WEBVTT

NOTE duration:"01:05:56.2450000"

NOTE language:en-us

NOTE Confidence: 0.759806

00:00:00.000 --> 00:00:03.040 Mike is a social professor of medicine and

NOTE Confidence: 0.759806

00:00:03.040 --> 00:00:05.198 internal medicine and medical oncology

NOTE Confidence: 0.759806

00:00:05.198 --> 00:00:07.413 shares patients or cancer patients,

NOTE Confidence: 0.759806

00:00:07.420 --> 00:00:08.590 fraternity or cancers.

NOTE Confidence: 0.759806

00:00:08.590 --> 00:00:10.930 As part of the smiling prostate,

NOTE Confidence: 0.759806

00:00:10.930 --> 00:00:13.549 your logic cancer program.

NOTE Confidence: 0.759806

00:00:13.550 --> 00:00:15.780 Alright, joining Allen 2009 Doctor Hertz

NOTE Confidence: 0.759806

00:00:15.780 --> 00:00:17.925 was instructor of medicine at Harvard

NOTE Confidence: 0.759806

00:00:17.925 --> 00:00:20.145 and attending physician in medicine at

NOTE Confidence: 0.759806

00:00:20.145 --> 00:00:21.709 the Massachusetts General Hospital.

NOTE Confidence: 0.759806

00:00:21.710 --> 00:00:23.570 MIKES graduate of Harvard College.

NOTE Confidence: 0.759806

00:00:23.570 --> 00:00:26.090 He received his doctorate degree in cell

NOTE Confidence: 0.759806

00:00:26.090 --> 00:00:27.723 Biology from Rockville University's

NOTE Confidence: 0.759806

00:00:27.723 --> 00:00:30.198 medical degree from Cornell University.

NOTE Confidence: 0.759806

00:00:30.200 --> 00:00:32.336 He completed a fellowship in Archology,

NOTE Confidence: 0.759806

00:00:32.340 --> 00:00:34.115 Dana Farber and postdoctoral fellowship

NOTE Confidence: 0.759806

00:00:34.115 --> 00:00:36.310 in Biology, the Masters in Massachusetts,

NOTE Confidence: 0.759806

00:00:36.310 --> 00:00:38.160 Channel MIT Institution might still

NOTE Confidence: 0.759806

00:00:38.160 --> 00:00:40.554 be talking about the silk yellow cell

NOTE Confidence: 0.759806

00:00:40.554 --> 00:00:42.300 therapy program for solid tumors.

NOTE Confidence: 0.759806

00:00:42.300 --> 00:00:43.724 Mike take it away.

NOTE Confidence: 0.759806

00:00:43.724 --> 00:00:44.446 Thanks, Dan.

NOTE Confidence: 0.759806

00:00:44.446 --> 00:00:46.276 Yeah, thanks everyone for inviting

NOTE Confidence: 0.759806

00:00:46.276 --> 00:00:48.000 us from that from the

NOTE Confidence: 0.7214773

00:00:48.000 --> 00:00:49.536 therapy dog to talk.

NOTE Confidence: 0.7214773

00:00:49.536 --> 00:00:51.840 I'm going to talk obviously about

NOTE Confidence: 0.7214773

00:00:51.916 --> 00:00:54.254 the solid tumor side and then the

NOTE Confidence: 0.7214773

00:00:54.254 --> 00:00:57.004 other half is going to be here as

NOTE Confidence: 0.7214773

00:00:57.004 --> 00:00:59.050 this would be talking about liquid.

NOTE Confidence: 0.7214773

00:00:59.050 --> 00:01:00.900 So were the newest art.

NOTE Confidence: 0.7214773

00:01:00.900 --> 00:01:02.355 And we really started right

NOTE Confidence: 0.7214773

00:01:02.355 --> 00:01:04.124 before covid so we don't have

NOTE Confidence: 0.7214773

00:01:04.124 --> 00:01:05.660 a whole lot of trials open,

NOTE Confidence: 0.7214773

00:01:05.660 --> 00:01:07.522 so I think that this talk is

NOTE Confidence: 0.7214773

00:01:07.522 --> 00:01:09.858 going to be sort of short on data,

NOTE Confidence: 0.7214773

00:01:09.860 --> 00:01:12.919 but I hope it's going to be

NOTE Confidence: 0.7214773

00:01:12.919 --> 00:01:14.230 long on potential.

NOTE Confidence: 0.7214773

00:01:14.230 --> 00:01:17.002 OK, let me see if I can move my

NOTE Confidence: 0.7214773

00:01:17.002 --> 00:01:19.977 thing forward here in my disclosures.

NOTE Confidence: 0.7214773

00:01:19.980 --> 00:01:22.324 So the main therapies I'm going to talk

NOTE Confidence: 0.7214773

00:01:22.324 --> 00:01:25.003 about today are car T cells and till

NOTE Confidence: 0.7214773

00:01:25.003 --> 00:01:26.359 or tumor infiltrating lymphocytes.

NOTE Confidence: 0.7214773

00:01:26.360 --> 00:01:28.238 And I think that everybody is

NOTE Confidence: 0.7214773

00:01:28.238 --> 00:01:29.870 somewhat familiar with these terms.

NOTE Confidence: 0.7214773

00:01:29.870 --> 00:01:32.206 I know that a lot of people know

NOTE Confidence: 0.7214773

00:01:32.206 --> 00:01:34.340 a lot about these so far,

NOTE Confidence: 0.7214773

00:01:34.340 --> 00:01:35.930 but but they're really quite

NOTE Confidence: 0.7214773

00:01:35.930 --> 00:01:36.566 different therapies,

NOTE Confidence: 0.7214773

00:01:36.570 --> 00:01:38.818 and I do want to talk a little

NOTE Confidence: 0.7214773

00:01:38.818 --> 00:01:40.720 bit about the basic biology.

NOTE Confidence: 0.7214773

00:01:40.720 --> 00:01:42.628 So for those who are immunologists,

NOTE Confidence: 0.7214773

00:01:42.630 --> 00:01:43.587 bear with us.

NOTE Confidence: 0.7214773

00:01:43.587 --> 00:01:45.182 Maybe read the newspaper for

NOTE Confidence: 0.7214773

00:01:45.182 --> 00:01:47.443 a minute or two while I give

NOTE Confidence: 0.7214773

00:01:47.443 --> 00:01:49.003 you my very simple oncologist.

NOTE Confidence: 0.7214773

00:01:49.010 --> 00:01:50.171 View of immunology.

NOTE Confidence: 0.7214773

00:01:50.171 --> 00:01:52.880 So adaptive immunity is where T cells

NOTE Confidence: 0.7214773

00:01:52.950 --> 00:01:55.055 primarily recognize things that are

NOTE Confidence: 0.7214773

00:01:55.055 --> 00:01:57.570 foreign and used in attack them.

NOTE Confidence: 0.7214773

00:01:57.570 --> 00:01:57.909 Now,

NOTE Confidence: 0.7214773

00:01:57.909 --> 00:02:00.282 one of the reasons we don't attack

NOTE Confidence: 0.7214773

00:02:00.282 --> 00:02:02.224 ourselves is that we're always

NOTE Confidence: 0.7214773

00:02:02.224 --> 00:02:04.612 taking little chunks of our proteins,

NOTE Confidence: 0.7214773

00:02:04.620 --> 00:02:06.205 expressing them on the surface

NOTE Confidence: 0.7214773

00:02:06.205 --> 00:02:07.790 in something called the major

NOTE Confidence: 0.7214773

00:02:07.851 --> 00:02:09.438 history compatibility complex,

NOTE Confidence: 0.7214773

00:02:09.440 --> 00:02:11.300 and the T cell receptors.

NOTE Confidence: 0.7214773

00:02:11.300 --> 00:02:11.672 Basically,

NOTE Confidence: 0.7214773

00:02:11.672 --> 00:02:13.904 when when were you know your

NOTE Confidence: 0.7214773

00:02:13.904 --> 00:02:15.380 own a little bit?

NOTE Confidence: 0.7214773

00:02:15.380 --> 00:02:17.684 After that all the T cell

NOTE Confidence: 0.7214773

00:02:17.684 --> 00:02:20.268 receptors that we have the T cells.

NOTE Confidence: 0.7214773

00:02:20.270 --> 00:02:22.830 That that recognized groups.

NOTE Confidence: 0.7214773

00:02:22.830 --> 00:02:25.770 That recognize.

NOTE Confidence: 0.7214773

00:02:25.770 --> 00:02:26.974 The energy is well,

NOTE Confidence: 0.7214773

00:02:26.974 --> 00:02:27.576 get deleted,

NOTE Confidence: 0.7214773

00:02:27.580 --> 00:02:29.996 or at least they get turned off OK,

NOTE Confidence: 0.7214773

00:02:30.000 --> 00:02:31.510 so generally we don't respond

NOTE Confidence: 0.7214773

00:02:31.510 --> 00:02:32.718 to our own antigens,

NOTE Confidence: 0.7214773

00:02:32.720 --> 00:02:34.532 But if you get a foreign

NOTE Confidence: 0.7214773

00:02:34.532 --> 00:02:35.740 antigen like a bacteria,

NOTE Confidence: 0.7214773

00:02:35.740 --> 00:02:37.195 what happens is let's say

NOTE Confidence: 0.7214773

00:02:37.195 --> 00:02:39.060 if they go into a cell,

NOTE Confidence: 0.7214773

00:02:39.060 --> 00:02:40.866 the cell chops up the proteins.

NOTE Confidence: 0.7214773

00:02:40.870 --> 00:02:42.564 The proteins get put on MHC and

NOTE Confidence: 0.7214773

00:02:42.564 --> 00:02:44.253 the T cell receptor is going

NOTE Confidence: 0.7214773

00:02:44.253 --> 00:02:45.753 to recognize there's going to

NOTE Confidence: 0.7214773

00:02:45.753 --> 00:02:47.509 be a strong interaction,

NOTE Confidence: 0.7214773

00:02:47.510 --> 00:02:49.020 but that isn't enough to

NOTE Confidence: 0.7214773

00:02:49.020 --> 00:02:49.926 actually cause killing.

NOTE Confidence: 0.7214773

00:02:49.930 --> 00:02:51.742 It's only when you get something

NOTE Confidence: 0.7214773

00:02:51.742 --> 00:02:52.648 called costimulation OK,

NOTE Confidence: 0.7214773

00:02:52.650 --> 00:02:54.160 and that's via another pathway.

NOTE Confidence: 0.7214773

00:02:54.160 --> 00:02:55.444 Another set of receptors.

NOTE Confidence: 0.7214773

00:02:55.444 --> 00:02:57.989 And then you actually get killed all right.

NOTE Confidence: 0.7214773

00:02:57.990 --> 00:03:00.069 So how can we use that information

NOTE Confidence: 0.7214773

00:03:00.069 --> 00:03:01.390 to kill cancer cells?

NOTE Confidence: 0.7214773

00:03:01.390 --> 00:03:03.658 So let me say a little bit more and

NOTE Confidence: 0.7214773

00:03:03.658 --> 00:03:05.934 go a little bit more in depth into

NOTE Confidence: 0.7214773

00:03:05.934 --> 00:03:08.498 the T cell receptor signaling first.

NOTE Confidence: 0.7214773

00:03:08.500 --> 00:03:10.354 So this is a schematic of

NOTE Confidence: 0.7214773

00:03:10.354 --> 00:03:11.590 the T cell receptor,

NOTE Confidence: 0.7214773

00:03:11.590 --> 00:03:14.094 the Alpha beta chains are the ones that

NOTE Confidence: 0.7214773

00:03:14.094 --> 00:03:15.908 actually recognize the antigens and MHC,

NOTE Confidence: 0.7214773

00:03:15.910 --> 00:03:17.460 and there are signaling molecules,

NOTE Confidence: 0.7214773

00:03:17.460 --> 00:03:19.616 the Zeta chain and the associated CD3.

NOTE Confidence: 0.7214773

00:03:19.620 --> 00:03:21.790 So T cell receptors only recognize proteins.

NOTE Confidence: 0.7214773

00:03:21.790 --> 00:03:24.191 They only work if the antigen is

NOTE Confidence: 0.7214773

00:03:24.191 --> 00:03:25.719 expressed is presented by MHC.

NOTE Confidence: 0.7214773

00:03:25.720 --> 00:03:26.900 And they require Co stimulation.

NOTE Confidence: 0.7214773

00:03:26.900 --> 00:03:28.300 And as I said,

NOTE Confidence: 0.7214773

00:03:28.300 --> 00:03:30.970 the signaling are through these two things.

NOTE Confidence: 0.7214773

00:03:30.970 --> 00:03:32.278 Antibodies another way that

NOTE Confidence: 0.7214773

00:03:32.278 --> 00:03:33.913 we recognize things that are

NOTE Confidence: 0.7214773

00:03:33.913 --> 00:03:35.489 formed were quite differently.

NOTE Confidence: 0.7214773

00:03:35.490 --> 00:03:37.578 They can recognize any type of

NOTE Confidence: 0.7214773

00:03:37.578 --> 00:03:38.970 management doesn't have protein.

NOTE Confidence: 0.8157049

00:03:38.970 --> 00:03:40.362 They don't use MHC,

NOTE Confidence: 0.8157049

00:03:40.362 --> 00:03:42.552 and antibodies are much, much stronger,

NOTE Confidence: 0.8157049

00:03:42.552 --> 00:03:44.532 their interactions with their antigens

NOTE Confidence: 0.8157049

00:03:44.532 --> 00:03:47.338 and T cell receptors are with their

NOTE Confidence: 0.8157049

00:03:47.338 --> 00:03:49.672 antigen that makes the interactions up

NOTE Confidence: 0.8157049

00:03:49.743 --> 00:03:52.279 to 1000 and 10,000 fold stronger in fact.

NOTE Confidence: 0.8157049

00:03:52.280 --> 00:03:53.900 So someone had the bright idea

NOTE Confidence: 0.8157049

00:03:53.900 --> 00:03:56.032 of taking the back end of a T

NOTE Confidence: 0.8157049

00:03:56.032 --> 00:03:57.272 cell receptor and connecting it

NOTE Confidence: 0.8157049

00:03:57.272 --> 00:03:59.175 to the front end of an antibody.

NOTE Confidence: 0.8157049

00:03:59.180 --> 00:04:01.343 And we call those guys get chimeric

NOTE Confidence: 0.8157049

00:04:01.343 --> 00:04:03.099 antigen receptors and so this is

NOTE Confidence: 0.8157049

00:04:03.099 --> 00:04:04.629 the first generation car and this

NOTE Confidence: 0.8157049

00:04:04.629 --> 00:04:06.140 is actually in the 1990s.

NOTE Confidence: 0.8157049

00:04:06.140 --> 00:04:08.750 It was awhile ago so this is the antibody.

NOTE Confidence: 0.8157049

00:04:08.750 --> 00:04:10.814 OK on the outside of the cell and

NOTE Confidence: 0.8157049

00:04:10.814 --> 00:04:13.098 this is part of the solar spectrum.

NOTE Confidence: 0.8157049

00:04:13.100 --> 00:04:15.710 The inside of the cell worked a little bit,

NOTE Confidence: 0.8157049

00:04:15.710 --> 00:04:17.258 but not terribly well.

NOTE Confidence: 0.8157049

00:04:17.258 --> 00:04:19.193 A huge breakthrough though came

NOTE Confidence: 0.8157049

00:04:19.193 --> 00:04:21.148 in the second generation.

NOTE Confidence: 0.8157049

00:04:21.150 --> 00:04:23.616 And here what was done is they add

NOTE Confidence: 0.8157049

00:04:23.616 --> 00:04:26.187 a domain to the protein of CD 28.

NOTE Confidence: 0.8157049

00:04:26.190 --> 00:04:27.414 And what's that? Whoops,

NOTE Confidence: 0.8157049

00:04:27.414 --> 00:04:29.660 that of course is the costimulatory signal,

NOTE Confidence: 0.8157049

00:04:29.660 --> 00:04:32.005 and so when you put the customer

NOTE Confidence: 0.8157049

00:04:32.005 --> 00:04:33.440 let costimulator right in it,

NOTE Confidence: 0.8157049

00:04:33.440 --> 00:04:35.330 these are much, much more powerful,

NOTE Confidence: 0.8157049

00:04:35.330 --> 00:04:36.900 and these are really what

NOTE Confidence: 0.8157049

00:04:36.900 --> 00:04:38.156 we mostly use today.

NOTE Confidence: 0.8157049

00:04:38.160 --> 00:04:39.740 There are even stronger ones.

NOTE Confidence: 0.8157049

00:04:39.740 --> 00:04:41.000 The third generations that

NOTE Confidence: 0.8157049

00:04:41.000 --> 00:04:42.260 use two costimulatory signals,

NOTE Confidence: 0.8157049

00:04:42.260 --> 00:04:43.830 and there's the 4th generation,

NOTE Confidence: 0.8157049

00:04:43.830 --> 00:04:46.140 which is a combination of cars

NOTE Confidence: 0.8157049

00:04:46.140 --> 00:04:48.765 plus other genes that are put in

NOTE Confidence: 0.8157049

00:04:48.765 --> 00:04:50.787 to make the cells work better.

NOTE Confidence: 0.8157049

00:04:50.790 --> 00:04:53.300 So.

NOTE Confidence: 0.8157049

00:04:53.300 --> 00:04:55.256 When you actually the mechanics of

NOTE Confidence: 0.8157049

00:04:55.256 --> 00:04:57.569 this and in patients are complicated,

NOTE Confidence: 0.8157049

00:04:57.570 --> 00:04:59.706 just like all cell therapies are,

NOTE Confidence: 0.8157049

00:04:59.710 --> 00:05:01.130 whether it's transplant or

NOTE Confidence: 0.8157049

00:05:01.130 --> 00:05:02.195 something like this.

NOTE Confidence: 0.8157049

00:05:02.200 --> 00:05:05.760 In this case you need to isolate the T cells.

NOTE Confidence: 0.8157049

00:05:05.760 --> 00:05:08.070 They have to get activated and then

NOTE Confidence: 0.8157049

00:05:08.070 --> 00:05:09.893 their transduced with the chimeric

NOTE Confidence: 0.8157049

00:05:09.893 --> 00:05:11.808 antigen receptor and then expanded

NOTE Confidence: 0.8157049

00:05:11.808 --> 00:05:14.041 and then reinfused in the meantime

NOTE Confidence: 0.8157049

00:05:14.041 --> 00:05:15.751 patients get lympho depleted and

NOTE Confidence: 0.8157049

00:05:15.751 --> 00:05:19.268 the reason for that is that.

NOTE Confidence: 0.8157049

00:05:19.270 --> 00:05:20.155 Probably twofold reasons.

NOTE Confidence: 0.8157049

00:05:20.155 --> 00:05:21.040 For some reasons,

NOTE Confidence: 0.8157049

00:05:21.040 --> 00:05:22.410 you're actually treating the cancer

NOTE Confidence: 0.8157049

00:05:22.410 --> 00:05:24.290 to some degree by lympho depleting,

NOTE Confidence: 0.8157049

00:05:24.290 --> 00:05:26.650 but that isn't the case for all cancers.

NOTE Confidence: 0.8157049

00:05:26.650 --> 00:05:27.240 For some,

NOTE Confidence: 0.8157049

00:05:27.240 --> 00:05:29.954 you're doing it to have a niche for the

NOTE Confidence: 0.8157049

00:05:29.954 --> 00:05:32.546 T cells to actually live in and grow it.

NOTE Confidence: 0.8157049

00:05:32.550 --> 00:05:33.730 As you might imagine,

NOTE Confidence: 0.8157049

00:05:33.730 --> 00:05:35.500 this does not take a day.

NOTE Confidence: 0.8157049

00:05:35.500 --> 00:05:36.716 This takes several weeks,

NOTE Confidence: 0.8157049

00:05:36.716 --> 00:05:39.192 so one of the things about this kind

NOTE Confidence: 0.8157049

00:05:39.192 --> 00:05:41.243 of treatment is patients have to be

NOTE Confidence: 0.8157049

00:05:41.243 --> 00:05:43.245 well enough to survive those weeks and

NOTE Confidence: 0.8157049

00:05:43.245 --> 00:05:45.229 to be able to tolerate the therapy.

NOTE Confidence: 0.77227306

00:05:47.400 --> 00:05:49.974 I'm not going to go into this in detail,

NOTE Confidence: 0.77227306

00:05:49.980 --> 00:05:51.793 but there are a lot of toxicities

NOTE Confidence: 0.77227306

00:05:51.793 --> 00:05:53.140 associated with these treatments.

NOTE Confidence: 0.77227306

00:05:53.140 --> 00:05:54.862 The three famous ones are cited

NOTE Confidence: 0.77227306

00:05:54.862 --> 00:05:56.010 kind of release syndrome,

NOTE Confidence: 0.77227306

00:05:56.010 --> 00:05:57.900 which has to do with a lot

NOTE Confidence: 0.77227306

00:05:57.900 --> 00:06:00.027 of T cells at the same time,

NOTE Confidence: 0.77227306

00:06:00.030 --> 00:06:01.892 seeing antigen and then causing lots of

NOTE Confidence: 0.77227306

00:06:01.892 --> 00:06:03.760 cytokines to go into the circulation.

NOTE Confidence: 0.77227306

00:06:03.760 --> 00:06:05.544 There's also neurotoxicity called

NOTE Confidence: 0.77227306

00:06:05.544 --> 00:06:07.774 crests or cans and probably

NOTE Confidence: 0.77227306

00:06:07.774 --> 00:06:10.008 the most severe of these HLH.

NOTE Confidence: 0.77227306

00:06:10.010 --> 00:06:12.946 Alright, So what are we doing at Yale?

NOTE Confidence: 0.77227306

00:06:12.950 --> 00:06:15.032 We have one party study open

NOTE Confidence: 0.77227306

00:06:15.032 --> 00:06:17.000 right now for solid tumors.

NOTE Confidence: 0.77227306

00:06:17.000 --> 00:06:19.576 This is a kidney cancer trial done

NOTE Confidence: 0.77227306

00:06:19.576 --> 00:06:21.522 by the company, CRISPR Therapeutics.

NOTE Confidence: 0.77227306

00:06:21.522 --> 00:06:24.469 It's anti CD 70 which is highly

NOTE Confidence: 0.77227306

00:06:24.469 --> 00:06:27.036 expressed on clear cell kidney cancers

NOTE Confidence: 0.77227306

00:06:27.036 --> 00:06:29.106 and then there's some expression

NOTE Confidence: 0.77227306

00:06:29.183 --> 00:06:31.360 on a few lymphoid type of cells.

NOTE Confidence: 0.77227306

00:06:31.360 --> 00:06:33.888 Now it's very long name for the trial.

NOTE Confidence: 0.77227306

00:06:33.890 --> 00:06:35.774 The reason is that it's actually

NOTE Confidence: 0.77227306

00:06:35.774 --> 00:06:37.401 a little more complicated than

NOTE Confidence: 0.77227306

00:06:37.401 --> 00:06:38.936 even what I described before.

NOTE Confidence: 0.77227306

00:06:38.940 --> 00:06:40.525 'cause these are allogeneic engineered

NOTE Confidence: 0.77227306

00:06:40.525 --> 00:06:43.710 T cells. And what does that mean?

NOTE Confidence: 0.77227306

00:06:43.710 --> 00:06:46.078 So these are T cells that actually don't

NOTE Confidence: 0.77227306

00:06:46.078 --> 00:06:48.326 come from the patient they come from.

NOTE Confidence: 0.77227306

00:06:48.330 --> 00:06:50.346 Sort of healthy weight healthy donors

NOTE Confidence: 0.77227306

00:06:50.346 --> 00:06:52.517 in whom there they're having the car

NOTE Confidence: 0.77227306

00:06:52.517 --> 00:06:54.696 put into their own T cells and they

NOTE Confidence: 0.77227306

00:06:54.696 --> 00:06:56.646 this company using CRISPR CAS nine.

NOTE Confidence: 0.77227306

00:06:56.650 --> 00:06:59.233 I think a lot of us are familiar with

NOTE Confidence: 0.77227306

00:06:59.233 --> 00:07:01.935 that to knock out certain other genes in

NOTE Confidence: 0.77227306

00:07:01.935 --> 00:07:04.647 these T cells to make them work in us.

NOTE Confidence: 0.77227306

00:07:04.650 --> 00:07:07.898 So what do I mean by that?

NOTE Confidence: 0.77227306

00:07:07.900 --> 00:07:08.208 Well,

NOTE Confidence: 0.77227306

00:07:08.208 --> 00:07:10.364 if you take someone else T cells

NOTE Confidence: 0.77227306

00:07:10.364 --> 00:07:11.990 and put them into you,

NOTE Confidence: 0.77227306

00:07:11.990 --> 00:07:14.825 they will attack you and you will attack it.

NOTE Confidence: 0.77227306

00:07:14.830 --> 00:07:16.720 It won't be an effective therapy.

NOTE Confidence: 0.77227306

00:07:16.720 --> 00:07:18.562 They will get destroyed pretty quickly

NOTE Confidence: 0.77227306

00:07:18.562 --> 00:07:20.180 by the endogenous immune system,

NOTE Confidence: 0.77227306

00:07:20.180 --> 00:07:22.301 and they're going to have off target

NOTE Confidence: 0.77227306

00:07:22.301 --> 00:07:24.589 effects tube via their T cell receptors,

NOTE Confidence: 0.77227306

00:07:24.590 --> 00:07:24.946 potentially.

NOTE Confidence: 0.77227306

00:07:24.946 --> 00:07:27.082 So what they've done this CRISPR

NOTE Confidence: 0.77227306

00:07:27.082 --> 00:07:28.748 therapeutics is in addition to

NOTE Confidence: 0.77227306

00:07:28.748 --> 00:07:30.884 putting in the car to these T cells.

NOTE Confidence: 0.77227306

00:07:30.890 --> 00:07:32.780 They've also put in using CRISPR.

NOTE Confidence: 0.77227306

00:07:32.780 --> 00:07:35.636 They've removed the T cell receptor OK.

NOTE Confidence: 0.77227306

00:07:35.640 --> 00:07:36.880 They've also removed something

NOTE Confidence: 0.77227306

00:07:36.880 --> 00:07:38.120 called beta two microglobulin,

NOTE Confidence: 0.77227306

00:07:38.120 --> 00:07:40.290 which is part of MHC class one,

NOTE Confidence: 0.77227306

00:07:40.290 --> 00:07:42.578 and the result is is that our immune

NOTE Confidence: 0.77227306

00:07:42.578 --> 00:07:44.197 system doesn't recognize that it

NOTE Confidence: 0.77227306

00:07:44.197 --> 00:07:46.177 very well except by some something.

NOTE Confidence: 0.77227306

00:07:46.180 --> 00:07:47.420 All natural killer cells.

NOTE Confidence: 0.77227306

00:07:47.420 --> 00:07:48.970 It doesn't do that much,

NOTE Confidence: 0.77227306

00:07:48.970 --> 00:07:50.640 and it doesn't really recognize

NOTE Confidence: 0.77227306

00:07:50.640 --> 00:07:52.690 us except via the anti CD 7.

NOTE Confidence: 0.77227306

00:07:52.690 --> 00:07:53.001 Alright,

NOTE Confidence: 0.77227306

00:07:53.001 --> 00:07:55.489 so there are a bunch of advantages here

NOTE Confidence: 0.77227306

00:07:55.489 --> 00:07:57.613 of using T cells from someone else

NOTE Confidence: 0.77227306

00:07:57.613 --> 00:08:00.129 and not from the patient one is speed.

NOTE Confidence: 0.77227306

00:08:00.130 --> 00:08:01.650 These cells are waiting.

NOTE Confidence: 0.77227306

00:08:01.650 --> 00:08:03.930 The patients don't have to wait.

NOTE Confidence: 0.77227306

00:08:03.930 --> 00:08:04.214 Secondly,

NOTE Confidence: 0.77227306

00:08:04.214 --> 00:08:05.918 these cells are for someone with

NOTE Confidence: 0.77227306

00:08:05.918 --> 00:08:07.615 an immune with Acton intact immune

NOTE Confidence: 0.77227306

00:08:07.615 --> 00:08:09.463 system and a lot of patients with

NOTE Confidence: 0.77227306

00:08:09.517 --> 00:08:11.012 extensive cancers may not have

NOTE Confidence: 0.77227306

00:08:11.012 --> 00:08:12.796 intact immune systems and the T

NOTE Confidence: 0.77227306

00:08:12.796 --> 00:08:14.226 cells may be somewhat dysfunctional,

NOTE Confidence: 0.77227306

00:08:14.230 --> 00:08:16.006 and obviously it leads to the

NOTE Confidence: 0.77227306

00:08:16.006 --> 00:08:17.659 potential for more of a drug,

NOTE Confidence: 0.77227306

00:08:17.660 --> 00:08:19.268 something that can be done with

NOTE Confidence: 0.77227306

00:08:19.268 --> 00:08:21.005 high levels of production out there

NOTE Confidence: 0.77227306

00:08:21.005 --> 00:08:22.229 for everybody we've enrolled.

NOTE Confidence: 0.77227306

00:08:22.230 --> 00:08:22.834 One patient,

NOTE Confidence: 0.77227306

00:08:22.834 --> 00:08:24.948 we're going to be enrolling one patient

NOTE Confidence: 0.77227306

00:08:24.948 --> 00:08:26.519 another patient in a few months,

NOTE Confidence: 0.77227306

00:08:26.520 --> 00:08:28.236 or at the dose escalation phase,

NOTE Confidence: 0.77227306

00:08:28.240 --> 00:08:30.235 and we'll see how this trial goes.

NOTE Confidence: 0.8159389

00:08:30.240 --> 00:08:32.235 What else is going on at yelled,

NOTE Confidence: 0.8159389

00:08:32.240 --> 00:08:34.564 oh, oh, sorry before I, I go there,

NOTE Confidence: 0.8159389

00:08:34.564 --> 00:08:36.948 let me just. Say that So what?

NOTE Confidence: 0.8159389

00:08:36.948 --> 00:08:40.190 Some of the challenges are for car T cells.

NOTE Confidence: 0.8159389

00:08:40.190 --> 00:08:41.646 Specifically in solid tumors.

NOTE Confidence: 0.8159389

00:08:41.646 --> 00:08:43.466 Well, in general there can

NOTE Confidence: 0.8159389

00:08:43.466 --> 00:08:45.286 be an issue with persistence.

NOTE Confidence: 0.8159389

00:08:45.290 --> 00:08:46.742 The car T cells.

NOTE Confidence: 0.8159389

00:08:46.742 --> 00:08:48.194 They may not last,

NOTE Confidence: 0.8159389

00:08:48.200 --> 00:08:50.748 but these are big issues for solitaire.

NOTE Confidence: 0.8159389

00:08:50.750 --> 00:08:53.060 So one there is almost no answers

NOTE Confidence: 0.8159389

00:08:53.060 --> 00:08:55.479 in a solid tumor cannot lose.

NOTE Confidence: 0.8159389

00:08:55.480 --> 00:08:58.168 And when you give something like CAR T

NOTE Confidence: 0.8159389

00:08:58.168 --> 00:09:00.208 therapy against a particular antigen,

NOTE Confidence: 0.8159389

00:09:00.210 --> 00:09:02.274 it's very likely that the tumor

NOTE Confidence: 0.8159389

00:09:02.274 --> 00:09:04.536 will just mutate or or lower

NOTE Confidence: 0.8159389

00:09:04.536 --> 00:09:06.156 expression of that antigen.

NOTE Confidence: 0.8159389

00:09:06.160 --> 00:09:08.830 And become resistant to it.

NOTE Confidence: 0.8159389

00:09:08.830 --> 00:09:10.086 In addition to that,

NOTE Confidence: 0.8159389

00:09:10.086 --> 00:09:12.278 the micro environment of the tumor is

NOTE Confidence: 0.8159389

00:09:12.278 --> 00:09:14.254 very toxic to a lot of immune cells,

NOTE Confidence: 0.8159389

00:09:14.260 --> 00:09:15.112 including T cells.

NOTE Confidence: 0.8159389

00:09:15.112 --> 00:09:17.699 It's hard to infiltrate into a lot of tumors.

NOTE Confidence: 0.8159389

00:09:17.700 --> 00:09:19.130 There's a lot of necrosis.

NOTE Confidence: 0.8159389

00:09:19.130 --> 00:09:21.410 Many of the cells have low blood supply,

NOTE Confidence: 0.8159389

00:09:21.410 --> 00:09:21.672 etc.

NOTE Confidence: 0.8159389

00:09:21.672 --> 00:09:22.196 And finally,

NOTE Confidence: 0.8159389

00:09:22.196 --> 00:09:24.030 the toxicity is that that I sort

NOTE Confidence: 0.8159389

00:09:24.082 --> 00:09:25.129 of mentioned before.

NOTE Confidence: 0.8159389

00:09:25.130 --> 00:09:27.722 So one of the things that's being done here

NOTE Confidence: 0.8159389

00:09:27.722 --> 00:09:30.274 is being done by the lab of City Chen.

NOTE Confidence: 0.8159389

00:09:30.280 --> 00:09:32.845 His is the only 11 going to talk about,

NOTE Confidence: 0.8159389

00:09:32.850 --> 00:09:35.090 but it's worth pointing out there are many

NOTE Confidence: 0.8159389

00:09:35.090 --> 00:09:37.428 labs here working on car T type therapies.

NOTE Confidence: 0.8159389

00:09:37.430 --> 00:09:38.990 City Shuns Lab has developed.

NOTE Confidence: 0.8159389

00:09:38.990 --> 00:09:39.624 A modular,

NOTE Confidence: 0.8159389

00:09:39.624 --> 00:09:41.526 high throughput way of developing cartis,

NOTE Confidence: 0.8159389

00:09:41.530 --> 00:09:43.120 and it's the system that

NOTE Confidence: 0.8159389

00:09:43.120 --> 00:09:44.710 that again is very complex.

NOTE Confidence: 0.8159389

00:09:44.710 --> 00:09:47.110 There's a there's no time for me to

NOTE Confidence: 0.8159389

00:09:47.110 --> 00:09:49.995 for me to describe it and and be I

NOTE Confidence: 0.8159389

00:09:49.995 --> 00:09:52.658 wouldn't be able to do very well anyway.

NOTE Confidence: 0.8159389

00:09:52.660 --> 00:09:55.204 But this is a slide from from CD,

NOTE Confidence: 0.8159389

00:09:55.210 --> 00:09:55.764 but again,

NOTE Confidence: 0.8159389

00:09:55.764 --> 00:09:57.980 this is his own system that he is

NOTE Confidence: 0.8159389

00:09:58.046 --> 00:10:00.436 designed using adeno associated virus.

NOTE Confidence: 0.8159389

00:10:00.440 --> 00:10:01.586 To make parties,

NOTE Confidence: 0.8159389

00:10:01.586 --> 00:10:03.878 it enables rapid building of new

NOTE Confidence: 0.8159389

00:10:03.878 --> 00:10:05.863 modules because because modular we

NOTE Confidence: 0.8159389

00:10:05.863 --> 00:10:08.753 can put in many different cars into a

NOTE Confidence: 0.8159389

00:10:08.753 --> 00:10:11.210 lot of cells and look at them in parallel.

NOTE Confidence: 0.8159389

00:10:11.210 --> 00:10:13.370 And it also allows for knockout

NOTE Confidence: 0.8159389

00:10:13.370 --> 00:10:15.598 of other genes in the cell just

NOTE Confidence: 0.8159389

00:10:15.598 --> 00:10:17.800 to make to try to improve the

NOTE Confidence: 0.8159389

00:10:17.800 --> 00:10:18.830 cell's capabilities.

NOTE Confidence: 0.8152212

00:10:21.740 --> 00:10:23.635 And therefore we're looking for

NOTE Confidence: 0.8152212

00:10:23.635 --> 00:10:25.530 is superior cancer killing based

NOTE Confidence: 0.8152212

00:10:25.591 --> 00:10:27.623 on a lot of the platforms that are

NOTE Confidence: 0.8152212

00:10:27.623 --> 00:10:29.557 used now in the short term goal,

NOTE Confidence: 0.8152212

00:10:29.560 --> 00:10:31.438 of course, is to generate better

NOTE Confidence: 0.8152212

00:10:31.438 --> 00:10:32.690 parties against kidney cancer.

NOTE Confidence: 0.8152212

00:10:32.690 --> 00:10:34.568 He's actually looking at kidney cancer,

NOTE Confidence: 0.8152212

00:10:34.570 --> 00:10:36.280 which is great. 'cause that's a

NOTE Confidence: 0.8152212

00:10:36.280 --> 00:10:38.329 lot of what I'm interested in,

NOTE Confidence: 0.8152212

00:10:38.330 --> 00:10:39.895 and we're also working with

NOTE Confidence: 0.8152212

00:10:39.895 --> 00:10:41.460 Doctor Krueger on this area.

NOTE Confidence: 0.8152212

00:10:41.460 --> 00:10:43.623 Cougar, but also he can engineer in

NOTE Confidence: 0.8152212

00:10:43.623 --> 00:10:45.918 safety control so that if the T cells

NOTE Confidence: 0.8152212

00:10:45.918 --> 00:10:48.339 are causing some of these severe toxicities,

NOTE Confidence: 0.8152212

00:10:48.340 --> 00:10:51.070 they can be turned off.

NOTE Confidence: 0.8152212

00:10:51.070 --> 00:10:53.527 And you know the long term goal,

NOTE Confidence: 0.8152212

00:10:53.530 --> 00:10:55.642 of course, is to optimize better

NOTE Confidence: 0.8152212

00:10:55.642 --> 00:10:57.050 parties across solid tumors.

NOTE Confidence: 0.8152212

00:10:57.050 --> 00:11:00.070 Anan maybe liquid tumors too.

NOTE Confidence: 0.8152212

00:11:00.070 --> 00:11:01.906 In the first step of that,

NOTE Confidence: 0.8152212

00:11:01.910 --> 00:11:04.059 hopefully will be once his lab develops,

NOTE Confidence: 0.8152212

00:11:04.060 --> 00:11:05.896 but he makes a great car.

NOTE Confidence: 0.8152212

00:11:05.900 --> 00:11:07.742 Is for us to actually put

NOTE Confidence: 0.8152212

00:11:07.742 --> 00:11:08.970 it into trials alright,

NOTE Confidence: 0.8152212

00:11:08.970 --> 00:11:10.951 moving on to till let's go back

NOTE Confidence: 0.8152212

00:11:10.951 --> 00:11:12.659 very quickly again into immunity.

NOTE Confidence: 0.8152212

00:11:12.660 --> 00:11:14.766 So remember something for and it's

NOTE Confidence: 0.8152212

00:11:14.766 --> 00:11:17.092 a strong interaction by the T cell

NOTE Confidence: 0.8152212

00:11:17.092 --> 00:11:19.087 receptor and the MHC complex you get

NOTE Confidence: 0.8152212

00:11:19.148 --> 00:11:21.266 Co stimulation and you get killing.

NOTE Confidence: 0.8152212

00:11:21.270 --> 00:11:21.523 Alright,

NOTE Confidence: 0.8152212

00:11:21.523 --> 00:11:24.243 but how do you get a T cell that actually

NOTE Confidence: 0.8152212

00:11:24.243 --> 00:11:26.517 kills something that's not for it,

NOTE Confidence: 0.8152212

00:11:26.520 --> 00:11:26.876 right?

NOTE Confidence: 0.8152212

00:11:26.876 --> 00:11:27.944 As mentioned before,

NOTE Confidence: 0.8152212

00:11:27.944 --> 00:11:30.080 we don't interact very well with

NOTE Confidence: 0.8152212

00:11:30.141 --> 00:11:31.149 our own antigens.

NOTE Confidence: 0.8152212

00:11:31.150 --> 00:11:31.403 Now,

NOTE Confidence: 0.8152212

00:11:31.403 --> 00:11:33.174 cancer has sort of solved that a

NOTE Confidence: 0.8152212

00:11:33.174 --> 00:11:35.212 little bit for us in that cancer

NOTE Confidence: 0.8152212

00:11:35.212 --> 00:11:36.687 proteins are often mutated because

NOTE Confidence: 0.8152212

00:11:36.747 --> 00:11:38.203 cancer causing mutations and

NOTE Confidence: 0.8152212

00:11:38.203 --> 00:11:39.659 therefore the peptides actually

NOTE Confidence: 0.8152212

00:11:39.659 --> 00:11:42.646 can look for and and so you can

NOTE Confidence: 0.8152212

00:11:42.646 --> 00:11:44.940 actually get T cells to kill.

NOTE Confidence: 0.8152212

00:11:44.940 --> 00:11:46.450 As we all know though,

NOTE Confidence: 0.8152212

00:11:46.450 --> 00:11:49.177 it doesn't really work very well on its own.

NOTE Confidence: 0.8152212

00:11:49.180 --> 00:11:51.301 We need to give things like immune

NOTE Confidence: 0.8152212

00:11:51.301 --> 00:11:52.210 checkpoint inhibitors because

NOTE Confidence: 0.8152212

00:11:52.261 --> 00:11:53.726 of the toxic micro environment,

NOTE Confidence: 0.8152212

00:11:53.730 --> 00:11:55.548 so I thought that was developed

NOTE Confidence: 0.8152212

00:11:55.548 --> 00:11:57.360 began developing back in the 1980s.

NOTE Confidence: 0.8152212

00:11:57.360 --> 00:11:57.890 Was well,

NOTE Confidence: 0.8152212

00:11:57.890 --> 00:12:00.460 maybe if we take the two T cells out

NOTE Confidence: 0.8152212

00:12:00.460 --> 00:12:02.509 of that environment, grow them up,

NOTE Confidence: 0.8152212

00:12:02.509 --> 00:12:04.024 enhance their function with cytokines,

NOTE Confidence: 0.8152212

00:12:04.030 --> 00:12:06.244 maybe we can cause cell killing

NOTE Confidence: 0.8152212

00:12:06.244 --> 00:12:08.898 if we re infuse those T cells.

NOTE Confidence: 0.8152212

00:12:08.900 --> 00:12:10.886 And that's what 'til therapy is.

NOTE Confidence: 0.8152212

00:12:10.890 --> 00:12:12.550 So much like I described,

NOTE Confidence: 0.8152212

00:12:12.550 --> 00:12:13.878 the car T cells,

NOTE Confidence: 0.8152212

00:12:13.878 --> 00:12:15.870 you respect the tumors from patients.

NOTE Confidence: 0.8152212

00:12:15.870 --> 00:12:18.194 T cells are isolated from those tumors.

NOTE Confidence: 0.8152212

00:12:18.200 --> 00:12:20.517 They are activated an expanded in vitro,

NOTE Confidence: 0.8152212

00:12:20.520 --> 00:12:21.948 generally using Interleukin 2,

NOTE Confidence: 0.8152212

00:12:21.948 --> 00:12:24.090 but there are other interventions we

NOTE Confidence: 0.8152212

00:12:24.151 --> 00:12:26.495 use and then they reinfuse with the patient.

NOTE Confidence: 0.8152212

00:12:26.500 --> 00:12:27.493 In the meantime,

NOTE Confidence: 0.8152212

00:12:27.493 --> 00:12:29.148 agents have been limited depleted,

NOTE Confidence: 0.8152212

00:12:29.150 --> 00:12:31.496 which is extremely important for this

NOTE Confidence: 0.8152212

00:12:31.496 --> 00:12:33.953 therapy because we not only have to

NOTE Confidence: 0.8152212

00:12:33.953 --> 00:12:36.460 have a niche for the cells to go into,

NOTE Confidence: 0.8152212

00:12:36.460 --> 00:12:39.826 we have to get rid of T regulatory cells.

NOTE Confidence: 0.8152212

00:12:39.830 --> 00:12:41.050 And the Immune system Act

NOTE Confidence: 0.8152212

00:12:41.050 --> 00:12:42.270 as a sighted kind sink,

NOTE Confidence: 0.8152212

00:12:42.270 --> 00:12:44.111 sucking up all the good side accounts

NOTE Confidence: 0.8152212

00:12:44.111 --> 00:12:46.170 that we want to go to these T cells.

NOTE Confidence: 0.8152212

00:12:46.170 --> 00:12:48.662 'cause when we infuse these T cells

NOTE Confidence: 0.8152212

00:12:48.662 --> 00:12:50.828 we give patients in alluding to.

NOTE Confidence: 0.8152212

00:12:50.830 --> 00:12:52.769 Now before I move on with that

NOTE Confidence: 0.8152212

00:12:52.769 --> 00:12:55.060 with till I think a lot of the

NOTE Confidence: 0.8152212

00:12:55.060 --> 00:12:57.380 time when I tell people that were

NOTE Confidence: 0.8152212

00:12:57.380 --> 00:12:59.100 interested in cell therapies,

NOTE Confidence: 0.8152212

00:12:59.100 --> 00:13:01.008 they say oh it's cortisol therapy.

NOTE Confidence: 0.8152212

00:13:01.010 --> 00:13:02.480 But there's a huge difference

NOTE Confidence: 0.8152212

00:13:02.480 --> 00:13:03.950 is really between CAR T

NOTE Confidence: 0.7871327

00:13:04.014 --> 00:13:05.458 cell therapies and tilsen.

NOTE Confidence: 0.7871327

00:13:05.460 --> 00:13:07.996 I think of them is really entirely different.

NOTE Confidence: 0.7871327

00:13:08.000 --> 00:13:08.954 As some examples.

NOTE Confidence: 0.7871327

00:13:08.954 --> 00:13:11.456 You know, car T cells are MHC totally

NOTE Confidence: 0.7871327

00:13:11.456 --> 00:13:13.409 independent right there using an antibody,

NOTE Confidence: 0.7871327

00:13:13.410 --> 00:13:15.318 whereas 'til therapy is totally dependent.

NOTE Confidence: 0.7871327

00:13:15.320 --> 00:13:16.416 CAR T cells don't?

NOTE Confidence: 0.7871327

00:13:16.416 --> 00:13:18.535 They can look at sugars or other

NOTE Confidence: 0.7871327

00:13:18.535 --> 00:13:21.780 non protein antigens. Tills do not.

NOTE Confidence: 0.7871327

00:13:21.780 --> 00:13:23.480 Cars are pretty ineffective at

NOTE Confidence: 0.7871327

00:13:23.480 --> 00:13:24.840 looking at intracellular proteins.

NOTE Confidence: 0.7871327

00:13:24.840 --> 00:13:26.204 They're working on that,

NOTE Confidence: 0.7871327

00:13:26.204 --> 00:13:28.580 so maybe we'll get there one day,

NOTE Confidence: 0.7871327

00:13:28.580 --> 00:13:30.488 but right now they can't really

NOTE Confidence: 0.7871327

00:13:30.488 --> 00:13:32.659 recognize a lot of the proteins.

NOTE Confidence: 0.7871327

00:13:32.660 --> 00:13:35.380 And the key thing is that you know,

NOTE Confidence: 0.7871327

00:13:35.380 --> 00:13:38.440 till can look at any antigens that they see.

NOTE Confidence: 0.7871327

00:13:38.440 --> 00:13:39.352 So for example,

NOTE Confidence: 0.7871327

00:13:39.352 --> 00:13:41.937 when we take tumors out of patience and

NOTE Confidence: 0.7871327

00:13:41.937 --> 00:13:43.877 isolate the lymphocytes from those,

NOTE Confidence: 0.7871327

00:13:43.880 --> 00:13:45.920 that's going to be a diverse,

NOTE Confidence: 0.7871327

00:13:45.920 --> 00:13:47.620 diverse type of T cells,

NOTE Confidence: 0.7871327

00:13:47.620 --> 00:13:48.300 probably recognizing

NOTE Confidence: 0.7871327

00:13:48.300 --> 00:13:49.320 multiple different antigens.

NOTE Confidence: 0.7871327

00:13:49.320 --> 00:13:51.020 And, as I said before,

NOTE Confidence: 0.7871327

00:13:51.020 --> 00:13:53.477 a big disadvantage of car T cells.

NOTE Confidence: 0.7871327

00:13:53.480 --> 00:13:55.258 Is that you can lose the one

NOTE Confidence: 0.7871327

00:13:55.258 --> 00:13:56.497 antigen they recognized in their

NOTE Confidence: 0.7871327

00:13:56.497 --> 00:13:58.177 useless and that may not be as big

NOTE Confidence: 0.7871327

00:13:58.232 --> 00:13:59.798 of an issue with 'til therapies.

NOTE Confidence: 0.7871327

00:13:59.800 --> 00:14:00.840 And Lastly,

NOTE Confidence: 0.7871327

00:14:00.840 --> 00:14:03.440 there toxicities are quite different.

NOTE Confidence: 0.7871327

00:14:03.440 --> 00:14:06.360 Alright, So what are we doing at Yale?

NOTE Confidence: 0.7871327

00:14:06.360 --> 00:14:08.864 We have a trial right now for looking

NOTE Confidence: 0.7871327

00:14:08.864 --> 00:14:11.098 at triple negative breast cancer.

NOTE Confidence: 0.7871327

00:14:11.100 --> 00:14:13.655 This is an IIT that I'm doing

NOTE Confidence: 0.7871327

00:14:13.655 --> 00:14:14.750 with IMS Therapeutics.

NOTE Confidence: 0.7871327

00:14:14.750 --> 00:14:16.922 This is the first dedicated breast

NOTE Confidence: 0.7871327

00:14:16.922 --> 00:14:19.130 cancer till trial world we've been.

NOTE Confidence: 0.7871327

00:14:19.130 --> 00:14:21.320 We've enrolled two patients so far,

NOTE Confidence: 0.7871327

00:14:21.320 --> 00:14:23.875 and one of the reasons were interesting.

NOTE Confidence: 0.7871327

00:14:23.880 --> 00:14:26.070 Breast is that there's lab here.

NOTE Confidence: 0.7871327

00:14:26.070 --> 00:14:26.798 Tristan Park,

NOTE Confidence: 0.7871327

00:14:26.798 --> 00:14:28.618 who's a surgical oncologist here,

NOTE Confidence: 0.7871327

00:14:28.620 --> 00:14:30.606 an expert on breast cancer and

NOTE Confidence: 0.7871327

00:14:30.606 --> 00:14:32.640 on breast cancer cell therapies?

NOTE Confidence: 0.7871327

00:14:32.640 --> 00:14:33.478 Who's actually?

NOTE Confidence: 0.7871327

00:14:33.478 --> 00:14:35.992 Looking at the samples we get

NOTE Confidence: 0.7871327

00:14:35.992 --> 00:14:38.093 analyzing for the immune infiltrates

NOTE Confidence: 0.7871327

00:14:38.093 --> 00:14:40.872 and working with us on the trial.

NOTE Confidence: 0.7871327

00:14:40.880 --> 00:14:42.630 Just to say a little bit more

NOTE Confidence: 0.7871327

00:14:42.630 --> 00:14:44.429 about what it actually entails.

NOTE Confidence: 0.7871327

00:14:44.430 --> 00:14:46.306 It's there's a lot of for any

NOTE Confidence: 0.7871327

00:14:46.306 --> 00:14:47.690 sort of cell therapy.

NOTE Confidence: 0.7871327

00:14:47.690 --> 00:14:49.714 There's a lot of work that goes into

NOTE Confidence: 0.7871327

00:14:49.714 --> 00:14:51.268 it because these are complicated

NOTE Confidence: 0.7871327

00:14:51.268 --> 00:14:53.571 therapies that require a good timing so

NOTE Confidence: 0.7871327

00:14:53.629 --> 00:14:55.680 you know once a patient signs consent,

NOTE Confidence: 0.7871327

00:14:55.680 --> 00:14:57.456 they have to get their surgeries.

NOTE Confidence: 0.7871327

00:14:57.460 --> 00:14:58.940 Only then do you initiate.

NOTE Confidence: 0.7871327

00:14:58.940 --> 00:15:00.420 Of course the till culture,

NOTE Confidence: 0.7871327

00:15:00.420 --> 00:15:02.190 then it's going to be going

NOTE Confidence: 0.7871327

00:15:02.190 --> 00:15:03.075 for several weeks,

NOTE Confidence: 0.7871327

00:15:03.080 --> 00:15:04.850 and once you know the till

NOTE Confidence: 0.7871327

00:15:04.850 --> 00:15:05.735 is growing appropriately,

NOTE Confidence: 0.7871327

00:15:05.740 --> 00:15:07.594 only then are you going to

NOTE Confidence: 0.7871327

00:15:07.594 --> 00:15:09.569 limited Lee the patient and then

NOTE Confidence: 0.7871327

00:15:09.569 --> 00:15:11.249 infuse that into the patient.

NOTE Confidence: 0.7871327

00:15:11.250 --> 00:15:12.214 And then of course,

NOTE Confidence: 0.7871327

00:15:12.214 --> 00:15:12.937 as I said,

NOTE Confidence: 0.7871327

00:15:12.940 --> 00:15:14.380 these people require oil to afterwards,

NOTE Confidence: 0.7871327

00:15:14.380 --> 00:15:16.052 and they're going to be in the hospital

NOTE Confidence: 0.7871327

00:15:16.052 --> 00:15:18.031 for a lot of this because they're going

NOTE Confidence: 0.7871327

00:15:18.031 --> 00:15:19.928 to depleted and then once they recover,

NOTE Confidence: 0.7871327

00:15:19.930 --> 00:15:21.274 they go home.

NOTE Confidence: 0.7871327

00:15:21.274 --> 00:15:22.618 We follow them.

NOTE Confidence: 0.7871327

00:15:22.620 --> 00:15:23.007 So,

NOTE Confidence: 0.7871327

00:15:23.007 --> 00:15:26.490 so how might we improve some of these things?

NOTE Confidence: 0.7871327

00:15:26.490 --> 00:15:26.877 Well,

NOTE Confidence: 0.7871327

00:15:26.877 --> 00:15:29.199 I think infusion and reception isolation.

NOTE Confidence: 0.7871327

00:15:29.200 --> 00:15:31.516 That's not where the money is,

NOTE Confidence: 0.7871327

00:15:31.520 --> 00:15:34.118 but clearly we can maybe improve

NOTE Confidence: 0.7871327

00:15:34.118 --> 00:15:35.850 activating and expanding these

NOTE Confidence: 0.7871327

00:15:35.922 --> 00:15:38.328 cells and make them better killers.

NOTE Confidence: 0.7871327

00:15:38.330 --> 00:15:40.370 And the people who are the best at

NOTE Confidence: 0.7871327

00:15:40.370 --> 00:15:42.467 growing up and activating these cells.

NOTE Confidence: 0.7871327

00:15:42.470 --> 00:15:45.044 Of course that you are the people of the

NOTE Confidence: 0.7871327

00:15:45.044 --> 00:15:47.208 Advanced Therapy Lab run by Alexi Burst.

NOTE Confidence: 0.7871327

00:15:47.210 --> 00:15:48.520 Never die across and they

NOTE Confidence: 0.7871327

00:15:48.520 --> 00:15:49.830 have a huge amount of

NOTE Confidence: 0.7965901

00:15:49.895 --> 00:15:51.347 expertise over many years.

NOTE Confidence: 0.7965901

00:15:51.350 --> 00:15:53.780 Looking at till type therapies.

NOTE Confidence: 0.7965901

00:15:53.780 --> 00:15:56.349 They've grown up a lot of different

NOTE Confidence: 0.7965901

00:15:56.349 --> 00:15:58.628 cell products for use in patients,

NOTE Confidence: 0.7965901

00:15:58.630 --> 00:16:00.495 and I actually hold Inds

NOTE Confidence: 0.7965901

00:16:00.495 --> 00:16:01.987 for growing Melanoma till,

NOTE Confidence: 0.7965901

00:16:01.990 --> 00:16:04.573 but of course they actually did it

NOTE Confidence: 0.7965901

00:16:04.573 --> 00:16:06.863 and we're working together right now

NOTE Confidence: 0.7965901

00:16:06.863 --> 00:16:09.446 to grow up lung cancer till four,

NOTE Confidence: 0.7965901

00:16:09.450 --> 00:16:12.750 ideally to eventually put into patients.

NOTE Confidence: 0.7965901

00:16:12.750 --> 00:16:14.290 Just quickly to point out,

NOTE Confidence: 0.7965901

00:16:14.290 --> 00:16:16.770 they are very good at growing up selves.

NOTE Confidence: 0.7965901

00:16:16.770 --> 00:16:18.822 This is 1 experiment which they

NOTE Confidence: 0.7965901

00:16:18.822 --> 00:16:20.844 actually separated out the PD one

NOTE Confidence: 0.7965901

00:16:20.844 --> 00:16:22.319 positive from negative cells and

NOTE Confidence: 0.7965901

00:16:22.319 --> 00:16:24.650 show a lot of expansion in both of

NOTE Confidence: 0.7965901

00:16:24.650 --> 00:16:26.937 them and this just kind of shows one

NOTE Confidence: 0.7965901

00:16:26.937 --> 00:16:28.731 experiment of theirs that the cells

NOTE Confidence: 0.7965901

00:16:28.731 --> 00:16:30.669 they get are actually quite good.

NOTE Confidence: 0.7965901

00:16:30.670 --> 00:16:32.524 So here till they've isolated out

NOTE Confidence: 0.7965901

00:16:32.524 --> 00:16:34.469 and these are assays for interferon

NOTE Confidence: 0.7965901

00:16:34.469 --> 00:16:36.425 gamma production which is an essay

NOTE Confidence: 0.7965901

00:16:36.425 --> 00:16:38.536 of sort of it's a surrogate for

NOTE Confidence: 0.7965901

00:16:38.536 --> 00:16:40.684 cell killing and when you take this

NOTE Confidence: 0.7965901

00:16:40.684 --> 00:16:43.660 pill and you and you you put him.

NOTE Confidence: 0.7965901

00:16:43.660 --> 00:16:43.938 Alone,

NOTE Confidence: 0.7965901

00:16:43.938 --> 00:16:46.162 they don't make a lot of interferon gamma.

NOTE Confidence: 0.7965901

00:16:46.170 --> 00:16:48.116 As soon as you put them with

NOTE Confidence: 0.7965901

00:16:48.116 --> 00:16:48.672 autologous tumor,

NOTE Confidence: 0.7965901

00:16:48.680 --> 00:16:49.792 or they recognize antigens

NOTE Confidence: 0.7965901

00:16:49.792 --> 00:16:51.182 in the setting of MHC,

NOTE Confidence: 0.7965901

00:16:51.190 --> 00:16:52.726 they make tons of interferon gamma

NOTE Confidence: 0.7965901

00:16:52.726 --> 00:16:54.705 and then if you give them someone

NOTE Confidence: 0.7965901

00:16:54.705 --> 00:16:56.210 elses tumor that has emerged,

NOTE Confidence: 0.7965901

00:16:56.210 --> 00:16:57.890 they don't recognize they don't kill.

NOTE Confidence: 0.7965901

00:16:57.890 --> 00:16:59.584 So they're very good at making cells

NOTE Confidence: 0.7965901

00:16:59.584 --> 00:17:01.240 that kill and kill specifically,

NOTE Confidence: 0.7965901

00:17:01.240 --> 00:17:02.908 which is exactly what we need.

NOTE Confidence: 0.89995277

00:17:05.150 --> 00:17:09.200 So what can we do to actually improve things?

NOTE Confidence: 0.89995277

00:17:09.200 --> 00:17:11.420 To make these, what are we

NOTE Confidence: 0.89995277

00:17:11.420 --> 00:17:12.900 interested in doing here?

NOTE Confidence: 0.89995277

00:17:12.900 --> 00:17:14.750 Yale to improve these therapies?

NOTE Confidence: 0.89995277

00:17:14.750 --> 00:17:17.387 Well, the South therapy the AC T lab is

NOTE Confidence: 0.89995277

00:17:17.387 --> 00:17:19.709 doing experiments to look at adjusting

NOTE Confidence: 0.89995277

00:17:19.709 --> 00:17:22.594 the growth medium that that they do

NOTE Confidence: 0.89995277

00:17:22.594 --> 00:17:24.739 it in different cytokine combinations,

NOTE Confidence: 0.89995277

00:17:24.740 --> 00:17:26.590 different levels of cytokines and

NOTE Confidence: 0.89995277

00:17:26.590 --> 00:17:28.070 those experiments are ongoing.

NOTE Confidence: 0.89995277

00:17:28.070 --> 00:17:29.895 But. It's actually striking how

NOTE Confidence: 0.89995277

00:17:29.895 --> 00:17:32.093 little we know about what happens

NOTE Confidence: 0.89995277

00:17:32.093 --> 00:17:34.200 between when we take the cells out

NOTE Confidence: 0.89995277

00:17:34.200 --> 00:17:36.537 of a person and we expand them.

NOTE Confidence: 0.89995277

00:17:36.540 --> 00:17:37.808 We don't really know

NOTE Confidence: 0.89995277

00:17:37.808 --> 00:17:39.076 which cells get expanded.

NOTE Confidence: 0.89995277

00:17:39.080 --> 00:17:41.792 We don't know whether the T cell maturation

NOTE Confidence: 0.89995277

00:17:41.792 --> 00:17:44.170 states whether they are more naive or more.

NOTE Confidence: 0.89995277

00:17:44.170 --> 00:17:45.442 Effector cells dictate which

NOTE Confidence: 0.89995277

00:17:45.442 --> 00:17:46.396 cells that expanded.

NOTE Confidence: 0.89995277

00:17:46.400 --> 00:17:48.704 We don't know how this concept of T

NOTE Confidence: 0.89995277

00:17:48.704 --> 00:17:50.530 cell exhaustion relates to expansion,

NOTE Confidence: 0.89995277

00:17:50.530 --> 00:17:52.406 and we have very little idea about

NOTE Confidence: 0.89995277

00:17:52.406 --> 00:17:53.622 how homogeneous or heterogeneous

NOTE Confidence: 0.89995277

00:17:53.622 --> 00:17:55.417 that essential traits are between

NOTE Confidence: 0.89995277

00:17:55.417 --> 00:17:57.210 tumors or between tumor types.

NOTE Confidence: 0.89995277

00:17:57.210 --> 00:17:58.650 So and can we.

NOTE Confidence: 0.89995277

00:17:58.650 --> 00:18:00.810 Can we actually do experiments to

NOTE Confidence: 0.89995277

00:18:00.894 --> 00:18:03.150 figure some of this stuff out?

NOTE Confidence: 0.89995277

00:18:03.150 --> 00:18:04.900 And the approach that we're

NOTE Confidence: 0.89995277

00:18:04.900 --> 00:18:06.300 going to take here,

NOTE Confidence: 0.89995277

00:18:06.300 --> 00:18:08.050 and we've actually begun taking,

NOTE Confidence: 0.89995277

00:18:08.050 --> 00:18:10.213 is to do single cell RNA sequencing

NOTE Confidence: 0.89995277

00:18:10.213 --> 00:18:12.151 and paired with TCR sequencing so

NOTE Confidence: 0.89995277

00:18:12.151 --> 00:18:14.356 that we can follow specific T cell

NOTE Confidence: 0.89995277

00:18:14.423 --> 00:18:16.483 clones through growth and figure

NOTE Confidence: 0.89995277

00:18:16.483 --> 00:18:18.131 out which maturation phenotypes

NOTE Confidence: 0.89995277

00:18:18.131 --> 00:18:22.018 are the ones that grow the best.

NOTE Confidence: 0.89995277

00:18:22.020 --> 00:18:23.886 And whether exhaustion has an effect,

NOTE Confidence: 0.89995277

00:18:23.890 --> 00:18:25.941 and then we're going to do this

NOTE Confidence: 0.89995277

00:18:25.941 --> 00:18:27.640 across a number of subjects,

NOTE Confidence: 0.89995277

00:18:27.640 --> 00:18:29.422 so I should say that that's

NOTE Confidence: 0.89995277

00:18:29.422 --> 00:18:31.379 already been done a little bit.

NOTE Confidence: 0.89995277

00:18:31.380 --> 00:18:32.940 One it's being done beginning,

NOTE Confidence: 0.89995277

00:18:32.940 --> 00:18:35.436 and Sam Katz is lab by Sam Kerr,

NOTE Confidence: 0.89995277

00:18:35.440 --> 00:18:37.000 one of his graduate students,

NOTE Confidence: 0.89995277

00:18:37.000 --> 00:18:38.824 and I'll be doing some of

NOTE Confidence: 0.89995277

00:18:38.824 --> 00:18:40.430 these studies on long till.

NOTE Confidence: 0.89995277

00:18:40.430 --> 00:18:42.296 But really, the person doing this,

NOTE Confidence: 0.89995277

00:18:42.300 --> 00:18:44.880 Ben Lewin, the Hafler lab.

NOTE Confidence: 0.89995277

00:18:44.880 --> 00:18:46.158 I have no time around this,

NOTE Confidence: 0.89995277

00:18:46.160 --> 00:18:48.040 so I don't know where I am on time and

NOTE Confidence: 0.89995277

00:18:48.090 --> 00:18:50.018 someone told me I've got a little time.

NOTE Confidence: 0.89995277

00:18:50.020 --> 00:18:50.230 OK,

NOTE Confidence: 0.89995277

00:18:50.230 --> 00:18:50.440 good.

NOTE Confidence: 0.83190864

00:18:52.660 --> 00:18:54.772 So let me say one last set of

NOTE Confidence: 0.83190864

00:18:54.772 --> 00:18:56.686 experiments that are being done at Yale.

NOTE Confidence: 0.83190864

00:18:56.690 --> 00:18:58.510 Looking at some basic science that could

NOTE Confidence: 0.83190864

00:18:58.510 --> 00:19:00.729 have a big impact on T cell therapies.

NOTE Confidence: 0.83190864

00:19:00.730 --> 00:19:03.142 And by the way, I should point out that,

NOTE Confidence: 0.83190864

00:19:03.150 --> 00:19:04.470 you know, I've mentioned a

NOTE Confidence: 0.83190864

00:19:04.470 --> 00:19:06.110 few people who are doing work,

NOTE Confidence: 0.83190864

00:19:06.110 --> 00:19:08.522 but there are many others doing work at Yale.

NOTE Confidence: 0.83190864

00:19:08.530 --> 00:19:10.138 I they don't have time unfortunately,

NOTE Confidence: 0.83190864

00:19:10.140 --> 00:19:11.754 but but I don't mean to

NOTE Confidence: 0.83190864

00:19:11.754 --> 00:19:12.830 leave other people out.

NOTE Confidence: 0.83190864

00:19:12.830 --> 00:19:14.648 We're doing really vital stuff that

NOTE Confidence: 0.83190864

00:19:14.648 --> 00:19:16.599 in fact probably there are a lot

NOTE Confidence: 0.83190864

00:19:16.599 --> 00:19:18.202 of things I don't know about that.

NOTE Confidence: 0.83190864

00:19:18.210 --> 00:19:19.210 I wish I did.

NOTE Confidence: 0.83190864

00:19:19.210 --> 00:19:21.438 So one of the things that Sam Katz's

NOTE Confidence: 0.83190864

00:19:21.438 --> 00:19:23.734 lab is working on for quite awhile.

NOTE Confidence: 0.83190864

00:19:23.740 --> 00:19:25.960 So some invoices lab is Weismann's

NOTE Confidence: 0.83190864

00:19:25.960 --> 00:19:28.584 lab is working on is the idea

NOTE Confidence: 0.83190864

00:19:28.584 --> 00:19:30.008 of M RNA reprogramming?

NOTE Confidence: 0.83190864

00:19:30.010 --> 00:19:31.730 So he's using something called

NOTE Confidence: 0.83190864

00:19:31.730 --> 00:19:34.248 crisper I which is a crisper based

NOTE Confidence: 0.83190864

00:19:34.248 --> 00:19:36.432 technique to knock down genes but

NOTE Confidence: 0.83190864

00:19:36.432 --> 00:19:38.385 not to actually cause mutations

NOTE Confidence: 0.83190864

00:19:38.385 --> 00:19:41.073 or or or changes the actual DNA.

NOTE Confidence: 0.83190864

00:19:41.080 --> 00:19:43.216 The advantages of this technique is

NOTE Confidence: 0.83190864

00:19:43.216 --> 00:19:46.249 that you can do multiple RNAs at once.

NOTE Confidence: 0.83190864

00:19:46.250 --> 00:19:49.045 Sorry bout that. The.

NOTE Confidence: 0.83190864

00:19:49.045 --> 00:19:51.055 Other thing about this of course

NOTE Confidence: 0.83190864

00:19:51.055 --> 00:19:53.710 is when you do these things by RNA.

NOTE Confidence: 0.83190864

00:19:53.710 --> 00:19:54.544 RNA is temporary,

NOTE Confidence: 0.83190864

00:19:54.544 --> 00:19:56.212 so there are pluses to that

NOTE Confidence: 0.83190864

00:19:56.212 --> 00:19:57.460 and minuses to that.

NOTE Confidence: 0.83190864

00:19:57.460 --> 00:20:00.196 The pluses are that it's a lot safer.

NOTE Confidence: 0.83190864

00:20:00.200 --> 00:20:01.528 Not permanently altering itself.

NOTE Confidence: 0.83190864

00:20:01.528 --> 00:20:02.856 OK, the negative, however,

NOTE Confidence: 0.83190864

00:20:02.856 --> 00:20:04.516 is that it's only temporary,

NOTE Confidence: 0.83190864

00:20:04.520 --> 00:20:06.725 so if you want to have effects

NOTE Confidence: 0.83190864

00:20:06.725 --> 00:20:08.499 that last a long time,

NOTE Confidence: 0.83190864

00:20:08.500 --> 00:20:12.865 this might not be the method to do it.

NOTE Confidence: 0.83190864

00:20:12.870 --> 00:20:15.054 But you can imagine situations where using

NOTE Confidence: 0.83190864

00:20:15.054 --> 00:20:17.462 this kind of technique you could really

NOTE Confidence: 0.83190864

00:20:17.462 --> 00:20:20.089 turbocharge a cell for short period of time.

NOTE Confidence: 0.83190864

00:20:20.090 --> 00:20:21.440 So for example,

NOTE Confidence: 0.83190864

00:20:21.440 --> 00:20:24.590 we could have a car T cell.

NOTE Confidence: 0.83190864

00:20:24.590 --> 00:20:26.636 And you could use his technique

NOTE Confidence: 0.83190864

00:20:26.636 --> 00:20:28.998 to make the groups make them

NOTE Confidence: 0.83190864

00:20:28.998 --> 00:20:30.390 particularly proliferative at

NOTE Confidence: 0.83190864

00:20:30.390 --> 00:20:32.710 the time at inside accounts,

NOTE Confidence: 0.83190864

00:20:32.710 --> 00:20:35.140 for example to happen particularly powerful

NOTE Confidence: 0.83190864

00:20:35.140 --> 00:20:37.580 and killing stimulators of other things,

NOTE Confidence: 0.83190864

00:20:37.580 --> 00:20:39.200 you could have inhibitors

NOTE Confidence: 0.83190864

00:20:39.200 --> 00:20:40.415 of negative regulators,

NOTE Confidence: 0.83190864

00:20:40.420 --> 00:20:43.004 and in fact Sam is shown in his

NOTE Confidence: 0.83190864

00:20:43.004 --> 00:20:45.810 lab and from Weismans lab that for

NOTE Confidence: 0.83190864

00:20:45.810 --> 00:20:48.926 example they can at the same time

NOTE Confidence: 0.83190864

00:20:48.926 --> 00:20:51.788 using their CRISPR RNA I techniques,

NOTE Confidence: 0.83190864

00:20:51.790 --> 00:20:53.065 Christmas learning techniques

NOTE Confidence: 0.83190864

00:20:53.065 --> 00:20:56.040 to increase IL two in a cell.

NOTE Confidence: 0.83190864

00:20:56.040 --> 00:20:57.740 And decrease BCL type proteins

NOTE Confidence: 0.83190864

00:20:57.740 --> 00:21:00.070 which are made up tatic proteins.

NOTE Confidence: 0.83190864

00:21:00.070 --> 00:21:02.730 So again when you think about what

NOTE Confidence: 0.83190864

00:21:02.730 --> 00:21:04.819 I've talked about so far with,

NOTE Confidence: 0.83190864

00:21:04.820 --> 00:21:07.308 let's say the city Chen Lab in which

NOTE Confidence: 0.83190864

00:21:07.308 --> 00:21:09.611 they can do multiple different things

NOTE Confidence: 0.83190864

00:21:09.611 --> 00:21:12.510 to design sort of permanent T cells,

NOTE Confidence: 0.83190864

00:21:12.510 --> 00:21:14.706 that car T cells that are

NOTE Confidence: 0.83190864

00:21:14.706 --> 00:21:15.438 particularly powerful.

NOTE Confidence: 0.83190864

00:21:15.440 --> 00:21:17.384 You could also imagine adding in

NOTE Confidence: 0.83190864

00:21:17.384 --> 00:21:20.366 these M RNA's to those same cells and

NOTE Confidence: 0.83190864

00:21:20.366 --> 00:21:22.386 making turbochargers even more so.

NOTE Confidence: 0.83190864

00:21:22.390 --> 00:21:24.415 There's a huge amount of

NOTE Confidence: 0.83190864

00:21:24.415 --> 00:21:26.720 combinatorial things that we could do.

NOTE Confidence: 0.83190864

00:21:26.720 --> 00:21:28.160 To improve his cell therapies,

NOTE Confidence: 0.83190864

00:21:28.160 --> 00:21:30.716 and there's a lot of excitement

NOTE Confidence: 0.83190864

00:21:30.716 --> 00:21:32.420 for all those things.

NOTE Confidence: 0.83190864

00:21:32.420 --> 00:21:34.330 Last but certainly not least,

NOTE Confidence: 0.83190864

00:21:34.330 --> 00:21:37.186 I just want to acknowledge all that

NOTE Confidence: 0.83190864

00:21:37.186 --> 00:21:40.060 people have been doing a lot of work.

NOTE Confidence: 0.83190864

00:21:40.060 --> 00:21:43.116 So what first assault therapy DART 3 docs?

NOTE Confidence: 0.83190864

00:21:43.120 --> 00:21:45.856 Who do it right now or are nearest

NOTE Confidence: 0.83190864

00:21:45.856 --> 00:21:48.253 Stewart and I Alex is our CDT

NOTE Confidence: 0.83190864

00:21:48.253 --> 00:21:49.888 N as fantastic Sharon days

NOTE Confidence: 0.7628183

00:21:49.966 --> 00:21:52.732 are relatively new but also fantastic

NOTE Confidence: 0.7628183

00:21:52.732 --> 00:21:55.292 research nurse Ann Pavan or CRA.

NOTE Confidence: 0.7628183

00:21:55.292 --> 00:21:57.784 I'm not impressed but and then we

NOTE Confidence: 0.7628183

00:21:57.784 --> 00:22:00.309 have an amazing team here doing,

NOTE Confidence: 0.7628183

00:22:00.310 --> 00:22:03.327 you know regulatory and and pharmacy etc.

NOTE Confidence: 0.7628183

00:22:03.330 --> 00:22:06.690 Also, of course, the AC T lab.

NOTE Confidence: 0.7628183

00:22:06.690 --> 00:22:08.424 Which you know is really going

NOTE Confidence: 0.7628183

00:22:08.424 --> 00:22:10.320 to be the people developing.

NOTE Confidence: 0.7628183

00:22:10.320 --> 00:22:11.640 Sorry the next therapies

NOTE Confidence: 0.7628183

00:22:11.640 --> 00:22:13.620 that we that we do here,

NOTE Confidence: 0.7628183

00:22:13.620 --> 00:22:15.600 I mentioned the Melanoma team because,

NOTE Confidence: 0.7628183

00:22:15.600 --> 00:22:17.220 really, we've been doing till

NOTE Confidence: 0.7628183

00:22:17.220 --> 00:22:19.230 at Yale for very long time.

NOTE Confidence: 0.7628183

00:22:19.230 --> 00:22:21.442 And the person who got us started

NOTE Confidence: 0.7628183

00:22:21.442 --> 00:22:23.647 here was Mary Otional and a lot

NOTE Confidence: 0.7628183

00:22:23.647 --> 00:22:25.856 of the ideas that I talked about

NOTE Confidence: 0.7628183

00:22:25.856 --> 00:22:28.397 with regards to how to study these

NOTE Confidence: 0.7628183

00:22:28.397 --> 00:22:30.117 things really came from Mario.

NOTE Confidence: 0.7628183

00:22:30.117 --> 00:22:32.420 Harriet has done the most to have

NOTE Confidence: 0.7628183

00:22:32.493 --> 00:22:34.754 anybody here and has done a huge

NOTE Confidence: 0.7628183

00:22:34.754 --> 00:22:36.778 amount and Sarah Weiss has seen.

NOTE Confidence: 0.7628183

00:22:36.780 --> 00:22:39.335 A lot of the patients as well,

NOTE Confidence: 0.7628183

00:22:39.340 --> 00:22:40.036 Katrina Bezak,

NOTE Confidence: 0.7628183

00:22:40.036 --> 00:22:43.272 is is the person who is really a point

NOTE Confidence: 0.7628183

00:22:43.272 --> 00:22:46.296 person for a lot of salt therapies here,

NOTE Confidence: 0.7628183

00:22:46.300 --> 00:22:47.764 and she's actually also

NOTE Confidence: 0.7628183

00:22:47.764 --> 00:22:49.960 key for setting us up for.

NOTE Confidence: 0.7628183

00:22:49.960 --> 00:22:50.935 As I said,

NOTE Confidence: 0.7628183

00:22:50.935 --> 00:22:52.560 the very very likely approval

NOTE Confidence: 0.7628183

00:22:52.560 --> 00:22:54.911 of heart till in Melanoma people

NOTE Confidence: 0.7628183

00:22:54.911 --> 00:22:56.539 probably don't know this,

NOTE Confidence: 0.7628183

00:22:56.540 --> 00:22:58.906 but we have our own something called

NOTE Confidence: 0.7628183

00:22:58.906 --> 00:23:01.300 CDC which is for cell therapies.

NOTE Confidence: 0.7628183

00:23:01.300 --> 00:23:03.412 It's a committee to look at

NOTE Confidence: 0.7628183

00:23:03.412 --> 00:23:05.670 really usage and whether we have

NOTE Confidence: 0.7628183

00:23:05.670 --> 00:23:07.605 the capability and the capacity.

NOTE Confidence: 0.7628183

00:23:07.610 --> 00:23:11.130 To do all the different trials we want to do,

NOTE Confidence: 0.7628183

00:23:11.130 --> 00:23:14.427 none of this would be possible without

NOTE Confidence: 0.7628183

00:23:14.427 --> 00:23:17.188 the nursing staff on 11/12 North.

NOTE Confidence: 0.7628183

00:23:17.190 --> 00:23:19.008 A pheresis machine, Hendrickson the RSL,

NOTE Confidence: 0.7628183

00:23:19.010 --> 00:23:21.128 Audrey King, and of course, the lab.

NOTE Confidence: 0.7628183

00:23:21.128 --> 00:23:23.550 As I mentioned, and I should point out,

NOTE Confidence: 0.7628183

00:23:23.550 --> 00:23:24.690 that as I said,

NOTE Confidence: 0.7628183

00:23:24.690 --> 00:23:26.400 we're trying to get an Ind

NOTE Confidence: 0.7628183

00:23:26.470 --> 00:23:28.100 right now for long till.

NOTE Confidence: 0.7628183

00:23:28.100 --> 00:23:29.560 And that's based on funding

NOTE Confidence: 0.7628183

00:23:29.560 --> 00:23:31.430 we got from the office floor,

NOTE Confidence: 0.7628183

00:23:31.430 --> 00:23:34.966 and I think I'll leave it at that.

NOTE Confidence: 0.7628183

00:23:34.970 --> 00:23:35.660 Thanks everybody.

NOTE Confidence: 0.90003246

00:23:40.260 --> 00:23:45.150 My great presentation. Really excellent.

NOTE Confidence: 0.90003246

00:23:45.150 --> 00:23:47.064 Let's see if there any questions

NOTE Confidence: 0.90003246

00:23:47.064 --> 00:23:48.980 from the audience chat room here.

NOTE Confidence: 0.7520829

00:23:54.300 --> 00:23:56.120 So this is from God.

NOTE Confidence: 0.7520829

00:23:56.120 --> 00:23:57.940 Looks like you're so excited.

NOTE Confidence: 0.7520829

00:23:57.940 --> 00:24:00.040 Talk research on adding tablets and

NOTE Confidence: 0.7520829

00:24:00.040 --> 00:24:02.532 margin molecules or modules in T cells

NOTE Confidence: 0.7520829

00:24:02.532 --> 00:24:04.252 to get around challenging metabolic

NOTE Confidence: 0.7520829

00:24:04.252 --> 00:24:05.950 environment for exhaustion times.

NOTE Confidence: 0.7520829

00:24:05.950 --> 00:24:09.219 So there are there have been, you know, a

NOTE Confidence: 0.7520829

00:24:09.220 --> 00:24:12.226 lot of they're going to have a bunch of

NOTE Confidence: 0.7520829

00:24:12.226 --> 00:24:15.045 studies in mice that are really fantastic.

NOTE Confidence: 0.7520829

00:24:15.050 --> 00:24:17.228 Actually, some of the best ones.

NOTE Confidence: 0.7520829

00:24:17.230 --> 00:24:19.420 I think we're from Sue Keck,

NOTE Confidence: 0.7520829

00:24:19.420 --> 00:24:22.692 used to have a cancer biology lab cancer

NOTE Confidence: 0.7520829

00:24:22.692 --> 00:24:25.286 Menology lab here and now she's at.

NOTE Confidence: 0.7520829

00:24:25.290 --> 00:24:28.231 Assault or or scripts.

NOTE Confidence: 0.7520829

00:24:28.231 --> 00:24:29.339 I don't know which,

NOTE Confidence: 0.7520829

00:24:29.340 --> 00:24:32.208 but she's in California, but absolutely.

NOTE Confidence: 0.7520829

00:24:32.210 --> 00:24:33.902 So there's no question that in

NOTE Confidence: 0.7520829

00:24:33.902 --> 00:24:36.064 mice you can knock down metabolic

NOTE Confidence: 0.7520829

00:24:36.064 --> 00:24:37.516 certain metabolic pathways,

NOTE Confidence: 0.7520829

00:24:37.520 --> 00:24:40.160 making T cells much more tolerant of the

NOTE Confidence: 0.7520829

00:24:40.160 --> 00:24:42.478 toxic micro environment in the tumor.

NOTE Confidence: 0.7520829

00:24:42.480 --> 00:24:45.304 Now that hasn't yet been done in people.

NOTE Confidence: 0.7520829

00:24:45.310 --> 00:24:47.788 I don't think, or I should say,

NOTE Confidence: 0.7520829

00:24:47.790 --> 00:24:49.286 it's not entirely true.

NOTE Confidence: 0.7520829

00:24:49.286 --> 00:24:51.919 People have been doing screens to look

NOTE Confidence: 0.7520829

00:24:51.919 --> 00:24:54.159 at to make T cells more effective,

NOTE Confidence: 0.7520829

00:24:54.160 --> 00:24:55.930 and either party or till,

NOTE Confidence: 0.7520829

00:24:55.930 --> 00:24:58.352 and so there might be a company

NOTE Confidence: 0.7520829

00:24:58.352 --> 00:25:00.530 out there that has done that,

NOTE Confidence: 0.7520829

00:25:00.530 --> 00:25:02.660 or we just don't know.

NOTE Confidence: 0.7520829

00:25:02.660 --> 00:25:03.318 But absolutely,

NOTE Confidence: 0.7520829

00:25:03.318 --> 00:25:05.292 that's a huge area of research

NOTE Confidence: 0.7520829

00:25:05.292 --> 00:25:06.919 by a lot of people,

NOTE Confidence: 0.7520829

00:25:06.920 --> 00:25:08.840 and I think we will definitely

NOTE Confidence: 0.7520829

00:25:08.840 --> 00:25:11.188 at some point the future be seen.

NOTE Confidence: 0.7520829

00:25:11.190 --> 00:25:12.830 Carty cells that have metabolic

NOTE Confidence: 0.7520829

00:25:12.830 --> 00:25:14.470 pathways altered based on this.

NOTE Confidence: 0.6099074

00:25:16.010 --> 00:25:18.836 This is some recent data looking

NOTE Confidence: 0.6099074

00:25:18.836 --> 00:25:21.210 Dyson kinase and using that

NOTE Confidence: 0.6099074

00:25:21.210 --> 00:25:23.605 as a way of overcoming, I'll.

NOTE Confidence: 0.6099074

00:25:23.605 --> 00:25:24.790 Basic resistance checkpoint.

NOTE Confidence: 0.6099074

00:25:24.790 --> 00:25:27.810 There being no troubles me design right now.

NOTE Confidence: 0.8437354

00:25:29.970 --> 00:25:32.070 Look at this picture.

NOTE Confidence: 0.63548505

00:25:35.910 --> 00:25:38.346 Next comment is from Marcus Poison Bird.

NOTE Confidence: 0.63548505

00:25:38.350 --> 00:25:41.860 Nice presentation, just to mention.

NOTE Confidence: 0.63548505

00:25:41.860 --> 00:25:43.344 Let's try this myself.

NOTE Confidence: 0.63548505

00:25:43.344 --> 00:25:44.828 Every efforts include developing

NOTE Confidence: 0.63548505

00:25:44.828 --> 00:25:45.570 Massapequa tillmanns.

NOTE Confidence: 0.63548505

00:25:45.570 --> 00:25:46.310 Yes, absolutely.

NOTE Confidence: 0.63548505

00:25:46.310 --> 00:25:48.540 I need to talk to you.

NOTE Confidence: 0.63548505

00:25:48.540 --> 00:25:49.650 And Marcus, yes,

NOTE Confidence: 0.6581466

00:25:49.650 --> 00:25:51.130 very excited about that.

NOTE Confidence: 0.7907089

00:25:52.890 --> 00:25:53.454 Ask questions.

NOTE Confidence: 0.7907089

00:25:53.454 --> 00:25:54.864 Have party studies been performed

NOTE Confidence: 0.7907089

00:25:54.864 --> 00:25:56.132 patients in multiple Kartik

NOTE Confidence: 0.7907089

00:25:56.132 --> 00:25:57.254 loans simultaneously against

NOTE Confidence: 0.7907089

00:25:57.254 --> 00:25:58.376 multiple different energies?

NOTE Confidence: 0.7907089

00:25:58.380 --> 00:25:59.668 How many tourists again,

NOTE Confidence: 0.7907089

00:25:59.668 --> 00:26:00.956 is it generally available?

NOTE Confidence: 0.7907089

00:26:00.960 --> 00:26:02.252 Is detention targets in

NOTE Confidence: 0.7907089

00:26:02.252 --> 00:26:03.867 different types of solid tumors?

NOTE Confidence: 0.7907089

00:26:03.870 --> 00:26:05.158 So I don't know

NOTE Confidence: 0.7907089

00:26:05.160 --> 00:26:06.520 the answer to that,

NOTE Confidence: 0.7907089

00:26:06.520 --> 00:26:09.358 but I can tell you what I do now.

NOTE Confidence: 0.7907089

00:26:09.360 --> 00:26:11.572 So I think the idea of using

NOTE Confidence: 0.7907089

00:26:11.572 --> 00:26:12.920 multiple parties at once.

NOTE Confidence: 0.7907089

00:26:12.920 --> 00:26:15.006 I think there's a worry that when

NOTE Confidence: 0.7907089

00:26:15.006 --> 00:26:17.628 you do that and I think their data

NOTE Confidence: 0.7907089

00:26:17.628 --> 00:26:19.683 for this that multiple ones within

NOTE Confidence: 0.7907089

00:26:19.683 --> 00:26:22.283 a cell result in a decrement of the

NOTE Confidence: 0.7907089

00:26:22.283 --> 00:26:24.908 actual response that you need to have.

NOTE Confidence: 0.7907089

00:26:24.910 --> 00:26:25.970 A lot of the same.

NOTE Confidence: 0.8840049

00:26:29.320 --> 00:26:32.570 You need to have sort of.

NOTE Confidence: 0.8840049

00:26:32.570 --> 00:26:34.810 The same cars activate it all at

NOTE Confidence: 0.8840049

00:26:34.810 --> 00:26:37.198 once to really get a good response.

NOTE Confidence: 0.8840049

00:26:37.200 --> 00:26:38.860 We have too many androgens.

NOTE Confidence: 0.8840049

00:26:38.860 --> 00:26:40.108 It doesn't, I think,

NOTE Confidence: 0.8840049

00:26:40.108 --> 00:26:41.980 work as well like you basically

NOTE Confidence: 0.8840049

00:26:42.047 --> 00:26:43.487 dilute out the response.

NOTE Confidence: 0.8840049

00:26:43.490 --> 00:26:44.814 That's what I think.

NOTE Confidence: 0.8840049

00:26:44.814 --> 00:26:46.138 He basically diluted out.

NOTE Confidence: 0.8840049

00:26:46.140 --> 00:26:49.332 Now there are there have been people who

NOTE Confidence: 0.8840049

00:26:49.332 --> 00:26:52.200 are designing right now parties that are.

NOTE Confidence: 0.8840049

00:26:52.200 --> 00:26:52.868 Their heritage,

NOTE Confidence: 0.8840049

00:26:52.868 --> 00:26:53.870 their their heterodimers,

NOTE Confidence: 0.8840049

00:26:53.870 --> 00:26:55.545 so one of the antibody

NOTE Confidence: 0.8840049

00:26:55.545 --> 00:26:57.220 chains is to one target.

NOTE Confidence: 0.8840049

00:26:57.220 --> 00:26:59.642 One of the antibody chains to another

NOTE Confidence: 0.8840049

00:26:59.642 --> 00:27:02.205 target that's only going to work if you

NOTE Confidence: 0.8840049

00:27:02.205 --> 00:27:04.589 have really high levels of both antigens.

NOTE Confidence: 0.8840049

00:27:04.590 --> 00:27:05.978 Obviously on the cell,

NOTE Confidence: 0.8840049

00:27:05.978 --> 00:27:08.060 but those are inexperienced or those

NOTE Confidence: 0.8840049

00:27:08.121 --> 00:27:09.993 are being experimented on right now

NOTE Confidence: 0.8840049

00:27:09.993 --> 00:27:12.298 and we'll see how those those work.

NOTE Confidence: 0.8840049

00:27:12.300 --> 00:27:15.306 There's a real question about if you do that,

NOTE Confidence: 0.8840049

00:27:15.310 --> 00:27:17.739 you're not going to get the binding

NOTE Confidence: 0.8840049

00:27:17.739 --> 00:27:20.739 is not going to be as good regarding

NOTE Confidence: 0.8840049

00:27:20.739 --> 00:27:23.350 the number of tumor specific antigens.

NOTE Confidence: 0.8840049

00:27:23.350 --> 00:27:23.863 Again,

NOTE Confidence: 0.8840049

00:27:23.863 --> 00:27:27.967 it probably varies from from cell to cell.

NOTE Confidence: 0.8840049

00:27:27.970 --> 00:27:29.860 That the older studies seem to indicate

NOTE Confidence: 0.8840049

00:27:29.860 --> 00:27:31.569 that these are very old studies,

NOTE Confidence: 0.8840049

00:27:31.570 --> 00:27:34.054 so it's very hard to know what that means.

NOTE Confidence: 0.8840049

00:27:34.060 --> 00:27:36.028 But for the till studies in in some

NOTE Confidence: 0.8840049

00:27:36.028 --> 00:27:38.338 of the patients, when I looked at

NOTE Confidence: 0.8840049

00:27:38.338 --> 00:27:40.930 the ones who had really good responses.

NOTE Confidence: 0.8840049

00:27:40.930 --> 00:27:43.440 It did look as though.

NOTE Confidence: 0.8840049

00:27:43.440 --> 00:27:45.486 It was usually one dominant clone.

NOTE Confidence: 0.8840049

00:27:45.490 --> 00:27:49.246 Sometimes there were two dominant clowns.

NOTE Confidence: 0.8840049

00:27:49.250 --> 00:27:51.162 It's hard to know exactly what those data

NOTE Confidence: 0.8840049

00:27:51.162 --> 00:27:53.358 are was a very limited number of patients,

NOTE Confidence: 0.8840049

00:27:53.360 --> 00:27:55.103 and it's hard to know that they

NOTE Confidence: 0.8840049

00:27:55.103 --> 00:27:56.700 were looking at the right time.

NOTE Confidence: 0.8840049

00:27:56.700 --> 00:27:58.380 Like maybe the clone was there did

NOTE Confidence: 0.8840049

00:27:58.380 --> 00:28:00.556 a lot of what it's supposed to do,

NOTE Confidence: 0.8840049

00:28:00.560 --> 00:28:02.275 and then a lot of it disappeared

NOTE Confidence: 0.8840049

00:28:02.275 --> 00:28:03.899 from the blood for some reason,

NOTE Confidence: 0.8840049

00:28:03.900 --> 00:28:05.442 so it's very hard to know

NOTE Confidence: 0.8840049

00:28:05.442 --> 00:28:06.470 how much that's real.

NOTE Confidence: 0.8840049

00:28:06.470 --> 00:28:08.229 The last thing I would say, though,

NOTE Confidence: 0.8840049

00:28:08.229 --> 00:28:09.981 is that it looks as though the most

NOTE Confidence: 0.8840049

00:28:09.981 --> 00:28:11.608 important antigens are private neoantigens,

NOTE Confidence: 0.8840049

00:28:11.610 --> 00:28:12.634 meaning they're not these

NOTE Confidence: 0.8840049

00:28:12.634 --> 00:28:13.914 big targets that we do,

NOTE Confidence: 0.8840049

00:28:13.920 --> 00:28:15.090 and that's really a worry

NOTE Confidence: 0.8840049

00:28:15.090 --> 00:28:16.750 for car T cells in general,

NOTE Confidence: 0.8840049

00:28:16.750 --> 00:28:17.575 for solid tumors.

NOTE Confidence: 0.8840049

00:28:17.575 --> 00:28:19.920 So that is sort of a separate issue.

NOTE Confidence: 0.6741931

00:28:21.880 --> 00:28:24.100 Terrific Mike is always great presentation,

NOTE Confidence: 0.6741931

00:28:24.100 --> 00:28:27.430 so like to move on to our second speaker,

NOTE Confidence: 0.6741931

00:28:27.430 --> 00:28:29.280 Doctor IRA, Sufi doctor Susan,

NOTE Confidence: 0.6741931

00:28:29.280 --> 00:28:30.390 System Professor of

NOTE Confidence: 0.6741931

00:28:30.390 --> 00:28:31.870 Medicine and Hematology Co.

NOTE Confidence: 0.6741931

00:28:31.870 --> 00:28:34.090 Directed the adult Carty salty program.

NOTE Confidence: 0.6741931

00:28:34.090 --> 00:28:35.770 She received her medical emergency

NOTE Confidence: 0.6741931

00:28:35.770 --> 00:28:38.299 nurse in New York at Stony Brook

NOTE Confidence: 0.6741931

00:28:38.299 --> 00:28:40.645 and completed a fellowship at Yale

NOTE Confidence: 0.6741931

00:28:40.645 --> 00:28:42.230 University School of Medicine.

NOTE Confidence: 0.6741931

00:28:42.230 --> 00:28:44.827 Doctor seems clever work is in the

NOTE Confidence: 0.6741931

00:28:44.827 --> 00:28:46.669 area of hematological in season.

NOTE Confidence: 0.6741931

00:28:46.670 --> 00:28:48.510 Tallest algic stem cell transplantation

NOTE Confidence: 0.6741931

00:28:48.510 --> 00:28:51.586 for his commissions as part of New Sweden

NOTE Confidence: 0.6741931

00:28:51.586 --> 00:28:53.154 legacy programming transplant teams.

NOTE Confidence: 0.6741931

00:28:53.160 --> 00:28:54.845 She developed a strong interest

NOTE Confidence: 0.6741931

00:28:54.845 --> 00:28:55.856 in the president,

NOTE Confidence: 0.6741931

00:28:55.860 --> 00:28:57.550 promised she's focused her efforts

NOTE Confidence: 0.6741931

00:28:57.550 --> 00:28:59.240 in treating patients with aggressive,

NOTE Confidence: 0.6741931

00:28:59.240 --> 00:29:00.962 more focus as part of clinical

NOTE Confidence: 0.6741931

00:29:00.962 --> 00:29:02.976 trials solid in the response to

NOTE Confidence: 0.6741931

00:29:02.976 --> 00:29:04.986 treatment without August or outdated.

NOTE Confidence: 0.6741931

00:29:04.990 --> 00:29:07.655 Translate based on the specifics

NOTE Confidence: 0.6741931

00:29:07.655 --> 00:29:09.254 of specific seeds.

NOTE Confidence: 0.6741931

00:29:09.260 --> 00:29:11.825 As to director of the car T cell therapy

NOTE Confidence: 0.6741931

00:29:11.825 --> 00:29:14.246 product Spell Cancer hospital doctor Soupy.

NOTE Confidence: 0.6741931

00:29:14.250 --> 00:29:16.329 As part of a team that brings

NOTE Confidence: 0.6741931

00:29:16.329 --> 00:29:17.623 interview Milliman therapy treatments

NOTE Confidence: 0.6741931

00:29:17.623 --> 00:29:19.373 options to patients with certain

NOTE Confidence: 0.6741931

00:29:19.373 --> 00:29:21.250 types of blood cancers doctors.

NOTE Confidence: 0.91277057

00:29:22.460 --> 00:29:24.728 Thank you very much for having me.

NOTE Confidence: 0.8840676

00:29:36.100 --> 00:29:37.360 Can you see my slides?

NOTE Confidence: 0.8292955

00:29:39.860 --> 00:29:44.660 Now you know. Well, you know I have.

NOTE Confidence: 0.8093776

00:29:51.770 --> 00:29:53.358 Sorry, just have to share.

NOTE Confidence: 0.8826748

00:30:15.820 --> 00:30:16.290 Yeah.

NOTE Confidence: 0.8732482

00:30:19.060 --> 00:30:19.999 Yep, that's great.

NOTE Confidence: 0.8223237

00:30:22.050 --> 00:30:24.654 Thank you so my focus today is

NOTE Confidence: 0.8223237

00:30:24.654 --> 00:30:27.358 going to be in South therapist

NOTE Confidence: 0.8223237

00:30:27.358 --> 00:30:30.340 for him to logic malignancies and

NOTE Confidence: 0.8223237

00:30:30.340 --> 00:30:33.585 and what we're doing here at Yale.

NOTE Confidence: 0.8223237

00:30:33.590 --> 00:30:35.810 I'm a clinical investigator in

NOTE Confidence: 0.8223237

00:30:35.810 --> 00:30:37.586 lymphoma and cell therapies.

NOTE Confidence: 0.8603855

00:30:41.590 --> 00:30:44.908 I have a couple of bad disclosures.

NOTE Confidence: 0.8641138

00:30:47.220 --> 00:30:50.748 So the I'd like to update you today on

NOTE Confidence: 0.8641138

00:30:50.748 --> 00:30:53.837 some of the FDA approved indications

NOTE Confidence: 0.8641138

00:30:53.837 --> 00:30:57.720 for cell therapies and he malignancies,

NOTE Confidence: 0.8641138

00:30:57.720 --> 00:31:00.720 which are growing by the day.

NOTE Confidence: 0.8641138

00:31:00.720 --> 00:31:03.492 Some of our research strategies to

NOTE Confidence: 0.8641138

00:31:03.492 --> 00:31:05.977 improve response rates and prevent

NOTE Confidence: 0.8641138

00:31:05.977 --> 00:31:08.217 resistance to cell therapies.

NOTE Confidence: 0.8641138

00:31:08.220 --> 00:31:11.220 Some of the challenges we're facing

NOTE Confidence: 0.8641138

00:31:11.220 --> 00:31:13.220 clinically and research wise.

NOTE Confidence: 0.8641138

00:31:13.220 --> 00:31:18.098 And then I'd like to end the presentation by.

NOTE Confidence: 0.8641138

00:31:18.100 --> 00:31:21.306 I'm giving you an idea about the

NOTE Confidence: 0.8641138

00:31:21.306 --> 00:31:24.840 work that we're doing here at DL as

NOTE Confidence: 0.8641138

00:31:24.840 --> 00:31:28.176 part of our immune cell therapy dart

NOTE Confidence: 0.8641138

00:31:28.176 --> 00:31:30.544 for hematologic malignancies and

NOTE Confidence: 0.8641138

00:31:30.544 --> 00:31:34.066 then some of the Inter institutional

NOTE Confidence: 0.8641138

00:31:34.066 --> 00:31:36.358 research collaborations that we

NOTE Confidence: 0.8641138

00:31:36.358 --> 00:31:38.970 have started to work on.

NOTE Confidence: 0.8641138

00:31:38.970 --> 00:31:40.898 So, as Mike mentioned,

NOTE Confidence: 0.8641138

00:31:40.898 --> 00:31:43.308 there's been an evolution in

NOTE Confidence: 0.8641138

00:31:43.308 --> 00:31:45.319 chimeric antigen receptors.

NOTE Confidence: 0.8641138

00:31:45.320 --> 00:31:45.780 Overtime,

NOTE Confidence: 0.8641138

00:31:45.780 --> 00:31:49.460 the once we are still using in the

NOTE Confidence: 0.8641138

00:31:49.460 --> 00:31:52.717 clinic that are commercially approve,

NOTE Confidence: 0.8641138

00:31:52.720 --> 00:31:54.716 our second generation cars,

NOTE Confidence: 0.8641138

00:31:54.716 --> 00:31:57.710 but there is some innovative card

NOTE Confidence: 0.8641138

00:31:57.800 --> 00:32:00.295 design going on including suicide

NOTE Confidence: 0.8641138

00:32:00.295 --> 00:32:03.515 cars as a control mechanism for

NOTE Confidence: 0.8641138

00:32:03.515 --> 00:32:05.420 better toxicity management.

NOTE Confidence: 0.8641138

00:32:05.420 --> 00:32:08.978 This dual targeting cars that express.

NOTE Confidence: 0.8641138

00:32:08.980 --> 00:32:11.488 Two different antigen specific

NOTE Confidence: 0.8641138

00:32:11.488 --> 00:32:15.250 cars by specifics where you have.

NOTE Confidence: 0.8641138

00:32:15.250 --> 00:32:19.303 Add two linked SF Sfes within one

NOTE Confidence: 0.8641138

00:32:19.303 --> 00:32:23.114 core vector and then these TCR

NOTE Confidence: 0.8641138

00:32:23.114 --> 00:32:27.014 mimic cars that are important to

NOTE Confidence: 0.8641138

00:32:27.014 --> 00:32:31.100 address HLA presented antigen swear.

NOTE Confidence: 0.8641138

00:32:31.100 --> 00:32:34.190 You're directing the CFP domain

NOTE Confidence: 0.8641138

00:32:34.190 --> 00:32:37.280 against a peptide HLA complex.

NOTE Confidence: 0.8141577

00:32:39.620 --> 00:32:42.868 Initially the the target was CD 19 for

NOTE Confidence: 0.8141577

00:32:42.868 --> 00:32:45.729 B cell malignancies because as you

NOTE Confidence: 0.8141577

00:32:45.729 --> 00:32:49.380 all know it's a pan bissan marker,

NOTE Confidence: 0.8141577

00:32:49.380 --> 00:32:51.470 its expression is generally restricted

NOTE Confidence: 0.8141577

00:32:51.470 --> 00:32:54.664 to B cells and their precursors and

NOTE Confidence: 0.8141577

00:32:54.664 --> 00:32:57.748 represent it's it's it's surface molecules,

NOTE Confidence: 0.8141577

00:32:57.750 --> 00:33:00.605 so it's represented irrational target

NOTE Confidence: 0.8141577

00:33:00.605 --> 00:33:03.460 for therapy and he malignancies

NOTE Confidence: 0.8141577

00:33:03.546 --> 00:33:06.586 and so all of the agents that are

NOTE Confidence: 0.8141577

00:33:06.586 --> 00:33:08.680 approved for commercial use.

NOTE Confidence: 0.8141577

00:33:08.680 --> 00:33:11.510 Or directed at city 19.

NOTE Confidence: 0.8141577

00:33:11.510 --> 00:33:15.479 So we started initially back in 2019.

NOTE Confidence: 0.8141577

00:33:15.480 --> 00:33:18.888 The first approval with that DISA,

NOTE Confidence: 0.8141577

00:33:18.890 --> 00:33:22.256 gentle occlusal in pediatric LL and

NOTE Confidence: 0.8141577

00:33:22.256 --> 00:33:26.281 subsequent to that we've had a series

NOTE Confidence: 0.8141577

00:33:26.281 --> 00:33:29.086 of approvals including this agenda,

NOTE Confidence: 0.8141577

00:33:29.090 --> 00:33:32.414 Cluzel and Axicabtagene Silo Loosle for

NOTE Confidence: 0.8141577

00:33:32.414 --> 00:33:35.899 aggressive diffuse large B cell lymphoma,

NOTE Confidence: 0.8141577

00:33:35.900 --> 00:33:39.900 transformed follicular lymphoma and then.

NOTE Confidence: 0.8141577

00:33:39.900 --> 00:33:41.304 Lisso catagen merilou.

NOTE Confidence: 0.8141577

00:33:41.304 --> 00:33:45.152 So where you are giving the cells differently

NOTE Confidence: 0.8141577

00:33:45.152 --> 00:33:49.016 because it's a defined CD4 to CD8 ratio,

NOTE Confidence: 0.8141577

00:33:49.020 --> 00:33:51.702 so there is some novelty compared

NOTE Confidence: 0.8141577

00:33:51.702 --> 00:33:54.124 to the two previously approved

NOTE Confidence: 0.8141577

00:33:54.124 --> 00:33:57.394 products and then more recently Brexit

NOTE Confidence: 0.8141577

00:33:57.394 --> 00:34:00.389 catagen auto loosle just in the

NOTE Confidence: 0.8141577

00:34:00.389 --> 00:34:02.939 last year for mantle cell lymphoma.

NOTE Confidence: 0.8141577

00:34:02.940 --> 00:34:03.804 Anan, finally,

NOTE Confidence: 0.8141577

00:34:03.804 --> 00:34:06.828 you know just a few weeks ago

NOTE Confidence: 0.8141577

00:34:06.828 --> 00:34:09.769 Axicabtagene Silo Loosle for relapsed

NOTE Confidence: 0.8141577

00:34:09.769 --> 00:34:11.590 refractory follicular lymphoma.

NOTE Confidence: 0.8141577

00:34:11.590 --> 00:34:14.452 So the response rates that we

NOTE Confidence: 0.8141577

00:34:14.452 --> 00:34:16.360 see with these drugs,

NOTE Confidence: 0.8141577

00:34:16.360 --> 00:34:18.268 particularly in low grade

NOTE Confidence: 0.8141577

00:34:18.268 --> 00:34:19.699 lymphomas like follicular,

NOTE Confidence: 0.8141577

00:34:19.700 --> 00:34:22.220 are extremely good with very high

NOTE Confidence: 0.8141577

00:34:22.220 --> 00:34:24.537 overall response rate and complete

NOTE Confidence: 0.8141577

00:34:24.537 --> 00:34:27.327 response rates in pretreated patients,

NOTE Confidence: 0.8141577

00:34:27.330 --> 00:34:30.571 and then in diffuse large B cell

NOTE Confidence: 0.8141577

00:34:30.571 --> 00:34:33.618 lymphoma and aggressive deal BCL or

NOTE Confidence: 0.8141577

00:34:33.618 --> 00:34:35.706 transformed the complete response

NOTE Confidence: 0.8141577

00:34:35.706 --> 00:34:38.117 rates have varied anywhere from

NOTE Confidence: 0.8141577

00:34:38.117 --> 00:34:41.200 30 to 50% even though the initial

NOTE Confidence: 0.8141577

00:34:41.200 --> 00:34:42.655 overall response rates.

NOTE Confidence: 0.8141577

00:34:42.660 --> 00:34:43.833 Are very high,

NOTE Confidence: 0.8141577

00:34:43.833 --> 00:34:46.570 so these are still very good outcomes.

NOTE Confidence: 0.8141577

00:34:46.570 --> 00:34:48.916 Don't get me wrong for this

NOTE Confidence: 0.8141577

00:34:48.916 --> 00:34:50.089 group of patients,

NOTE Confidence: 0.8141577

00:34:50.090 --> 00:34:52.430 you know the predicted long term.

NOTE Confidence: 0.8141577

00:34:52.430 --> 00:34:55.171 Survival is typically less than 10% when

NOTE Confidence: 0.8141577

00:34:55.171 --> 00:34:58.690 they go on to get CAR T cell therapies.

NOTE Confidence: 0.8141577

00:34:58.690 --> 00:35:01.410 So we've really been able to to cure

NOTE Confidence: 0.8141577

00:35:01.410 --> 00:35:04.158 a good subset of those patients.

NOTE Confidence: 0.8141577

00:35:04.160 --> 00:35:06.120 But as you can see,

NOTE Confidence: 0.8141577

00:35:06.120 --> 00:35:09.369 you know we still have a long way to

NOTE Confidence: 0.8141577

00:35:09.369 --> 00:35:12.890 go in aggressive lymphomas be cause.

NOTE Confidence: 0.8141577

00:35:12.890 --> 00:35:15.050 Even of the patients were cheap

NOTE Confidence: 0.8141577

00:35:15.050 --> 00:35:17.146 complete remission only about 2/3 are

NOTE Confidence: 0.8141577

00:35:17.146 --> 00:35:19.350 able to maintain that, but it's very.

NOTE Confidence: 0.8141577

00:35:19.350 --> 00:35:21.390 It's very exciting because just in

NOTE Confidence: 0.8141577

00:35:21.390 --> 00:35:23.522 the last couple of years we now

NOTE Confidence: 0.8141577

00:35:23.522 --> 00:35:25.879 have all of these products that are

NOTE Confidence: 0.8141577

00:35:25.879 --> 00:35:27.769 commercially approved for use and

NOTE Confidence: 0.8141577

00:35:27.769 --> 00:35:31.860 that we are already using here at Yale.

NOTE Confidence: 0.8141577

00:35:31.860 --> 00:35:35.190 So the other rational target was

NOTE Confidence: 0.8141577

00:35:35.190 --> 00:35:38.370 BCM may in multiple myeloma,

NOTE Confidence: 0.8141577

00:35:38.370 --> 00:35:41.330 which is highly expressed on

NOTE Confidence: 0.8141577

00:35:41.330 --> 00:35:43.106 malignant plasma cells.

NOTE Confidence: 0.8141577

00:35:43.110 --> 00:35:46.548 And we know that higher concentrations

NOTE Confidence: 0.8141577

00:35:46.548 --> 00:35:50.138 of soluble soluble BCM mayor also

NOTE Confidence: 0.8141577

00:35:50.138 --> 00:35:52.542 associated with poor outcomes

NOTE Confidence: 0.8141577

00:35:52.542 --> 00:35:54.946 in in multiple myeloma.

NOTE Confidence: 0.8141577

00:35:54.950 --> 00:35:58.835 This is very essential in regulating B

NOTE Confidence: 0.8141577

00:35:58.835 --> 00:36:02.130 cell maturation and differentiation.

NOTE Confidence: 0.8141577

00:36:02.130 --> 00:36:04.713 And so there have been a series of phase

NOTE Confidence: 0.8141577

00:36:04.713 --> 00:36:07.089 one and two studies looking at PCM.

NOTE Confidence: 0.8141577

00:36:07.090 --> 00:36:10.080 A directed car T cells.

NOTE Confidence: 0.8141577

00:36:10.080 --> 00:36:13.517 And particularly the first one I did,

NOTE Confidence: 0.8141577

00:36:13.520 --> 00:36:14.996 captain be cluzel,

NOTE Confidence: 0.8141577

00:36:14.996 --> 00:36:17.948 is actually very close to approval.

NOTE Confidence: 0.8141577

00:36:17.950 --> 00:36:20.485 These were very heavily pretreated

NOTE Confidence: 0.8141577

00:36:20.485 --> 00:36:23.020 patients with a median number

NOTE Confidence: 0.8141577

00:36:23.108 --> 00:36:25.328 of treatments being about 6.

NOTE Confidence: 0.8141577

00:36:25.330 --> 00:36:27.790 And as you can see,

NOTE Confidence: 0.8141577

00:36:27.790 --> 00:36:30.916 the overall response rates are extremely

NOTE Confidence: 0.8141577

00:36:30.916 --> 00:36:34.330 good and even complete response rates.

NOTE Confidence: 0.8141577

00:36:34.330 --> 00:36:35.800 I'm.

NOTE Confidence: 0.8141577

00:36:35.800 --> 00:36:38.278 Are are very good and so.

NOTE Confidence: 0.7992763

00:36:40.300 --> 00:36:42.905 There is of course toxicity

NOTE Confidence: 0.7992763

00:36:42.905 --> 00:36:46.259 like we saw with anti CD 19,

NOTE Confidence: 0.7992763

00:36:46.260 --> 00:36:47.754 particularly cytokinin release

NOTE Confidence: 0.7992763

00:36:47.754 --> 00:36:49.248 and neurologic toxicity,

NOTE Confidence: 0.7992763

00:36:49.250 --> 00:36:52.799 but again this is a very difficult

NOTE Confidence: 0.7992763

00:36:52.799 --> 00:36:55.209 population of patients to treat.

NOTE Confidence: 0.7992763

00:36:55.210 --> 00:36:58.577 The majority of them were what we

NOTE Confidence: 0.7992763

00:36:58.577 --> 00:37:01.630 call triple refractory to emits an

NOTE Confidence: 0.7992763

00:37:01.630 --> 00:37:04.155 proteasome inhibitors and about 25%

NOTE Confidence: 0.7992763

00:37:04.160 --> 00:37:06.640 of patients were pent. Artifactory,

NOTE Confidence: 0.7992763

00:37:06.640 --> 00:37:10.288 including city 38 monoclonal antibodies so.

NOTE Confidence: 0.7992763

00:37:10.290 --> 00:37:13.237 These are extremely good outcomes for this.

NOTE Confidence: 0.7992763

00:37:13.240 --> 00:37:15.580 For this patient population.

NOTE Confidence: 0.7992763

00:37:15.580 --> 00:37:19.090 And there's now a race to

NOTE Confidence: 0.7992763

00:37:19.204 --> 00:37:22.240 get FDA approval in the USA.

NOTE Confidence: 0.7992763

00:37:22.240 --> 00:37:25.180 Not just only for I decapped

NOTE Confidence: 0.7992763

00:37:25.180 --> 00:37:28.130 agenda cluzel but but also for.

NOTE Confidence: 0.7992763

00:37:28.130 --> 00:37:30.455 For several other products and

NOTE Confidence: 0.7992763

00:37:30.455 --> 00:37:33.316 there are efforts being made to

NOTE Confidence: 0.7992763

00:37:33.316 --> 00:37:35.601 introduce them earlier in earlier

NOTE Confidence: 0.7992763

00:37:35.601 --> 00:37:37.966 phases of disease and comparing

NOTE Confidence: 0.7992763

00:37:37.966 --> 00:37:41.165 them to the standard of care which

NOTE Confidence: 0.7992763

00:37:41.165 --> 00:37:43.439 is autologous stem cell transplant.

NOTE Confidence: 0.7992763

00:37:43.439 --> 00:37:46.610 And then there are already efforts being

NOTE Confidence: 0.7992763

00:37:46.688 --> 00:37:49.978 made to mitigate antigen escape by combining.

NOTE Confidence: 0.7992763

00:37:49.980 --> 00:37:53.332 For example, PC MA Carty with CD19 CAR

NOTE Confidence: 0.7992763

00:37:53.332 --> 00:37:57.298 T or targeting other other antigens.

NOTE Confidence: 0.7992763

00:37:57.300 --> 00:38:02.076 So the same cannot be said for acute

NOTE Confidence: 0.7992763

00:38:02.076 --> 00:38:03.866 myeloid leukemia, unfortunately,

NOTE Confidence: 0.7992763

00:38:03.866 --> 00:38:06.846 which has been, you know,

NOTE Confidence: 0.7992763

00:38:06.850 --> 00:38:10.426 a great challenge over the years.

NOTE Confidence: 0.7992763

00:38:10.430 --> 00:38:14.133 And because many of the potential target

NOTE Confidence: 0.7992763

00:38:14.133 --> 00:38:17.000 antigens are actually intracellular,

NOTE Confidence: 0.7992763

00:38:17.000 --> 00:38:19.944 their tumor associated antigens

NOTE Confidence: 0.7992763

00:38:19.944 --> 00:38:23.624 or or NEO antigens and.

NOTE Confidence: 0.7992763

00:38:23.630 --> 00:38:26.198 And the proteins that are expressed on the

NOTE Confidence: 0.7992763

00:38:26.198 --> 00:38:28.659 surface of the malignant leukemic cells,

NOTE Confidence: 0.7992763

00:38:28.660 --> 00:38:29.659 like City 33,

NOTE Confidence: 0.7992763

00:38:29.659 --> 00:38:31.657 you know some of those markers

NOTE Confidence: 0.7992763

00:38:31.657 --> 00:38:33.319 are also expressed on.

NOTE Confidence: 0.69286615

00:38:35.350 --> 00:38:39.690 Hammer away **** stem cells and so.

NOTE Confidence: 0.69286615

00:38:39.690 --> 00:38:45.858 The trials going on have had to consolidate.

NOTE Confidence: 0.69286615

00:38:45.860 --> 00:38:48.602 Cortisol therapy or or rescue I

NOTE Confidence: 0.69286615

00:38:48.602 --> 00:38:52.370 should say the the mirror with an

NOTE Confidence: 0.69286615

00:38:52.370 --> 00:38:54.826 allogeneic stem cell transplant.

NOTE Confidence: 0.69286615

00:38:54.830 --> 00:38:57.320 So there are several critical

NOTE Confidence: 0.69286615

00:38:57.320 --> 00:39:00.392 and resolved issues with car T

NOTE Confidence: 0.69286615

00:39:00.392 --> 00:39:02.827 cell therapy in he malignancies,

NOTE Confidence: 0.69286615

00:39:02.830 --> 00:39:05.830 and I would categorize them in

NOTE Confidence: 0.69286615

00:39:05.830 --> 00:39:07.830 failure to achieve remission,

NOTE Confidence: 0.69286615

00:39:07.830 --> 00:39:08.834 disease, relapse,

NOTE Confidence: 0.69286615

00:39:08.834 --> 00:39:11.846 toxicities with car T cell and

NOTE Confidence: 0.69286615

00:39:11.846 --> 00:39:14.329 then some of the toxicity.

NOTE Confidence: 0.69286615

00:39:14.330 --> 00:39:17.662 Some of the challenges in moving beyond

NOTE Confidence: 0.69286615

00:39:17.662 --> 00:39:21.828 Bissell LL and diffuse large B cell lymphoma,

NOTE Confidence: 0.69286615

00:39:21.830 --> 00:39:25.330 two other diseases that may not necessarily.

NOTE Confidence: 0.77998555

00:39:27.910 --> 00:39:31.095 Have high expression of of surface markers.

NOTE Confidence: 0.77998555

00:39:31.100 --> 00:39:34.355 Easy to visit that are easy to

NOTE Confidence: 0.77998555

00:39:34.355 --> 00:39:37.154 target with with cortisol therapy

NOTE Confidence: 0.77998555

00:39:37.154 --> 00:39:40.404 or or certain diseases where.

NOTE Confidence: 0.77998555

00:39:40.410 --> 00:39:43.050 Malignant clone, residing inside a lymph

NOTE Confidence: 0.77998555

00:39:43.050 --> 00:39:46.169 node and not necessarily in the circulation.

NOTE Confidence: 0.77998555

00:39:46.170 --> 00:39:49.466 Like with Abyssal LL and so there's that

NOTE Confidence: 0.77998555

00:39:49.466 --> 00:39:52.012 challenge of the tumor microenvironment

NOTE Confidence: 0.77998555

00:39:52.012 --> 00:39:55.827 prohibiting the T cells from getting there.

NOTE Confidence: 0.77998555

00:39:55.830 --> 00:40:00.226 So. What is it that?

NOTE Confidence: 0.77998555

00:40:00.226 --> 00:40:03.040 Predicts outcome from a patient perspective.

NOTE Confidence: 0.77998555

00:40:03.040 --> 00:40:06.768 Ann and risk factors that we can outline

NOTE Confidence: 0.77998555

00:40:06.768 --> 00:40:10.208 before they go onto car T cell therapy.

NOTE Confidence: 0.77998555

00:40:10.210 --> 00:40:12.912 So there was this large study that

NOTE Confidence: 0.77998555

00:40:12.912 --> 00:40:15.726 looked at baseline factors that were

NOTE Confidence: 0.77998555

00:40:15.726 --> 00:40:18.351 associated with worse overall survival

NOTE Confidence: 0.77998555

00:40:18.351 --> 00:40:20.717 and progression free survival in

NOTE Confidence: 0.77998555

00:40:20.717 --> 00:40:23.195 patients who got standard of care.

NOTE Confidence: 0.77998555

00:40:23.200 --> 00:40:23.647 Axicabtagene,

NOTE Confidence: 0.77998555

00:40:23.647 --> 00:40:27.223 Sila Loosle and as you can see here,

NOTE Confidence: 0.77998555

00:40:27.230 --> 00:40:30.032 there were several factors that were

NOTE Confidence: 0.77998555

00:40:30.032 --> 00:40:31.433 statistically significantly associated.

NOTE Confidence: 0.77998555

00:40:31.440 --> 00:40:36.588 With worse outcomes and in particular.

NOTE Confidence: 0.77998555

00:40:36.590 --> 00:40:40.294 I would outline here patients that had high

NOTE Confidence: 0.77998555

00:40:40.294 --> 00:40:44.039 bulk of disease and patients that had,

NOTE Confidence: 0.77998555

00:40:44.040 --> 00:40:45.058 for example,

NOTE Confidence: 0.77998555

00:40:45.058 --> 00:40:47.603 elevated LDH levels pre transplant

NOTE Confidence: 0.77998555

00:40:47.603 --> 00:40:49.633 patients who required bridging

NOTE Confidence: 0.77998555

00:40:49.633 --> 00:40:52.159 therapy also were at higher risk

NOTE Confidence: 0.77998555

00:40:52.159 --> 00:40:54.653 of having worse overall survival

NOTE Confidence: 0.77998555

00:40:54.653 --> 00:40:56.965 and progression free survival,

NOTE Confidence: 0.77998555

00:40:56.970 --> 00:41:00.330 perhaps because both of these things are

NOTE Confidence: 0.77998555

00:41:00.330 --> 00:41:03.917 a surrogate for a higher disease burden,

NOTE Confidence: 0.77998555

00:41:03.920 --> 00:41:07.070 and then Interestingly some of the other

NOTE Confidence: 0.77998555

00:41:07.070 --> 00:41:10.438 factors that were associated with outcomes.

NOTE Confidence: 0.77998555

00:41:10.440 --> 00:41:13.065 Were younger age and also

NOTE Confidence: 0.77998555

00:41:13.065 --> 00:41:16.120 male gender and and that is.

NOTE Confidence: 0.77998555

00:41:16.120 --> 00:41:19.990 Very different from what we see.

NOTE Confidence: 0.77998555

00:41:19.990 --> 00:41:22.790 Included in our prognostic indices

NOTE Confidence: 0.77998555

00:41:22.790 --> 00:41:25.030 for lymphomas where actually

NOTE Confidence: 0.77998555

00:41:25.030 --> 00:41:27.788 older patients tend to do worse,

NOTE Confidence: 0.77998555

00:41:27.790 --> 00:41:32.470 and and this means that we need to really,

NOTE Confidence: 0.77998555

00:41:32.470 --> 00:41:35.380 really look at our prognostic markers

NOTE Confidence: 0.77998555

00:41:35.380 --> 00:41:39.247 in the era of cell therapy and

NOTE Confidence: 0.77998555

00:41:39.247 --> 00:41:42.292 and really redefine what relevant

NOTE Confidence: 0.77998555

00:41:42.292 --> 00:41:44.750 clinical risk factors are.

NOTE Confidence: 0.77998555

00:41:44.750 --> 00:41:48.110 So this is showing a multivariable

NOTE Confidence: 0.77998555

00:41:48.110 --> 00:41:51.103 model of Afexa cottage inside

NOTE Confidence: 0.77998555

00:41:51.103 --> 00:41:53.699 a looser treated patients,

NOTE Confidence: 0.77998555

00:41:53.700 --> 00:41:57.108 where again having.

NOTE Confidence: 0.77998555

00:41:57.110 --> 00:41:59.150 Poor performance status and

NOTE Confidence: 0.77998555

00:41:59.150 --> 00:42:01.190 also having high elevated,

NOTE Confidence: 0.77998555

00:42:01.190 --> 00:42:03.740 high LDH levels is associated

NOTE Confidence: 0.77998555

00:42:03.740 --> 00:42:05.270 with worse progression,

NOTE Confidence: 0.77998555

00:42:05.270 --> 00:42:09.240 free survival and overall survival.

NOTE Confidence: 0.77998555

00:42:09.240 --> 00:42:12.030 And then what about, you know,

NOTE Confidence: 0.77998555

00:42:12.030 --> 00:42:14.350 the the the disease itself?

NOTE Confidence: 0.77998555

00:42:14.350 --> 00:42:18.214 One of the things that we already know

NOTE Confidence: 0.77998555

00:42:18.214 --> 00:42:22.214 is that about 25 to 30% of patients

NOTE Confidence: 0.77998555

00:42:22.214 --> 00:42:26.953 who relapse after car T cell therapy.

NOTE Confidence: 0.77998555

00:42:26.960 --> 00:42:30.272 Experienced loss of CD 19 and

NOTE Confidence: 0.77998555

00:42:30.272 --> 00:42:31.928 this was demonstrated.

NOTE Confidence: 0.77998555

00:42:31.930 --> 00:42:34.540 Inazuma 1 trial and the US

NOTE Confidence: 0.77998555

00:42:34.540 --> 00:42:35.845 Carty Lymphoma consortium.

NOTE Confidence: 0.77998555

00:42:35.850 --> 00:42:38.909 So it's not the majority of patients,

NOTE Confidence: 0.77998555

00:42:38.910 --> 00:42:40.275 particularly in lymphoma,

NOTE Confidence: 0.77998555

00:42:40.275 --> 00:42:45.009 but it is a good subset and so you know what.

NOTE Confidence: 0.77998555

00:42:45.010 --> 00:42:47.770 What can we do?

NOTE Confidence: 0.77998555

00:42:47.770 --> 00:42:50.925 To prevent antigen loss and

NOTE Confidence: 0.77998555

00:42:50.925 --> 00:42:55.250 and then also this PD One PDL,

NOTE Confidence: 0.77998555

00:42:55.250 --> 00:43:00.008 one mediated cortisol inhibition and so.

NOTE Confidence: 0.77998555

00:43:00.010 --> 00:43:03.958 Because we know that PDL one up

NOTE Confidence: 0.77998555

00:43:03.958 --> 00:43:06.510 regulation is actually contributing

NOTE Confidence: 0.77998555

00:43:06.510 --> 00:43:09.518 to Carty exhaustion so.

NOTE Confidence: 0.77998555

00:43:09.520 --> 00:43:11.835 We have this publication nice

NOTE Confidence: 0.77998555

00:43:11.835 --> 00:43:14.580 publication in Nature Medicine from 2020,

NOTE Confidence: 0.77998555

00:43:14.580 --> 00:43:15.040 where.

NOTE Confidence: 0.47944975

00:43:17.140 --> 00:43:21.476 Nirav Shah at. In Wisconsin,

NOTE Confidence: 0.47944975

00:43:21.476 --> 00:43:24.577 actually looked at point of care manufactured

NOTE Confidence: 0.47944975

00:43:24.577 --> 00:43:27.381 by specific anti CD 20 and anti CD 19

NOTE Confidence: 0.47944975

00:43:27.381 --> 00:43:30.240 CAR T cells in relapsed malignancies.

NOTE Confidence: 0.47944975

00:43:30.240 --> 00:43:33.516 In some of these patients had already

NOTE Confidence: 0.47944975

00:43:33.516 --> 00:43:36.889 undergone anti CD 19 CAR T cell therapy.

NOTE Confidence: 0.47944975

00:43:36.890 --> 00:43:39.788 And they do see ongoing responses

NOTE Confidence: 0.47944975

00:43:39.788 --> 00:43:42.204 in about 40% of patients,

NOTE Confidence: 0.47944975

00:43:42.204 --> 00:43:46.192 I think out of about 60% that responded

NOTE Confidence: 0.47944975

00:43:46.192 --> 00:43:50.560 initially and they did not observe loss of

NOTE Confidence: 0.47944975

00:43:50.663 --> 00:43:54.499 CD 19 in progressing patients when they.

NOTE Confidence: 0.47944975

00:43:54.500 --> 00:43:57.620 Target at the tumor with the by specifics.

NOTE Confidence: 0.47944975

00:43:57.620 --> 00:43:59.960 So really very very exciting data.

NOTE Confidence: 0.47944975

00:43:59.960 --> 00:44:03.030 And then just this year.

NOTE Confidence: 0.47944975

00:44:03.030 --> 00:44:06.960 Just this past year at ASCO.

NOTE Confidence: 0.47944975

00:44:06.960 --> 00:44:10.334 They presented results of a first CD

NOTE Confidence: 0.47944975

00:44:10.334 --> 00:44:14.124 19 and CD 22 targeting Bicistronic

NOTE Confidence: 0.47944975

00:44:14.124 --> 00:44:17.854 which is dual antigen targeting.

NOTE Confidence: 0.47944975

00:44:17.860 --> 00:44:19.552 With humanized binders,

NOTE Confidence: 0.47944975

00:44:19.552 --> 00:44:21.808 to reduce image unicity,

NOTE Confidence: 0.47944975

00:44:21.810 --> 00:44:25.765 and in addition to 41 BB costimulatory,

NOTE Confidence: 0.47944975

00:44:25.770 --> 00:44:31.346 they also edit OX 40 to improve persistence.

NOTE Confidence: 0.47944975

00:44:31.350 --> 00:44:35.550 So based on that?

NOTE Confidence: 0.47944975

00:44:35.550 --> 00:44:38.214 Data they went on to do a single

NOTE Confidence: 0.47944975

00:44:38.214 --> 00:44:40.908 arm open label multicenter phase.

NOTE Confidence: 0.47944975

00:44:40.910 --> 00:44:44.151 One two study where they did tool

NOTE Confidence: 0.47944975

00:44:44.151 --> 00:44:47.086 dual targeting of CD 19 and CD 22.

NOTE Confidence: 0.47944975

00:44:47.090 --> 00:44:50.338 But they also added Pember Lizum app

NOTE Confidence: 0.47944975

00:44:50.338 --> 00:44:52.868 for relapsed refractory diffuse large

NOTE Confidence: 0.47944975

00:44:52.868 --> 00:44:55.518 B cell lymphoma and Interestingly.

NOTE Confidence: 0.47944975

00:44:55.520 --> 00:44:58.148 What they saw is there is a high rate

NOTE Confidence: 0.47944975

00:44:58.148 --> 00:45:00.780 of complete response is about 66%,

NOTE Confidence: 0.47944975

00:45:00.780 --> 00:45:03.939 although it's too early to say you know how.

NOTE Confidence: 0.47944975

00:45:03.940 --> 00:45:06.088 If they're going to be durable

NOTE Confidence: 0.47944975

00:45:06.088 --> 00:45:08.159 and how durable they will be,

NOTE Confidence: 0.47944975

00:45:08.160 --> 00:45:10.668 because right now they.

NOTE Confidence: 0.47944975

00:45:10.670 --> 00:45:14.156 They only have short term a data,

NOTE Confidence: 0.47944975

00:45:14.160 --> 00:45:16.998 but Interestingly there was very little

NOTE Confidence: 0.47944975

00:45:16.998 --> 00:45:19.650 toxicity with this particular construct.

NOTE Confidence: 0.47944975

00:45:19.650 --> 00:45:23.754 They did not see any grade three or four

NOTE Confidence: 0.47944975

00:45:23.754 --> 00:45:27.198 cytokine release or neurologic toxicity.

NOTE Confidence: 0.47944975

00:45:27.200 --> 00:45:29.960 And that perhaps really is

NOTE Confidence: 0.47944975

00:45:29.960 --> 00:45:32.168 a reflection of this.

NOTE Confidence: 0.47944975

00:45:32.170 --> 00:45:34.648 Really novel novel technology that they're

NOTE Confidence: 0.47944975

00:45:34.648 --> 00:45:37.589 using with a novel pentameric spacer,

NOTE Confidence: 0.47944975

00:45:37.590 --> 00:45:40.254 and this humanized binders so this

NOTE Confidence: 0.47944975

00:45:40.254 --> 00:45:42.854 data is very exciting because it's

NOTE Confidence: 0.47944975

00:45:42.854 --> 00:45:45.830 a therapy that we might be able to

NOTE Confidence: 0.47944975

00:45:45.916 --> 00:45:49.054 use if approved eventually in the

NOTE Confidence: 0.47944975

00:45:49.054 --> 00:45:51.146 outpatient setting and delivered

NOTE Confidence: 0.47944975

00:45:51.150 --> 00:45:53.254 in the outpatient setting.

NOTE Confidence: 0.47944975

00:45:53.254 --> 00:45:55.884 And that's where they're really

NOTE Confidence: 0.47944975

00:45:55.884 --> 00:45:58.744 going with this. So I'm.

NOTE Confidence: 0.47944975

00:45:58.744 --> 00:46:03.728 What else do we know about the?

NOTE Confidence: 0.47944975

00:46:03.730 --> 00:46:07.984 The disease aspect itself that may

NOTE Confidence: 0.47944975

00:46:07.984 --> 00:46:11.890 make response to cortisol therapy.

NOTE Confidence: 0.47944975

00:46:11.890 --> 00:46:12.392 Challenging,

NOTE Confidence: 0.47944975

00:46:12.392 --> 00:46:15.906 so this data from the Juliet study,

NOTE Confidence: 0.47944975

00:46:15.910 --> 00:46:19.109 which was the global phase two trial

NOTE Confidence: 0.47944975

00:46:19.109 --> 00:46:21.116 of tisagenlecleucel in relapsed

NOTE Confidence: 0.47944975

00:46:21.116 --> 00:46:24.434 refractory diffuse large B cell lymphoma.

NOTE Confidence: 0.47944975

00:46:24.440 --> 00:46:28.052 They looked at the Myc expression and

NOTE Confidence: 0.47944975

00:46:28.052 --> 00:46:31.470 tumor infiltrating T cells in that study,

NOTE Confidence: 0.47944975

00:46:31.470 --> 00:46:34.008 and what they actually found was

NOTE Confidence: 0.47944975

00:46:34.008 --> 00:46:36.333 that baseline mic negative status

NOTE Confidence: 0.47944975

00:46:36.333 --> 00:46:38.569 was actually associated with

NOTE Confidence: 0.47944975

00:46:38.569 --> 00:46:40.246 significantly improved outcome

NOTE Confidence: 0.47944975

00:46:40.246 --> 00:46:43.090 compared to Nick positive patients.

NOTE Confidence: 0.47944975

00:46:43.090 --> 00:46:46.408 And that included also longer median

NOTE Confidence: 0.47944975

00:46:46.408 --> 00:46:50.259 duration of response and overall survival.

NOTE Confidence: 0.47944975

00:46:50.260 --> 00:46:53.062 And when they looked at the

NOTE Confidence: 0.47944975

00:46:53.062 --> 00:46:54.463 tumor microenvironment analysis

NOTE Confidence: 0.47944975

00:46:54.463 --> 00:46:56.670 of the baseline biopsies,

NOTE Confidence: 0.47944975

00:46:56.670 --> 00:46:59.798 what they saw is that lack or low

NOTE Confidence: 0.47944975

00:46:59.798 --> 00:47:01.685 frequency of tumor infiltrating

NOTE Confidence: 0.47944975

00:47:01.685 --> 00:47:05.255 CD 3 positive T cells was also

NOTE Confidence: 0.47944975

00:47:05.255 --> 00:47:07.533 associated with short progression

NOTE Confidence: 0.47944975

00:47:07.533 --> 00:47:10.338 free survival compared to patients

NOTE Confidence: 0.47944975

00:47:10.338 --> 00:47:15.960 that had more than 3% CD 3T cells.

NOTE Confidence: 0.47944975

00:47:15.960 --> 00:47:18.876 In the tumor so taken together,

NOTE Confidence: 0.47944975

00:47:18.880 --> 00:47:21.700 these results suggest that make

NOTE Confidence: 0.47944975

00:47:21.700 --> 00:47:23.956 overexpression or an unfavorable

NOTE Confidence: 0.47944975

00:47:23.956 --> 00:47:25.519 immunosuppressive tumor microenvironment

NOTE Confidence: 0.47944975

00:47:25.519 --> 00:47:28.285 with a restricted T cell response

NOTE Confidence: 0.47944975

00:47:28.285 --> 00:47:30.520 may impact score efficacy in

NOTE Confidence: 0.47944975

00:47:30.520 --> 00:47:32.998 patients with large B cell lymphoma.

NOTE Confidence: 0.8249064

00:47:37.860 --> 00:47:40.795 And then this publication and

NOTE Confidence: 0.8249064

00:47:40.795 --> 00:47:43.730 Oncotarget looked at mutations or

NOTE Confidence: 0.8249064

00:47:43.831 --> 00:47:47.184 copy number losses of CD58 and TP53.

NOTE Confidence: 0.8249064

00:47:47.190 --> 00:47:50.368 Genes in diffuse large B cell lymphoma

NOTE Confidence: 0.8249064

00:47:50.368 --> 00:47:53.837 and showed that these are independent

NOTE Confidence: 0.8249064

00:47:53.837 --> 00:47:56.529 unfavorable prognostic markers so.

NOTE Confidence: 0.891362

00:47:58.900 --> 00:48:04.588 What we know about City 58 is that.

NOTE Confidence: 0.891362

00:48:04.590 --> 00:48:08.027 This is actually binds CD two and

NOTE Confidence: 0.891362

00:48:08.027 --> 00:48:12.137 the T cells and T cell mediated

NOTE Confidence: 0.891362

00:48:12.137 --> 00:48:15.929 cytotoxicity and also NK cell mediated

NOTE Confidence: 0.891362

00:48:16.047 --> 00:48:20.517 cytotoxicity is actually quite important.

NOTE Confidence: 0.891362

00:48:20.520 --> 00:48:23.180 And quite dependent on the

NOTE Confidence: 0.891362

00:48:23.180 --> 00:48:25.308 expression of CD 58.

NOTE Confidence: 0.891362

00:48:25.310 --> 00:48:28.388 On the on the tumor tissue.

NOTE Confidence: 0.891362

00:48:28.390 --> 00:48:31.659 So in Ash 2020 they presented data

NOTE Confidence: 0.891362

00:48:31.659 --> 00:48:34.698 looking at city 58 mutations and

NOTE Confidence: 0.891362

00:48:34.698 --> 00:48:37.268 circulating tumor DNA is tumor

NOTE Confidence: 0.891362

00:48:37.268 --> 00:48:40.674 DNA and they showed that this

NOTE Confidence: 0.891362

00:48:40.674 --> 00:48:43.529 was associated with poor outcome.

NOTE Confidence: 0.891362

00:48:43.530 --> 00:48:46.890 After Axicabtagene sila loosle.

NOTE Confidence: 0.891362

00:48:46.890 --> 00:48:50.117 So these 358 mutations are or loss

NOTE Confidence: 0.891362

00:48:50.117 --> 00:48:53.334 are common and they occur in about

NOTE Confidence: 0.891362

00:48:53.334 --> 00:48:55.960 20% of patients with diffuse large

NOTE Confidence: 0.891362

00:48:55.960 --> 00:48:59.161 B cell lymphoma and then in addition

NOTE Confidence: 0.891362

00:48:59.161 --> 00:49:02.395 to that the protein City 58 protein

NOTE Confidence: 0.891362

00:49:02.395 --> 00:49:04.782 expression is also directly related

NOTE Confidence: 0.891362

00:49:04.782 --> 00:49:08.467 somewhere between 60 to 80% to 70% of

NOTE Confidence: 0.891362

00:49:08.467 --> 00:49:11.680 patients with diffuse large B cell lymphoma.

NOTE Confidence: 0.891362

00:49:11.680 --> 00:49:13.785 His do regulate have deregulation

NOTE Confidence: 0.891362

00:49:13.785 --> 00:49:16.830 of the CD 58 protein expression.

NOTE Confidence: 0.891362

00:49:16.830 --> 00:49:19.278 And as you can see here,

NOTE Confidence: 0.891362

00:49:19.280 --> 00:49:22.288 they were able to show that loss of

NOTE Confidence: 0.891362

00:49:22.288 --> 00:49:24.420 this expression was also associated

NOTE Confidence: 0.891362

00:49:24.420 --> 00:49:27.024 with worst outcomes were in blue.

NOTE Confidence: 0.891362

00:49:27.030 --> 00:49:30.208 Here you see 5058 wild type and

NOTE Confidence: 0.891362

00:49:30.208 --> 00:49:33.469 in Red City 58 alteration so.

NOTE Confidence: 0.891362

00:49:33.470 --> 00:49:36.158 Fewer patients that had loss of

NOTE Confidence: 0.891362

00:49:36.158 --> 00:49:38.529 CD 58 expression actually went

NOTE Confidence: 0.891362

00:49:38.529 --> 00:49:41.019 on to achieve complete remission.

NOTE Confidence: 0.891362

00:49:41.020 --> 00:49:43.995 The majority either did not respond or

NOTE Confidence: 0.891362

00:49:43.995 --> 00:49:46.689 they achieved only partial remission.

NOTE Confidence: 0.891362

00:49:46.690 --> 00:49:50.458 And then they went on to to progress,

NOTE Confidence: 0.891362

00:49:50.460 --> 00:49:50.930 unfortunately.

NOTE Confidence: 0.36321577

00:49:56.180 --> 00:50:00.660 So, meisner. Amazing group.

NOTE Confidence: 0.36321577

00:50:00.660 --> 00:50:03.220 Presented this data very,

NOTE Confidence: 0.36321577

00:50:03.220 --> 00:50:06.142 very interesting this year at ASH

NOTE Confidence: 0.36321577

00:50:06.142 --> 00:50:08.755 where they showed that integrating

NOTE Confidence: 0.36321577

00:50:08.755 --> 00:50:12.199 City 22 costimulation within cars was

NOTE Confidence: 0.36321577

00:50:12.199 --> 00:50:15.680 actually able to overcome City 58 loss

NOTE Confidence: 0.36321577

00:50:15.680 --> 00:50:19.166 in in tumor cells and they tried this

NOTE Confidence: 0.36321577

00:50:19.166 --> 00:50:22.582 both insists an entrance and it wasn't

NOTE Confidence: 0.36321577

00:50:22.582 --> 00:50:25.111 until they integrated it entrance

NOTE Confidence: 0.36321577

00:50:25.111 --> 00:50:28.660 that they saw that they saw these.

NOTE Confidence: 0.36321577

00:50:28.660 --> 00:50:30.076 These results so.

NOTE Confidence: 0.36321577

00:50:30.076 --> 00:50:34.230 This was very eye opening for us because,

NOTE Confidence: 0.36321577

00:50:34.230 --> 00:50:38.108 you know, we used to think that.

NOTE Confidence: 0.36321577

00:50:38.110 --> 00:50:41.680 All of the Co stimulation is

NOTE Confidence: 0.36321577

00:50:41.680 --> 00:50:44.880 coming from from other cells.

NOTE Confidence: 0.36321577

00:50:44.880 --> 00:50:48.720 And we didn't really realize how

NOTE Confidence: 0.36321577

00:50:48.720 --> 00:50:52.501 important actually ceded to City to

NOTE Confidence: 0.36321577

00:50:52.501 --> 00:50:56.400 was in in in car mediated cytotoxicity.

NOTE Confidence: 0.36321577

00:50:56.400 --> 00:50:58.689 So City 5862 was a very novel

NOTE Confidence: 0.36321577

00:50:58.689 --> 00:51:01.530 axis of car resistance that was

NOTE Confidence: 0.36321577

00:51:01.530 --> 00:51:03.894 uncovered through deep correlative

NOTE Confidence: 0.36321577

00:51:03.894 --> 00:51:06.665 studies in patients getting cell

NOTE Confidence: 0.36321577

00:51:06.665 --> 00:51:08.945 therapies and city 58 loss,

NOTE Confidence: 0.36321577

00:51:08.950 --> 00:51:11.740 or mutation pretends a poor outcome,

NOTE Confidence: 0.36321577

00:51:11.740 --> 00:51:14.974 but perhaps we can overcome that by

NOTE Confidence: 0.36321577

00:51:14.974 --> 00:51:17.303 engineering these cars that integrates

NOTE Confidence: 0.36321577

00:51:17.303 --> 00:51:20.313 it is 2 signaling in entrance and

NOTE Confidence: 0.36321577

00:51:20.313 --> 00:51:23.257 this is important because City 58

NOTE Confidence: 0.36321577

00:51:23.257 --> 00:51:26.115 Lawson mutations are also common in.

NOTE Confidence: 0.36321577

00:51:26.115 --> 00:51:28.665 Other cancers in are likely able

NOTE Confidence: 0.36321577

00:51:28.665 --> 00:51:31.101 to mediate resistance to other

NOTE Confidence: 0.36321577

00:51:31.101 --> 00:51:32.727 cars and immunotherapeutics,

NOTE Confidence: 0.36321577

00:51:32.730 --> 00:51:36.293 so it could perhaps be applied in

NOTE Confidence: 0.36321577

00:51:36.293 --> 00:51:38.424 other other malignancies outside

NOTE Confidence: 0.36321577

00:51:38.424 --> 00:51:41.508 of diffuse large B cell lymphoma.

NOTE Confidence: 0.36321577

00:51:41.510 --> 00:51:43.982 So I've spoken to you about

NOTE Confidence: 0.36321577

00:51:43.982 --> 00:51:45.630 the relapse reflect setting,

NOTE Confidence: 0.36321577

00:51:45.630 --> 00:51:49.102 but we are now doing studies pushing these

NOTE Confidence: 0.36321577

00:51:49.102 --> 00:51:51.399 cellular therapies in the second line,

NOTE Confidence: 0.36321577

00:51:51.400 --> 00:51:54.277 and even in the first line settings,

NOTE Confidence: 0.36321577

00:51:54.280 --> 00:51:57.440 Uma 12 looked at very high risk patients

NOTE Confidence: 0.36321577

00:51:57.440 --> 00:52:00.047 with high grade B cell lymphoma.

NOTE Confidence: 0.36321577

00:52:00.050 --> 00:52:01.286 With Myc, BCL,

NOTE Confidence: 0.36321577

00:52:01.286 --> 00:52:03.346 two and BCL 6 translocations,

NOTE Confidence: 0.36321577

00:52:03.350 --> 00:52:05.870 and they did pet directed therapy

NOTE Confidence: 0.36321577

00:52:05.870 --> 00:52:08.443 and for patients who still had

NOTE Confidence: 0.36321577

00:52:08.443 --> 00:52:11.285 disease after two cycles by PET scan.

NOTE Confidence: 0.36321577

00:52:11.290 --> 00:52:14.622 They actually went on to get their

NOTE Confidence: 0.36321577

00:52:14.622 --> 00:52:17.708 T cells collected and then receive.

NOTE Confidence: 0.36321577

00:52:17.710 --> 00:52:23.540 Car T cell therapy. So these are the results.

NOTE Confidence: 0.36321577

00:52:23.540 --> 00:52:26.994 They saw a very high 85% of the

NOTE Confidence: 0.36321577

00:52:26.994 --> 00:52:29.526 overall response rate with 74% CRS.

NOTE Confidence: 0.36321577

00:52:29.526 --> 00:52:32.088 This is a difficult group of patients

NOTE Confidence: 0.36321577

00:52:32.088 --> 00:52:35.108 for us to treat because F oftentimes

NOTE Confidence: 0.36321577

00:52:35.108 --> 00:52:37.894 they do not achieve remission and

NOTE Confidence: 0.36321577

00:52:37.894 --> 00:52:40.389 they progress right through therapy.

NOTE Confidence: 0.36321577

00:52:40.390 --> 00:52:42.545 And then Interestingly also or

NOTE Confidence: 0.36321577

00:52:42.545 --> 00:52:43.838 maybe as expected.

NOTE Confidence: 0.36321577

00:52:43.840 --> 00:52:47.710 The car T cell expansion was greater in this

NOTE Confidence: 0.36321577

00:52:47.710 --> 00:52:51.405 study when compared to Zuma one which were.

NOTE Confidence: 0.36321577

00:52:51.410 --> 00:52:53.778 Patients with relapsed refractory

NOTE Confidence: 0.36321577

00:52:53.778 --> 00:52:57.330 disease was were treated so so

NOTE Confidence: 0.36321577

00:52:57.423 --> 00:53:00.657 higher quality T cells with higher,

NOTE Confidence: 0.36321577

00:53:00.660 --> 00:53:03.548 with higher higher proliferation

NOTE Confidence: 0.36321577

00:53:03.548 --> 00:53:05.714 and higher expansion.

NOTE Confidence: 0.36321577

00:53:05.720 --> 00:53:07.324 So this has not.

NOTE Confidence: 0.36321577

00:53:07.324 --> 00:53:10.229 Obviously it's not prime time for us

NOTE Confidence: 0.36321577

00:53:10.229 --> 00:53:12.314 to change our decision-making and

NOTE Confidence: 0.36321577

00:53:12.314 --> 00:53:15.589 move this to to first line therapy,

NOTE Confidence: 0.36321577

00:53:15.590 --> 00:53:18.410 but there is definitely improved T

NOTE Confidence: 0.36321577

00:53:18.410 --> 00:53:21.149 cell fitness in first line treatment

NOTE Confidence: 0.36321577

00:53:21.149 --> 00:53:24.734 and this may be the wave of the future

NOTE Confidence: 0.36321577

00:53:24.734 --> 00:53:27.597 when we get more long term data.

NOTE Confidence: 0.36321577

00:53:27.600 --> 00:53:31.024 So just to sort of recap for you,

NOTE Confidence: 0.36321577

00:53:31.030 --> 00:53:34.414 some of the studies in relapsed

NOTE Confidence: 0.36321577

00:53:34.414 --> 00:53:36.106 refractory disease and.

NOTE Confidence: 0.36321577

00:53:36.110 --> 00:53:38.606 Also to include some data with

NOTE Confidence: 0.36321577

00:53:38.606 --> 00:53:41.110 CLL and mantle cell lymphoma,

NOTE Confidence: 0.36321577

00:53:41.110 --> 00:53:44.309 as you can see very high overall

NOTE Confidence: 0.36321577

00:53:44.309 --> 00:53:46.658 response rates across the board

NOTE Confidence: 0.36321577

00:53:46.658 --> 00:53:49.310 and then somewhere between 50 and

NOTE Confidence: 0.36321577

00:53:49.310 --> 00:53:51.924 75% complete remission rates in

NOTE Confidence: 0.36321577

00:53:51.924 --> 00:53:53.547 in relapse patients.

NOTE Confidence: 0.36321577

00:53:53.550 --> 00:53:56.609 So where are we going with this?

NOTE Confidence: 0.36321577

00:53:56.610 --> 00:53:57.900 As I mentioned,

NOTE Confidence: 0.36321577

00:53:57.900 --> 00:54:00.910 we're trying to introduce them earlier in

NOTE Confidence: 0.8410666

00:54:00.992 --> 00:54:02.728 the lines of therapies.

NOTE Confidence: 0.8410666

00:54:02.730 --> 00:54:05.650 So many phase three studies looking at second

NOTE Confidence: 0.8410666

00:54:05.650 --> 00:54:08.408 line for transplant eligible patients,

NOTE Confidence: 0.8410666

00:54:08.410 --> 00:54:10.760 randomizing them to transplant versus

NOTE Confidence: 0.8410666

00:54:10.760 --> 00:54:13.961 Carty and then and then perhaps eventually

NOTE Confidence: 0.8410666

00:54:13.961 --> 00:54:17.563 in the front line and then in a LL

NOTE Confidence: 0.8410666

00:54:17.563 --> 00:54:20.197 patients looking at patients one or

NOTE Confidence: 0.8410666

00:54:20.197 --> 00:54:23.020 MRD positive after one line of therapy.

NOTE Confidence: 0.8410666

00:54:23.020 --> 00:54:25.717 And then hopefully some of these phase

NOTE Confidence: 0.8410666

00:54:25.717 --> 00:54:28.342 three data in adults will result in

NOTE Confidence: 0.8410666

00:54:28.342 --> 00:54:30.492 an approval because we still don't

NOTE Confidence: 0.8410666

00:54:30.492 --> 00:54:33.312 have an approval in a LL for patients

NOTE Confidence: 0.8410666

00:54:33.312 --> 00:54:35.367 over the age of 25.

NOTE Confidence: 0.8410666

00:54:35.370 --> 00:54:38.220 So what about alginate cars is,

NOTE Confidence: 0.8410666

00:54:38.220 --> 00:54:41.678 as you know, there are some limitations

NOTE Confidence: 0.8410666

00:54:41.678 --> 00:54:43.919 with autologous CAR T cells,

NOTE Confidence: 0.8410666

00:54:43.920 --> 00:54:46.488 particularly in terms of cost harvesting

NOTE Confidence: 0.8410666

00:54:46.488 --> 00:54:48.819 and manufacturing failures and disease

NOTE Confidence: 0.8410666

00:54:48.819 --> 00:54:51.039 really progressing during manufacture,

NOTE Confidence: 0.8410666

00:54:51.040 --> 00:54:54.554 and we can really bypass a lot

NOTE Confidence: 0.8410666

00:54:54.554 --> 00:54:57.819 of that with donor derived.

NOTE Confidence: 0.8410666

00:54:57.820 --> 00:55:01.020 Sales where we can really reduce the time

NOTE Confidence: 0.8410666

00:55:01.020 --> 00:55:03.239 to infusion significantly and actually

NOTE Confidence: 0.8410666

00:55:03.239 --> 00:55:06.890 be able to take more patients to Carty.

NOTE Confidence: 0.8410666

00:55:06.890 --> 00:55:09.315 And there's an increased probability

NOTE Confidence: 0.8410666

00:55:09.315 --> 00:55:12.252 of healthy cortisol generation and the

NOTE Confidence: 0.8410666

00:55:12.252 --> 00:55:14.886 convenient of repeat dosing if necessary.

NOTE Confidence: 0.8410666

00:55:14.890 --> 00:55:17.417 So these are some of the investigational

NOTE Confidence: 0.8410666

00:55:17.417 --> 00:55:20.280 allogeneic CAR T cells for him malignancies.

NOTE Confidence: 0.7589539

00:55:22.620 --> 00:55:23.991 Targeting different antigens

NOTE Confidence: 0.7589539

00:55:23.991 --> 00:55:25.819 both in lymphomas AALL,

NOTE Confidence: 0.7589539

00:55:25.820 --> 00:55:28.100 but also in multiple myeloma.

NOTE Confidence: 0.7589539

00:55:28.100 --> 00:55:32.213 This is still early phase one phase two data,

NOTE Confidence: 0.7589539

00:55:32.220 --> 00:55:35.604 but I think that this is going to

NOTE Confidence: 0.7589539

00:55:35.604 --> 00:55:39.528 be the wave of the future in Carty,

NOTE Confidence: 0.7589539

00:55:39.530 --> 00:55:42.834 so I'm going to now shift gears to

NOTE Confidence: 0.7589539

00:55:42.834 --> 00:55:45.683 just briefly talk about our cortisol

NOTE Confidence: 0.7589539

00:55:45.683 --> 00:55:48.581 therapy program here at heel we

NOTE Confidence: 0.7589539

00:55:48.676 --> 00:55:51.924 started our efforts in 2018 and were.

NOTE Confidence: 0.7589539

00:55:51.930 --> 00:55:54.305 Able to eventually treat our

NOTE Confidence: 0.7589539

00:55:54.305 --> 00:55:57.289 first patients in January of 2019

NOTE Confidence: 0.7589539

00:55:57.289 --> 00:56:00.391 and then were able to actually

NOTE Confidence: 0.7589539

00:56:00.391 --> 00:56:02.587 achieve fact accreditation after

NOTE Confidence: 0.7589539

00:56:02.587 --> 00:56:05.367 extensive auditing of our program.

NOTE Confidence: 0.7589539

00:56:05.370 --> 00:56:08.466 So this is our organizational chart.

NOTE Confidence: 0.7589539

00:56:08.470 --> 00:56:11.578 As you can see, it includes.

NOTE Confidence: 0.78538793

00:56:13.690 --> 00:56:15.460 Collaboration between multiple

NOTE Confidence: 0.78538793

00:56:15.460 --> 00:56:16.640 different departments.

NOTE Confidence: 0.78538793

00:56:16.640 --> 00:56:19.004 Physicians nursing program self

NOTE Confidence: 0.78538793

00:56:19.004 --> 00:56:21.959 therapy with Diane and alexianne.

NOTE Confidence: 0.78538793

00:56:21.960 --> 00:56:25.310 Also a pheresis with it's

NOTE Confidence: 0.78538793

00:56:25.310 --> 00:56:27.990 neither and Jeannie Hendrickson.

NOTE Confidence: 0.78538793

00:56:27.990 --> 00:56:31.318 We have a really trained group of people

NOTE Confidence: 0.78538793

00:56:31.318 --> 00:56:34.237 being able to freeze the patients and

NOTE Confidence: 0.78538793

00:56:34.237 --> 00:56:36.960 then and then give the conditioning

NOTE Confidence: 0.78538793

00:56:36.960 --> 00:56:40.155 therapy and manage the toxicities.

NOTE Confidence: 0.78538793

00:56:40.160 --> 00:56:43.376 So what have we done in the last

NOTE Confidence: 0.78538793

00:56:43.376 --> 00:56:46.009 two years with 357 patients,

NOTE Confidence: 0.78538793

00:56:46.010 --> 00:56:48.710 some of them with axicabtagene, sidlu,

NOTE Confidence: 0.78538793

00:56:48.710 --> 00:56:50.510 sillence, amethys agenda, cluzel?

NOTE Confidence: 0.78538793

00:56:50.510 --> 00:56:52.630 We're just starting to actually

NOTE Confidence: 0.78538793

00:56:52.630 --> 00:56:54.750 expand to mantle cell lymphoma

NOTE Confidence: 0.78538793

00:56:54.824 --> 00:56:56.808 and then follicular lymphoma.

NOTE Confidence: 0.78538793

00:56:56.810 --> 00:56:59.967 And we've also treated 11 patients on

NOTE Confidence: 0.78538793

00:56:59.967 --> 00:57:02.286 clinical trial for multiple myeloma

NOTE Confidence: 0.78538793

00:57:02.286 --> 00:57:05.359 with anti BCMAM RNA CAR T cells.

NOTE Confidence: 0.78538793

00:57:05.360 --> 00:57:07.994 And as Mike mentioned there are

NOTE Confidence: 0.78538793

00:57:07.994 --> 00:57:11.070 some there is much less toxicity.

NOTE Confidence: 0.78538793

00:57:11.070 --> 00:57:15.070 But there are also challenges in terms of.

NOTE Confidence: 0.78538793

00:57:15.070 --> 00:57:19.270 In terms of the short life of the M RNA,

NOTE Confidence: 0.78538793

00:57:19.270 --> 00:57:21.622 and perhaps the need for frequent

NOTE Confidence: 0.78538793

00:57:21.622 --> 00:57:24.203 dosing or or maybe introducing this

NOTE Confidence: 0.78538793

00:57:24.203 --> 00:57:27.005 in earlier lines of therapy where

NOTE Confidence: 0.78538793

00:57:27.005 --> 00:57:29.942 patients do not have are not very

NOTE Confidence: 0.78538793

00:57:29.942 --> 00:57:32.255 heavily pretreated and do not have

NOTE Confidence: 0.78538793

00:57:32.255 --> 00:57:34.180 an extensive burden of disease

NOTE Confidence: 0.78538793

00:57:34.180 --> 00:57:36.722 with a new approval and multiple

NOTE Confidence: 0.78538793

00:57:36.722 --> 00:57:38.586 myeloma expected this year,

NOTE Confidence: 0.78538793

00:57:38.590 --> 00:57:40.490 there's actually an anticipated

NOTE Confidence: 0.78538793

00:57:40.490 --> 00:57:42.865 significant rise in numbers of

NOTE Confidence: 0.78538793

00:57:42.865 --> 00:57:45.415 patients that were going to be treated.

NOTE Confidence: 0.78538793

00:57:45.420 --> 00:57:48.244 And what that means is that we can

NOTE Confidence: 0.78538793

00:57:48.244 --> 00:57:51.007 collect a lot more data and and do a

NOTE Confidence: 0.78538793

00:57:51.007 --> 00:57:54.665 lot of a lot of studies on patient samples.

NOTE Confidence: 0.78538793

00:57:54.670 --> 00:57:57.575 So this is the yellow advanced cell

NOTE Confidence: 0.78538793

00:57:57.575 --> 00:58:00.689 therapy lab and then this is our

NOTE Confidence: 0.78538793

00:58:00.689 --> 00:58:02.924 immune effector cell therapy dart

NOTE Confidence: 0.78538793

00:58:02.924 --> 00:58:05.621 that Mike and I call lead and and

NOTE Confidence: 0.78538793

00:58:05.621 --> 00:58:08.530 we have a team as he spoke about.

NOTE Confidence: 0.78538793

00:58:08.530 --> 00:58:10.050 I won't belabor this,

NOTE Confidence: 0.78538793

00:58:10.050 --> 00:58:13.224 but we wouldn't be able to do what

NOTE Confidence: 0.78538793

00:58:13.224 --> 00:58:15.660 we do without their amazing work.

NOTE Confidence: 0.78538793

00:58:15.660 --> 00:58:17.640 So this is our portfolio.

NOTE Confidence: 0.78538793

00:58:17.640 --> 00:58:20.016 We have some studies that were

NOTE Confidence: 0.78538793

00:58:20.016 --> 00:58:21.600 opened and finished accrual,

NOTE Confidence: 0.78538793

00:58:21.600 --> 00:58:26.160 but as you can see we have a large number of.

NOTE Confidence: 0.78538793

00:58:26.160 --> 00:58:29.286 Pending studies at the majority of

NOTE Confidence: 0.78538793

00:58:29.286 --> 00:58:32.586 which are very novel because they

NOTE Confidence: 0.78538793

00:58:32.586 --> 00:58:36.499 are either by specific cars or their

NOTE Confidence: 0.78538793

00:58:36.499 --> 00:58:39.808 allogenic cars sitting 19 NK cars and.

NOTE Confidence: 0.84343517

00:58:43.360 --> 00:58:46.168 You know, really also these comparative

NOTE Confidence: 0.84343517

00:58:46.168 --> 00:58:48.040 randomized comparative studies introducing

NOTE Confidence: 0.84343517

00:58:48.105 --> 00:58:50.616 car T cells in the earlier lines of therapy.

NOTE Confidence: 0.84343517

00:58:50.620 --> 00:58:53.824 You know, we really took a set back with

NOTE Confidence: 0.84343517

00:58:53.824 --> 00:58:57.340 with Chobit, but we really hope to be able

NOTE Confidence: 0.84343517

00:58:57.340 --> 00:59:01.103 to open all of these studies in the next

NOTE Confidence: 0.84343517

00:59:01.103 --> 00:59:04.590 few months and start enrolling patients.

NOTE Confidence: 0.84343517

00:59:04.590 --> 00:59:09.725 So this is. These are some of our

NOTE Confidence: 0.84343517

00:59:09.725 --> 00:59:11.849 instruct intra institutional research

NOTE Confidence: 0.84343517

00:59:11.849 --> 00:59:14.027 collaborations with Doctor Mina Xuan,

NOTE Confidence: 0.84343517

00:59:14.030 --> 00:59:16.510 Doctor Jordan Pober in Pathology,

NOTE Confidence: 0.84343517

00:59:16.510 --> 00:59:19.090 looking at the vasculature in the

NOTE Confidence: 0.84343517

00:59:19.090 --> 00:59:21.502 human lymphoma nodal micro environment

NOTE Confidence: 0.84343517

00:59:21.502 --> 00:59:23.966 collaboration with shall issue.

NOTE Confidence: 0.84343517

00:59:23.970 --> 00:59:27.183 Looking at these phase cars for low

NOTE Confidence: 0.84343517

00:59:27.183 --> 00:59:30.244 antigen expressing B cell cancers and

NOTE Confidence: 0.84343517

00:59:30.244 --> 00:59:32.909 then collaborations with City Chen.

NOTE Confidence: 0.84343517

00:59:32.910 --> 00:59:35.898 So in the interest of time,

NOTE Confidence: 0.84343517

00:59:35.900 --> 00:59:38.188 I will just briefly.

NOTE Confidence: 0.84343517

00:59:38.188 --> 00:59:40.887 Discuss these collaborations, but.

NOTE Confidence: 0.84343517

00:59:40.887 --> 00:59:43.818 As you know.

NOTE Confidence: 0.84343517

00:59:43.820 --> 00:59:47.260 Getting the T cells to the tumor tissue

NOTE Confidence: 0.84343517

00:59:47.260 --> 00:59:49.658 and increasing homing is actually

NOTE Confidence: 0.84343517

00:59:49.658 --> 00:59:52.574 quite a challenge for most patients,

NOTE Confidence: 0.84343517

00:59:52.580 --> 00:59:55.442 and there have been several attempts

NOTE Confidence: 0.84343517

00:59:55.442 --> 00:59:58.443 overtime looking at how we can

NOTE Confidence: 0.84343517

00:59:58.443 --> 01:00:00.459 improve homing for lymphocytes.

NOTE Confidence: 0.84343517

01:00:00.460 --> 01:00:02.280 Including cell surface painting,

NOTE Confidence: 0.84343517

01:00:02.280 --> 01:00:03.190 for example,

NOTE Confidence: 0.84343517

01:00:03.190 --> 01:00:05.006 to insert alphabeta integrin

NOTE Confidence: 0.84343517

01:00:05.006 --> 01:00:06.368 into primary lymphocytes,

NOTE Confidence: 0.84343517

01:00:06.370 --> 01:00:09.100 including glyco engineering CAR T cells,

NOTE Confidence: 0.84343517

01:00:09.100 --> 01:00:10.084 for example,

NOTE Confidence: 0.84343517

01:00:10.084 --> 01:00:12.544 to enforce E selectin binding

NOTE Confidence: 0.84343517

01:00:12.544 --> 01:00:15.467 because as many of you may know,

NOTE Confidence: 0.84343517

01:00:15.470 --> 01:00:18.333 car T cells do not express sialyl

NOTE Confidence: 0.84343517

01:00:18.333 --> 01:00:21.840 Lewis X and do not bind deselecting,

NOTE Confidence: 0.84343517

01:00:21.840 --> 01:00:24.624 but we can actually achieve enforce

NOTE Confidence: 0.84343517

01:00:24.624 --> 01:00:28.345 their display on human CAR T cells by

NOTE Confidence: 0.84343517

01:00:28.345 --> 01:00:30.570 surface fucosylation and this will.

NOTE Confidence: 0.84343517

01:00:30.570 --> 01:00:34.050 Results in very robust E selectin

NOTE Confidence: 0.84343517

01:00:34.050 --> 01:00:37.068 binding even under conditions of

NOTE Confidence: 0.84343517

01:00:37.068 --> 01:00:40.662 hemodynamic shear and then also gene

NOTE Confidence: 0.84343517

01:00:40.662 --> 01:00:43.224 therapy using genetically modified

NOTE Confidence: 0.84343517

01:00:43.224 --> 01:00:46.584 lymphocytes targeting VEGF or two

NOTE Confidence: 0.84343517

01:00:46.584 --> 01:00:49.272 in highly vascularized tumors.

NOTE Confidence: 0.84343517

01:00:49.280 --> 01:00:51.905 But unfortunately all of this data is

NOTE Confidence: 0.84343517

01:00:51.905 --> 01:00:55.260 in mice and we don't really know what's

NOTE Confidence: 0.84343517

01:00:55.260 --> 01:00:58.100 happening in the human tumor vessels,

NOTE Confidence: 0.84343517

01:00:58.100 --> 01:01:01.061 and we do not have any idea about the

NOTE Confidence: 0.84343517

01:01:01.061 --> 01:01:04.028 spatial relations of these two of

NOTE Confidence: 0.84343517

01:01:04.028 --> 01:01:06.076 these tumor infiltrating lymphocytes,

NOTE Confidence: 0.84343517

01:01:06.080 --> 01:01:08.620 and so the aim of our study is to employ

NOTE Confidence: 0.84343517

01:01:08.686 --> 01:01:10.324 highly multiplexed immunofluorescent

NOTE Confidence: 0.84343517

01:01:10.324 --> 01:01:13.600 imaging of human lymphomas to specially

NOTE Confidence: 0.84343517

01:01:13.600 --> 01:01:15.739 specially correlate and phenotype.

NOTE Confidence: 0.84343517

01:01:15.740 --> 01:01:17.930 The infiltrating even of sites

NOTE Confidence: 0.84343517

01:01:17.930 --> 01:01:19.682 using formalin fixed and.

NOTE Confidence: 0.84343517

01:01:19.690 --> 01:01:21.870 Not been embedded tissue specimens,

NOTE Confidence: 0.84343517

01:01:21.870 --> 01:01:24.733 and then we want to apply these

NOTE Confidence: 0.84343517

01:01:24.733 --> 01:01:26.970 results to investigate the informer

NOTE Confidence: 0.84343517

01:01:26.970 --> 01:01:29.295 vasculature in car T patients.

NOTE Confidence: 0.84343517

01:01:29.300 --> 01:01:30.611 Pretreatment and posttreatment.

NOTE Confidence: 0.84343517

01:01:30.611 --> 01:01:32.359 This is Nathan Paulsen,

NOTE Confidence: 0.84343517

01:01:32.360 --> 01:01:34.976 one of the residents in pathology,

NOTE Confidence: 0.84343517

01:01:34.980 --> 01:01:38.310 and he's already looked at some.

NOTE Confidence: 0.84343517

01:01:38.310 --> 01:01:40.650 Or lymphoma tissue samples showing that

NOTE Confidence: 0.84343517

01:01:40.650 --> 01:01:42.776 there are differences in expression

NOTE Confidence: 0.84343517

01:01:42.776 --> 01:01:45.266 levels of vascular adhesion molecules.

NOTE Confidence: 0.84343517

01:01:45.270 --> 01:01:46.140 For example,

NOTE Confidence: 0.84343517

01:01:46.140 --> 01:01:48.750 between diffuse large B cell lymphoma,

NOTE Confidence: 0.84343517

01:01:48.750 --> 01:01:51.788 classical Hodgkin lymphoma and T cell rich,

NOTE Confidence: 0.84343517

01:01:51.790 --> 01:01:53.322 large B cell lymphoma.

NOTE Confidence: 0.84343517

01:01:53.322 --> 01:01:56.956 And so we want to do high dimensional

NOTE Confidence: 0.84343517

01:01:56.956 --> 01:02:00.071 phenotyping of these vascular cell

NOTE Confidence: 0.84343517

01:02:00.071 --> 01:02:03.027 in FPED identified tumor samples

NOTE Confidence: 0.84343517

01:02:03.027 --> 01:02:05.507 looking and all of these,

NOTE Confidence: 0.84343517

01:02:05.510 --> 01:02:08.000 all of these vascular markers and

NOTE Confidence: 0.84343517

01:02:08.000 --> 01:02:10.734 the we anticipate to find some

NOTE Confidence: 0.84343517

01:02:10.734 --> 01:02:13.229 correlation of the vessel phenotypes

NOTE Confidence: 0.84343517

01:02:13.229 --> 01:02:16.329 with the abundance and phenotype of

NOTE Confidence: 0.84343517

01:02:16.329 --> 01:02:18.864 the leukocytic infiltrates and to

NOTE Confidence: 0.84343517

01:02:18.864 --> 01:02:22.032 correlate there this with the patients

NOTE Confidence: 0.84343517

01:02:22.032 --> 01:02:25.260 outcomes post car T cell therapy.

NOTE Confidence: 0.84343517

01:02:25.260 --> 01:02:27.400 And.

NOTE Confidence: 0.84343517

01:02:27.400 --> 01:02:28.606 If we're lucky,

NOTE Confidence: 0.84343517

01:02:28.606 --> 01:02:31.986 we're going to be able to show that

NOTE Confidence: 0.84343517

01:02:31.986 --> 01:02:34.346 some two rationale for combining

NOTE Confidence: 0.84343517

01:02:34.346 --> 01:02:38.079 these CAR T cell therapies with

NOTE Confidence: 0.84343517

01:02:38.079 --> 01:02:41.860 antiangiogenic therapies, particularly.

NOTE Confidence: 0.84343517

01:02:41.860 --> 01:02:44.170 And this can be a launching point

NOTE Confidence: 0.84343517

01:02:44.170 --> 01:02:45.160 for us to

NOTE Confidence: 0.8898998

01:02:45.236 --> 01:02:47.192 actually eventually in the

NOTE Confidence: 0.8898998

01:02:47.192 --> 01:02:49.148 future consider a trial.

NOTE Confidence: 0.8898998

01:02:49.150 --> 01:02:52.118 So this is some of the data

NOTE Confidence: 0.8898998

01:02:52.118 --> 01:02:55.040 from Chalet Sues Lab where he's

NOTE Confidence: 0.8898998

01:02:55.040 --> 01:02:57.630 using these face cars where.

NOTE Confidence: 0.809262499999999

01:03:00.190 --> 01:03:02.450 Targeting specifically low density

NOTE Confidence: 0.809262499999999

01:03:02.450 --> 01:03:06.340 surface antigen and he's been able to

NOTE Confidence: 0.809262499999999

01:03:06.340 --> 01:03:08.842 show that car signaling is different

NOTE Confidence: 0.809262499999999

01:03:08.842 --> 01:03:12.405 from T cell receptor signaling and that

NOTE Confidence: 0.809262499999999

01:03:12.405 --> 01:03:15.741 it bypasses certain proteins like latch.

NOTE Confidence: 0.809262499999999

01:03:15.750 --> 01:03:18.886 And has a different pathway that results

NOTE Confidence: 0.809262499999999

01:03:18.886 --> 01:03:21.510 in acting polar MIS polymerization

NOTE Confidence: 0.809262499999999

01:03:21.510 --> 01:03:26.080 compared to TCR signaling, and he's.

NOTE Confidence: 0.809262499999999

01:03:26.080 --> 01:03:28.430 Actually using this information to

NOTE Confidence: 0.809262499999999

01:03:28.430 --> 01:03:31.320 develop these phase cars on lipid

NOTE Confidence: 0.809262499999999

01:03:31.320 --> 01:03:34.050 bilayers that he can modulate to

NOTE Confidence: 0.809262499999999

01:03:34.050 --> 01:03:36.789 recognize low density surface antigens.

NOTE Confidence: 0.809262499999999

01:03:36.790 --> 01:03:40.030 So this is again some of the data that

NOTE Confidence: 0.809262499999999

01:03:40.030 --> 01:03:43.378 he is generated in his lab where he's

NOTE Confidence: 0.809262499999999

01:03:43.378 --> 01:03:47.383 been able to show that Corti signaling

NOTE Confidence: 0.809262499999999

01:03:47.383 --> 01:03:50.055 bypasses this important scaffold

NOTE Confidence: 0.809262499999999

01:03:50.055 --> 01:03:54.610 protein promoting phase separation and.

NOTE Confidence: 0.809262499999999

01:03:54.610 --> 01:03:57.158 He's been able to build this face

NOTE Confidence: 0.809262499999999

01:03:57.158 --> 01:03:59.844 cars where they contain and you

NOTE Confidence: 0.809262499999999

01:03:59.844 --> 01:04:02.369 control modality that can leverage

NOTE Confidence: 0.809262499999999

01:04:02.369 --> 01:04:05.132 domains affecting phase separation to

NOTE Confidence: 0.809262499999999

01:04:05.132 --> 01:04:07.360 modulate Carty activity recognizing

NOTE Confidence: 0.809262499999999

01:04:07.360 --> 01:04:09.574 low density surface antigens.

NOTE Confidence: 0.809262499999999

01:04:09.574 --> 01:04:12.244 He's constructed Roger B cells

NOTE Confidence: 0.809262499999999

01:04:12.244 --> 01:04:15.768 expressing low to High City 19 and

NOTE Confidence: 0.809262499999999

01:04:15.768 --> 01:04:18.360 this is just some very preliminary

NOTE Confidence: 0.809262499999999

01:04:18.360 --> 01:04:21.634 data that he has showing that this

NOTE Confidence: 0.809262499999999

01:04:21.634 --> 01:04:23.961 point phase cars display superior

NOTE Confidence: 0.809262499999999

01:04:23.961 --> 01:04:26.416 activity compared to control parties.

NOTE Confidence: 0.809262499999999

01:04:26.420 --> 01:04:26.881 Again,

NOTE Confidence: 0.809262499999999

01:04:26.881 --> 01:04:30.569 low against low CD 19 so we are

NOTE Confidence: 0.809262499999999

01:04:30.569 --> 01:04:34.651 hoping to look now at some of our

NOTE Confidence: 0.809262499999999

01:04:34.651 --> 01:04:37.289 patients blood samples that have.

NOTE Confidence: 0.809262499999999

01:04:37.290 --> 01:04:40.350 Low CD19 expressing he malignancy's

NOTE Confidence: 0.809262499999999

01:04:40.350 --> 01:04:43.410 either at baseline or following

NOTE Confidence: 0.809262499999999

01:04:43.509 --> 01:04:46.708 treatment with CD19 CAR T cell therapy

NOTE Confidence: 0.809262499999999

01:04:46.708 --> 01:04:49.853 and and and showing how these pace

NOTE Confidence: 0.809262499999999

01:04:49.853 --> 01:04:53.384 cars will be able to to act against

NOTE Confidence: 0.809262499999999

01:04:53.384 --> 01:04:55.894 these low CD19 expressing tumors.

NOTE Confidence: 0.809262499999999

01:04:55.900 --> 01:04:59.092 And then we're also hoping the

NOTE Confidence: 0.809262499999999

01:04:59.092 --> 01:05:01.811 future to collaborate with City

NOTE Confidence: 0.809262499999999

01:05:01.811 --> 01:05:04.781 Chen looking at these dual knock

NOTE Confidence: 0.809262499999999

01:05:04.781 --> 01:05:08.039 in knockout CAR T cells that he's.

NOTE Confidence: 0.809262499999999

01:05:08.040 --> 01:05:12.464 Engineered in his lab targeting two different

NOTE Confidence: 0.809262499999999

01:05:12.464 --> 01:05:15.800 antigens on lymphoma cells and and.

NOTE Confidence: 0.6449524

01:05:19.690 --> 01:05:23.658 Doing PT one knockout.

NOTE Confidence: 0.6449524

01:05:23.660 --> 01:05:26.155 So this is our.

NOTE Confidence: 0.6449524

01:05:26.155 --> 01:05:29.580 This is our group and.

NOTE Confidence: 0.6449524

01:05:29.580 --> 01:05:30.972 Dedicated really dedicated

NOTE Confidence: 0.6449524

01:05:30.972 --> 01:05:33.756 group of people and I'm very

NOTE Confidence: 0.6449524

01:05:33.756 --> 01:05:35.889 thankful for their work and I

NOTE Confidence: 0.6449524

01:05:35.889 --> 01:05:38.323 went a little over time so I'm

NOTE Confidence: 0.6449524

01:05:38.323 --> 01:05:40.238 happy to answer any questions.

NOTE Confidence: 0.87382656

01:05:45.330 --> 01:05:47.110 So I don't think there's

NOTE Confidence: 0.87382656

01:05:47.110 --> 01:05:48.534 any questions on the.

NOTE Confidence: 0.87382656

01:05:48.540 --> 01:05:51.870 Chatroom at this point so.

NOTE Confidence: 0.87382656

01:05:51.870 --> 01:05:54.030 I was thank you for a

NOTE Confidence: 0.87382656

01:05:54.030 --> 01:05:54.750 terrific presentation.

NOTE Confidence: 0.87382656

01:05:54.750 --> 01:05:56.242 Thank you, thank you.