphomas typically come back with treatment whereas if we wait, and actually it is not so much waiting as actually surveying, so if the patient has indolent disease and indolent lymphoma, we watch them very closely and over time if we detect symptoms, we start treatment and it seems that active surveillance is the best way of treating the indolent processes in lymphomas.

- Gore So the outcomes are not better if you treat it early?
- Huntington That is exactly right, yes.
- Gore And why aren't those patients easily cured?
- Huntington How I think of it is an indolent lymphoma has many cancer cells that are basically dormant and so they are not replicating, so we now give chemotherapy to these patients, that gets rid of the replicating portion but there are plenty of cells that are basically dormant and resistant to active chemotherapy. When you take that to the aggressive lymphoma, like diffuse large B-cell or Burkitt's, where all the lymphoma cells are replicating quite quickly, our chemotherapy can eradicate all of that and so really the pathophysiology and the basis of the lymphomas does explain some of the activity of how chemotherapy works and whether the patient can be cured and whether they can be rendered in a very good remission that can last years potentially and be treated over time. So the indolent process, we typically try to convert into a more chronic disease where patients hopefully do not have a lot of symptoms from the disease and also do not have a lot of symptoms from our treatment, that is the goal when I see a patient with indolent, whereas the goal is very different if someone comes in with aggressive lymphoma, my goal is to get rid of it for good and not have it come back.
- Gore Can you walk us through what happens to a patient if they find a lump or somebody finds a lump, is that going to turn out to be a lymphoma, how does that all play out?
- Huntington Many things can cause lumps and lymphadenopathy and infection, so if someone has a viral illness, they may have a lump under their neck or throat and it could certainly go away as part of the healing process and getting over infections. If lumps persist for weeks potentially and do not wax and wane, then that may be a signal that this is something else besides a normal inflammatory process and so frequently what we do if someone has a lump is that we need a biopsy whether it be a needle or actually more commonly an excision, actually taking that lymph node and looking it under the microscope.
- Gore Okay so you send me to someone who has taken out my lump and you send it to the lab and I am thinking that I just had the flu and now you are going to tell me that I have cancer and I am going to be mad at you, then what happens?
- Huntington When we take out the lymph node, there are a number of things that go on, looking at how they look under the microscope, how their genes are arranged to help us classify if this is lymphoma. If it is a lymphoma, we further classify as to whether it needs treatment or not and ways that we could do that is doing imaging. Frequently we do staging procedures where we might do a CT scan, a CAT scan, x-ray machine or nuclear medicine scan to get a sense of where the lymphoma is and depending on the stage of the disease, the lymphoma, we might have slightly different treatment, maybe it is only chemotherapy alone. Other times, if there is only limited stage or we have only a few spots, we might do chemotherapy along with radiation for those patients.

- Gore But there is always chemotherapy?
- Huntington Typically, there is always chemotherapy that is quite effective for patients with lymphoma.
- Gore Interesting, so I stop being mad at you because you are doing the best for me and I say okay, Dr. Huntington you can go ahead and treat me and you have given me chemotherapy, how long does that last for usually?
- Huntington Yes, well your classic chemotherapy for lymphoma typically lasts on the order of 4-6 months. And the goal of that frequently is to get this in remission where we are unable to detect lymphoma and if it is an aggressive lymphoma, we are hoping that the remission stays forever, that we are curing these patients. If it is in the more indolent process, we typically know that our treatments can render disease in remission but over time, months, years, potentially even decades, the lymphomas are likely to come back in those cases and so most importantly, when I see a patient I determine if I can cure them with my treatment and if I can, I am going to do everything I can to do that. If we cannot, then we have to balance the pros and cons of our treatment, the side effects of the treatment and also the side effects of the lymphoma and so it is really an important thing to think about patients when they come to see you and what the goal of our treatment is.
- Gore Do you tell the patients that and do you tell your patients you are not going to cure them?
- Huntington I think it is a process, so when patients in particular have indolent lymphoma, then I tell them we are going to likely need to treat this at some point but I see us treating it in the future, that is the first step that we need to overcome with the provider and the patient, the idea that we may not need treatment emergently for indolent lymphomas. The second process is getting over the idea that our treatments are going to be effective and this is likely something that you will be dealing with for the rest of your life and what we are finding out is that as new treatments become available, we have so many different lines of therapy for indolent lymphomas, that our goal really is to convert it into a chronic disease that potentially does not impact your quality of life significantly. It is moving towards minimizing toxicities of our treatment so we have a number of newer agents that are not traditional chemotherapies but are actually oral medications, much like you would take for say high blood pressure or diabetes, and our goal is to render lymphomas into a very, very treatable disease without the significant side effects.
- Gore And if I still am resisting this and I say I do not like this kind of watch and wait thing and I want to be cured, could I go somewhere else and have somebody tell me differently?
- Huntington There is quite a consensus in terms of indolent versus aggressive lymphomas. There are occasionally things that we can do, I talked about radiation in early stage disease or these more advanced approaches like allogenic stem cell transplant sometimes can render patients cured, but those have significant side effects and I think there is a wide consensus that the aggressive lymphomas, we treat aggressively; we really want to cure those patients and get them in remission

that is long lasting, whereas the indolent process, we are now trying to figure out how do we minimize our treatment toxicities because these patients live very well with their disease and it is a new process that we use for both the provider and the patient to help them overcome and to live with their disease.

Gore I am counting on you to talk me through this one but before you do, we are going to take a short break for a medical minute. Please stay tuned to learn more about lymphoma with our guest, Dr. Scott Huntington.

*Medical
Minute*

There are many obstacles to face when quitting smoking as smoking involves the potent drug nicotine, but it is a very important lifestyle change especially for patients undergoing cancer treatment. Quitting smoking has been shown to positively impact response to treatments, decrease the likelihood that the patients will develop second malignancies and increase rates of survival. Tobacco treatment programs are currently being offered at federally designated comprehensive cancer centers such as Yale Cancer Center and at Smilow Cancer Hospital. Smilow Cancer Hospital's Tobacco Treatment Program operates on the principles of the US Public Health Service Clinical Practice Guidelines. All treatment components are evidence based and therefore all patients are treated with FDA approved first line medications for smoking cessation as well as smoking cessation counseling that stresses appropriate coping skills. More information is available at yalecancercenter.org. You are listening to WNPR, Connecticut's Public Media Source for news and ideas.

Gore Welcome back to Yale Cancer Answers. This is Dr. Steven Gore and I am talking with my guest, Dr. Scott Huntington about lymphoma. Scott before the break, we were talking about the fact that there are some lymphomas where people live quite well but they are likely not to be cured and I was imagining that there must be patients who push back on that because our society is focused so much on, I am going to beat this cancer, I am going to fight this cancer, but you are proposing for some cancers and some lymphomas, learning to live well with the cancer may be the more noble goal or may be the only realistic goal.

Huntington It is not an easy thing to overcome and it takes time, so when the patient comes to my office and learns that they have a lymphoma diagnosis, whether it is aggressive and we are going to treat it aggressively, or whether it is indolent where we may actually not treat it for years, it is a process of coping and education and learning more about the disease. I think what is really encouraging is that for both aggressive lymphomas and for the indolent lymphomas, we are learning more about the disease and our treatments are getting ever better, so for the indolent processes, minimizing the side effects of our treatments and moving more towards the non-chemotherapeutic approach, is something that many of us are enthusiastic about both clinicians and patients and we really do have a future that is very bright in terms of the current treatment and also for patients who have indolent lymphomas.

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- Gore I guess one of the ways that we all learn about the newer treatments and the newer biology is by going to international meetings where this information is shared and you recently had one of those meetings right?
- Huntington Yes, we just returned from San Diego where the American Society of Hematology Annual Meeting was held and this is a meeting of about 20,000 to 30,000 hematologists and basic scientists throughout the world that come each year and the goal is to really review and discuss the most pressing up-to-date research in blood disorders and there were definitely some high profile and important studies that were presented this year and will likely impact how we are going to be treating patients for the next year with lymphomas.
- Gore What did you find exciting or what did you learn that was new that our listeners might find interesting?
- Huntington For the two most common lymphomas, one being the aggressive diffuse large B-cell lymphoma, the other being an indolent lymphoma called follicular lymphoma, there were a number of large studies that were reported at ASH. In the diffuse large B-cell realm, there was a study comparing a therapy that is a little bit more intensive treatment to what is typically used and this was a study that we knew was underway and as a lymphoma community, we were really anxiously awaiting. To some surprise, the standard treatment to less intensive treatment actually had the same outcomes to more intensive treatment but actually had fewer side effects and so that trial was important. It is what we call a negative study but it reassured that what we are doing is actually the current standard and that will likely impact how we think about patients going forward.
- Gore Of course it is kind of disappointing if you felt that the standard must have been having some failings or shortcomings, we would not have tried to make it better and then the way you tried to make it better, turned out not to. It is kind of disappointing right?
- Huntington It is disappointing. I would say that the outcomes for the standard treatment are actually quite good and this typical treatment called CHOP or R-CHOP which has been a standard for a number of years has bested other treatments in the past, so historically, this is a really good treatment that is generally well tolerated and it does not mean that we are not going to try to make it better and so there are other trials going on currently trying to again advance the needle for treatment of large cell lymphoma but this treatment in general, the more intensive therapy, did not win out in this round.
- Gore Large cell lymphoma is not just one disease either, right?
- Huntington Yeah that is true. There are a number of different forms of large cell lymphomas, the most common is diffuse large B-cell lymphoma and that is the most common lymphoma in general, but there are T-cell lymphomas that can be large and aggressive and so this trial was really limited to the large B-cell lymphomas. On the other end of the spectrum, there was a clinical trial looking at follicular lymphoma and follicular lymphoma again is a very treatable lymphoma with either chemotherapy or what we call immunotherapy, and there is an immunotherapy that has been

around for about 15 years and really is a mainstay of treatment for B-cell lymphomas and this trial compared the immunotherapy that has been around for 15 years to a newer therapy and in this clinical trial, the newer therapy did seem to improve the outcome, so it is likely that many lymphoma providers over the next years will be transitioning in some settings to this newer immunotherapy treatment.

Gore So the newer therapy was also an immunotherapy?

Huntington It was, yes.

Gore And these immunotherapies, they are not oral like what you are talking about the newer more exciting drugs, these are all infusions right?

Huntington Yes, the immunotherapies are still infusions and they are typically given alongside chemotherapy. They augment the chemotherapy and also impact how our own immune system might recognize the lymphoma cells and so it is an important component but it also is typically given as an infusion either weekly or sometimes after every month or two months.

Gore But you said some of the new therapies are oral, is that right?

Huntington That is correct, there are a number of newer therapies that are currently in clinic and usually are used on a single agent basis, so you may be on a therapy that you take every day that we hope will keep your lymphoma at bay for a long period of time, years potentially. What we are trying to figure out is whether combining therapies for things like infectious diseases where if we had a cocktail of treatments that were well tolerated, we might be able to improve our outcomes and we are trying to find that cocktail for lymphoma as well for these new oral agents.

Gore If I were a patient with a diagnosis of lymphoma, whether it is a new lymphoma or a recurrent lymphoma, how would I even learn about whether there is a study that I could go on if I wanted to because it seems to me that I might want to know what is the latest and greatest, most promising to be part of if I could.

Huntington There are a number of available websites, the Leukemia and Lymphoma Society has a great website that has active clinical trials. You also can go on the Smilow Cancer website where it has clinical trials. I think as lymphoma specialists, it is really important for patients to recognize that the diagnosis, having to be sure about the diagnosis is the first step. Again, there are 60 different types of lymphomas and you need to have hematopathologists, the doctors that look at your tissue, to confirm what type of lymphoma, that is the first step. The second step is going invasively, being seen by a clinician that is comfortable in treating lymphomas and so I think those are the 2 metrics of starting a lymphoma process. In terms of care, making sure that the diagnosis is there and #2, that your treating provider has knowledge about the treatment and also knowledge about ongoing clinical trials.

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- Gore And I guess from the numbers that you stated, if lymphomas are 5% of cancers or 8% of cancers, many general oncologists might not see a lot of lymphoma.
- Huntington That potentially is true. The more common lymphomas, diffuse large B-cell, follicular lymphoma, there are some moving pieces in terms of further sub-classifying diffuse large B-cell lymphoma but for the more rare diseases, providers may only see a few of those every couple of years, so I think we are recognizing that centers of excellence where patients are seen by providers that are lymphomas clinicians or hematopathologist that really focus on lymphoma, are likely to be increasingly important as this world of personalized medicine shifts how we think about lymphoma and treatment of lymphoma.
- Gore It certainly is reasonable to consider a second opinion even if you are very comfortable with your oncologist and your oncologist may be comfortable treating lymphoma in general, it would not hurt to see a lymphoma expert to at least check, is that what is going on and make sure everything is appropriate, right?
- Huntington I think that is a good point and I also think that having a second opinion, but also receiving potential treatment locally is important. It is important that providers and centers of excellence work together and collaborate to make sure that the diagnosis is 100% sure and also that the treatment is on the right path, but it is frequent that patients can be treated locally under the guidance of their local oncologist.
- Gore I know that is something we have worked very carefully to do at Yale Cancer Center to have our center be available in local sites from Torrington down to North Haven and now out to L and M Hospital, so that patients can get the same care essentially without having to come down to New Haven.
- Huntington I think that has worked quite well. We have weekly meetings where we discuss with clinicians and radiation oncologists and radiologists and pathologists. We come together and discuss the cases that have some uncertainty and we invite providers that are outside the New Haven campus to call in and teleconference in and I think that is likely the way that we are going for the treatment of most cancers. As we learn more about the cancer and further sub-classify we are likely to need experts that really focus on one disease process but we have to recognize that we as a community as a healthcare provider in the system that we need to reach out to those providers that are actually in the front lines that are actually doing the treatment and welcoming them into that process. I have been very happy and have been here for about 2 years; I have been very happy with how the process is working in terms of the care centers and in terms of the multidisciplinary and collaboration that has been going on.
- Gore You started sounding like somebody who thinks about ways that healthcare should be delivered in a larger sense, I am sensing there is another side of your interests that are not only just singularly disease focused.

Huntington I wear two hats, one is a lymphoma clinician and the other as a health services researcher, so I think about translating our clinical trials into real world care, ensuring that patients not only in academic centers but throughout the United States have access to high quality cancer care, so that is my research focus when I am not in the clinic. When I am not in the wards, I am really focused on what is going on in the real world practice of oncology and what sort of barriers might we be able to overcome to improve patient outcomes.

Gore How do you even measure that, do you make phone calls, focus groups, surveys, how do you figure out what is going on out there?

Huntington There are many different methods to study this and sometimes it is just patient groups, having patients come in and we talk qualitative research, learning their experience because that can be really helpful. The opposite end is actually doing big data research, looking at things like insurance claims and certain potential barriers to treatment or out-of-pocket cost. Those are the things that we actually do here in the cancer group that I am part of, these are very large scale insurance based designs for clinical trials, not clinical trials but client based trials.

Gore So you have got the information about what insurance paid for, for individual patients, and you see what is going on across the country, is that what happens?

Huntington Yes, we can look at what provider a patient saw, what health system a patient saw and we can actually look at what care they received and we can try to look at some of the characteristics that go into high quality care. If we identify that, then our goal is to disseminate the kind of special sauce to the other providers that are providing high quality cancer care.

Dr. Scott Huntington is an Assistant Professor of Medicine at Yale School of Medicine. If you have questions, go to yalecancercenter.org where you will also find past episodes in audio and written form. I am Bruce Barber reminding you to tune in every Sunday night to learn more about the progress being made in the fight against cancer here on WNPR, Connecticut's Public Media Source for news and ideas.