0:00:00 –> 0:00:11.032 Support for Yale Cancer Answers comes from AstraZeneca, proud partner in personalized medicine and developing tailored treatments for cancer patients.

0:00:11.13 –> 0:00:18.16 Learn more at astrazeneca-us.com. Welcome to Yale Cancer Answers with doctor Anees Chagpar.

0:00:18.16 –> 0:00:28.629 Yale Cancer Answers features the latest information on cancer care by welcoming oncologists and specialists who are on the forefront of the battle to fight cancer.

0:00:28.629 –> 0:00:32.82 This week, it's a conversation about lymphoma with Dr. Shalin Kothari.

0:00:32.82 –> 0:00:38.399 Doctor Kothari is an Assistant Professor of Medicine and Hematology at the Yale School of Medicine

0:00:38.399 –> 0:00:42.329 where Doctor Chagpar is a Professor of Surgery.

0:00:42.329 –> 0:00:42.759 Start by

0:00:42.759 –> 0:00:46.219 telling us a little bit about yourself

0:00:46.219 –> 0:00:50.969 and about what you do as a hematologist and oncologist.

0:00:50.969 –> 0:01:03.929 I joined Yale Cancer Center three months ago and my specialty and my focus is lymphoma, lymphoma patients, treating them and researching newer

0:01:03.929 –> 0:01:06.519 therapies for lymphoma.

0:01:06.519 –> 0:01:09.109 Tell us a little bit more about lymphoma.

0:01:09.109 –> 0:01:12.76 I mean, it seems like a broad term

0:01:12.76 –> 0:01:15.31 that encompasses many different things.

0:01:15.31 –> 0:01:16.159 Yeah, you're

0:01:16.159 –> 0:01:20.409 right. There are approximately 65 different types of lymphomas,

0:01:20.409 –> 0:01:29.76 so when we talk about lymphoma we really have to get granular because every different type of lymphoma has a different treatment,

0:01:29.76 –> 0:01:34.439 and many times we can even wait and watch.

0:01:34.439 –> 0:01:42.95 So it is very important to figure out what the sub type of lymphoma is before jumping to any therapies.

0:01:42.95 –> 0:01:53.159 And one of the things that is very important to keep in mind is that lymphomas usually require a big chunk of tissue for a good diagnosis.

0:01:53.159 –> 0:02:02.23 So one of the things that typically can go wrong and does go wrong frequently at centers is that we don't have enough tissue,

0:02:02.23 –> 0:02:05.629 and that's why we are left in the dark

0:02:05.629 –> 0:02:08.28 as to what the exact diagnosis is.

0:02:08.28 –> 0:02:13.219 But to tell you what lymphoma is in general,

0:02:13.219 –> 0:02:21.55 lymphoma is essentially a cancer of immune cells and immune cells live in different areas of the body,

0:02:21.55 –> 0:02:30.83 such as lymph nodes. And one of the biggest lymph nodes that we have in our body is the spleen,

0:02:30.83 –> 0:02:35.389 and in the belly and sometimes even in the liver.

0:02:35.389 –> 0:02:43.139 So these are the most common sites where lymph nodes can get enlarged and that can lead

0:02:43.139 –> 0:02:47.25 to lymphoma.

0:02:47.25 –> 0:02:48.61 How do people present with lymphoma? I mean do

0:02:48.61 –> 0:03:01.9 they present with big lymph nodes?

0:03:01.9 –> 0:03:04.65 That is one of the possible signs or symptoms rather but it can also present as just a very subtle blood abnormality. Which is detected by a blood test.

0:03:04.65 –> 0:03:07.4 So the symptoms range from fevers,

0:03:07.4 –> 0:03:10.939 night sweats, weight-loss along with a swollen lymph node.

0:03:10.939 –> 0:03:13.689 Either it could be in the neck.

0:03:13.689 –> 0:03:16.05 It could be in the chest,

0:03:16.05 –> 0:03:26.659 in the belly, or it could just be as indolent as just a small abnormality in the blood that can only be detected by a blood test.

0:03:26.659 –> 0:03:29.8 Many of those, the latter types of lymphomas,

0:03:29.8 –> 0:03:34.15 are detected by a routine blood test that was done.

0:03:34.15 –> 0:03:36.9 It is more often an incidental finding.

0:03:36.9 –> 0:03:40 In either case, how do you make that diagnosis?

0:03:40 –> 0:03:46.53 You mentioned that you would need a sufficient amount of tissue if you just had a routine blood test,

0:03:46.53 –> 0:03:49.289 you've been feeling a little under the weather,

0:03:49.289 –> 0:03:54.789 you thought, maybe it's just a cold and feeling a little rundown,

0:03:54.789 –> 0:03:56.509 a little tired.

0:03:56.509 –> 0:03:59.949 I've got a bit of night sweats and fevers,

0:03:59.949 –> 0:04:02.36 but I thought it was a cold.

0:04:02.36 –> 0:04:04.419 So I went to the doctor,

0:04:04.419 –> 0:04:06.569 he drew some routine blood tests

0:04:06.569 –> 0:04:10.05 and now you're telling me that he suspicious of lymphoma.

0:04:10.05 –> 0:04:13.879 How do we get from that to actually making a diagnosis?

0:04:13.879 –> 0:04:15.62 That's a great question. Typically

0:04:15.62 –> 0:04:17.709 we start with a blood test,

0:04:17.709 –> 0:04:23.62 but before that the doctor that you are going to see would do a full physical exam.

0:04:23.62 –> 0:04:28.839 So one of the things that if the patient is not complaining him or herself,

0:04:28.839 –> 0:04:35.11 then they would do a full physical exam to make sure that there are no swollen lymph nodes.

0:04:35.11 –> 0:04:37.959 Typical areas that we look at our the

0:04:37.959 –> 0:04:50.889 neck, under the armpits or at the groin crease so there are these typical areas that we look for lymph nodes and then we do a

0:04:50.889 –> 0:04:53.05 comprehensive lung and abdominal exam,

0:04:53.05 –> 0:04:58.649 so that is just to look at whether there is anything swollen.

0:04:58.649 –> 0:05:01.23 We can feel just by hand.

0:05:01.23 –> 0:05:08.149 But then the next steps are to look at different sub types of white blood cells

0:05:08.149 –> 0:05:20.129 in in the blood, and look at whether they are increased in number or do they show any signs of markers on the surface of the cells which shouldn't

0:05:20.129 –> 0:05:23.839 be there.

0:05:23.839 –> 0:05:26.319 And that's another blood test, correct? And so you do that,

0:05:26.319 –> 0:05:27.97 and then what happens?

0:05:27.97 –> 0:05:33.339 Well then we figure out what type of lymphoma it is.

0:05:33.339 –> 0:05:39.569 As I said before there are 65 different types of lymphomas

0:05:39.569 –> 0:05:42.16 as given by WHO classification,

0:05:42.16 –> 0:05:55.6 so it is absolutely crucial to figure out what the type of lymphoma is and that happens by putting together the entire spectrum of data.

0:05:55.6 –> 0:06:00.25 So that includes the way the patient presented,

0:06:00.25 –> 0:06:02.839 what are the symptoms?

0:06:02.839 –> 0:06:09.579 What did those tests in the blood show and also the biopsy specimen?

0:06:09.579 –> 0:06:14.72 We put all three pieces of information together,

0:06:14.72 –> 0:06:18.389 figure out the subtype, figure out the stage of lymphoma,

0:06:18.389 –> 0:06:22.43 and decide whether we need to treat the patient or not.

0:06:22.43 –> 0:06:23.529 So what do

0:06:23.529 –> 0:06:25.36 you biopsy in that situation?

0:06:25.36 –> 0:06:29.399 You're feeling a little under the weather,

0:06:29.399 –> 0:06:31.6 they did a routine blood test,

0:06:31.6 –> 0:06:35.639 they said, your white count is out of wack,

0:06:35.639 –> 0:06:39.31 you go to the oncologist,

0:06:39.31 –> 0:06:43.379 or the hematologist who does this full physical exam,

0:06:43.379 –> 0:06:46.72 And if you did not have Lymphadenopathy

0:06:46.72 –> 0:06:49.31 your lymph nodes were not swollen up,

0:06:49.31 –> 0:06:57.85 they're going to run this special blood test to look at the different types of white blood cells and so on so forth,

0:06:57.85 –> 0:06:59.329 but then what do

0:06:59.329 –> 0:07:02.67 you biopsy in that particular case that you're describing?

0:07:02.67 –> 0:07:11.269 There is nothing to biopsy and the most common type of lymphoma that presents the way you described is CLL.

0:07:11.269 –> 0:07:19.25 Or chronic lymphocytic leukemia, where the lymphoma cells are there circulating in the blood so there is nothing really to biopsy.

0:07:19.25 –> 0:07:30.269 We just acquire a few tubes of blood and do all the tests that we would have done on a biopsy specimen but on a blood specimen instead.

0:07:30.269 –> 0:07:35.259 Sometimes we also have to do a bone marrow biopsy which is

0:07:35.259 –> 0:07:45.399 a test looking at the hollow part of the bone that's the factory of all the cells that I just described that can become

0:07:45.399 –> 0:07:55.54 cancerous but you know the field is trying to move away from doing bone marrow biopsies because our tests in the peripheral blood and tissue are getting more and more

0:07:55.54 –> 0:08:00.61 sensitive. We can get most of the information that we need but that being said,

0:08:00.61 –> 0:08:05.339 there are still many situations where we have to do a bone marrow biopsy.

0:08:05.509 –> 0:08:11.279 And so if somebody presents on the other side of the spectrum,

0:08:11.279 –> 0:08:13.689 feeling terrible, fevers,

0:08:13.689 –> 0:08:17.54 chills, night sweats, losing weight for no reason,

0:08:17.54 –> 0:08:19.939 notices a lump in the neck,

0:08:19.939 –> 0:08:22.829 then feeling more,

0:08:22.829 –> 0:08:26.189 lumps in the groin,

0:08:26.189 –> 0:08:28.6 you go to the doctor,

0:08:28.6 –> 0:08:31.019 and the doctor gets worried.

0:08:31.019 –> 0:08:33.57 What then? Do they do

0:08:33.57 –> 0:08:36.12 a biopsy of the lymph nodes?

0:08:36.12 –> 0:08:40.799 Is that how that works in that scenario that you're describing?

0:08:40.799 –> 0:08:48.019 Biopsy becomes very, very important and we work very closely with our interventional radiologists or even surgeons

0:08:48.019 –> 0:08:52.269 sometimes, depending on the location of the swollen lymph node.

0:08:52.269 –> 0:08:54.399 So either surgeons or an Interventional

0:08:54.399 –> 0:08:56.519 Radiologist would biopsy the specimen,

0:08:56.519 –> 0:09:01.23 and then that specimen would go to the pathologist who would

0:09:01.23 –> 0:09:04.57 look at that tissue under the microscope,

0:09:04.57 –> 0:09:11.62 stain it with different markers that we already know may be positive in these different types of lymphomas,

0:09:11.62 –> 0:09:22.379 and then we figure out the subtype of the lymphoma and within usually within a week or two we are ready to start the therapy.

0:09:22.379 –> 0:09:25.72 If the patient is really sick at that time,

0:09:25.72 –> 0:09:32.779 then sometimes we even have to admit the patient while all these results are back and just give some

0:09:32.779 –> 0:09:35.36 medications to temporize rather than starting

0:09:35.36 –> 0:09:41.24 full blown therapy that we would have given that we would give in the future.

0:09:41.24 –> 0:09:42.35 So what's the

0:09:42.35 –> 0:09:44.19 most common kind of lymphoma?

0:09:44.19 –> 0:09:47.129 I mean, you say there's 65 different types,

0:09:47.129 –> 0:09:49.34 your head could spin,

0:09:49.34 –> 0:09:51.919 especially with all of the different therapies.

0:09:51.919 –> 0:09:54.86 If each one of these is treated differently,

0:09:54.86 –> 0:09:55.23 what's

0:09:55.23 –> 0:09:58.909 most common?

0:09:58.909 –> 0:10:03.37 That's also a tricky question to answer, and the reason is that we branch the way we classify lymphomas.

0:10:03.37 –> 0:10:07.94 The broad categories are Hodgkin lymphoma and non Hodgkin's lymphoma,

0:10:07.94 –> 0:10:12.919 but then it gets complicated very quickly so that classification,

0:10:12.919 –> 0:10:15.82 Non Hodgkin Lymphoma, is the most common,

0:10:15.82 –> 0:10:17.899 so how do you know

0:10:17.899 –> 0:10:21.629 what's a Hodgkin's lymphoma? What's a non Hodgkin's lymphoma?

0:10:22.049 –> 0:10:27.029 Hodgkin's lymphoma has a very classic appearance on the tissue biopsy specimen,

0:10:27.029 –> 0:10:34.5 so that's something that the pathologist would tell us that it is either Hodgkin or non Hodgkin lymphoma.

0:10:35.74 –> 0:10:39.029 And you were saying Non Hodgkin's is the most common

0:10:39.029 –> 0:10:43.289 right? So pretty much everything else falls under Hodgkin's.

0:10:43.289 –> 0:10:53.129 The way I like to think about it is what is the origin of the cancer cells?

0:10:53.129 –> 0:10:54.769 There are different types of lymphocytes.

0:10:54.769 –> 0:11:01 The immune cells that we talked about before, so it could be B cell or a T cell.

0:11:01 –> 0:11:05.6 There are Non Hodgkin's lymphoma's that originate from a B cell,

0:11:05.6 –> 0:11:07.74 so they're called B cell lymphoma's.

0:11:07.74 –> 0:11:15.149 Those that are Non Hodgkin Lymphoma that originate from T cells and they're called T cell lymphomas.

0:11:15.149 –> 0:11:20.71 Then the way I think about it next is under B cell lymphoma,

0:11:20.71 –> 0:11:23.879 which is the most common out of B and T cell lymphomas,

0:11:23.879 –> 0:11:27.46 is looking at whether they're

0:11:27.46 –> 0:11:31.029 aggressive in presentation or indolent in presentation,

0:11:31.029 –> 0:11:33.409 so that's how I like to

0:11:33.409 –> 0:11:35.399 broadly classify them

0:11:35.399 –> 0:11:39.759 And when we had talked about that first case,

0:11:39.759 –> 0:11:46.509 which was really indolent cancer where somebody was picked up on a routine blood test,

0:11:46.509 –> 0:11:51.61 you called it CLL you called it a leukemia.

0:11:51.61 –> 0:11:54.19 What's the difference between a leukemia,

0:11:54.19 –> 0:11:56.779 and a lymphoma or are they the

0:11:56.779 –> 0:11:59.799 same?

0:11:59.799 –> 0:12:01.95 They are not the same, but this leukemia in general,

0:12:01.95 –> 0:12:14.45 means that there are cancer cells circulating in the blood and most of the time when we talk about the routine leukemias,

0:12:14.45 –> 0:12:16.61 I don't treat leukemia patients,

0:12:16.61 –> 0:12:19.649 But CLL is an exception because

0:12:19.649 –> 0:12:24.519 that particular type of cell circulating in the blood is a lymphocyte,

0:12:24.519 –> 0:12:33.45 but it has not honed into a lymph node or something that is tangible or can be seen on a physical exam.

0:12:33.45 –> 0:12:38.33 So that's why it's sort of not really a misnomer,

0:12:38.33 –> 0:12:40.759 but it can get people confused.

0:12:41.49 –> 0:12:49.07 You had mentioned earlier that 65 different types of lymphomas are all treated differently,

0:12:49.07 –> 0:12:53.7 and for some of them you can actually just watch them.

0:12:53.7 –> 0:12:54.12 That is correct,

0:12:54.12 –> 0:13:02.539 and that's exactly why the classification and working very closely with the pathologist is absolutely crucial.

0:13:02.539 –> 0:13:07.59 The subtype that we talked about, CLL, many times

0:13:07.59 –> 0:13:10.12 we can just wait and watch.

0:13:10.12 –> 0:13:16.789 And one of the things we want to look at is whether the cell burden,

0:13:16.789 –> 0:13:30.2 the cancer cell burden in the body is large enough to either compress on our normal organs or prevent production of other cell lines such as platelets or red blood

0:13:30.2 –> 0:13:33.33 cells. So if we see those signs,

0:13:33.33 –> 0:13:38.24 then that's when we pull the trigger to start the treatment,

0:13:38.24 –> 0:13:41.879 but many of the times, particularly for CLL,

0:13:41.879 –> 0:13:44.19 we can wait and watch,

0:13:44.19 –> 0:13:53.61 but that being said, there are many other indolent lymphomas such as follicular lymphoma and even very minor subsets of mantle cell lymphoma.

0:13:54.019 –> 0:14:01.44 Lots of great information, but we're going to have to take a short break for a medical minute.

0:14:01.44 –> 0:14:05.559 Please stay tuned to learn more about lymphoma and early

0:14:05.559 –> 0:14:08.029 phase clinical trials with my guest

0:14:08.029 –> 0:14:18.83 Doctor Shalin Kothari. Support for Yale Cancer Answers comes from AstraZeneca dedicated to providing innovative treatment options for people living with cancer. Learn more at astrazeneca-us.com.

0:14:18.83 –> 0:14:21.6 This is a medical minute about melanoma.

0:14:21.6 –> 0:14:24.36 While Melanoma accounts for only about 4%

0:14:24.36 –> 0:14:29.889 of skin cancer cases, it causes the most skin cancer deaths. When detected early,

0:14:29.889 –> 0:14:33.45 however, melanoma is easily treated and highly curable. Clinical

0:14:33.45 –> 0:14:38.19 trials are currently underway to test innovative new treatments for melanoma.

0:14:38.19 –> 0:14:50.226 The goal of the specialized programs of research excellence in skin cancer, or SPORE grant, is to better understand the biology of skin cancer with a focus on discovering targets

0:14:50.293 –> 0:14:53.46 that will lead to improved diagnosis and treatment.

0:14:53.46 –> 0:14:56.6 More information is available at yalecancercenter.org.

0:14:56.6 –> 0:15:00.769 You're listening to Connecticut Public Radio.

0:15:00.769 –> 0:15:01.21 Welcome

0:15:01.21 –> 0:15:03.429 back to Yale Cancer Answers.

0:15:03.429 –> 0:15:10.96 This is doctor Anees Chagpar and I'm joined tonight by my guest doctor Shalin Kothari.

0:15:10.96 –> 0:15:14.95 We're talking about lymphoma and early phase clinical trials.

0:15:14.95 –> 0:15:17.159 Now, right before the break,

0:15:17.159 –> 0:15:25.139 Shalin was telling us about lymphoma being this really large basket of 64 different types of cancers,

0:15:25.139 –> 0:15:30.009 essentially all of which are bound together by this term lymphoma.

0:15:30.009 –> 0:15:32.669 Because they are cancers of lymphocytes,

0:15:32.669 –> 0:15:35.779 those immune cells that all of us

0:15:35.779 –> 0:15:37.919 need to help fight infections.

0:15:37.919 –> 0:15:41.769 Some of these present in a really indolent fashion,

0:15:41.769 –> 0:15:49.899 some of them present with symptoms of fevers and night sweats and weight loss and enlarged lymph nodes,

0:15:49.899 –> 0:15:52.47 and even getting your spleen enlarged.

0:15:52.47 –> 0:16:02.32 And we talked a little bit about how the diagnosis can sometimes be made on something as simple as a routine blood test,

0:16:02.32 –> 0:16:05.789 but other times really requires a tissue biopsy.

0:16:05.789 –> 0:16:16.87 Right before the break you were saying that some cancers don't require any treatment and that you can simply wait and watch.

0:16:16.87 –> 0:16:19.519 But other cancers do require treatment.

0:16:19.519 –> 0:16:32.37 Can you tell us a little bit more about how lymphoma is classically treated and a bit about some of the research that's going on in terms of treatment

0:16:32.37 –> 0:16:35.919 of lymphomas?

0:16:35.919 –> 0:16:37.95 Classically lymphoma is treated, and

0:16:37.95 –> 0:16:43.21 it becomes a bit challenging because every subtype is again treated very different,

0:16:43.21 –> 0:16:46.86 but let's say we talk about B cell lymphoma's,

0:16:46.86 –> 0:16:54.549 then most of the regimens that we use for the first year as a frontline therapy for the patient,

0:16:54.549 –> 0:17:00.22 we would use a antibody drug called Rituximab or a CD20 antibody,

0:17:00.22 –> 0:17:04.68 which is one of the very common markers on B cells.

0:17:04.68 –> 0:17:05.079 So

0:17:05.079 –> 0:17:08.73 are these like chemotherapies? Is that what it is?

0:17:08.769 –> 0:17:12.73 I would say they are more of a protein infusion.

0:17:12.73 –> 0:17:15.109 It's more of an antibody infusion.

0:17:15.109 –> 0:17:19.46 That particular drug that I talked about is not a chemotherapy,

0:17:19.46 –> 0:17:26.99 but it is typically combined with two or three or even four different types of chemotherapy drugs in combination.

0:17:26.99 –> 0:17:32.93 So usually we have to find different ways to trick the cancer cell into dying,

0:17:32.93 –> 0:17:34.91 and that requires different tools,

0:17:34.91 –> 0:17:39.68 so that the cancer cell is attacked from different angles.

0:17:39.68 –> 0:17:46 That's why we combine these therapies together as a cocktail which has been studied for many years,

0:17:46 –> 0:17:50.21 and we have a good idea of what goes with what and what regimen,

0:17:50.21 –> 0:17:51.97 what cycle, how many cycles,

0:17:51.97 –> 0:17:53.72 how many weeks of a break,

0:17:53.72 –> 0:18:03.9 all of that has been figured out over a period of time and that is a good segue to what you were asking me about the research.

0:18:03.9 –> 0:18:07.759 All of these questions as to what drug to use,

0:18:07.759 –> 0:18:10.599 how do cancer cells figure it out?

0:18:10.599 –> 0:18:18.009 A way to survive with these therapies and what is the dose of the drug to use?

0:18:18.009 –> 0:18:24.99 What is a dose of a drug that doesn't cost too much toxicity through the patient?

0:18:24.99 –> 0:18:28.91 What is the schedule of that combination of drugs?

0:18:28.91 –> 0:18:32.4 All of that is studied in clinical trials,

0:18:32.4 –> 0:18:35.45 so, for example at Yale for lymphomas,

0:18:35.45 –> 0:18:40.759 we have around 60 to 70 different types of clinical trials ongoing.

0:18:40.759 –> 0:18:44.4 And they can range from early phase clinical trials,

0:18:44.4 –> 0:18:46.42 to late phase clinical trials.

0:18:46.42 –> 0:18:49.24 And my team,

0:18:49.24 –> 0:19:01.359 we are actively involved in enrolling patients into these clinical trials so that they can benefit and they can help other patients benefit in the future because any therapy that

0:19:01.359 –> 0:19:11.869 we use today at some point in the past was studied as a clinical trial which is now benefiting everyone who has lymphoma.

0:19:11.93 –> 0:19:15.259 But a lot of patients may think,

0:19:15.259 –> 0:19:17.109 I just want what is standard.

0:19:17.109 –> 0:19:20.44 I don't want to be a human Guinea pig.

0:19:20.44 –> 0:19:23.4 Somebody else can be a human Guinea pig.

0:19:23.4 –> 0:19:28.21 How do I know that what you're giving me is going to work?

0:19:28.21 –> 0:19:30.799 Or is going to work better than

0:19:30.799 –> 0:19:41.9 standard? What do you say to patients who say that?

0:19:41.9 –> 0:19:54.96 That's an excellent question and a lot goes into research before we decide to introduce the drug as a clinical trial. Typically a drug is studied for years and when I say years, it could be even a decade or at least four to five years before we

0:19:54.96 –> 0:19:57.17 even think of

0:19:57.17 –> 0:20:02.92 designing a clinical trial for use in patients and the way we do that is,

0:20:02.92 –> 0:20:12.2 we start with testing lymphoma cells with that drug in a Petri Dish in a Translational Research Laboratory.

0:20:12.2 –> 0:20:14.91 And then we move on to

0:20:14.91 –> 0:20:26.92 lymphomas in mammals. So we use either mice or other mammals just to see what the drug does in those animals through those phases, and

0:20:26.92 –> 0:20:29.069 we figure out the dose,

0:20:29.069 –> 0:20:38.509 or at least the range that we should study in humans because we have a lot of

0:20:38.509 –> 0:20:45.039 formulas and calculations that we can do to figure out

0:20:45.039 –> 0:20:51.48 where to start as a starting dose for the drug in a particular patient.

0:20:51.48 –> 0:20:52.4 So with all of these

0:20:52.4 –> 0:20:58.38 different types of lymphoma and all of these different therapies,

0:20:58.38 –> 0:21:05.279 what do you think is the most exciting in terms of where research is going?

0:21:05.279 –> 0:21:12.64 The research is definitely moving towards using less and less of what you described as chemotherapy,

0:21:12.64 –> 0:21:17.75 and for good reasons. Chemotherapy can cause a lot of toxicity.

0:21:17.75 –> 0:21:23.99 which of course is very effective in killing cancer cells,

0:21:23.99 –> 0:21:35.45 but it can also cause other unwanted toxicities and the research is moving very very fast towards using novel therapeutic agents

0:21:35.45 –> 0:21:44.049 which really look at genetic and even cellular level to figure out what exactly is driving the cancer cell.

0:21:44.049 –> 0:21:51.869 What is that genetic change that is leading that cancer cell to go from 2 cells to four cells,

0:21:51.869 –> 0:21:55.39 4 to 8 and so on and so forth.

0:21:55.39 –> 0:21:57.74 And once we figure that out,

0:21:57.74 –> 0:22:02.039 we can use a drug that directly targets that particular mutation,

0:22:02.039 –> 0:22:07.63 or a pathway that we think is crucial for that cancer cell to survive.

0:22:07.63 –> 0:22:09.63 So as you can imagine,

0:22:09.63 –> 0:22:16.029 if are that selective then we can reduce the toxicities that drug would cause otherwise.

0:22:16.029 –> 0:22:17.23 Yeah, that makes

0:22:17.23 –> 0:22:22.244 sense. That's like all of this personalized medicine that people are talking.

0:22:22.321 –> 0:22:24.008 Yes in some ways, yeah.

0:22:24.084 –> 0:22:26.43 So tell us about your research.

0:22:26.43 –> 0:22:26.829 Do

0:22:26.829 –> 0:22:28.829 you work in that field?

0:22:28.829 –> 0:22:31.63 Yeah, I dedicate 50%

0:22:31.63 –> 0:22:37.23 of my time into a translational research laboratory where I study mantle cell lymphoma.

0:22:37.23 –> 0:22:39.66 We're trying to figure out

0:22:39.66 –> 0:22:42.859 newer therapies for mantle cell lymphoma,

0:22:42.859 –> 0:22:49.799 which is a subtype of aggressive B cell lymphoma's for the most part.

0:22:49.799 –> 0:22:56.4 And currently there are a couple of drugs that are already known,

0:22:56.4 –> 0:23:01.829 these novel therapies that are already known to be active in mantle cell lymphoma,

0:23:01.829 –> 0:23:06.869 but many or most versions will eventually develop resistance to those drugs,

0:23:06.869 –> 0:23:15.019 so we have to find newer therapies that will work after those two drugs or three drugs stop working.

0:23:15.019 –> 0:23:20.109 So that's what my focus is in the research laboratory to figure out.

0:23:20.109 –> 0:23:26.032 And how do you do that?

0:23:26.104 –> 0:23:28.92 As I discussed before,

0:23:28.92 –> 0:23:31.98 we take lymphoma cells in a Petri dish,

0:23:31.98 –> 0:23:35.809 one of the first steps that we start with and

0:23:35.809 –> 0:23:38.88 we first figure out

0:23:38.88 –> 0:23:41.94 what is driving the cancer cell to divide.

0:23:41.94 –> 0:23:45.96 So then we get, let's say a list of

0:23:45.96 –> 0:23:49.47 10 different genes and five different pathways to target.

0:23:49.47 –> 0:24:01.17 Then we look at previous research that has already been done and see what can we target in that pathway and then try to design either a designer drug or collaborate

0:24:01.17 –> 0:24:10.92 with other laboratories around the world that have already designed a drug for that particular pathway and see if that works against the lymphoma cells.

0:24:12.089 –> 0:24:19.47 When you say that you're trying to find therapies that will help in the cases of resistant lymphoma

0:24:19.47 –> 0:24:24.339 when you're looking at pathways that cause cancer cells to divide,

0:24:24.339 –> 0:24:30.029 I would think that those would help even up front as frontline therapies do.

0:24:30.029 –> 0:24:38.549 Do you try to figure out why they were resistant to the first line chemotherapy or the first line drug?

0:24:38.549 –> 0:24:45.049 Because presumably those already were targeting certain pathways that made cancer cells divide to begin with.

0:24:45.049 –> 0:24:47.48 That is true, and that really,

0:24:47.48 –> 0:24:50.329 again depends on the type of lymphoma.

0:24:50.329 –> 0:25:01.849 For example, mantle cell lymphoma is the frontline therapy that we use even to this date with Rituximab that I talked about in combination

0:25:01.849 –> 0:25:04.869 with other chemotherapy agents and to be honest,

0:25:04.869 –> 0:25:10.92 most of the lymphoma frontline therapy is still that cocktail of chemotherapy with Rituximab,

0:25:10.92 –> 0:25:20.369 and for good reason the bar is so high for these novel therapies to be used in front line.

0:25:20.369 –> 0:25:22.71 We don't want to harm patients.

0:25:22.71 –> 0:25:30.98 We have to find those novel drugs that will either improve, further the response to the frontline therapy and

0:25:30.98 –> 0:25:38.809 if not, then most most of the time they end up being used in second or third line.

0:25:38.809 –> 0:25:42.289 If the patients develop resistance to the frontline

0:25:42.289 –> 0:25:48.38 therapy.

0:25:48.38 –> 0:25:49.68 How often do patients with mantle cell lymphoma actually become resistant?

0:25:49.68 –> 0:25:55.38 Mantle cell lymphoma is one of the areas where there's a lot of research that needs to be done.

0:25:55.38 –> 0:25:59.4 In mantle cell,

0:25:59.4 –> 0:26:01.64 for example,

0:26:01.64 –> 0:26:04.769 I would say almost 70 to 80%

0:26:04.769 –> 0:26:08.339 of patients develop resistance to the frontline therapy.

0:26:08.339 –> 0:26:10.579 And as you can imagine,

0:26:10.579 –> 0:26:15.94 we already know that's what to use in second line third line.

0:26:15.94 –> 0:26:21.895 But then eventually most patients develop resistance to all these lines of therapy.

0:26:21.99 –> 0:26:25.39 And why is that? That's the $1,000,000 question.

0:26:25.39 –> 0:26:28.13 It's not easy to figure that out,

0:26:28.13 –> 0:26:31.549 but we do know that there are

0:26:31.549 –> 0:26:35.64 different mutations that the cancer cell can

0:26:35.64 –> 0:26:40.7 keep evolving. That's probably the best way to think about it.

0:26:40.7 –> 0:26:44.589 So if you introduce frontline therapy to a cancer cell,

0:26:44.589 –> 0:26:48.089 and let's say there are 10 cells to kill,

0:26:48.089 –> 0:26:59.759 maybe 8 of them get killed but the other two they find a way to change their path of dividing and circumvent the way the frontline

0:26:59.759 –> 0:27:02.869 therapies worked. So now they have become smarter.

0:27:02.869 –> 0:27:04.819 They have acquired new mutations,

0:27:04.819 –> 0:27:06.809 new genetic changes that

0:27:06.809 –> 0:27:12.069 weren't there the first time and then you introduce second line therapy and again,

0:27:12.069 –> 0:27:16.68 the same thing happens where you kill most of the cells but not all,

0:27:16.68 –> 0:27:19.64 and then those few cells that are left behind,

0:27:19.64 –> 0:27:23.92 they eventually start dividing again because they have acquired newer mutations.

0:27:24.579 –> 0:27:34.45 It sounds a lot like what our audience might be familiar with in terms of antibiotic resistance that you see one antibiotic and the idea is that

0:27:34.45 –> 0:27:37.41 you don't want to keep taking different antibiotics,

0:27:37.41 –> 0:27:39.42 especially when you don't need them.

0:27:39.42 –> 0:27:45.68 Because then you have the generation of super bugs that are resistant to all antibiotics.

0:27:45.68 –> 0:27:46.089 Is

0:27:46.089 –> 0:27:48.589 that a similar kind of concept?

0:27:48.589 –> 0:27:58.609 Similar concept, but we are not worried about a generation of superbugs in this case because most lymphomas if not treated can be deadly.

0:27:58.609 –> 0:28:02.089 If they need treatment, if they're aggressive kinds of lymphomas,

0:28:02.089 –> 0:28:04.18 and if they are not treated,

0:28:04.18 –> 0:28:10.089 they can be deadly, so we don't typically worry about what will happen to that cancer cell, and

0:28:10.089 –> 0:28:13.23 what different types of mutations they're going to acquire.

0:28:13.23 –> 0:28:17.049 Because we really don't have the time in that particular patient,

0:28:17.049 –> 0:28:18.99 so in other words,

0:28:18.99 –> 0:28:25.529 we typically switch from one line of therapy to the next line of therapy very quickly.

0:28:25.529 –> 0:28:30.849 The moment we know that this particular patients lymphoma stopped responding,

0:28:30.849 –> 0:28:42.299 then we quickly move to the next line because it's crucial to try to keep it at a very low level of burden or even completely cure it.

0:28:42.99 –> 0:28:49.23 Doctor Shalin Kothari is an Assistant Professor of Medicine and Hematology at the Yale School of Medicine.

0:28:49.23 –> 0:28:57.67 If you have questions, the address is canceranswers@yale.edu and past editions of the program are available in audio and written form at Yalecancercenter.org.

0:28:57.67 –> 0:29:06.314 We hope you'll join us next week to learn more about the fight against cancer here on Connecticut Public Radio.