WEBVTT

1 00:00:00.000 --> 00:00:11.032 Support for Yale Cancer Answers comes from AstraZeneca, proud partner in personalized medicine and developing tailored treatments for cancer patients.

2 00:00:11.130 --> 00:00:18.160 Learn more at astrazeneca-us.com. Welcome to Yale Cancer Answers with doctor Anees Chagpar.

3 00:00:18.160 --> 00:00:28.629 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.

4 00:00:28.629 --> 00:00:32.820 This week, it's a conversation about lymphoma with Dr. Shalin Kothari.

5 00:00:32.820 --> 00:00:38.399 Doctor Kothari is an Assistant Professor of Medicine and Hematology at the Yale School of Medicine

6 00:00:38.399 --> 00:00:42.329 where Doctor Chagpar is a Professor of Surgery.

7 00:00:42.329 --> 00:00:42.759 Start by

8 00:00:42.759 --> 00:00:46.219 telling us a little bit about yourself

9 00:00:46.219 --> 00:00:50.969 and about what you do as a hematologist and oncologist.

10 00:00:50.969 --> 00:01:03.929 I joined Yale Cancer Center three months ago and my specialty and my focus is lymphoma, lymphoma patients, treating them and researching newer

11 00:01:03.929 --> 00:01:06.519 therapies for lymphoma.

12 00:01:06.519 --> 00:01:09.109 Tell us a little bit more about lymphoma.

13 00:01:09.109 --> 00:01:12.760 I mean, it seems like a broad term

14 00:01:12.760 --> 00:01:15.310 that encompasses many different things.

15 00:01:15.310 --> 00:01:16.159 Yeah, you're

16 00:01:16.159 --> 00:01:20.409 right. There are approximately 65 different types of lymphomas,

17 00:01:20.409 --> 00:01:29.760 so when we talk about lymphoma we really have to get granular because every different type of lymphoma has a different treatment,

18 00:01:29.760 --> 00:01:34.439 and many times we can even wait and watch.

19 00:01:34.439 --> 00:01:42.950 So it is very important to figure out what the sub type of lymphoma is before jumping to any therapies.

20 00:01:42.950 --> 00:01:53.159 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.

21 00:01:53.159 --> 00:02:02.230 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,

22 00:02:02.230 --> 00:02:05.629 and that's why we are left in the dark

23 00:02:05.629 --> 00:02:08.280 as to what the exact diagnosis is.

24 00:02:08.280 --> 00:02:13.219 But to tell you what lymphoma is in general,

25 00:02:13.219 --> 00:02:21.550 lymphoma is essentially a cancer of immune cells and immune cells live in different areas of the body,

26 00:02:21.550 --> 00:02:30.830 such as lymph nodes. And one of the biggest lymph nodes that we have in our body is the spleen,

27 00:02:30.830 --> 00:02:35.389 and in the belly and sometimes even in the liver.

28 00:02:35.389 --> 00:02:43.139 So these are the most common sites where lymph nodes can get enlarged and that can lead

29 00:02:43.139 --> 00:02:47.250 to lymphoma.

30 00:02:47.250 --> 00:02:48.610 How do people present with lymphoma? I mean do

31 00:02:48.610 --> 00:03:01.900 they present with big lymph nodes?

32 00:03:01.900 --> 00:03:04.650 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.

33 00:03:04.650 --> 00:03:07.400 So the symptoms range from fevers,

34 00:03:07.400 --> 00:03:10.939 night sweats, weight-loss along with a swollen lymph node.

35 00:03:10.939 --> 00:03:13.689 Either it could be in the neck.

36 00:03:13.689 --> 00:03:16.050 It could be in the chest,

37 00:03:16.050 --> 00:03:26.659 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.

38 00:03:26.659 --> 00:03:29.800 Many of those, the latter types of lymphomas,

39 00:03:29.800 --> 00:03:34.150 are detected by a routine blood test that was done.

40 00:03:34.150 --> 00:03:36.900 It is more often an incidental finding.

41 00:03:36.900 --> 00:03:40.000 In either case, how do you make that diagnosis?

42 00:03:40.000 --> 00:03:46.530 You mentioned that you would need a sufficient amount of tissue if you just had a routine blood test,

43 00:03:46.530 --> 00:03:49.289 you've been feeling a little under the weather,

44 00:03:49.289 --> 00:03:54.789 you thought, maybe it's just a cold and feeling a little rundown,

45 00:03:54.789 --> 00:03:56.509 a little tired.

46 00:03:56.509 --> 00:03:59.949 I've got a bit of night sweats and fevers,

47 00:03:59.949 --> 00:04:02.360 but I thought it was a cold.

48 00:04:02.360 --> 00:04:04.419 So I went to the doctor,

49 00:04:04.419 --> 00:04:06.569 he drew some routine blood tests

50 00:04:06.569 --> 00:04:10.050 and now you're telling me that he suspicious of lymphoma.

51 00:04:10.050 --> 00:04:13.879 How do we get from that to actually making a diagnosis?

52 00:04:13.879 --> 00:04:15.620 That's a great question. Typically

53 00:04:15.620 --> 00:04:17.709 we start with a blood test,

54 00:04:17.709 --> 00:04:23.620 but before that the doctor that you are going to see would do a full physical exam.

55 00:04:23.620 --> 00:04:28.839 So one of the things that if the patient is not complaining him or herself,

56 00:04:28.839 --> 00:04:35.110 then they would do a full physical exam to make sure that there are no swollen lymph nodes.

57 00:04:35.110 --> 00:04:37.959 Typical areas that we look at our the

58 00:04:37.959 --> 00:04:50.889 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

59 00:04:50.889 --> 00:04:53.050 comprehensive lung and abdominal exam,

60 00:04:53.050 --> 00:04:58.649 so that is just to look at whether there is anything swollen.

61 00:04:58.649 --> 00:05:01.230 We can feel just by hand.

62 00:05:01.230 --> 00:05:08.149 But then the next steps are to look at different sub types of white blood cells

63 00:05:08.149 --> 00:05:20.129 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

64 00:05:20.129 --> 00:05:23.839 be there.

65 00:05:23.839 --> 00:05:26.319 And that's another blood test, correct? And so you do that,

66 00:05:26.319 --> 00:05:27.970 and then what happens?

67 00:05:27.970 --> 00:05:33.339 Well then we figure out what type of lymphoma it is.

68 00:05:33.339 --> 00:05:39.569 As I said before there are 65 different types of lymphomas

69 00:05:39.569 --> 00:05:42.160 as given by WHO classification,

70 00:05:42.160 --> 00:05:55.600 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.

71 00:05:55.600 --> 00:06:00.250 So that includes the way the patient presented,

72 00:06:00.250 --> 00:06:02.839 what are the symptoms?

73 00:06:02.839 --> 00:06:09.579 What did those tests in the blood show and also the biopsy specimen?

74 00:06:09.579 --> 00:06:14.720 We put all three pieces of information together,

75 00:06:14.720 --> 00:06:18.389 figure out the subtype, figure out the stage of lymphoma,

76 00:06:18.389 --> 00:06:22.430 and decide whether we need to treat the patient or not.

77 00:06:22.430 --> 00:06:23.529 So what do

78 00:06:23.529 --> 00:06:25.360 you biopsy in that situation?

79 00:06:25.360 --> 00:06:29.399 You're feeling a little under the weather,

80 00:06:29.399 --> 00:06:31.600 they did a routine blood test,

81 00:06:31.600 --> 00:06:35.639 they said, your white count is out of wack,

82 00:06:35.639 --> 00:06:39.310 you go to the oncologist,

83 00:06:39.310 --> 00:06:43.379 or the hematologist who does this full physical exam,

84 00:06:43.379 --> 00:06:46.720 And if you did not have Lymphadenopathy

85 00:06:46.720 --> 00:06:49.310 your lymph nodes were not swollen up,

86 00:06:49.310 --> 00:06:57.850 they're going to run this special blood test to look at the different types of white blood cells and so on so forth,

87 00:06:57.850 --> 00:06:59.329 but then what do

88 00:06:59.329 --> 00:07:02.670 you biopsy in that particular case that you're describing?

89 00:07:02.670 --> 00:07:11.269 There is nothing to biopsy and the most common type of lymphoma that presents the way you described is CLL.

90 00:07:11.269 --> 00:07:19.250 Or chronic lymphocytic leukemia, where the lymphoma cells are there circulating in the blood so there is nothing really to biopsy.

91 00:07:19.250 --> 00:07:30.269 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.

92 00:07:30.269 --> 00:07:35.259 Sometimes we also have to do a bone marrow biopsy which is

93 00:07:35.259 --> 00:07:45.399 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

94 00:07:45.399 --> 00:07:55.540 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

95 00:07:55.540 --> 00:08:00.610 sensitive. We can get most of the information that we need but that being said,

96 00:08:00.610 --> 00:08:05.339 there are still many situations where we have to do a bone marrow biopsy.

97 00:08:05.509 --> 00:08:11.279 And so if somebody presents on the other side of the spectrum,

98 00:08:11.279 --> 00:08:13.689 feeling terrible, fevers,

99 00:08:13.689 --> 00:08:17.540 chills, night sweats, losing weight for no reason,

100 00:08:17.540 --> 00:08:19.939 notices a lump in the neck,

101 00:08:19.939 --> 00:08:22.829 then feeling more,

102 00:08:22.829 --> 00:08:26.189 lumps in the groin,

103 00:08:26.189 --> 00:08:28.600 you go to the doctor,

104 00:08:28.600 --> 00:08:31.019 and the doctor gets worried.

105 00:08:31.019 --> 00:08:33.570 What then? Do they do

106 00:08:33.570 --> 00:08:36.120 a biopsy of the lymph nodes?

107 00:08:36.120 --> 00:08:40.799 Is that how that works in that scenario that you're describing?

108 00:08:40.799 --> 00:08:48.019 Biopsy becomes very, very important and we work very closely with our interventional radiologists or even surgeons

109 00:08:48.019 --> 00:08:52.269 sometimes, depending on the location of the swollen lymph node.

110 00:08:52.269 --> 00:08:54.399 So either surgeons or an Interventional

111 00:08:54.399 --> 00:08:56.519 Radiologist would biopsy the specimen,

112 00:08:56.519 --> 00:09:01.230 and then that specimen would go to the pathologist who would

113 00:09:01.230 --> 00:09:04.570 look at that tissue under the microscope,

114 00:09:04.570 --> 00:09:11.620 stain it with different markers that we already know may be positive in these different types of lymphomas,

115 00:09:11.620 --> 00:09:22.379 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.

116 00:09:22.379 --> 00:09:25.720 If the patient is really sick at that time,

117 00:09:25.720 --> 00:09:32.779 then sometimes we even have to admit the patient while all these results are back and just give some

118 00:09:32.779 --> 00:09:35.360 medications to temporize rather than starting

119 00:09:35.360 --> 00:09:41.240 full blown therapy that we would have given that we would give in the future.

120 00:09:41.240 --> 00:09:42.350 So what's the

121 00:09:42.350 --> 00:09:44.190 most common kind of lymphoma?

122 00:09:44.190 --> 00:09:47.129 I mean, you say there's 65 different types,

123 00:09:47.129 --> 00:09:49.340 your head could spin,

124 00:09:49.340 --> 00:09:51.919 especially with all of the different therapies.

125 00:09:51.919 --> 00:09:54.860 If each one of these is treated differently,

126 00:09:54.860 --> 00:09:55.230 what's

127 00:09:55.230 --> 00:09:58.909 most common?

128 00:09:58.909 --> 00:10:03.370 That's also a tricky question to answer, and the reason is that we branch the way we classify lymphomas.

129 00:10:03.370 --> 00:10:07.940 The broad categories are Hodgkin lymphoma and non Hodgkin's lymphoma,

130 00:10:07.940 --> 00:10:12.919 but then it gets complicated very quickly so that classification,

131 00:10:12.919 --> 00:10:15.820 Non Hodgkin Lymphoma, is the most common,

132 00:10:15.820 --> 00:10:17.899 so how do you know

133 00:10:17.899 --> 00:10:21.629 what's a Hodgkin's lymphoma? What's a non Hodgkin's lymphoma?

135 00:10:22.049 --> 00:10:27.029 Hodgkin's lymphoma has a very classic appearance on the tissue biopsy specimen,

136 00:10:27.029 --> 00:10:34.500 so that's something that the pathologist would tell us that it is either Hodgkin or non Hodgkin lymphoma.

138 00:10:35.740 --> 00:10:39.029 And you were saying Non Hodgkin's is the most common

139 00:10:39.029 --> 00:10:43.289 right? So pretty much everything else falls under Hodgkin's.

140 00:10:43.289 --> 00:10:53.129 The way I like to think about it is what is the origin of the cancer cells?

141 00:10:53.129 --> 00:10:54.769 There are different types of lymphocytes.

142 00:10:54.769 --> 00:11:01.000 The immune cells that we talked about before, so it could be B cell or a T cell.

143 00:11:01.000 --> 00:11:05.600 There are Non Hodgkin's lymphoma's that originate from a B cell,

144 00:11:05.600 --> 00:11:07.740 so they're called B cell lymphoma's.

145 00:11:07.740 --> 00:11:15.149 Those that are Non Hodgkin Lymphoma that originate from T cells and they're called T cell lymphomas.

146 00:11:15.149 --> 00:11:20.710 Then the way I think about it next is under B cell lymphoma,

147 00:11:20.710 --> 00:11:23.879 which is the most common out of B and T cell lymphomas,

148 00:11:23.879 --> 00:11:27.460 is looking at whether they're

149 00:11:27.460 --> 00:11:31.029 aggressive in presentation or indolent in presentation,

150 00:11:31.029 --> 00:11:33.409 so that's how I like to

151 00:11:33.409 --> 00:11:35.399 broadly classify them

152 00:11:35.399 --> 00:11:39.759 And when we had talked about that first case,

153 00:11:39.759 --> 00:11:46.509 which was really indolent cancer where somebody was picked up on a routine blood test,

154 00:11:46.509 --> 00:11:51.610 you called it CLL you called it a leukemia.

155 00:11:51.610 --> 00:11:54.190 What's the difference between a leukemia,

156 00:11:54.190 --> 00:11:56.779 and a lymphoma or are they the

157 00:11:56.779 --> 00:11:59.799 same?

158 00:11:59.799 --> 00:12:01.950 They are not the same, but this leukemia in general,

159 00:12:01.950 --> 00:12:14.450 means that there are cancer cells circulating in the blood and most of the time when we talk about the routine leukemias,

160 00:12:14.450 --> 00:12:16.610 I don't treat leukemia patients,

161 00:12:16.610 --> 00:12:19.649 But CLL is an exception because

162 00:12:19.649 --> 00:12:24.519 that particular type of cell circulating in the blood is a lymphocyte,

163 00:12:24.519 --> 00:12:33.450 but it has not honed into a lymph node or something that is tangible or can be seen on a physical exam.

164 00:12:33.450 --> 00:12:38.330 So that's why it's sort of not really a misnomer,

165 00:12:38.330 --> 00:12:40.759 but it can get people confused.

166 00:12:41.490 --> 00:12:49.070 You had mentioned earlier that 65 different types of lymphomas are all treated differently,

167 00:12:49.070 --> 00:12:53.700 and for some of them you can actually just watch them.

168 00:12:53.700 --> 00:12:54.120 That is correct,

169 00:12:54.120 --> 00:13:02.539 and that's exactly why the classification and working very closely with the pathologist is absolutely crucial.

170 00:13:02.539 --> 00:13:07.590 The subtype that we talked about, CLL, many times

171 00:13:07.590 --> 00:13:10.120 we can just wait and watch.

172 00:13:10.120 --> 00:13:16.789 And one of the things we want to look at is whether the cell burden,

173 00:13:16.789 --> 00:13:30.200 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

174 00:13:30.200 --> 00:13:33.330 cells. So if we see those signs,

175 00:13:33.330 --> 00:13:38.240 then that's when we pull the trigger to start the treatment,

176 00:13:38.240 --> 00:13:41.879 but many of the times, particularly for CLL,

177 00:13:41.879 --> 00:13:44.190 we can wait and watch,

178 00:13:44.190 --> 00:13:53.610 but that being said, there are many other indolent lymphomas such as follicular lymphoma and even very minor subsets of mantle cell lymphoma.

180 00:13:54.019 --> 00:14:01.440 Lots of great information, but we're going to have to take a short break for a medical minute.

181 00:14:01.440 --> 00:14:05.559 Please stay tuned to learn more about lymphoma and early

182 00:14:05.559 --> 00:14:08.029 phase clinical trials with my guest

183 00:14:08.029 --> 00:14:18.830 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.

184 00:14:18.830 --> 00:14:21.600 This is a medical minute about melanoma.

185 00:14:21.600 --> 00:14:24.360 While Melanoma accounts for only about 4%

186 00:14:24.360 --> 00:14:29.889 of skin cancer cases, it causes the most skin cancer deaths. When detected early,

187 00:14:29.889 --> 00:14:33.450 however, melanoma is easily treated and highly curable. Clinical

188 00:14:33.450 --> 00:14:38.190 trials are currently underway to test innovative new treatments for melanoma.

189 00:14:38.190 --> 00:14:50.226 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

190 00:14:50.293 --> 00:14:53.460 that will lead to improved diagnosis and treatment.

191 00:14:53.460 --> 00:14:56.600 More information is available at yalecancercenter.org.

192 00:14:56.600 --> 00:15:00.769 You're listening to Connecticut Public Radio.

193 00:15:00.769 --> 00:15:01.210 Welcome

194 00:15:01.210 --> 00:15:03.429 back to Yale Cancer Answers.

195 00:15:03.429 --> 00:15:10.960 This is doctor Anees Chagpar and I'm joined tonight by my guest doctor Shalin Kothari.

196 00:15:10.960 --> 00:15:14.950 We're talking about lymphoma and early phase clinical trials.

197 00:15:14.950 --> 00:15:17.159 Now, right before the break,

198 00:15:17.159 --> 00:15:25.139 Shalin was telling us about lymphoma being this really large basket of 64 different types of cancers,

199 00:15:25.139 --> 00:15:30.009 essentially all of which are bound together by this term lymphoma.

200 00:15:30.009 --> 00:15:32.669 Because they are cancers of lymphocytes,

201 00:15:32.669 --> 00:15:35.779 those immune cells that all of us

202 00:15:35.779 --> 00:15:37.919 need to help fight infections.

203 00:15:37.919 --> 00:15:41.769 Some of these present in a really indolent fashion,

204 00:15:41.769 --> 00:15:49.899 some of them present with symptoms of fevers and night sweats and weight loss and enlarged lymph nodes,

205 00:15:49.899 --> 00:15:52.470 and even getting your spleen enlarged.

206 00:15:52.470 --> 00:16:02.320 And we talked a little bit about how the diagnosis can sometimes be made on something as simple as a routine blood test,

207 00:16:02.320 --> 00:16:05.789 but other times really requires a tissue biopsy.

208 00:16:05.789 --> 00:16:16.870 Right before the break you were saying that some cancers don't require any treatment and that you can simply wait and watch.

209 00:16:16.870 --> 00:16:19.519 But other cancers do require treatment.

210 00:16:19.519 --> 00:16:32.370 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

211 00:16:32.370 --> 00:16:35.919 of lymphomas?

212 00:16:35.919 --> 00:16:37.950 Classically lymphoma is treated, and

213 00:16:37.950 --> 00:16:43.210 it becomes a bit challenging because every subtype is again treated very different,

214 00:16:43.210 --> 00:16:46.860 but let's say we talk about B cell lymphoma's,

215 00:16:46.860 --> 00:16:54.549 then most of the regimens that we use for the first year as a frontline therapy for the patient,

216 00:16:54.549 --> 00:17:00.220 we would use a antibody drug called Rituximab or a CD20 antibody,

217 00:17:00.220 --> 00:17:04.680 which is one of the very common markers on B cells.

218 00:17:04.680 --> 00:17:05.079 So

219 00:17:05.079 --> 00:17:08.730 are these like chemotherapies? Is that what it is?

220 00:17:08.769 --> 00:17:12.730 I would say they are more of a protein infusion.

221 00:17:12.730 --> 00:17:15.109 It's more of an antibody infusion.

222 00:17:15.109 --> 00:17:19.460 That particular drug that I talked about is not a chemotherapy,

223 00:17:19.460 --> 00:17:26.990 but it is typically combined with two or three or even four different types of chemotherapy drugs in combination.

224 00:17:26.990 --> 00:17:32.930 So usually we have to find different ways to trick the cancer cell into dying,

225 00:17:32.930 --> 00:17:34.910 and that requires different tools,

226 00:17:34.910 --> 00:17:39.680 so that the cancer cell is attacked from different angles.

227 00:17:39.680 --> 00:17:46.000 That's why we combine these therapies together as a cocktail which has been studied for many years,

228 00:17:46.000 --> 00:17:50.210 and we have a good idea of what goes with what and what regimen,

229 00:17:50.210 --> 00:17:51.970 what cycle, how many cycles,

230 00:17:51.970 --> 00:17:53.720 how many weeks of a break,

231 00:17:53.720 --> 00:18:03.900 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.

232 00:18:03.900 --> 00:18:07.759 All of these questions as to what drug to use,

233 00:18:07.759 --> 00:18:10.599 how do cancer cells figure it out?

234 00:18:10.599 --> 00:18:18.009 A way to survive with these therapies and what is the dose of the drug to use?

235 00:18:18.009 --> 00:18:24.990 What is a dose of a drug that doesn't cost too much toxicity through the patient?

236 00:18:24.990 --> 00:18:28.910 What is the schedule of that combination of drugs?

237 00:18:28.910 --> 00:18:32.400 All of that is studied in clinical trials,

238 00:18:32.400 --> 00:18:35.450 so, for example at Yale for lymphomas,

239 00:18:35.450 --> 00:18:40.759 we have around 60 to 70 different types of clinical trials ongoing.

240 00:18:40.759 --> 00:18:44.400 And they can range from early phase clinical trials,

241 00:18:44.400 --> 00:18:46.420 to late phase clinical trials.

242 00:18:46.420 --> 00:18:49.240 And my team,

243 00:18:49.240 --> 00:19:01.359 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

244 00:19:01.359 --> 00:19:11.869 we use today at some point in the past was studied as a clinical trial which is now benefiting everyone who has lymphoma.

245 00:19:11.930 --> 00:19:15.259 But a lot of patients may think,

246 00:19:15.259 --> 00:19:17.109 I just want what is standard.

247 00:19:17.109 --> 00:19:20.440 I don't want to be a human Guinea pig.

248 00:19:20.440 --> 00:19:23.400 Somebody else can be a human Guinea pig.

249 00:19:23.400 --> 00:19:28.210 How do I know that what you're giving me is going to work?

250 00:19:28.210 --> 00:19:30.799 Or is going to work better than

251 00:19:30.799 --> 00:19:41.900 standard? What do you say to patients who say that?

252 00:19:41.900 --> 00:19:54.960 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

253 00:19:54.960 --> 00:19:57.170 even think of

254 00:19:57.170 --> 00:20:02.920 designing a clinical trial for use in patients and the way we do that is,

255 00:20:02.920 --> 00:20:12.200 we start with testing lymphoma cells with that drug in a Petri Dish in a Translational Research Laboratory.

256 00:20:12.200 --> 00:20:14.910 And then we move on to

257 00:20:14.910 --> 00:20:26.920 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

258 00:20:26.920 --> 00:20:29.069 we figure out the dose,

259 00:20:29.069 --> 00:20:38.509 or at least the range that we should study in humans because we have a lot of

260 00:20:38.509 --> 00:20:45.039 formulas and calculations that we can do to figure out

261 00:20:45.039 --> 00:20:51.480 where to start as a starting dose for the drug in a particular patient.

262 00:20:51.480 --> 00:20:52.400 So with all of these

263 00:20:52.400 --> 00:20:58.380 different types of lymphoma and all of these different therapies,

264 00:20:58.380 --> 00:21:05.279 what do you think is the most exciting in terms of where research is going?

265 00:21:05.279 --> 00:21:12.640 The research is definitely moving towards using less and less of what you described as chemotherapy,

266 00:21:12.640 --> 00:21:17.750 and for good reasons. Chemotherapy can cause a lot of toxicity.

267 00:21:17.750 --> 00:21:23.990 which of course is very effective in killing cancer cells,

268 00:21:23.990 --> 00:21:35.450 but it can also cause other unwanted toxicities and the research is moving very very fast towards using novel therapeutic agents

269 00:21:35.450 --> 00:21:44.049 which really look at genetic and even cellular level to figure out what exactly is driving the cancer cell.

270 00:21:44.049 --> 00:21:51.869 What is that genetic change that is leading that cancer cell to go from 2 cells to four cells,

271 00:21:51.869 --> 00:21:55.390 4 to 8 and so on and so forth.

272 00:21:55.390 --> 00:21:57.740 And once we figure that out,

273 00:21:57.740 --> 00:22:02.039 we can use a drug that directly targets that particular mutation,

274 00:22:02.039 --> 00:22:07.630 or a pathway that we think is crucial for that cancer cell to survive.

275 00:22:07.630 --> 00:22:09.630 So as you can imagine,

276 00:22:09.630 --> 00:22:16.029 if are that selective then we can reduce the toxicities that drug would cause otherwise.

277 00:22:16.029 --> 00:22:17.230 Yeah, that makes

278 00:22:17.230 --> 00:22:22.244 sense. That's like all of this personalized medicine that people are talking.

279 00:22:22.321 --> 00:22:24.008 Yes in some ways, yeah.

280 00:22:24.084 --> 00:22:26.430 So tell us about your research.

281 00:22:26.430 --> 00:22:26.829 Do

282 00:22:26.829 --> 00:22:28.829 you work in that field?

283 00:22:28.829 --> 00:22:31.630 Yeah, I dedicate 50%

284 00:22:31.630 --> 00:22:37.230 of my time into a translational research laboratory where I study mantle cell lymphoma.

285 00:22:37.230 --> 00:22:39.660 We're trying to figure out

286 00:22:39.660 --> 00:22:42.859 newer therapies for mantle cell lymphoma,

287 00:22:42.859 --> 00:22:49.799 which is a subtype of aggressive B cell lymphoma's for the most part.

288 00:22:49.799 --> 00:22:56.400 And currently there are a couple of drugs that are already known,

289 00:22:56.400 --> 00:23:01.829 these novel therapies that are already known to be active in mantle cell lymphoma,

290 00:23:01.829 --> 00:23:06.869 but many or most versions will eventually develop resistance to those drugs,

291 00:23:06.869 --> 00:23:15.019 so we have to find newer therapies that will work after those two drugs or three drugs stop working.

292 00:23:15.019 --> 00:23:20.109 So that's what my focus is in the research laboratory to figure out.

293 00:23:20.109 --> 00:23:26.032 And how do you do that?

294 00:23:26.104 --> 00:23:28.920 As I discussed before,

295 00:23:28.920 --> 00:23:31.980 we take lymphoma cells in a Petri dish,

296 00:23:31.980 --> 00:23:35.809 one of the first steps that we start with and

297 00:23:35.809 --> 00:23:38.880 we first figure out

298 00:23:38.880 --> 00:23:41.940 what is driving the cancer cell to divide.

299 00:23:41.940 --> 00:23:45.960 So then we get, let's say a list of

300 00:23:45.960 --> 00:23:49.470 10 different genes and five different pathways to target.

301 00:23:49.470 --> 00:24:01.170 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

302 00:24:01.170 --> 00:24:10.920 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.

304 00:24:12.089 --> 00:24:19.470 When you say that you're trying to find therapies that will help in the cases of resistant lymphoma

305 00:24:19.470 --> 00:24:24.339 when you're looking at pathways that cause cancer cells to divide,

306 00:24:24.339 --> 00:24:30.029 I would think that those would help even up front as frontline therapies do.

307 00:24:30.029 --> 00:24:38.549 Do you try to figure out why they were resistant to the first line chemotherapy or the first line drug?

308 00:24:38.549 --> 00:24:45.049 Because presumably those already were targeting certain pathways that made cancer cells divide to begin with.

309 00:24:45.049 --> 00:24:47.480 That is true, and that really,

310 00:24:47.480 --> 00:24:50.329 again depends on the type of lymphoma.

311 00:24:50.329 --> 00:25:01.849 For example, mantle cell lymphoma is the frontline therapy that we use even to this date with Rituximab that I talked about in combination

312 00:25:01.849 --> 00:25:04.869 with other chemotherapy agents and to be honest,

313 00:25:04.869 --> 00:25:10.920 most of the lymphoma frontline therapy is still that cocktail of chemotherapy with Rituximab,

314 00:25:10.920 --> 00:25:20.369 and for good reason the bar is so high for these novel therapies to be used in front line.

315 00:25:20.369 --> 00:25:22.710 We don't want to harm patients.

316 00:25:22.710 --> 00:25:30.980 We have to find those novel drugs that will either improve, further the response to the frontline therapy and

317 00:25:30.980 --> 00:25:38.809 if not, then most most of the time they end up being used in second or third line.

318 00:25:38.809 --> 00:25:42.289 If the patients develop resistance to the frontline

319 00:25:42.289 --> 00:25:48.380 therapy.

320 00:25:48.380 --> 00:25:49.680 How often do patients with mantle cell lymphoma actually become resistant?

321 00:25:49.680 --> 00:25:55.380 Mantle cell lymphoma is one of the areas where there's a lot of research that needs to be done.

322 00:25:55.380 --> 00:25:59.400 In mantle cell,

323 00:25:59.400 --> 00:26:01.640 for example,

324 00:26:01.640 --> 00:26:04.769 I would say almost 70 to 80%

325 00:26:04.769 --> 00:26:08.339 of patients develop resistance to the frontline therapy.

326 00:26:08.339 --> 00:26:10.579 And as you can imagine,

327 00:26:10.579 --> 00:26:15.940 we already know that's what to use in second line third line.

328 00:26:15.940 --> 00:26:21.895 But then eventually most patients develop resistance to all these lines of therapy.

329 00:26:21.990 --> 00:26:25.390 And why is that? That's the $1,000,000 question.

330 00:26:25.390 --> 00:26:28.130 It's not easy to figure that out,

331 00:26:28.130 --> 00:26:31.549 but we do know that there are

332 00:26:31.549 --> 00:26:35.640 different mutations that the cancer cell can

333 00:26:35.640 --> 00:26:40.700 keep evolving. That's probably the best way to think about it.

334 00:26:40.700 --> 00:26:44.589 So if you introduce frontline therapy to a cancer cell,

335 00:26:44.589 --> 00:26:48.089 and let's say there are 10 cells to kill,

336 00:26:48.089 --> 00:26:59.759 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

337 00:26:59.759 --> 00:27:02.869 therapies worked. So now they have become smarter.

338 00:27:02.869 --> 00:27:04.819 They have acquired new mutations,

339 00:27:04.819 --> 00:27:06.809 new genetic changes that

340 00:27:06.809 --> 00:27:12.069 weren't there the first time and then you introduce second line therapy and again,

341 00:27:12.069 --> 00:27:16.680 the same thing happens where you kill most of the cells but not all,

342 00:27:16.680 --> 00:27:19.640 and then those few cells that are left behind,

343 00:27:19.640 --> 00:27:23.920 they eventually start dividing again because they have acquired newer mutations.

345 00:27:24.579 --> 00:27:34.450 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

346 00:27:34.450 --> 00:27:37.410 you don't want to keep taking different antibiotics,

347 00:27:37.410 --> 00:27:39.420 especially when you don't need them.

348 00:27:39.420 --> 00:27:45.680 Because then you have the generation of super bugs that are resistant to all antibiotics.

349 00:27:45.680 --> 00:27:46.089 Is

350 00:27:46.089 --> 00:27:48.589 that a similar kind of concept?

351 00:27:48.589 --> 00:27:58.609 Similar concept, but we are not worried about a generation of superbugs in this case because most lymphomas if not treated can be deadly.

352 00:27:58.609 --> 00:28:02.089 If they need treatment, if they're aggressive kinds of lymphomas,

353 00:28:02.089 --> 00:28:04.180 and if they are not treated,

354 00:28:04.180 --> 00:28:10.089 they can be deadly, so we don't typically worry about what will happen to that cancer cell, and

355 00:28:10.089 --> 00:28:13.230 what different types of mutations they're going to acquire.

356 00:28:13.230 --> 00:28:17.049 Because we really don't have the time in that particular patient,

357 00:28:17.049 --> 00:28:18.990 so in other words,

358 00:28:18.990 --> 00:28:25.529 we typically switch from one line of therapy to the next line of therapy very quickly.

359 00:28:25.529 --> 00:28:30.849 The moment we know that this particular patients lymphoma stopped responding,

360 00:28:30.849 --> 00:28:42.299 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.

361 00:28:42.990 --> 00:28:49.230 Doctor Shalin Kothari is an Assistant Professor of Medicine and Hematology at the Yale School of Medicine.

362 00:28:49.230 --> 00:28:57.670 If you have questions, the address is cancer-answers@yale.edu and past editions of the program are available in audio and written form at Yalecancercenter.org.

363 00:28:57.670 --> 00:29:06.314 We hope you'll join us next week to learn more about the fight against cancer here on Connecticut Public Radio.