WEBVTT

00:00:00.000 --> 00:00:03.204 Funding for Yale Cancer Answers is

NOTE Confidence: 0.902802829090909

00:00:03.204 --> 00:00:06.240 provided by Smilow Cancer Hospital.

NOTE Confidence: 0.902802829090909

00:00:06.240 --> 00:00:08.420 Welcome to Yale Cancer Answers

NOTE Confidence: 0.902802829090909

00:00:08.420 --> 00:00:10.160 with Doctor Anees Chagpar.

NOTE Confidence: 0.902802829090909

00:00:10.160 --> 00:00:11.896 Yale Cancer Answers features the

NOTE Confidence: 0.902802829090909

00:00:11.896 --> 00:00:13.666 latest information on cancer care

NOTE Confidence: 0.902802829090909

00:00:13.666 --> 00:00:15.164 by welcoming oncologists and

NOTE Confidence: 0.902802829090909

00:00:15.164 --> 00:00:17.324 specialists who are on the forefront

NOTE Confidence: 0.902802829090909

00:00:17.324 --> 00:00:19.238 of the battle to fight cancer.

NOTE Confidence: 0.902802829090909

00:00:19.240 --> 00:00:21.928 This week it's a conversation about CAR T

NOTE Confidence: 0.902802829090909

00:00:21.928 --> 00:00:24.479 cell therapy with Doctor Timothy Robinson.

NOTE Confidence: 0.902802829090909

00:00:24.480 --> 00:00:26.450 Doctor Robinson is an assistant

NOTE Confidence: 0.902802829090909

00:00:26.450 --> 00:00:28.026 professor of Therapeutic radiology

NOTE Confidence: 0.902802829090909

00:00:28.026 --> 00:00:30.080 at the Yale School of Medicine

NOTE Confidence: 0.902802829090909

00:00:30.080 --> 00:00:30.672 where Dr. Chagpar

NOTE Confidence: 0.902802829090909

00:00:30.672 --> 00:00:32.152 is a professor

NOTE Confidence: 0.902802829090909

00:00:32.152 --> 00:00:33.040 of Surgical oncology.

NOTE Confidence: 0.935679327272727

00:00:34.280 --> 00:00:35.928 Tim, maybe we can start off by you

NOTE Confidence: 0.935679327272727

00:00:35.928 --> 00:00:37.468 telling us a little bit more about

NOTE Confidence: 0.935679327272727

00:00:37.468 --> 00:00:38.920 yourself and what it is you do.

NOTE Confidence: 0.9402536

00:00:39.600 --> 00:00:42.239 Sure. So I am a radiation oncologist,

NOTE Confidence: 0.9402536

00:00:42.240 --> 00:00:45.558 which means that I treat tumors or

NOTE Confidence: 0.9402536

00:00:45.558 --> 00:00:47.640 cancers using radiation therapy

NOTE Confidence: 0.9402536

00:00:47.640 --> 00:00:50.040 and I have a clinical presence,

NOTE Confidence: 0.9402536

00:00:50.040 --> 00:00:51.300 so I treat patients.

NOTE Confidence: 0.9402536

00:00:51.300 --> 00:00:53.667 I specialize in the treatment of hematologic

NOTE Confidence: 0.9402536

00:00:53.667 --> 00:00:56.115 malignancies as well as CNS disease.

NOTE Confidence: 0.9402536

00:00:56.120 --> 00:00:57.600 I also have a small lab that

NOTE Confidence: 0.9402536

00:00:57.600 --> 00:00:59.317 tries to work more on the research side,

NOTE Confidence: 0.9402536

00:00:59.320 --> 00:01:00.100 trying to figure out how

NOTE Confidence: 0.9402536

00:01:00.100 --> 00:01:00.880 to do these things better.

NOTE Confidence: 0.931531986666667

00:01:01.560 --> 00:01:04.016 And so tell us a little bit more

NOTE Confidence: 0.931531986666667

00:01:04.016 --> 00:01:05.996 about what your lab is up to.

NOTE Confidence: 0.933963975

00:01:07.280 --> 00:01:11.120 Sure, my lab has been working on

NOTE Confidence: 0.933963975

00:01:11.120 --> 00:01:13.980 ways to try and figure out with lymphoma

NOTE Confidence: 0.933963975

00:01:13.980 --> 00:01:16.560 how to make our treatments better.

NOTE Confidence: 0.933963975

00:01:16.560 --> 00:01:18.148 As a radiation oncologist,

NOTE Confidence: 0.933963975

00:01:18.148 --> 00:01:20.530 I think about radiation a lot.

NOTE Confidence: 0.933963975

00:01:20.530 --> 00:01:22.225 Lymphomas are unique in that

NOTE Confidence: 0.933963975

00:01:22.225 --> 00:01:24.250 in many cancers we use

NOTE Confidence: 0.933963975

00:01:24.250 --> 00:01:25.936 radiation to treat many

NOTE Confidence: 0.933963975

00:01:25.936 --> 00:01:27.450 different cancers and solid tumors,

NOTE Confidence: 0.933963975

00:01:27.450 --> 00:01:29.275 but lymphomas and other so called

NOTE Confidence: 0.933963975

00:01:29.275 --> 00:01:31.218 liquid tumors, so lymphoma,

NOTE Confidence: 0.933963975

00:01:31.218 --> 00:01:33.634 myelomas, leukemias are actually

NOTE Confidence: 0.933963975

00:01:33.634 --> 00:01:36.050 exquisitely sensitive to radiation

NOTE Confidence: 0.933963975

00:01:36.050 --> 00:01:39.278 and so it's another place where

NOTE Confidence: 0.933963975

00:01:39.278 --> 00:01:40.763 radiation can actually be helpful.

NOTE Confidence: 0.933963975

00:01:40.770 --> 00:01:42.260 However, even though in general

NOTE Confidence: 0.933963975

00:01:42.260 --> 00:01:44.145 these tumors tend to be very

NOTE Confidence: 0.933963975

00:01:44.145 --> 00:01:45.509 sensitive for aggressive lymphomas

NOTE Confidence: 0.933963975

00:01:45.509 --> 00:01:47.705 that have kind of blown through

NOTE Confidence: 0.933963975

00:01:47.705 --> 00:01:49.437 all the conventional treatments,

NOTE Confidence: 0.933963975

00:01:49.440 --> 00:01:50.802 we actually will sometimes even for

NOTE Confidence: 0.933963975

00:01:50.802 --> 00:01:52.560 them see that they will actually grow

NOTE Confidence: 0.933963975

00:01:52.560 --> 00:01:54.174 through radiation treatment and we don't

NOTE Confidence: 0.933963975

00:01:54.174 --> 00:01:55.998 have a good understanding of why that is.

NOTE Confidence: 0.933963975

00:01:56.000 --> 00:01:58.800 And so my lab is interested in

NOTE Confidence: 0.933963975

00:01:58.800 --> 00:02:01.040 understanding how those tumors

NOTE Confidence: 0.933963975

00:02:01.040 --> 00:02:03.246 become resistant to radiation and

NOTE Confidence: 0.933963975

00:02:03.246 --> 00:02:05.808 then also how are those tumors becoming

NOTE Confidence: 0.933963975

00:02:05.808 --> 00:02:08.129 resistant to some of these new and

NOTE Confidence: 0.933963975

00:02:08.129 --> 00:02:10.174 these emerging therapies like cellular

NOTE Confidence: 0.933963975

00:02:10.174 --> 00:02:12.720 therapies like CAR T cell therapy

NOTE Confidence: 0.933963975

00:02:12.720 --> 00:02:13.980 that have really kind of

NOTE Confidence: 0.933963975

00:02:13.980 --> 00:02:15.240 revolutionized our treatment of these tumors.

NOTE Confidence: 0.933963975

00:02:15.692 --> 00:02:17.048 But they still don't always work

NOTE Confidence: 0.933963975

00:02:17.048 --> 00:02:18.361 and we're trying to figure out

NOTE Confidence: 0.933963975

00:02:18.361 --> 00:02:19.591 ways to make them work better.

NOTE Confidence: 0.9352219

00:02:20.760 --> 00:02:23.440 So tell us a bit more about what

NOTE Confidence: 0.9352219

00:02:23.440 --> 00:02:25.557 exactly CAR T cell therapy is.

NOTE Confidence: 0.9352219

00:02:25.560 --> 00:02:27.240 I mean some of our audience may

NOTE Confidence: 0.9352219

00:02:27.240 --> 00:02:29.788 have heard of it, it seems to be

NOTE Confidence: 0.9352219

00:02:29.788 --> 00:02:32.073 something that is fairly novel.

NOTE Confidence: 0.9352219

00:02:32.080 --> 00:02:33.838 Many of our audience may know

NOTE Confidence: 0.9352219

00:02:33.840 --> 00:02:36.120 the standard surgery,

NOTE Confidence: 0.9352219

00:02:36.120 --> 00:02:37.292 chemotherapy, radiation,

NOTE Confidence: 0.9352219

00:02:37.292 --> 00:02:40.808 maybe even have heard about immunotherapy.

NOTE Confidence: 0.9352219

00:02:40.810 --> 00:02:43.042 But CAR T cell therapy sounds

NOTE Confidence: 0.9352219

00:02:43.042 --> 00:02:44.530 really new and interesting.

NOTE Confidence: 0.9352219

00:02:44.530 --> 00:02:46.555 So can you tell us a bit more about

NOTE Confidence: 0.9352219

00:02:46.555 --> 00:02:48.530 what it is and how it works?

NOTE Confidence: 0.938576366666667

00:02:48.530 --> 00:02:49.730 Well, it is new and interesting,

NOTE Confidence: 0.938576366666667

00:02:49.730 --> 00:02:51.010 you're correct.

NOTE Confidence: 0.938576366666667

00:02:51.010 --> 00:02:53.470 So CAR T cell therapy,

NOTE Confidence: 0.938576366666667

00:02:53.470 --> 00:02:55.726 what it stands for is chimeric

NOTE Confidence: 0.938576366666667

00:02:55.726 --> 00:02:58.109 antigen receptor, T cell therapy.

NOTE Confidence: 0.938576366666667

00:02:58.109 --> 00:03:01.140 So chimera meaning a mix and then

NOTE Confidence: 0.938576366666667

00:03:01.234 --> 00:03:03.538 antigen receptor is basically what

NOTE Confidence: 0.938576366666667

00:03:03.538 --> 00:03:05.610 they've done it's actually very cool.

NOTE Confidence: 0.938576366666667

00:03:05.610 --> 00:03:07.506 It almost sounds

NOTE Confidence: 0.938576366666667

00:03:07.506 --> 00:03:08.454 like science fiction.

NOTE Confidence: 0.938576366666667

00:03:08.460 --> 00:03:10.290 So what they can do is they can take your

NOTE Confidence: 0.938576366666667

00:03:10.340 --> 00:03:12.216 immune cells, or your T cells specifically,

NOTE Confidence: 0.938576366666667

00:03:12.220 --> 00:03:14.740 which is why it's called CAR T cell therapy.

NOTE Confidence: 0.938576366666667

00:03:14.740 --> 00:03:16.324 And your T cells are part of your

NOTE Confidence: 0.938576366666667

00:03:16.324 --> 00:03:17.866 immune system that can recognize of

NOTE Confidence: 0.938576366666667

00:03:17.866 --> 00:03:19.252 course foreign antigens, infections,

NOTE Confidence: 0.938576366666667

00:03:19.252 --> 00:03:21.460 but also potentially, cancers.

NOTE Confidence: 0.938576366666667

00:03:21.460 --> 00:03:25.230 And basically what you can do is

NOTE Confidence: 0.938576366666667

00:03:25.230 --> 00:03:28.660 you can take somebody's individual T cells,

NOTE Confidence: 0.938576366666667

00:03:28.660 --> 00:03:30.774 so let's say somebody has an aggressive,

NOTE Confidence: 0.938576366666667

00:03:30.780 --> 00:03:32.595 you know, lymphoma that's grown

NOTE Confidence: 0.938576366666667

00:03:32.595 --> 00:03:34.410 through all the chemotherapy treatments

NOTE Confidence: 0.938576366666667

00:03:34.468 --> 00:03:36.204 that are kind of standard of care.

NOTE Confidence: 0.938576366666667

00:03:36.210 --> 00:03:37.086 And they have this

NOTE Confidence: 0.938576366666667

00:03:37.090 --> 00:03:38.742 aggressive lymphoma that's just

NOTE Confidence: 0.938576366666667

00:03:38.742 --> 00:03:40.494 not responding for those patients.

NOTE Confidence: 0.938576366666667

00:03:40.494 --> 00:03:42.650 CAR T cell therapy has been approved.

NOTE Confidence: 0.938576366666667

00:03:42.650 --> 00:03:44.466 And what you can do is basically take

NOTE Confidence: 0.938576366666667

00:03:44.466 --> 00:03:46.206 the immune cells out of that patient,

NOTE Confidence: 0.938576366666667

00:03:46.210 --> 00:03:47.728 put them in a Petri dish,

NOTE Confidence: 0.938576366666667

00:03:47.730 --> 00:03:49.720 genetically engineer them to go

NOTE Confidence: 0.938576366666667

00:03:49.720 --> 00:03:52.170 after markers on those cancer cells,

NOTE Confidence: 0.938576366666667

00:03:52.170 --> 00:03:53.367 kind of have a pep rally in

NOTE Confidence: 0.938576366666667

00:03:53.367 --> 00:03:54.370 the Petri dish

NOTE Confidence: 0.938576366666667

00:03:54.370 --> 00:03:55.930 get them good and revved up and

NOTE Confidence: 0.938576366666667

00:03:55.930 --> 00:03:57.526 then inject them back into the patients.

NOTE Confidence: 0.938576366666667

00:03:57.530 --> 00:04:00.086 And then those CAR T cells

00:04:00.580 --> 00:04:02.050 they're chimera because they've now been

00:04:02.572 --> 00:04:04.138 put with a specific marker to

NOTE Confidence: 0.938576366666667

00:04:04.138 --> 00:04:05.718 kind of heat sink towards

NOTE Confidence: 0.938576366666667

00:04:05.720 --> 00:04:06.760 the cancer cells,

NOTE Confidence: 0.938576366666667

00:04:06.760 --> 00:04:08.320 so it's a chimera or mix

NOTE Confidence: 0.938576366666667

00:04:08.387 --> 00:04:09.717 of your normal T cells,

NOTE Confidence: 0.938576366666667

00:04:09.720 --> 00:04:11.250 but now kind of targeted

NOTE Confidence: 0.938576366666667

00:04:11.250 --> 00:04:12.474 towards the cancer cells.

NOTE Confidence: 0.938576366666667

00:04:12.480 --> 00:04:14.909 And with that approach we can actually

NOTE Confidence: 0.938576366666667

00:04:14.909 --> 00:04:16.939 cure people who previously really

NOTE Confidence: 0.938576366666667

00:04:16.939 --> 00:04:19.234 didn't have any curable options.

NOTE Confidence: 0.938576366666667

00:04:19.240 --> 00:04:20.913 And really what you need is kind

NOTE Confidence: 0.938576366666667

00:04:20.913 --> 00:04:22.678 of a specific target to go after.

NOTE Confidence: 0.938576366666667

00:04:22.680 --> 00:04:24.424 And this has been a very exciting area

NOTE Confidence: 0.938576366666667

00:04:24.424 --> 00:04:25.680 in cancer overall,

NOTE Confidence: 0.938576366666667

00:04:25.680 --> 00:04:27.425 but it's been very successful

NOTE Confidence: 0.938576366666667

00:04:27.425 --> 00:04:29.170 in pediatric leukemias but also

NOTE Confidence: 0.938576366666667

00:04:29.232 --> 00:04:30.318 in adult lymphomas.

NOTE Confidence: 0.938423890909091

00:04:31.640 --> 00:04:33.548 But you know when some of

NOTE Confidence: 0.938423890909091

00:04:33.548 --> 00:04:35.560 us hear the words lymphoma,

NOTE Confidence: 0.938423890909091

00:04:35.560 --> 00:04:37.160 we think about

NOTE Confidence: 0.938423890909091

00:04:37.160 --> 00:04:39.518 T cell lymphomas, B cell lymphomas.

NOTE Confidence: 0.938423890909091

00:04:39.520 --> 00:04:42.460 So if you're taking people's

NOTE Confidence: 0.938423890909091

00:04:42.460 --> 00:04:45.726 T cells out of them

NOTE Confidence: 0.938423890909091

00:04:45.726 --> 00:04:47.356 and they have a lymphoma,

NOTE Confidence: 0.938423890909091

00:04:47.360 --> 00:04:49.640 especially if they have a T cell lymphoma,

NOTE Confidence: 0.938423890909091

00:04:49.640 --> 00:04:51.280 how does that work exactly?

NOTE Confidence: 0.927464051428571

00:04:51.880 --> 00:04:53.917 Yeah, sure. So it's a great question.

NOTE Confidence: 0.927464051428571

00:04:53.920 --> 00:04:55.560 So the thing is that right now

NOTE Confidence: 0.927464051428571

00:04:55.560 --> 00:04:57.760 we're still figuring this out.

NOTE Confidence: 0.927464051428571

00:04:57.760 --> 00:05:00.680 And so right now CAR T cell therapy

NOTE Confidence: 0.927464051428571

00:05:00.680 --> 00:05:03.738 works great for B cell lymphomas because

NOTE Confidence: 0.927464051428571

00:05:03.740 --> 00:05:06.211 almost all B cell lymphomas and many

NOTE Confidence: 0.927464051428571

00:05:06.211 --> 00:05:08.540 B cell leukemias over-express a very

NOTE Confidence: 0.927464051428571

00:05:08.540 --> 00:05:11.340 specific kind of protein on their surface

NOTE Confidence: 0.927464051428571

00:05:11.407 --> 00:05:13.771 and it happens to be called CD19 and

NOTE Confidence: 0.927464051428571

00:05:13.771 --> 00:05:15.619 that's kind of the bullseye so to speak.

NOTE Confidence: 0.927464051428571

00:05:15.620 --> 00:05:18.156 It's a protein that is

NOTE Confidence: 0.927464051428571

00:05:18.156 --> 00:05:19.440 over-expressed on malignant

NOTE Confidence: 0.927464051428571

00:05:19.440 --> 00:05:21.580 B cells or lymphoma cells,

NOTE Confidence: 0.927464051428571

00:05:21.580 --> 00:05:22.890 but not really over-expressed on

NOTE Confidence: 0.927464051428571

00:05:22.890 --> 00:05:24.500 any other cells in the body.

NOTE Confidence: 0.927464051428571

00:05:24.500 --> 00:05:25.886 And that's the target that the

NOTE Confidence: 0.927464051428571

00:05:25.886 --> 00:05:27.180 CAR T cells go after.

NOTE Confidence: 0.927464051428571

00:05:27.180 --> 00:05:28.908 We're trying to figure out how

NOTE Confidence: 0.927464051428571

00:05:28.908 --> 00:05:31.172 could we go after T cell lymphomas

NOTE Confidence: 0.927464051428571

00:05:31.172 --> 00:05:32.564 which are very aggressive.

NOTE Confidence: 0.927464051428571

00:05:32.570 --> 00:05:33.330 But as you point out,

NOTE Confidence: 0.927464051428571

00:05:33.330 --> 00:05:34.446 those don't necessarily have

NOTE Confidence: 0.927464051428571

00:05:34.446 --> 00:05:36.120 the same markers and we haven't

NOTE Confidence: 0.927464051428571

00:05:36.172 --> 00:05:37.570 cracked that nut so to speak,

NOTE Confidence: 0.927464051428571

00:05:37.570 --> 00:05:38.818 but we are trying to figure

NOTE Confidence: 0.927464051428571

00:05:38.818 --> 00:05:40.113 out specific markers on T cell

NOTE Confidence: 0.927464051428571

00:05:40.113 --> 00:05:41.367 lymphomas that might work as well,

NOTE Confidence: 0.927464051428571

00:05:41.370 --> 00:05:42.930 but we haven't figured that out just yet.

NOTE Confidence: 0.937378342857143

00:05:43.930 --> 00:05:46.322 And so if you have these T cells

NOTE Confidence: 0.937378342857143

00:05:46.322 --> 00:05:48.374 that are going after these markers

NOTE Confidence: 0.937378342857143

00:05:48.374 --> 00:05:51.170 on B cells for B cell lymphoma,

NOTE Confidence: 0.939135444444444

00:05:53.490 --> 00:05:57.126 is it true that, it sounds like that's great,

NOTE Confidence: 0.939135444444444

00:05:57.130 --> 00:05:58.888 it sounds like you're just kind

NOTE Confidence: 0.939135444444444

00:05:58.888 --> 00:06:00.500 of getting your immune system

NOTE Confidence: 0.939135444444444

00:06:00.500 --> 00:06:04.334 to go after these cells and kill them off,

NOTE Confidence: 0.939135444444444

00:06:04.340 --> 00:06:07.098 some of our audience might get confused

NOTE Confidence: 0.939135444444444

00:06:07.098 --> 00:06:09.340 between that and immunotherapy.

NOTE Confidence: 0.939135444444444

00:06:09.340 --> 00:06:13.615 Is this a form of immunotherapy and if so,

NOTE Confidence: 0.939135444444444

00:06:13.620 --> 00:06:16.889 does it need to be administered with

NOTE Confidence: 0.939135444444444

00:06:16.889 --> 00:06:19.156 chemotherapy as immunotherapies do or is

NOTE Confidence: 0.939135444444444

00:06:19.156 --> 00:06:21.452 this something that is just

NOTE Confidence: 0.939135444444444

00:06:21.460 --> 00:06:25.086 your body being revved up and

NOTE Confidence: 0.939135444444444

00:06:25.090 --> 00:06:27.538 those T cells having gone to the pep

NOTE Confidence: 0.939135444444444

00:06:27.538 --> 00:06:30.075 rally in the Petri dish, as you say,

NOTE Confidence: 0.939135444444444

00:06:30.075 --> 00:06:32.290 just going out there and doing their job?

NOTE Confidence: 0.9452853

00:06:33.290 --> 00:06:35.190 Typically when we

NOTE Confidence: 0.9452853

00:06:35.190 --> 00:06:36.658 give this therapy, yeah,

NOTE Confidence: 0.9452853

00:06:36.658 --> 00:06:39.282 the conditioning so to speak is

NOTE Confidence: 0.9452853

00:06:39.290 --> 00:06:41.486 it's not given alongside

NOTE Confidence: 0.9452853

00:06:41.490 --> 00:06:43.450 cytotoxic chemotherapy or other agents.

NOTE Confidence: 0.9452853

00:06:43.450 --> 00:06:45.370 It really is kind of expected to act

NOTE Confidence: 0.9452853

00:06:45.370 --> 00:06:48.158 on its own and that's what they

NOTE Confidence: 0.9452853

00:06:48.158 --> 00:06:50.186 call lympho depleting chemotherapy.

NOTE Confidence: 0.9452853

00:06:50.190 --> 00:06:52.310 So what they will do is give you about 3

NOTE Confidence: 0.9452853

00:06:52.372 --> 00:06:54.382 days typically worth of chemotherapy that

NOTE Confidence: 0.9452853

00:06:54.382 --> 00:06:56.790 will kind of suppress your immune system,

NOTE Confidence: 0.9452853

00:06:56.790 --> 00:06:58.896 get your T cells that are there to kind

NOTE Confidence: 0.9452853

00:06:58.896 --> 00:07:01.029 of calm down and get out of the way.

NOTE Confidence: 0.9452853

00:07:01.030 --> 00:07:02.577 And then two days later they go

NOTE Confidence: 0.9452853

00:07:02.577 --> 00:07:04.254 ahead and inject the CAR T cells and

NOTE Confidence: 0.9452853

00:07:04.254 --> 00:07:05.868 they really do kind of on their own

NOTE Confidence: 0.9452853

00:07:05.870 --> 00:07:07.388 basically

NOTE Confidence: 0.9452853

00:07:07.390 --> 00:07:09.829 do the job of getting rid of the cancer.

NOTE Confidence: 0.9452853

00:07:09.830 --> 00:07:11.972 So on one hand it is the

NOTE Confidence: 0.9452853

00:07:11.972 --> 00:07:14.068 immune system going after the cancer,

NOTE Confidence: 0.9452853

00:07:14.070 --> 00:07:17.304 but on the other hand we kind of tend

NOTE Confidence: 0.9452853

00:07:17.304 --> 00:07:18.228 to distinguish

NOTE Confidence: 0.9452853

00:07:18.230 --> 00:07:19.970 CAR T is cellular therapies

NOTE Confidence: 0.9452853

00:07:19.970 --> 00:07:21.710 because you're taking cells out,

NOTE Confidence: 0.9452853

00:07:21.710 --> 00:07:23.058 you know genetic engineering

NOTE Confidence: 0.9452853

00:07:23.058 --> 00:07:24.743 then putting them back in.

NOTE Confidence: 0.9452853

00:07:24.750 --> 00:07:26.304 And so we tend to call those

NOTE Confidence: 0.9452853

00:07:26.304 --> 00:07:26.748 cellular therapies.

NOTE Confidence: 0.9452853

00:07:26.750 --> 00:07:27.590 But I mean it really is

NOTE Confidence: 0.9452853

00:07:27.590 --> 00:07:29.238 splitting hairs a little bit

NOTE Confidence: 0.9452853

00:07:29.238 --> 00:07:30.728 because it is still the immune system

NOTE Confidence: 0.9452853

00:07:30.728 --> 00:07:32.270 being used to go after the cancer.

NOTE Confidence: 0.9364797575

00:07:32.850 --> 00:07:36.370 Yeah. So I mean, it sounds really cool,

NOTE Confidence: 0.9364797575

00:07:36.370 --> 00:07:38.914 right? And it sounds like that would be

NOTE Confidence: 0.9364797575

00:07:38.914 --> 00:07:42.170 something that would be the ideal.

NOTE Confidence: 0.9364797575

00:07:42.170 --> 00:07:44.753 Here is one of the cells in your

NOTE Confidence: 0.9364797575

00:07:44.753 --> 00:07:47.565 body that has gone awry and created a cancer.

NOTE Confidence: 0.9364797575

00:07:47.570 --> 00:07:50.538 And now all you're doing is you're kind

NOTE Confidence: 0.9364797575

00:07:50.538 --> 00:07:53.459 of helping your body to target

NOTE Confidence: 0.9364797575

00:07:53.459 --> 00:07:55.720 those cancerous cells and fight them

NOTE Confidence: 0.9364797575

00:07:55.720 --> 00:07:58.769 off just like they were designed to do.

NOTE Confidence: 0.9364797575

00:07:58.770 --> 00:08:00.450 So what's the downside?

NOTE Confidence: 0.9364797575

00:08:00.450 --> 00:08:02.474 I mean are there

NOTE Confidence: 0.9364797575

00:08:02.474 --> 00:08:06.618 side effects to CAR T cell therapy

NOTE Confidence: 0.9364797575

00:08:06.620 --> 00:08:08.978 and what about the financial cost?

NOTE Confidence: 0.939247156

00:08:09.380 --> 00:08:10.980 Sure, these are all

NOTE Confidence: 0.939247156

00:08:10.980 --> 00:08:12.580 good points and

00:08:14.820 --> 00:08:16.060 first and foremost,

NOTE Confidence: 0.939247156

00:08:16.060 --> 00:08:18.340 it doesn't work all the time.

NOTE Confidence: 0.939247156

00:08:18.340 --> 00:08:20.260 So for patients with

NOTE Confidence: 0.939247156

00:08:20.260 --> 00:08:21.532 relapse refractory aggressive lymphomas,

NOTE Confidence: 0.939247156

00:08:21.532 --> 00:08:23.122 we're trying to figure out

NOTE Confidence: 0.939247156

00:08:23.122 --> 00:08:24.499 ways to make it work better.

NOTE Confidence: 0.939247156

00:08:24.500 --> 00:08:26.138 But for those patients

NOTE Confidence: 0.939247156

00:08:26.140 --> 00:08:27.928 their cure rates are quite low.

NOTE Confidence: 0.939247156

00:08:27.930 --> 00:08:29.210 With CAR T cell therapy,

NOTE Confidence: 0.939247156

00:08:29.210 --> 00:08:30.785 we appear to be getting about a

NOTE Confidence: 0.939247156

00:08:30.785 --> 00:08:32.242 40% durable response,

NOTE Confidence: 0.939247156

00:08:32.242 --> 00:08:34.090 which you could kind of call

NOTE Confidence: 0.939247156

00:08:34.149 --> 00:08:35.800 a cure for those patients.

NOTE Confidence: 0.939247156

00:08:35.800 --> 00:08:37.450 And so it's not perfect.

NOTE Confidence: 0.939247156

00:08:37.450 --> 00:08:38.800 It doesn't work for everybody and

NOTE Confidence: 0.939247156

00:08:38.800 --> 00:08:39.907 that's what we're actually trying

NOTE Confidence: 0.939247156

00:08:39.907 --> 00:08:41.083 to do is to make that better so

NOTE Confidence: 0.939247156

00:08:41.090 --> 00:08:41.934 that it does cure everybody,

00:08:42.570 --> 00:08:44.411 but 40 percent is a pretty good

NOTE Confidence: 0.939247156

00:08:44.411 --> 00:08:45.970 number when you're talking about

NOTE Confidence: 0.939247156

00:08:45.970 --> 00:08:48.754 a setting where almost

NOTE Confidence: 0.939247156

00:08:48.754 --> 00:08:50.610 nothing else works well.

NOTE Confidence: 0.939247156

00:08:50.610 --> 00:08:52.686 And 2nd, in terms of toxicity,

NOTE Confidence: 0.939247156

00:08:52.690 --> 00:08:55.600 first of all, the biologic toxicity,

00:08:55.964 --> 00:08:57.420 so one of the things that can happen

NOTE Confidence: 0.939247156

00:08:57.468 --> 00:08:58.910 is that there are some

NOTE Confidence: 0.939247156

00:08:58.910 --> 00:09:00.228 patients it actually is similar to

NOTE Confidence: 0.939247156

00:09:00.228 --> 00:09:01.536 immune therapy in that some patients

NOTE Confidence: 0.939247156

00:09:01.536 --> 00:09:03.116 will just sail right through it

NOTE Confidence: 0.939247156

00:09:03.116 --> 00:09:04.560 and won't even bat an eye.

NOTE Confidence: 0.939247156

00:09:04.560 --> 00:09:06.877 But then some patients can have dramatic

NOTE Confidence: 0.939247156

00:09:06.877 --> 00:09:09.152 side effects or toxicities and they

NOTE Confidence: 0.939247156

00:09:09.152 --> 00:09:11.680 tend to be self limited which is good.

NOTE Confidence: 0.939247156

00:09:11.680 --> 00:09:13.409 And the biggest one that we worry

NOTE Confidence: 0.939247156

00:09:13.409 --> 00:09:15.466 about with CAR T cell therapy is

NOTE Confidence: 0.939247156

00:09:15.466 --> 00:09:17.036 this thing called cytokine release

NOTE Confidence: 0.939247156

00:09:17.036 --> 00:09:18.520 syndrome or CRS and what that is,

00:09:19.484 --> 00:09:21.176 we've taken these T cells and

NOTE Confidence: 0.939247156

00:09:21.176 --> 00:09:23.240 thrown a PEP rally inject them in

NOTE Confidence: 0.939247156

00:09:23.240 --> 00:09:24.402 and then they see a lot of

NOTE Confidence: 0.939247156

00:09:24.402 --> 00:09:25.638 tumor and they get real excited.

00:09:25.975 --> 00:09:28.320 Your immune system when it revs up

NOTE Confidence: 0.939247156

00:09:28.320 --> 00:09:30.567 can secrete a lot of cytokines and

NOTE Confidence: 0.939247156

00:09:30.567 --> 00:09:32.452 sometimes it's such a powerful kind

NOTE Confidence: 0.939247156

00:09:32.452 --> 00:09:34.883 of storm of cytokines that it can

NOTE Confidence: 0.939247156

00:09:34.883 --> 00:09:36.718 actually cause a severe toxicity.

NOTE Confidence: 0.939247156

00:09:36.720 --> 00:09:38.940 Probably the most feared toxicity is

NOTE Confidence: 0.939247156

00:09:38.940 --> 00:09:41.432 something called ICANS or this kind

NOTE Confidence: 0.939247156

00:09:41.432 --> 00:09:45.144 of neurologic toxicity where it can

NOTE Confidence: 0.939247156

00:09:45.144 --> 00:09:48.168 actually result in something as severe as

NOTE Confidence: 0.939247156

00:09:48.170 --> 00:09:49.745 not being able to talk

NOTE Confidence: 0.939247156

00:09:49.745 --> 00:09:51.224 or even being temporarily paralyzed

NOTE Confidence: 0.939247156

00:09:51.224 --> 00:09:52.988 like a kind of Guillain Barre

NOTE Confidence: 0.939247156

00:09:52.988 --> 00:09:54.609 type syndrome in the hospital.

NOTE Confidence: 0.939247156

00:09:54.610 --> 00:09:56.338 And that happens

NOTE Confidence: 0.939247156

00:09:56.338 --> 00:09:57.202 actually not infrequently,

NOTE Confidence: 0.939247156

00:09:57.210 --> 00:09:59.569 it varies by the exact cellular product.

NOTE Confidence: 0.939247156

00:09:59.570 --> 00:10:01.260 But I mean in some of the products

NOTE Confidence: 0.939247156

00:10:01.260 --> 00:10:02.976 that can be as high as 30% rate

NOTE Confidence: 0.939247156

00:10:02.976 --> 00:10:04.698 of having a toxicity so bad that

NOTE Confidence: 0.939247156

00:10:04.698 --> 00:10:06.358 people can temporarily be

NOTE Confidence: 0.939247156

00:10:06.358 --> 00:10:08.284 stuck in the hospital not able to

NOTE Confidence: 0.939247156

00:10:08.284 --> 00:10:10.122 speak and the vast

NOTE Confidence: 0.939247156

00:10:10.122 --> 00:10:11.909 majority of those are self limited

NOTE Confidence: 0.939247156

00:10:11.909 --> 00:10:13.829 and go away with close monitoring.

NOTE Confidence: 0.939247156

00:10:13.830 --> 00:10:15.230 But there

NOTE Confidence: 0.939247156

00:10:15.230 --> 00:10:17.120 certainly is a potential

NOTE Confidence: 0.939247156

00:10:17.120 --> 00:10:19.010 for real toxicity especially in

NOTE Confidence: 0.939247156

00:10:19.073 --> 00:10:20.363 the acute setting chronically.

NOTE Confidence: 0.939247156

00:10:20.363 --> 00:10:21.881 So far, again, we don't have

NOTE Confidence: 0.939247156

00:10:21.881 --> 00:10:23.149 super long term follow up,

NOTE Confidence: 0.939247156

00:10:23.150 --> 00:10:26.030 but these patients seem to do well long term.

NOTE Confidence: 0.939247156

00:10:26.030 --> 00:10:28.310 It really is kind of that acute window.

NOTE Confidence: 0.939247156

00:10:28.310 --> 00:10:30.949 And then lastly on the financial toxicity,

NOTE Confidence: 0.939247156

00:10:30.950 --> 00:10:32.427 you know this is an expensive therapy,

NOTE Confidence: 0.939247156

00:10:32.430 --> 00:10:34.272 the number that I've heard cited

NOTE Confidence: 0.939247156

00:10:34.272 --> 00:10:35.500 most often because obviously

NOTE Confidence: 0.95283285

00:10:35.555 --> 00:10:37.150 our healthcare systems are complex

NOTE Confidence: 0.95283285

00:10:37.150 --> 00:10:39.864 and opaque and can

NOTE Confidence: 0.95283285

00:10:39.864 --> 00:10:41.820 be very difficult to navigate,

NOTE Confidence: 0.95283285

00:10:41.820 --> 00:10:43.434 but around $400,000 is

NOTE Confidence: 0.95283285

00:10:43.434 --> 00:10:45.170 the number that I've heard.

NOTE Confidence: 0.95283285

00:10:45.170 --> 00:10:47.739 Holy Dinah.

NOTE Confidence: 0.95283285

00:10:47.740 --> 00:10:49.360 Yeah, holy Dinah.

NOTE Confidence: 0.95283285

00:10:49.360 --> 00:10:51.790 And that's obviously

NOTE Confidence: 0.95283285

00:10:51.867 --> 00:10:53.457 a very high price tag.

NOTE Confidence: 0.95283285

00:10:53.460 --> 00:10:55.416 So insurance clearance is of importance.

NOTE Confidence: 0.95283285

00:10:55.420 --> 00:10:57.524 I mean the good news is that insurance

NOTE Confidence: 0.95283285

00:10:57.524 --> 00:10:59.524 does cover this and approve it when

NOTE Confidence: 0.95283285

00:10:59.524 --> 00:11:01.289 it's appropriate and the FDA approvals

NOTE Confidence: 0.95283285

00:11:01.289 --> 00:11:03.291 have kind of been moving up

NOTE Confidence: 0.95283285

00:11:03.291 --> 00:11:05.765 as appropriate

NOTE Confidence: 0.95283285

00:11:05.765 --> 00:11:07.950 for patients with bad disease.

NOTE Confidence: 0.95283285

00:11:07.950 --> 00:11:09.024 But that's the thing

NOTE Confidence: 0.95283285

00:11:09.024 --> 00:11:09.950 with cancer care these days.

NOTE Confidence: 0.95283285

00:11:09.950 --> 00:11:11.630 You could do a whole segment.

NOTE Confidence: 0.95283285

00:11:11.630 --> 00:11:12.782 I'm sure you've done many segments

NOTE Confidence: 0.95283285

00:11:12.782 --> 00:11:14.070 on the cost of cancer care,

NOTE Confidence: 0.95283285

00:11:14.070 --> 00:11:15.510 which is a rapidly moving target.

NOTE Confidence: 0.95283285

00:11:15.510 --> 00:11:17.590 So you know, on the one hand you could say,

NOTE Confidence: 0.95283285

00:11:17.590 --> 00:11:19.746 oh my gosh, $400,000, this is crazy,

NOTE Confidence: 0.95283285

00:11:19.750 --> 00:11:21.470 how is this ever going to be a real solution?

NOTE Confidence: 0.95283285

00:11:21.470 --> 00:11:22.990 We should just abandon this.

NOTE Confidence: 0.95283285

00:11:22.990 --> 00:11:24.382 But I would also say that

NOTE Confidence: 0.95283285

00:11:24.382 --> 00:11:25.310 technology improves over time.

NOTE Confidence: 0.95283285

00:11:25.310 --> 00:11:26.106 And so NOTE Confidence: 0.95283285

00:11:26.106 --> 00:11:27.590 as we get better at doing this, we

NOTE Confidence: 0.95283285

00:11:27.590 --> 00:11:29.466 figure out cheaper ways to do it,

NOTE Confidence: 0.95283285

00:11:29.470 --> 00:11:31.166 I think that will be a natural thing

NOTE Confidence: 0.95283285

00:11:31.166 --> 00:11:32.787 that will kind of evolve over time.

NOTE Confidence: 0.95283285

00:11:32.790 --> 00:11:34.160 Right now we're just excited

NOTE Confidence: 0.95283285

00:11:34.160 --> 00:11:35.960 to be curing folks who before

NOTE Confidence: 0.95283285

00:11:36.140 --> 00:11:37.400 we're kind of carrying a death sentence.

00:11:39.720 --> 00:11:42.087 I just have to take a

NOTE Confidence: 0.931028753333333

00:11:42.087 --> 00:11:45.212 breath at that, nearly half,

NOTE Confidence: 0.931028753333333

00:11:45.212 --> 00:11:48.077 $1,000,000 price tag for therapy,

NOTE Confidence: 0.931028753333333

00:11:48.080 --> 00:11:50.190 especially when you say that

NOTE Confidence: 0.931028753333333

00:11:50.190 --> 00:11:51.878 it doesn't always work.

NOTE Confidence: 0.931028753333333

00:11:51.880 --> 00:11:56.888 So how often does it not work and

NOTE Confidence: 0.931028753333333

00:11:56.890 --> 00:11:58.490 what do you do then?

NOTE Confidence: 0.931028753333333

00:11:58.490 --> 00:12:00.450 Is this something that you then repeat,

NOTE Confidence: 0.931028753333333

00:12:00.450 --> 00:12:03.969 so multiple courses of CAR T cell therapy at,

NOTE Confidence: 0.931028753333333

00:12:03.970 --> 00:12:06.490 you know, $400,000 a pop?

NOTE Confidence: 0.931028753333333

00:12:06.490 --> 00:12:09.130 And if so, how many times do you do that?

NOTE Confidence: 0.924439685714286

00:12:09.730 --> 00:12:11.249 Yeah, so to be

NOTE Confidence: 0.941371755555556

00:12:11.250 --> 00:12:12.535 honest, I think it's important

NOTE Confidence: 0.941371755555556

00:12:12.535 --> 00:12:13.850 to keep in mind,

NOTE Confidence: 0.941371755555556

00:12:13.850 --> 00:12:15.410 it's easy to kind of talk about this

NOTE Confidence: 0.949198844444445

00:12:16.170 --> 00:12:17.103 academically,

NOTE Confidence: 0.949198844444445

00:12:17.103 --> 00:12:18.969 which is great and very important.

NOTE Confidence: 0.949198844444445

00:12:18.970 --> 00:12:20.293 But I'll give you kind of an

NOTE Confidence: 0.949198844444445

00:12:20.293 --> 00:12:21.647 example of a case that I saw,

NOTE Confidence: 0.949198844444445

00:12:21.650 --> 00:12:24.000 one of the earlier cases.

NOTE Confidence: 0.949198844444445

00:12:24.000 --> 00:12:25.880 I had a gentleman who had been referred

NOTE Confidence: 0.949198844444445

00:12:25.880 --> 00:12:27.840 to the Cancer Center I was at where

NOTE Confidence: 0.949198844444445

00:12:27.840 --> 00:12:29.508 I'd actually started out at

NOTE Confidence: 0.949198844444445

00:12:29.508 --> 00:12:31.110 Moffitt Cancer Center before I came

NOTE Confidence: 0.949198844444445

00:12:31.110 --> 00:12:32.664 to Yale who happened to do

NOTE Confidence: 0.949198844444445

00:12:32.664 --> 00:12:34.280 some of the first CAR T therapies.

NOTE Confidence: 0.949198844444445

00:12:34.280 --> 00:12:35.358 And so they're a big center there.

NOTE Confidence: 0.949198844444445

00:12:35.360 --> 00:12:37.808 And anyway, this was in the early days

NOTE Confidence: 0.949198844444445

00:12:37.808 --> 00:12:41.438 around 2018 and I had a gentleman with

NOTE Confidence: 0.949198844444445

00:12:41.440 --> 00:12:43.533 a diffuse source B cell lymphoma that

NOTE Confidence: 0.949198844444445

00:12:43.533 --> 00:12:45.518 had been through 6 lines of therapy.

NOTE Confidence: 0.949198844444445

00:12:45.520 --> 00:12:46.584 And I don't know the price tags

NOTE Confidence: 0.949198844444445

00:12:46.584 --> 00:12:47.918 of all the therapies he went through,

NOTE Confidence: 0.949198844444445

00:12:47.920 --> 00:12:49.200 but they weren't small either.

NOTE Confidence: 0.949198844444445

00:12:49.200 --> 00:12:51.200 Chemotherapy, rituximab,

NOTE Confidence: 0.949198844444445

00:12:51.200 --> 00:12:53.336 he had a stem cell transplant.

NOTE Confidence: 0.949198844444445

00:12:53.340 --> 00:12:55.518 Two rounds of radiation and his

NOTE Confidence: 0.949198844444445

00:12:55.518 --> 00:12:57.778 cancer kept coming back,

00:12:59.620 --> 00:13:01.436 and it kept on coming back to the

NOTE Confidence: 0.949198844444445

00:13:01.436 --> 00:13:03.046 point that actually it caused his

NOTE Confidence: 0.949198844444445

00:13:03.046 --> 00:13:04.989 leg to necrose and he actually had

NOTE Confidence: 0.949198844444445

00:13:04.989 --> 00:13:06.690 to have an amputation

NOTE Confidence: 0.949198844444445

00:13:06.690 --> 00:13:08.551 from the lymphoma attacking it.

NOTE Confidence: 0.949198844444445

00:13:08.551 --> 00:13:12.404 And that's when I met him and

NOTE Confidence: 0.949198844444445

00:13:12.404 --> 00:13:14.612 so he came to see me,

NOTE Confidence: 0.949198844444445

00:13:14.620 --> 00:13:15.495 we did a little bit of chemo,

00:13:16.913 --> 00:13:19.257 got in the car T and he actually

NOTE Confidence: 0.949198844444445

00:13:19.257 --> 00:13:21.343 was able to survive for another

NOTE Confidence: 0.949198844444445

00:13:21.343 --> 00:13:22.727 two years cancer free.

NOTE Confidence: 0.949198844444445

00:13:22.730 --> 00:13:24.319 With the approach of radiation to

NOTE Confidence: 0.949198844444445

00:13:24.319 --> 00:13:26.162 kind of get him through that danger

NOTE Confidence: 0.949198844444445

00:13:26.162 --> 00:13:27.824 zone to temporarily control the tumor

NOTE Confidence: 0.949198844444445

00:13:27.879 --> 00:13:29.607 and then get the CAR T cell therapy.

NOTE Confidence: 0.949198844444445

00:13:29.610 --> 00:13:32.330 So kind of miraculous but

NOTE Confidence: 0.949198844444445

00:13:32.330 --> 00:13:34.538 I think that

NOTE Confidence: 0.949198844444445

00:13:34.538 --> 00:13:36.010 it's just when you're faced with these cases,

NOTE Confidence: 0.949198844444445

00:13:36.010 --> 00:13:37.050 I mean the NOTE Confidence: 0.949198844444445

00:13:37.050 --> 00:13:38.890 cold truth is that if you have a

NOTE Confidence: 0.949198844444445

00:13:38.890 --> 00:13:40.716 really refractory disease that's life

NOTE Confidence: 0.949198844444445

00:13:40.716 --> 00:13:42.768 threatening and if you don't fix it,

NOTE Confidence: 0.949198844444445

00:13:42.770 --> 00:13:44.170 I mean the alternative is death.

NOTE Confidence: 0.949198844444445

00:13:47.565 --> 00:13:48.904 and that's why we're really working

NOTE Confidence: 0.949198844444445

00:13:48.904 --> 00:13:50.544 to try and provide potentially

NOTE Confidence: 0.949198844444445

00:13:50.544 --> 00:13:53.540 curative options for these patients.

NOTE Confidence: 0.949198844444445

00:13:53.540 --> 00:13:55.500 And happy to speak on that more.

NOTE Confidence: 0.949198844444445

00:13:55.500 --> 00:13:57.804 I mean costs in the medical system is

NOTE Confidence: 0.949198844444445

00:13:57.804 --> 00:14:00.293 a whole ball of wax and I agree it's

NOTE Confidence: 0.949198844444445

00:14:00.293 --> 00:14:02.012 a high price tag and I think that's

NOTE Confidence: 0.949198844444445

00:14:02.012 --> 00:14:03.020 something we'll move in the future.

NOTE Confidence: 0.949198844444445

00:14:03.020 --> 00:14:03.820 But it's

NOTE Confidence: 0.949198844444445

00:14:03.820 --> 00:14:05.339 a whole other topic of discussion.

NOTE Confidence: 0.939338745454545

00:14:05.940 --> 00:14:08.670 Certainly, I mean I think

NOTE Confidence: 0.939338745454545

00:14:08.670 --> 00:14:11.724 that CAR T therapy has its place.

NOTE Confidence: 0.939338745454545

00:14:11.724 --> 00:14:14.580 We're going to learn more on the

NOTE Confidence: 0.939338745454545

00:14:14.672 --> 00:14:17.276 other side of the break about

NOTE Confidence: 0.939338745454545

00:14:17.280 --> 00:14:19.352 how it could fall short and some of

NOTE Confidence: 0.939338745454545

00:14:19.352 --> 00:14:21.503 the work that you've been doing to

NOTE Confidence: 0.939338745454545

00:14:21.503 --> 00:14:23.435 kind of improve outcomes in those

NOTE Confidence: 0.939338745454545

00:14:23.435 --> 00:14:25.277 patients right after we take a

NOTE Confidence: 0.939338745454545

00:14:25.277 --> 00:14:27.145 short break for a medical minute.

NOTE Confidence: 0.939338745454545

00:14:27.145 --> 00:14:29.035 Please stay tuned to learn more

NOTE Confidence: 0.939338745454545

00:14:29.035 --> 00:14:31.000 with my guest Dr. Tim Robinson.

NOTE Confidence: 0.89472673

00:14:31.640 --> 00:14:34.046 Funding for Yale Cancer Answers comes

NOTE Confidence: 0.89472673

00:14:34.046 --> 00:14:36.224 from Smilow Cancer Hospital where

NOTE Confidence: 0.89472673

00:14:36.224 --> 00:14:38.734 their oncodermatology program treats

NOTE Confidence: 0.89472673

00:14:38.734 --> 00:14:40.742 dermatologic concerns including very

NOTE Confidence: 0.89472673

00:14:40.808 --> 00:14:43.200 dry skin itching and skin changes that

NOTE Confidence: 0.89472673

00:14:43.200 --> 00:14:45.400 arise as side effects from chemotherapy.

NOTE Confidence: 0.9301903

00:14:47.510 --> 00:14:50.142 Smilowcancerhospital.org. Genetic

NOTE Confidence: 0.9301903

00:14:50.142 --> 00:14:52.014 testing can be useful for people

NOTE Confidence: 0.9301903

00:14:52.014 --> 00:14:53.799 with certain types of cancer that

NOTE Confidence: 0.9301903

00:14:53.799 --> 00:14:55.383 seem to run in their families.

NOTE Confidence: 0.9301903

00:14:55.390 --> 00:14:57.682 Genetic counseling is a process that

NOTE Confidence: 0.9301903

00:14:57.682 --> 00:14:59.671 includes collecting a detailed personal

NOTE Confidence: 0.9301903

00:14:59.671 --> 00:15:02.214 and family history, a risk assessment,

NOTE Confidence: 0.9301903

00:15:02.214 --> 00:15:05.350 and a discussion of genetic testing options.

NOTE Confidence: 0.9301903

00:15:05.350 --> 00:15:07.958 Only about 5 to 10% of all cancers

NOTE Confidence: 0.9301903

00:15:07.958 --> 00:15:09.923 are inherited, and genetic testing

NOTE Confidence: 0.9301903

00:15:09.923 --> 00:15:12.078 is not recommended for everyone.

NOTE Confidence: 0.9301903

00:15:12.080 --> 00:15:14.396 Individuals who have a personal and

NOTE Confidence: 0.9301903

00:15:14.396 --> 00:15:16.457 or family history that includes

NOTE Confidence: 0.9301903

00:15:16.457 --> 00:15:18.677 cancer at unusually early ages,

NOTE Confidence: 0.9301903

00:15:18.680 --> 00:15:20.684 Multiple relatives on the same side

NOTE Confidence: 0.9301903

00:15:20.684 --> 00:15:23.078 of the family with the same cancer,

NOTE Confidence: 0.9301903

00:15:23.080 --> 00:15:25.740 more than one diagnosis of cancer in

NOTE Confidence: 0.9301903

00:15:25.740 --> 00:15:27.682 the same individual, rare cancers,

NOTE Confidence: 0.9301903

00:15:27.682 --> 00:15:30.489 or family history of a known altered

NOTE Confidence: 0.9301903

00:15:30.489 --> 00:15:33.000 cancer predisposing gene could be

NOTE Confidence: 0.9301903

00:15:33.000 --> 00:15:35.040 candidates for genetic testing.

NOTE Confidence: 0.9301903

00:15:35.040 --> 00:15:37.030 Resources for genetic counseling and

NOTE Confidence: 0.9301903

00:15:37.030 --> 00:15:39.020 testing are available at federally

NOTE Confidence: 0.9301903

00:15:39.084 --> 00:15:41.328 designated comprehensive Cancer centers

NOTE Confidence: 0.9301903

00:15:41.330 --> 00:15:43.466 such as Yale Cancer Center and

NOTE Confidence: 0.9301903

00:15:43.466 --> 00:15:44.890 Smilow Cancer Hospital.

NOTE Confidence: 0.9301903

00:15:44.890 --> 00:15:47.258 More information is available

NOTE Confidence: 0.9301903

00:15:47.258 --> 00:15:48.284 at yalecancercenter.org.

NOTE Confidence: 0.9301903

00:15:48.284 --> 00:15:50.888 You're listening to Connecticut Public Radio.

NOTE Confidence: 0.950316926666667

00:15:51.610 --> 00:15:53.566 Welcome back to Yale Cancer Answers.

NOTE Confidence: 0.950316926666667

00:15:53.570 --> 00:15:55.130 This is Dr. Anees Chagpar

NOTE Confidence: 0.950316926666667

00:15:55.130 --> 00:15:57.781 and I'm joined tonight by my guest, Dr.

NOTE Confidence: 0.950316926666667

00:15:57.781 --> 00:15:58.603 Tim Robinson.

NOTE Confidence: 0.950316926666667

00:15:58.603 --> 00:16:00.658 We're talking about improving outcomes

NOTE Confidence: 0.950316926666667

00:16:00.658 --> 00:16:03.327 for patients undergoing CAR T cell therapy.

NOTE Confidence: 0.950316926666667

00:16:03.330 --> 00:16:05.830 And for those of you who are just joining us,

NOTE Confidence: 0.950316926666667

00:16:05.830 --> 00:16:07.346 right before the break,

NOTE Confidence: 0.950316926666667

00:16:07.346 --> 00:16:09.241 we were talking about this

NOTE Confidence: 0.950316926666667

00:16:09.241 --> 00:16:10.750 fairly novel treatment,

NOTE Confidence: 0.950316926666667

00:16:10.750 --> 00:16:14.350 cellular therapy with CAR T cells,

NOTE Confidence: 0.950316926666667

00:16:14.350 --> 00:16:17.518 which is basically taking out your

NOTE Confidence: 0.950316926666667

00:16:17.518 --> 00:16:20.605 own T cells, putting them into a Petri

NOTE Confidence: 0.950316926666667

00:16:20.605 --> 00:16:22.790 dish where they have a pep rally,

NOTE Confidence: 0.950316926666667

00:16:22.790 --> 00:16:25.961 as Tim would say, getting revved up

NOTE Confidence: 0.950316926666667

00:16:25.961 --> 00:16:29.150 to fight against particular antigens,

NOTE Confidence: 0.950316926666667

00:16:29.150 --> 00:16:31.562 and then they are reinjected into

NOTE Confidence: 0.950316926666667

00:16:31.562 --> 00:16:34.370 your body where they do their magic.

NOTE Confidence: 0.950316926666667

00:16:34.370 --> 00:16:35.846 And Tim, right before the break,

NOTE Confidence: 0.950316926666667

00:16:35.850 --> 00:16:38.433 he told us a nice case that you had

NOTE Confidence: 0.950316926666667

00:16:38.433 --> 00:16:40.989 seen early on in your career where

NOTE Confidence: 0.950316926666667

00:16:40.989 --> 00:16:44.223 somebody who had failed multiple lines

NOTE Confidence: 0.950316926666667

00:16:44.223 --> 00:16:47.080 of chemotherapy and Rituximab and

NOTE Confidence: 0.950316926666667

00:16:47.080 --> 00:16:49.965 radiation and stem cell transplant

NOTE Confidence: 0.950316926666667

00:16:49.970 --> 00:16:54.155 really got CAR T cell therapy and did

NOTE Confidence: 0.950316926666667

00:16:54.155 --> 00:16:56.570 well for at least two years thereafter.

NOTE Confidence: 0.950316926666667

00:16:56.570 --> 00:17:00.514 So certainly it has a role to play.

NOTE Confidence: 0.950316926666667

00:17:00.520 --> 00:17:03.118 But it is not without toxicity.

NOTE Confidence: 0.950316926666667

00:17:03.120 --> 00:17:05.235 It certainly has some biologic

NOTE Confidence: 0.950316926666667

00:17:05.235 --> 00:17:07.781 toxicities as we talked about before

NOTE Confidence: 0.950316926666667

00:17:07.781 --> 00:17:09.743 the break and a significant price

NOTE Confidence: 0.950316926666667

00:17:09.743 --> 00:17:12.080 tag for those of you just joining us.

NOTE Confidence: 0.950316926666667

00:17:12.080 --> 00:17:14.900 That price tag was estimated to

NOTE Confidence: 0.950316926666667

00:17:14.900 --> 00:17:16.193 be roughly $400,000.

NOTE Confidence: 0.950316926666667

00:17:16.193 --> 00:17:17.252 And so Tim,

NOTE Confidence: 0.950316926666667

00:17:17.252 --> 00:17:19.832 the part that I want to talk

NOTE Confidence: 0.950316926666667

00:17:19.832 --> 00:17:22.472 about in this next segment is

NOTE Confidence: 0.950316926666667

00:17:22.472 --> 00:17:24.936 the issue that you brought up in

NOTE Confidence: 0.950316926666667

00:17:24.936 --> 00:17:27.332 passing before the break, which is

NOTE Confidence: 0.950316926666667

00:17:27.332 --> 00:17:29.196 it doesn't always work.

NOTE Confidence: 0.950316926666667

00:17:29.200 --> 00:17:30.718 So tell us a bit more,

NOTE Confidence: 0.950316926666667

00:17:30.720 --> 00:17:35.355 how often does CAR T cell therapy not work?

NOTE Confidence: 0.950316926666667

00:17:35.360 --> 00:17:36.752 And why is that?

NOTE Confidence: 0.950316926666667

00:17:36.752 --> 00:17:39.369 Why is it that some people may

NOTE Confidence: 0.950316926666667

00:17:39.369 --> 00:17:42.484 have what seems to be a miraculous

NOTE Confidence: 0.950316926666667

00:17:42.484 --> 00:17:44.997 response whereas others not so much?

NOTE Confidence: 0.944279066

00:17:45.880 --> 00:17:48.328 Yeah, exactly. So that's the

NOTE Confidence: 0.944279066

00:17:48.328 --> 00:17:50.720 $400,000 question.

NOTE Confidence: 0.944279066

00:17:50.720 --> 00:17:52.470 What we have seen

NOTE Confidence: 0.944279066

00:17:52.470 --> 00:17:54.427 is where this is being

NOTE Confidence: 0.944279066

00:17:54.427 --> 00:17:56.620 actively studied by a lot of groups,

NOTE Confidence: 0.944279066

00:17:56.620 --> 00:17:58.846 why do some patients respond

NOTE Confidence: 0.944279066

00:17:58.846 --> 00:18:00.934 and others not respond and what

NOTE Confidence: 0.944279066

00:18:00.934 --> 00:18:02.519 are the mechanisms of resistance

NOTE Confidence: 0.944279066

00:18:02.519 --> 00:18:04.941 and what are the prognostic kind of

NOTE Confidence: 0.944279066

00:18:04.941 --> 00:18:07.053 factors that help us understand that.

NOTE Confidence: 0.944279066

00:18:07.060 --> 00:18:08.698 One of the major prognostic factors

NOTE Confidence: 0.944279066

00:18:08.698 --> 00:18:10.721 that we've seen is the total amount

NOTE Confidence: 0.944279066

00:18:10.721 --> 00:18:12.176 of disease that somebody has.

NOTE Confidence: 0.944279066

00:18:12.180 --> 00:18:13.496 So we quantify this

NOTE Confidence: 0.944279066

00:18:13.496 --> 00:18:15.470 using a term called

NOTE Confidence: 0.944279066

00:18:15.547 --> 00:18:17.899 metabolic tumor burden, or

NOTE Confidence: 0.944279066

00:18:17.899 --> 00:18:20.257 even just the size of the tumors.

NOTE Confidence: 0.944279066

00:18:20.260 --> 00:18:22.740 And we use the term metabolic tumor burden.

NOTE Confidence: 0.944279066

00:18:22.740 --> 00:18:24.498 If somebody gets a PET scan,

NOTE Confidence: 0.944279066

00:18:24.500 --> 00:18:26.376 these are scans that can

NOTE Confidence: 0.944279066

00:18:26.376 --> 00:18:27.902 trace the amount of metabolic

NOTE Confidence: 0.944279066

00:18:27.902 --> 00:18:29.218 activity in the cancer.

NOTE Confidence: 0.944279066

00:18:29.220 --> 00:18:30.957 Add that all up and we can

NOTE Confidence: 0.944279066

00:18:30.957 --> 00:18:32.599 get a volume of how much disease

NOTE Confidence: 0.944279066

00:18:32.599 --> 00:18:33.740 and how active it is.

NOTE Confidence: 0.944279066

00:18:33.740 --> 00:18:35.973 And we have seen repeatedly and multiple

NOTE Confidence: 0.944279066

00:18:35.973 --> 00:18:37.626 investigators have seen this, that

NOTE Confidence: 0.944279066

00:18:37.626 --> 00:18:39.580 when you have a high burden of disease,

NOTE Confidence: 0.944279066

00:18:39.580 --> 00:18:42.436 those patients don't do as well with

NOTE Confidence: 0.944279066

00:18:42.436 --> 00:18:44.616 CAR T. As we learn more about this,

NOTE Confidence: 0.944279066

00:18:44.620 --> 00:18:45.820 there's different mechanisms,

NOTE Confidence: 0.944279066

00:18:45.820 --> 00:18:48.700 but what we think is that basically

NOTE Confidence: 0.944279066

00:18:48.700 --> 00:18:50.877 there's many reasons why CAR T cells

NOTE Confidence: 0.944279066

00:18:50.877 --> 00:18:53.579 can fail and I will list a few.

NOTE Confidence: 0.944279066

00:18:53.580 --> 00:18:53.895 One,

NOTE Confidence: 0.944279066

00:18:53.895 --> 00:18:56.100 we have seen that sometimes the target

NOTE Confidence: 0.944279066

00:18:56.100 --> 00:18:58.652 they go after, the CD19 can

NOTE Confidence: 0.944279066

00:18:58.652 --> 00:19:00.820 become more elusive or down regulated

NOTE Confidence: 0.944279066

00:19:00.820 --> 00:19:03.142 and then that can be a way for cells

NOTE Confidence: 0.944279066

00:19:03.142 --> 00:19:05.256 to kind of evade this therapy.

NOTE Confidence: 0.944279066

00:19:05.260 --> 00:19:07.564 Fortunately for us the B cell lymphomas

NOTE Confidence: 0.944279066

00:19:07.564 --> 00:19:09.778 tend to be fairly dependent on that.

NOTE Confidence: 0.944279066

00:19:09.780 --> 00:19:11.124 So we don't think that's a

NOTE Confidence: 0.944279066

00:19:11.124 --> 00:19:12.020 major source of resistance,

NOTE Confidence: 0.944279066

00:19:12.020 --> 00:19:13.560 but it's theoretically

NOTE Confidence: 0.944279066

00:19:13.560 --> 00:19:15.670 there and it happens in leukemia.

NOTE Confidence: 0.944279066

00:19:15.670 --> 00:19:17.550 The other things that can happen,

00:19:18.062 --> 00:19:19.598 the biggest issue, is just a

NOTE Confidence: 0.944279066

00:19:19.598 --> 00:19:20.950 worn out immune system.

NOTE Confidence: 0.944279066

00:19:20.950 --> 00:19:22.483 And what we have learned is

NOTE Confidence: 0.944279066

00:19:22.483 --> 00:19:23.549 that if somebody's T cells,

NOTE Confidence: 0.944279066

00:19:23.550 --> 00:19:24.677 you can take them out of their

NOTE Confidence: 0.944279066

00:19:24.677 --> 00:19:25.390 body and

NOTE Confidence: 0.944279066

00:19:25.390 --> 00:19:26.610 genetically engineer them to

NOTE Confidence: 0.944279066

00:19:26.610 --> 00:19:27.830 put them back in.

NOTE Confidence: 0.944279066

00:19:27.830 --> 00:19:29.573 But if you look at many

NOTE Confidence: 0.944279066

00:19:29.573 --> 00:19:31.509 of these T cells in patients,

NOTE Confidence: 0.944279066

00:19:31.510 --> 00:19:33.550 especially patients who've gone through

00:19:34.402 --> 00:19:36.356 multiple rounds of chemotherapy and

NOTE Confidence: 0.944279066

00:19:36.356 --> 00:19:38.078 what we've seen is that the more

NOTE Confidence: 0.944279066

00:19:38.078 --> 00:19:39.294 chemotherapies that people have been

NOTE Confidence: 0.944279066

00:19:39.294 --> 00:19:40.862 through before they get the CAR T,

NOTE Confidence: 0.944279066

00:19:40.870 --> 00:19:42.652 the more worn out and exhausted

NOTE Confidence: 0.944279066

00:19:42.652 --> 00:19:44.469 their immune system is and probably

NOTE Confidence: 0.944279066

00:19:44.469 --> 00:19:45.605 the worse they do.

NOTE Confidence: 0.944279066

00:19:45.610 --> 00:19:47.394 And so we think that one possibility is

NOTE Confidence: 0.944279066

00:19:47.394 --> 00:19:49.567 that if somebody's immune system,

NOTE Confidence: 0.944279066

00:19:49.570 --> 00:19:50.506 if their T cells,

NOTE Confidence: 0.944279066

00:19:50.506 --> 00:19:52.264 they can only fight so

NOTE Confidence: 0.944279066

00:19:52.264 --> 00:19:53.769 much before they become exhausted.

NOTE Confidence: 0.944279066

00:19:56.730 --> 00:19:58.711 And then lastly something that my lab

NOTE Confidence: 0.944279066

00:19:58.711 --> 00:20:00.679 has been interested in

NOTE Confidence: 0.944279066

00:20:00.679 --> 00:20:02.415 actually really clinically is

NOTE Confidence: 0.944279066

00:20:02.415 --> 00:20:04.845 what about the tumor microenvironment.

NOTE Confidence: 0.944279066

00:20:04.850 --> 00:20:06.434 So again if you have a

NOTE Confidence: 0.944279066

00:20:06.434 --> 00:20:07.490 very large angry tumor,

NOTE Confidence: 0.944279066

00:20:07.490 --> 00:20:09.122 in a PET scan you'll see

NOTE Confidence: 0.944279066

00:20:09.122 --> 00:20:10.307 what's called a necrotic lesion

NOTE Confidence: 0.944279066

00:20:10.307 --> 00:20:12.008 oftentimes and we think that those are

NOTE Confidence: 0.877517055384615

00:20:12.058 --> 00:20:13.318 areas where there's a lot of

NOTE Confidence: 0.877517055384615

00:20:13.320 --> 00:20:15.096 those tumors are taking up a

NOTE Confidence: 0.877517055384615

00:20:15.096 --> 00:20:17.486 ton of sugar and burning it so fast that

NOTE Confidence: 0.877517055384615

00:20:17.486 --> 00:20:19.240 it's actually sucking up all the oxygen.

NOTE Confidence: 0.877517055384615

00:20:19.240 --> 00:20:20.722 So there's no oxygen or there's

NOTE Confidence: 0.877517055384615

00:20:20.722 --> 00:20:22.519 a lot of hypoxia.

NOTE Confidence: 0.877517055384615

00:20:22.520 --> 00:20:24.600 There can be a lot

NOTE Confidence: 0.877517055384615

00:20:24.600 --> 00:20:26.599 of lactic acid in these tumors.

NOTE Confidence: 0.877517055384615

00:20:26.600 --> 00:20:28.841 And if you put a T cell and exposure

NOTE Confidence: 0.877517055384615

00:20:28.841 --> 00:20:31.080 to hypoxia or acidosis,

NOTE Confidence: 0.877517055384615

00:20:31.080 --> 00:20:32.360 they can't really function.

NOTE Confidence: 0.877517055384615

00:20:32.360 --> 00:20:34.592 And so part of the rationale for radiation

NOTE Confidence: 0.877517055384615

00:20:34.592 --> 00:20:36.830 where I've become interested is,

NOTE Confidence: 0.877517055384615

00:20:36.830 --> 00:20:38.615 how do we prevent the CAR T

NOTE Confidence: 0.877517055384615

00:20:38.615 --> 00:20:40.480 cells from not getting worn out,

NOTE Confidence: 0.877517055384615

00:20:40.480 --> 00:20:41.825 from fighting just an enormous

NOTE Confidence: 0.877517055384615

00:20:41.825 --> 00:20:43.455 amount of tumor where it's just

NOTE Confidence: 0.877517055384615

00:20:43.455 --> 00:20:44.595 too much tumor to fight?

NOTE Confidence: 0.877517055384615

00:20:44.600 --> 00:20:46.070 How can we use radiation to help

NOTE Confidence: 0.877517055384615

00:20:46.070 --> 00:20:47.951 kind of get rid of these areas of

NOTE Confidence: 0.877517055384615

00:20:47.951 --> 00:20:49.440 hypoxy and acidosis that are just

NOTE Confidence: 0.877517055384615

00:20:49.440 --> 00:20:50.959 really defeating the T cells?

NOTE Confidence: 0.935222021666667

00:20:52.280 --> 00:20:54.656 So tell us more about that. I mean

NOTE Confidence: 0.935222021666667

00:20:54.656 --> 00:20:58.022 is the idea that maybe these people

NOTE Confidence: 0.935222021666667

00:20:58.022 --> 00:21:00.899 should have CAR T therapy upfront before

NOTE Confidence: 0.935222021666667

00:21:00.899 --> 00:21:03.960 they ever get chemotherapy, tell us more

NOTE Confidence: 0.935222021666667

00:21:03.960 --> 00:21:06.519 about what your findings are showing us?

NOTE Confidence: 0.941930944166666

00:21:06.880 --> 00:21:08.203 Yeah, sure. So I think you kind

NOTE Confidence: 0.941930944166666

00:21:08.203 --> 00:21:09.439 of mentioned 2 viable options,

NOTE Confidence: 0.941930944166666

00:21:09.440 --> 00:21:10.760 both of which are being pursued.

NOTE Confidence: 0.941930944166666

00:21:10.760 --> 00:21:11.796 So I'll start with the first one,

NOTE Confidence: 0.941930944166666

00:21:11.800 --> 00:21:12.944 which is,

NOTE Confidence: 0.941930944166666

00:21:12.944 --> 00:21:14.880 what about getting CAR T earlier up,

NOTE Confidence: 0.941930944166666

00:21:14.880 --> 00:21:16.680 on the docket?

NOTE Confidence: 0.941930944166666

00:21:16.680 --> 00:21:19.160 And that's being actively explored.

NOTE Confidence: 0.941930944166666

00:21:19.160 --> 00:21:20.980 And so you know, CAR T cell

NOTE Confidence: 0.941930944166666

00:21:20.980 --> 00:21:22.980 therapy when it first got approved,

NOTE Confidence: 0.941930944166666

00:21:22.980 --> 00:21:23.805 it was only for patients

NOTE Confidence: 0.941930944166666

00:21:23.805 --> 00:21:25.400 who'd been through two prior

NOTE Confidence: 0.941930944166666

00:21:25.400 --> 00:21:26.255 chemotherapies that didn't work.

NOTE Confidence: 0.941930944166666

00:21:26.255 --> 00:21:27.739 So that had to be the minimum,

NOTE Confidence: 0.941930944166666

00:21:27.740 --> 00:21:29.820 but typically they'd seen many more,

NOTE Confidence: 0.941930944166666

00:21:29.820 --> 00:21:31.032 five or six even.

NOTE Confidence: 0.941930944166666

00:21:31.032 --> 00:21:33.756 And that's where we got a 40% cure rate.

NOTE Confidence: 0.941930944166666

00:21:33.756 --> 00:21:36.220 But then what we saw is that there's

NOTE Confidence: 0.941930944166666

00:21:36.288 --> 00:21:38.724 been recently trials where after a

NOTE Confidence: 0.941930944166666

00:21:38.724 --> 00:21:41.139 single line of chemotherapy has failed,

NOTE Confidence: 0.941930944166666

00:21:41.140 --> 00:21:42.180 all those patients used to

NOTE Confidence: 0.941930944166666

00:21:42.180 --> 00:21:43.220 go to something called an

NOTE Confidence: 0.965412215

00:21:43.220 --> 00:21:45.740 autologous stem cell transplant.

NOTE Confidence: 0.965412215

00:21:45.740 --> 00:21:47.516 And again, this is not my area

NOTE Confidence: 0.965412215

00:21:47.516 --> 00:21:49.636 of expertise, but

NOTE Confidence: 0.965412215

00:21:49.636 --> 00:21:51.428 actually the cost of an autologous stem

NOTE Confidence: 0.948639766666667

00:21:51.430 --> 00:21:53.068 cell transplant from what I understand

NOTE Confidence: 0.948639766666667

00:21:53.068 --> 00:21:54.549 is actually quite pricey as well.

NOTE Confidence: 0.948639766666667

00:21:54.550 --> 00:21:55.542 So it may be quite comparable

NOTE Confidence: 0.948639766666667

00:21:55.542 --> 00:21:58.108 to CAR T cell therapy.

NOTE Confidence: 0.948639766666667

00:21:58.110 --> 00:21:59.640 And so anyway, they

NOTE Confidence: 0.948639766666667

00:21:59.640 --> 00:22:01.110 basically would try and do that.

NOTE Confidence: 0.948639766666667

00:22:01.110 --> 00:22:02.825 But there's randomized trials where

NOTE Confidence: 0.948639766666667

00:22:02.825 --> 00:22:04.919 they did autologous stem cell transplant

NOTE Confidence: 0.948639766666667

00:22:04.919 --> 00:22:06.815 versus CAR T for patients with

NOTE Confidence: 0.948639766666667

00:22:06.815 --> 00:22:08.749 bad disease that either came back,

NOTE Confidence: 0.948639766666667

00:22:08.750 --> 00:22:11.306 within 12 months after

NOTE Confidence: 0.948639766666667

00:22:11.310 --> 00:22:13.008 their chemo or they just blew

NOTE Confidence: 0.948639766666667

00:22:13.008 --> 00:22:14.780 through first line chemo altogether.

NOTE Confidence: 0.948639766666667

00:22:14.780 --> 00:22:16.787 And they saw that CAR T therapy did a

NOTE Confidence: 0.948639766666667

00:22:16.787 --> 00:22:18.888 much better job of getting rid of the

NOTE Confidence: 0.948639766666667

00:22:18.888 --> 00:22:20.899 disease than the stem cell transplants.

NOTE Confidence: 0.948639766666667

00:22:20.900 --> 00:22:22.839 So that's one thing that's been happening

NOTE Confidence: 0.948639766666667

00:22:22.839 --> 00:22:24.775 is that we've moved from third line

NOTE Confidence: 0.948639766666667

00:22:24.775 --> 00:22:26.699 to second line and now there's even

NOTE Confidence: 0.948639766666667

00:22:26.699 --> 00:22:28.481 trials for patients with first line

NOTE Confidence: 0.948639766666667

00:22:28.481 --> 00:22:30.132 treatment for high risk factors,

NOTE Confidence: 0.948639766666667

00:22:30.132 --> 00:22:30.884 for example,

NOTE Confidence: 0.948639766666667

00:22:30.884 --> 00:22:33.140 just patients with tumors

NOTE Confidence: 0.948639766666667

00:22:33.140 --> 00:22:35.779 we don't expect to respond to chemo,

NOTE Confidence: 0.948639766666667

00:22:35.780 --> 00:22:37.250 bad genomic markers, these kind of

NOTE Confidence: 0.948639766666667

00:22:37.250 --> 00:22:38.778 double hit or triple hit lymphomas,

NOTE Confidence: 0.948639766666667

00:22:38.780 --> 00:22:39.926 things like that.

NOTE Confidence: 0.948639766666667

00:22:39.926 --> 00:22:41.836 There's folks who are exploring

NOTE Confidence: 0.948639766666667

00:22:41.836 --> 00:22:44.008 introducing CAR T therapy at that line.

NOTE Confidence: 0.948639766666667

00:22:44.010 --> 00:22:45.762 And so really what you're getting

NOTE Confidence: 0.948639766666667

00:22:45.762 --> 00:22:47.885 is moving it further up in the process.

NOTE Confidence: 0.948639766666667

00:22:47.890 --> 00:22:49.528 So that's kind of one option and

NOTE Confidence: 0.948639766666667

00:22:49.528 --> 00:22:50.769 people are certainly doing that.

NOTE Confidence: 0.948639766666667

00:22:50.770 --> 00:22:52.834 The other option is well what about radiation

NOTE Confidence: 0.948639766666667

00:22:52.834 --> 00:22:54.648 and trying to reduce the tumor burden.

NOTE Confidence: 0.948639766666667

00:22:54.650 --> 00:22:57.674 And so this is another possibility and

NOTE Confidence: 0.948639766666667

00:22:57.674 --> 00:23:00.202 I certainly believe for some

NOTE Confidence: 0.948639766666667

00:23:00.202 --> 00:23:02.352 patients that this may actually be

NOTE Confidence: 0.948639766666667

00:23:02.352 --> 00:23:04.067 helping them out and we're trying to

NOTE Confidence: 0.948639766666667

00:23:04.067 --> 00:23:06.285 kind of figure out ways to confirm that.

NOTE Confidence: 0.948639766666667

00:23:06.290 --> 00:23:07.610 Right now there's many clinical

NOTE Confidence: 0.948639766666667

00:23:07.610 --> 00:23:09.244 trials that are getting up and

NOTE Confidence: 0.948639766666667

00:23:09.244 --> 00:23:10.564 running where that's exactly what

NOTE Confidence: 0.948639766666667

00:23:10.564 --> 00:23:12.230 we're doing is we're taking patients

NOTE Confidence: 0.948639766666667

00:23:12.230 --> 00:23:13.630 with large or bulky tumors

NOTE Confidence: 0.948639766666667

00:23:13.630 --> 00:23:15.304 and we're going to use radiation

NOTE Confidence: 0.948639766666667

00:23:15.304 --> 00:23:16.705 to basically shrink those tumors

NOTE Confidence: 0.948639766666667

00:23:16.705 --> 00:23:18.322 down right before they get the CAR

NOTE Confidence: 0.948639766666667

00:23:18.322 --> 00:23:19.991 T cell therapy to reduce the tumor

NOTE Confidence: 0.948639766666667

00:23:19.991 --> 00:23:21.510 burden to get rid of those

NOTE Confidence: 0.948639766666667

00:23:22.230 --> 00:23:24.030 acid laden and hypoxic environments

NOTE Confidence: 0.948639766666667

00:23:24.030 --> 00:23:26.253 and really just try and give the CAR

NOTE Confidence: 0.948639766666667

00:23:26.253 --> 00:23:28.189 T cells a better chance to fight.

NOTE Confidence: 0.948639766666667

00:23:28.190 --> 00:23:29.558 And there's also some evidence kind

NOTE Confidence: 0.948639766666667

00:23:29.558 --> 00:23:31.333 of which is very early stages that

NOTE Confidence: 0.948639766666667

00:23:31.333 --> 00:23:32.693 suggests that radiation may actually

NOTE Confidence: 0.948639766666667

00:23:32.693 --> 00:23:34.299 kind of help stimulate the immune

NOTE Confidence: 0.948639766666667

00:23:34.299 --> 00:23:36.606 system and may actually help the CAR T

NOTE Confidence: 0.948639766666667

00:23:36.606 --> 00:23:38.546 cells recognize these cancers better.

NOTE Confidence: 0.948639766666667

00:23:38.550 --> 00:23:40.349 And so we're exploring all those options.

NOTE Confidence: 0.921514121428571

00:23:40.640 --> 00:23:42.584 The other thing that

NOTE Confidence: 0.921514121428571

00:23:42.584 --> 00:23:44.198 our audience might be thinking about,

NOTE Confidence: 0.921514121428571

00:23:44.200 --> 00:23:46.955 especially when we talk about

NOTE Confidence: 0.921514121428571

00:23:46.955 --> 00:23:49.159 hypoxia and hypoxic environments,

NOTE Confidence: 0.921514121428571

00:23:49.160 --> 00:23:52.240 is the role of hyperbaric oxygen chambers.

NOTE Confidence: 0.921514121428571

00:23:52.240 --> 00:23:54.472 I mean a lot of people have heard about

NOTE Confidence: 0.921514121428571

00:23:54.480 --> 00:23:57.655 these hyperbaric oxygen chambers and

NOTE Confidence: 0.921514121428571

00:23:57.655 --> 00:24:00.610 maybe asking themselves,

NOTE Confidence: 0.921514121428571

00:24:00.610 --> 00:24:03.922 is that a role for

NOTE Confidence: 0.921514121428571

00:24:03.922 --> 00:24:06.650 CAR T therapy to kind of fight where

NOTE Confidence: 0.921514121428571

00:24:06.650 --> 00:24:08.858 maybe we can get more oxygen

NOTE Confidence: 0.921514121428571

00:24:08.858 --> 00:24:09.962 into these environments.

NOTE Confidence: 0.921514121428571

00:24:09.970 --> 00:24:13.874 Or is it more the tumor micro environment

NOTE Confidence: 0.921514121428571

00:24:13.874 --> 00:24:16.680 itself that may or may not be influenced

NOTE Confidence: 0.921514121428571

00:24:16.680 --> 00:24:18.729 by these hyperbaric oxygen chambers.

NOTE Confidence: 0.921514121428571

00:24:18.730 --> 00:24:20.200 Can you kind of

NOTE Confidence: 0.921514121428571

00:24:20.200 --> 00:24:21.530 shed some light on that?

00:24:24.250 --> 00:24:26.250 So the truth is that no one's looked at that.

NOTE Confidence: 0.938576366666667

00:24:26.250 --> 00:24:28.490 It's an interesting idea. However,

NOTE Confidence: 0.938576366666667

00:24:28.490 --> 00:24:31.766 I suspect it would be a very bad idea.

NOTE Confidence: 0.938576366666667

00:24:31.770 --> 00:24:34.272 The issue is that right now

NOTE Confidence: 0.938576366666667

00:24:34.272 --> 00:24:36.060 hyperbaric oxygen, at least in the

NOTE Confidence: 0.938576366666667

00:24:36.060 --> 00:24:37.650 radiation world where we use it,

NOTE Confidence: 0.938576366666667

00:24:37.650 --> 00:24:39.180 is that if somebody's had radiation

NOTE Confidence: 0.938576366666667

00:24:39.180 --> 00:24:40.984 therapy and they had to have high

NOTE Confidence: 0.938576366666667

00:24:40.984 --> 00:24:42.209 doses of radiation with chemo,

NOTE Confidence: 0.938576366666667

00:24:42.210 --> 00:24:44.121 and they have wound healing issues or

NOTE Confidence: 0.938576366666667

00:24:44.121 --> 00:24:45.690 some other toxicities from radiation,

NOTE Confidence: 0.938576366666667

00:24:45.690 --> 00:24:47.526 this is getting very high doses

NOTE Confidence: 0.938576366666667

00:24:47.526 --> 00:24:49.236 of radiation that we don't have

NOTE Confidence: 0.938576366666667

00:24:49.236 --> 00:24:50.808 to use as much in lymphoma.

NOTE Confidence: 0.938576366666667

00:24:50.810 --> 00:24:52.556 But hyperbaric oxygen can be a

NOTE Confidence: 0.938576366666667

00:24:52.556 --> 00:24:54.649 way to help with wound healing.

NOTE Confidence: 0.938576366666667

00:24:54.650 --> 00:24:56.562 And the reason why I mention that is

NOTE Confidence: 0.938576366666667

00:24:56.562 --> 00:24:58.395 that one of the big contraindications

NOTE Confidence: 0.938576366666667

00:24:58.395 --> 00:25:00.339 or sources of extreme caution is

NOTE Confidence: 0.938576366666667

00:25:00.400 --> 00:25:02.206 that if anybody has active cancer,

NOTE Confidence: 0.938576366666667

00:25:02.210 --> 00:25:04.658 they're very wary to do hyperbaric

NOTE Confidence: 0.938576366666667

00:25:04.658 --> 00:25:05.882 oxygen because anecdotally,

NOTE Confidence: 0.938576366666667

00:25:05.890 --> 00:25:07.350 they've seen cases where people

NOTE Confidence: 0.938576366666667

00:25:07.350 --> 00:25:09.096 have done hyperbaric oxygen and the

NOTE Confidence: 0.938576366666667

00:25:09.096 --> 00:25:10.488 cancer has sprung back to life.

NOTE Confidence: 0.938576366666667

00:25:10.490 --> 00:25:11.730 And so for example, I

NOTE Confidence: 0.938576366666667

00:25:11.730 --> 00:25:13.046 had a patient with CAR T therapy

NOTE Confidence: 0.938576366666667

00:25:13.046 --> 00:25:14.090 who I did radiation.

NOTE Confidence: 0.938576366666667

00:25:14.090 --> 00:25:16.310 We got rid of this giant, very angry tumor.

NOTE Confidence: 0.938576366666667

00:25:16.310 --> 00:25:17.450 It was ulcerating.

NOTE Confidence: 0.938576366666667

00:25:17.450 --> 00:25:19.039 And the tumor destroyed

NOTE Confidence: 0.938576366666667

00:25:19.039 --> 00:25:20.860 so much of the tissue around the

NOTE Confidence: 0.938576366666667

00:25:20.860 --> 00:25:22.486 leg that you still have ulcers,

NOTE Confidence: 0.938576366666667

00:25:22.490 --> 00:25:24.488 even though the cancer has been gone for a year.

NOTE Confidence: 0.938576366666667

00:25:24.490 --> 00:25:26.008 And they still are being cautious

NOTE Confidence: 0.938576366666667

00:25:26.008 --> 00:25:27.020 about doing hyperbaric oxygen

NOTE Confidence: 0.938576366666667

00:25:27.070 --> 00:25:28.295 because they're worried that if

NOTE Confidence: 0.938576366666667

00:25:28.295 --> 00:25:29.770 there's any cancer cells left over,

NOTE Confidence: 0.938576366666667

00:25:29.770 --> 00:25:31.618 they will kind of bring those

NOTE Confidence: 0.938576366666667

00:25:31.618 --> 00:25:32.850 back with the vengeance.

NOTE Confidence: 0.938576366666667

00:25:32.850 --> 00:25:33.984 The other point I would mention

NOTE Confidence: 0.938576366666667

00:25:33.984 --> 00:25:35.758 is that it's kind of more of a

NOTE Confidence: 0.938576366666667

00:25:35.758 --> 00:25:36.487 technical modeling perspective,

NOTE Confidence: 0.938576366666667

00:25:36.490 --> 00:25:37.290 but I think it's valid.

NOTE Confidence: 0.938576366666667

00:25:37.290 --> 00:25:37.846 Is that,

NOTE Confidence: 0.938576366666667

00:25:37.846 --> 00:25:39.514 I mean I think it's interesting

NOTE Confidence: 0.938576366666667

00:25:39.514 --> 00:25:41.640 is that if you look at a tumor and

NOTE Confidence: 0.938576366666667

00:25:41.640 --> 00:25:43.250 you see these hypoxic and

NOTE Confidence: 0.938576366666667

00:25:43.250 --> 00:25:46.530 low glucose, highly acidic environments.

NOTE Confidence: 0.938576366666667

00:25:46.530 --> 00:25:48.890 And you think, how am I going to fix that?

NOTE Confidence: 0.938576366666667

00:25:48.890 --> 00:25:51.809 Should you increase blood flow,

NOTE Confidence: 0.938576366666667

00:25:51.810 --> 00:25:53.214 should you

NOTE Confidence: 0.938576366666667

00:25:53.214 --> 00:25:54.969 increase oxygen as you're mentioning?

NOTE Confidence: 0.938576366666667

00:25:54.970 --> 00:25:55.970 And as it turns out,

NOTE Confidence: 0.938576366666667

00:25:55.970 --> 00:25:58.346 the most effective way to normalize

NOTE Confidence: 0.938576366666667

00:25:58.346 --> 00:26:00.352 the tumor microenvironment from a

NOTE Confidence: 0.938576366666667

00:26:00.352 --> 00:26:01.772 metabolic perspective is actually

NOTE Confidence: 0.938576366666667

00:26:01.772 --> 00:26:04.201 to turn the cancer cells off or

NOTE Confidence: 0.938576366666667

00:26:04.201 --> 00:26:05.089 kill cancer cells.

NOTE Confidence: 0.938576366666667

00:26:05.090 --> 00:26:06.062 Because the problem is,

NOTE Confidence: 0.938576366666667

00:26:06.062 --> 00:26:08.489 that you have this kind of,

00:26:08.868 --> 00:26:10.191 large number of tumor cells that are

NOTE Confidence: 0.938576366666667

00:26:10.191 --> 00:26:11.290 sitting there going at full tilt,

NOTE Confidence: 0.938576366666667

00:26:11.290 --> 00:26:13.756 you have this necrotic center oftentimes.

NOTE Confidence: 0.938576366666667

00:26:13.760 --> 00:26:14.840 And if you add more oxygen,

NOTE Confidence: 0.938576366666667

00:26:14.840 --> 00:26:16.360 all you're gonna do is

NOTE Confidence: 0.938576366666667

00:26:16.360 --> 00:26:18.114 feed the ones on the outside just as much.

NOTE Confidence: 0.938576366666667

00:26:18.120 --> 00:26:19.520 But then there's gonna be more to

NOTE Confidence: 0.938576366666667

00:26:19.520 --> 00:26:20.854 spill over towards the middle and

NOTE Confidence: 0.938576366666667

00:26:20.854 --> 00:26:22.240 there's plenty of cancer cells waiting,

NOTE Confidence: 0.938576366666667

00:26:22.240 --> 00:26:24.640 ready to go to soak up those resources.

NOTE Confidence: 0.938576366666667

00:26:24.640 --> 00:26:26.957 And so really from a modeling perspective,

NOTE Confidence: 0.938576366666667

00:26:26.960 --> 00:26:29.080 and this is one of my mentors from

NOTE Confidence: 0.938576366666667

00:26:29.080 --> 00:26:31.236 back at Duke, what they saw,

NOTE Confidence: 0.938576366666667

00:26:31.240 --> 00:26:32.686 was that really the most effective

NOTE Confidence: 0.938576366666667

00:26:32.686 --> 00:26:34.249 way to normalize the environment was

NOTE Confidence: 0.938576366666667

00:26:34.249 --> 00:26:36.020 really to slow down the metabolism

NOTE Confidence: 0.938576366666667

00:26:36.020 --> 00:26:37.545 or kill the tumor cells.

NOTE Confidence: 0.938576366666667

00:26:37.550 --> 00:26:38.782 And that trying just to kind of

NOTE Confidence: 0.938576366666667

00:26:38.782 --> 00:26:39.870 feed it more to normalize,

NOTE Confidence: 0.938576366666667

00:26:39.870 --> 00:26:41.244 it really doesn't work out that way.

NOTE Confidence: 0.8611976175

00:26:44.030 --> 00:26:46.484 So certainly people

NOTE Confidence: 0.8611976175

00:26:46.484 --> 00:26:49.163 are looking at how we can do

NOTE Confidence: 0.8611976175

00:26:49.163 --> 00:26:51.428 CAR T cell therapy better.

NOTE Confidence: 0.8611976175

00:26:51.430 --> 00:26:53.405 And so what's next for

NOTE Confidence: 0.8611976175

00:26:53.405 --> 00:26:54.985 your lab going forward?

NOTE Confidence: 0.93220288

00:26:57.070 --> 00:26:58.390 Yeah, so a few things.

NOTE Confidence: 0.93220288

00:26:58.390 --> 00:26:59.845 One, I'm excited about the

NOTE Confidence: 0.93220288

00:26:59.845 --> 00:27:01.510 clinical trials that are going on,

NOTE Confidence: 0.93220288

00:27:01.510 --> 00:27:04.174 trying to figure out what's the best way to

NOTE Confidence: 0.93220288

00:27:04.174 --> 00:27:07.417 combine radiation to make CAR T work better.

NOTE Confidence: 0.93220288

00:27:07.420 --> 00:27:08.820 And the thing that I'm excited about

NOTE Confidence: 0.93220288

00:27:08.820 --> 00:27:10.418 this is because it's just very pragmatic.

NOTE Confidence: 0.93220288

00:27:10.420 --> 00:27:11.540 We know radiation

NOTE Confidence: 0.93220288

00:27:11.540 --> 00:27:12.660 works to shrink down tumors.

NOTE Confidence: 0.93220288

00:27:12.660 --> 00:27:15.978 These tumors tend to be responsive.

NOTE Confidence: 0.93220288

00:27:15.980 --> 00:27:17.420 We know that can debulk tumors.

NOTE Confidence: 0.93220288

00:27:17.420 --> 00:27:19.010 There's been studies showing that

NOTE Confidence: 0.93220288

00:27:19.010 --> 00:27:20.979 if you do radiation before CAR T,

NOTE Confidence: 0.93220288

00:27:20.980 --> 00:27:22.688 I mentioned that the total

NOTE Confidence: 0.93220288

00:27:22.688 --> 00:27:24.579 amount of disease burden predicts outcome,

NOTE Confidence: 0.93220288

00:27:24.580 --> 00:27:26.060 well if you look at patients

NOTE Confidence: 0.93220288

00:27:26.060 --> 00:27:28.724 who get radiation, the

NOTE Confidence: 0.93220288

00:27:28.724 --> 00:27:30.244 tumor burden after radiation does

NOTE Confidence: 0.93220288

00:27:30.244 --> 00:27:32.252 the better job of predicting it

NOTE Confidence: 0.93220288

00:27:32.252 --> 00:27:34.077 than the tumor burden beforehand.

NOTE Confidence: 0.93220288

00:27:34.080 --> 00:27:35.898 So in other words we may be able to

NOTE Confidence: 0.93220288

00:27:35.898 --> 00:27:37.913 kind of convert high burden of disease

NOTE Confidence: 0.93220288

00:27:37.913 --> 00:27:39.735 patients to lower burden and give

NOTE Confidence: 0.93220288

00:27:39.735 --> 00:27:41.517 them more favorable outcomes.

NOTE Confidence: 0.93220288

00:27:41.520 --> 00:27:43.823 And I'm excited to see where

NOTE Confidence: 0.93220288

00:27:43.823 --> 00:27:45.354 these different clinical trials kind

NOTE Confidence: 0.93220288

00:27:45.354 --> 00:27:46.996 of end and these clinical trials

NOTE Confidence: 0.93220288

00:27:46.996 --> 00:27:48.441 using radiation with smaller doses

NOTE Confidence: 0.93220288

00:27:48.441 --> 00:27:50.124 to give novel ways to

NOTE Confidence: 0.93220288

00:27:50.124 --> 00:27:51.719 try to wake up the immune system.

NOTE Confidence: 0.93220288

00:27:51.720 --> 00:27:53.407 And so I'm very excited to see where these land.

00:27:55.370 --> 00:27:57.683 And then two is more on the molecular side.

NOTE Confidence: 0.93220288

00:27:57.690 --> 00:27:58.770 I haven't mentioned this too much,

NOTE Confidence: 0.93220288

00:27:58.770 --> 00:28:00.530 but I actually one of the things

NOTE Confidence: 0.93220288

00:28:00.530 --> 00:28:02.450 my lab studies is splicing and we think

NOTE Confidence: 0.93220288

00:28:02.450 --> 00:28:03.890 that alternative splicing may actually

NOTE Confidence: 0.93220288

00:28:03.890 --> 00:28:06.004 be one of the mechanisms by which

NOTE Confidence: 0.93220288

00:28:06.010 --> 00:28:09.210 CAR T cell therapy actually may not work.

NOTE Confidence: 0.93220288

00:28:09.210 --> 00:28:10.908 We actually think that there

NOTE Confidence: 0.93220288

00:28:10.908 --> 00:28:12.693 may be alternative splicing that is

NOTE Confidence: 0.93220288

00:28:12.693 --> 00:28:14.208 driving resistance in these lymphomas

NOTE Confidence: 0.93220288

00:28:14.210 --> 00:28:16.555 because splicing is something that

NOTE Confidence: 0.93220288

00:28:16.555 --> 00:28:18.900 occurs aberrantly

NOTE Confidence: 0.93220288

00:28:18.974 --> 00:28:20.230 in many hematologic malignancies.

NOTE Confidence: 0.93220288

00:28:20.230 --> 00:28:24.020 And my lab has been

NOTE Confidence: 0.93220288

00:28:24.020 --> 00:28:25.470 investigating this and so hopefully

NOTE Confidence: 0.93220288

00:28:25.470 --> 00:28:27.844 in the next, year or two,

NOTE Confidence: 0.93220288

00:28:27.844 --> 00:28:29.620 we'll kind of hot off the press

NOTE Confidence: 0.93220288

00:28:29.620 --> 00:28:30.596 we'll get that out.

NOTE Confidence: 0.93220288

00:28:30.596 --> 00:28:32.060 And that's something we're actively pursuing.

NOTE Confidence: 0.9454326275

00:28:32.700 --> 00:28:35.280 Dr. Timothy Robinson is an assistant

NOTE Confidence: 0.9454326275

00:28:35.280 --> 00:28:37.000 professor of therapeutic radiology

NOTE Confidence: 0.9454326275

00:28:37.062 --> 00:28:38.940 at the Yale School of Medicine.

NOTE Confidence: 0.9454326275

00:28:38.940 --> 00:28:40.740 If you have questions, the addresses,

NOTE Confidence: 0.9454326275

00:28:40.740 --> 00:28:42.995 cancer Answers at yale.edu and

NOTE Confidence: 0.9454326275

00:28:42.995 --> 00:28:45.729 past editions of the program are

NOTE Confidence: 0.9454326275

00:28:45.729 --> 00:28:47.734 available in audio and written

NOTE Confidence: 0.9454326275

00:28:47.734 --> 00:28:48.838 form at yalecancercenter.org.

NOTE Confidence: 0.9454326275

00:28:48.838 --> 00:28:51.222 We hope you'll join us next week to

NOTE Confidence: 0.9454326275

00:28:51.222 --> 00:28:53.046 learn more about the fight against

NOTE Confidence: 0.9454326275

00:28:53.046 --> 00:28:54.850 cancer here on Connecticut Public Radio.

NOTE Confidence: 0.9454326275

00:28:54.850 --> 00:28:57.496 Funding for Yale Cancer Answers is

NOTE Confidence: 0.9454326275

00:28:57.496 --> 00:29:00.000 provided by Smilow Cancer Hospital.