WEBVTT

00:00:00.000 --> 00:00:01.965 Funding for Yale Cancer Answers

NOTE Confidence: 0.95525706

00:00:01.965 --> 00:00:03.930 is provided by Smilow Cancer

NOTE Confidence: 0.95525706

00:00:03.997 --> 00:00:05.697 Hospital and AstraZeneca.

NOTE Confidence: 0.9654582

00:00:07.820 --> 00:00:09.240 Welcome to Yale Cancer Answers

00:00:10.660 --> 00:00:12.730 with your host Dr. Anees Chagpar.

NOTE Confidence: 0.9654582

00:00:12.730 --> 00:00:14.110 Yale Cancer Answers features the latest

NOTE Confidence: 0.9654582

00:00:14.171 --> 00:00:16.246 information on cancer care by

NOTE Confidence: 0.9654582

00:00:16.246 --> 00:00:17.906 welcoming oncologists and specialists

NOTE Confidence: 0.9654582

00:00:17.906 --> 00:00:20.136 who are on the forefront of the

NOTE Confidence: 0.9654582

00:00:20.136 --> 00:00:22.006 battle to fight cancer. This week,

NOTE Confidence: 0.9654582

00:00:22.006 --> 00:00:23.746 it's a conversation about Melanoma

NOTE Confidence: 0.9654582

00:00:23.746 --> 00:00:25.220 with Doctor Harriet Kluger.

NOTE Confidence: 0.9654582

00:00:25.220 --> 00:00:27.428 Doctor Kluger is a professor of

NOTE Confidence: 0.9654582

00:00:27.428 --> 00:00:28.900 medicine and medical oncology

NOTE Confidence: 0.9654582

00:00:28.960 --> 00:00:30.910 at the Yale School of Medicine

NOTE Confidence: 0.9654582

00:00:30.910 --> 00:00:33.002 where Doctor Chagpar is a

NOTE Confidence: 0.9654582

00:00:33.002 --> 00:00:34.450 professor of surgical oncology.

00:00:37.238 --> 00:00:40.320 I thought that we would dive

NOTE Confidence: 0.9624361

00:00:40.320 --> 00:00:42.960 right into the treatment of Melanoma.

NOTE Confidence: 0.9624361

00:00:42.960 --> 00:00:46.040 We've talked a lot on this show

NOTE Confidence: 0.9624361

00:00:46.040 --> 00:00:48.755 about Melanoma being one of the

NOTE Confidence: 0.9624361

00:00:48.755 --> 00:00:50.495 most deadly skin cancers.

NOTE Confidence: 0.9624361

00:00:50.500 --> 00:00:53.118 Can you talk a

NOTE Confidence: 0.9624361

00:00:53.118 --> 00:00:55.988 little bit about how we have

NOTE Confidence: 0.9624361

00:00:55.988 --> 00:00:57.647 traditionally treated Melanoma

NOTE Confidence: 0.9624361

00:00:57.647 --> 00:01:00.710 and where things might be going?

NOTE Confidence: 0.9624361

00:01:00.710 --> 00:01:03.030 Sure, when we

NOTE Confidence: 0.9802106

00:01:03.030 --> 00:01:05.306 think about oncologic treatments,

NOTE Confidence: 0.9802106

00:01:05.306 --> 00:01:08.151 there are three major categories.

NOTE Confidence: 0.9802106

00:01:08.151 --> 00:01:11.260 You can take a cancer out with surgery,

NOTE Confidence: 0.9802106

00:01:11.260 --> 00:01:14.211 you can do radiation, or you can

NOTE Confidence: 0.9802106

00:01:14.211 --> 00:01:16.941 give what we call systemic therapy,

NOTE Confidence: 0.9802106

00:01:16.950 --> 00:01:20.394 which is therapy that's given by mouth.

NOTE Confidence: 0.9802106

00:01:20.400 --> 00:01:23.168 But I feel the vast majority of melanomas

NOTE Confidence: 0.9802106

00:01:23.168 --> 00:01:25.660 are actually discovered really early on

NOTE Confidence: 0.9802106

00:01:25.660 --> 00:01:28.072 when people see a changing mole

NOTE Confidence: 0.9802106

00:01:28.072 --> 00:01:30.087 or a dermatologist might find

NOTE Confidence: 0.9802106

00:01:30.087 --> 00:01:32.055 one on a routine skin exam.

NOTE Confidence: 0.9802106

00:01:32.060 --> 00:01:34.685 Most of the melanomas are then excised,

NOTE Confidence: 0.9802106

00:01:34.690 --> 00:01:37.006 in other words, taken out and

NOTE Confidence: 0.9802106

00:01:37.006 --> 00:01:39.199 nothing further needs to be done,

NOTE Confidence: 0.9802106

00:01:39.200 --> 00:01:41.660 and patients are simply observed.

NOTE Confidence: 0.9802106

00:01:41.660 --> 00:01:43.676 Every so often patients come in

NOTE Confidence: 0.9802106

00:01:43.676 --> 00:01:45.358 without ever knowing that they

NOTE Confidence: 0.9802106

00:01:45.358 --> 00:01:46.978 had a Melanoma in the skin.

NOTE Confidence: 0.9802106

00:01:46.980 --> 00:01:49.170 So it's a Melanoma that has

NOTE Confidence: 0.9802106

00:01:49.170 --> 00:01:51.050 spread beyond the primary site.

NOTE Confidence: 0.9802106

00:01:51.050 --> 00:01:53.241 Or they might have had a primary

NOTE Confidence: 0.9802106

00:01:53.241 --> 00:01:55.368 Melanoma that was removed years ago,

NOTE Confidence: 0.9802106

00:01:55.370 --> 00:01:57.603 but a few cells escaped and are

NOTE Confidence: 0.9802106

00:01:57.603 --> 00:01:59.309 now developing into tumors in

NOTE Confidence: 0.9802106

00:01:59.309 --> 00:02:01.009 other locations in the body.

NOTE Confidence: 0.9802106

00:02:01.010 --> 00:02:03.692 What I do in my clinic is treat with

NOTE Confidence: 0.9802106

00:02:03.692 --> 00:02:05.854 systemic therapy so things that are

NOTE Confidence: 0.9802106

00:02:05.854 --> 00:02:07.980 administered by mouth or by IV

NOTE Confidence: 0.9802106

00:02:07.980 --> 00:02:10.484 so they go all over the body and

NOTE Confidence: 0.9802106

00:02:10.484 --> 00:02:12.956 that's what we're going to talk about

NOTE Confidence: 0.9708482

00:02:12.960 --> 00:02:14.172 primarily today.

NOTE Confidence: 0.9708482

00:02:14.172 --> 00:02:16.659 One of the questions that a lot of

NOTE Confidence: 0.9708482

00:02:16.659 --> 00:02:18.477 patients have is when they have

NOTE Confidence: 0.9708482

00:02:18.477 --> 00:02:20.269 that phenomenon of metastatic Melanoma,

NOTE Confidence: 0.9708482

00:02:20.270 --> 00:02:22.020 so the Melanoma has escaped.

NOTE Confidence: 0.9708482

00:02:22.020 --> 00:02:24.548 It's gone to other parts of the body

NOTE Confidence: 0.9708482

00:02:24.548 --> 00:02:26.687 where surgery really can't remove the

NOTE Confidence: 0.9708482

00:02:26.687 --> 00:02:28.847 Melanoma itself and where

NOTE Confidence: 0.9708482

00:02:28.916 --> 00:02:31.316 you're treating with systemic therapy

NOTE Confidence: 0.9708482

00:02:31.320 --> 00:02:33.235 people wonder about the prognosis

NOTE Confidence: 0.9708482

00:02:33.235 --> 00:02:35.562 and whether in fact they can

NOTE Confidence: 0.9708482

00:02:35.562 --> 00:02:37.267 never be quote cancer free.

NOTE Confidence: 0.9708482

00:02:37.270 --> 00:02:39.496 Can you talk a little bit

NOTE Confidence: 0.98686314

00:02:39.500 --> 00:02:40.541 about that?

NOTE Confidence: 0.98686314

00:02:40.541 --> 00:02:42.623 When I started treating patients

NOTE Confidence: 0.98686314

00:02:42.623 --> 00:02:44.709 with metastatic Melanoma in 2001,

NOTE Confidence: 0.98686314

00:02:44.710 --> 00:02:46.525 if somebody had cancer

NOTE Confidence: 0.98686314

00:02:46.525 --> 00:02:48.786 that had spread beyond the skin

NOTE Confidence: 0.98686314

00:02:48.786 --> 00:02:50.656 and into the internal organs,

NOTE Confidence: 0.98686314

00:02:50.660 --> 00:02:53.018 we would have a frank conversation

NOTE Confidence: 0.98686314

00:02:53.020 --> 00:02:55.620 with the patient and say we're really sorry,

00:02:56.595 --> 00:02:58.220 this is an incurable disease,

NOTE Confidence: 0.98686314

00:02:58.220 --> 00:02:59.845 and on average people live

NOTE Confidence: 0.98686314

00:02:59.845 --> 00:03:01.470 between 6 and 12 months.

NOTE Confidence: 0.98686314

00:03:01.470 --> 00:03:03.678 You should start getting your

NOTE Confidence: 0.98686314

00:03:03.678 --> 00:03:06.024 affairs in order and we will do

NOTE Confidence: 0.98686314

00:03:06.024 --> 00:03:08.300 what we can and hope for the best.

NOTE Confidence: 0.98686314

00:03:08.300 --> 00:03:10.436 At the time we had a chemotherapy called

NOTE Confidence: 0.98686314

00:03:10.436 --> 00:03:12.441 Dacarbazine and an immunotherapy

NOTE Confidence: 0.98686314

00:03:12.441 --> 00:03:14.565 called high dose interleukin two which

NOTE Confidence: 0.98686314

00:03:14.622 --> 00:03:16.417 was very difficult to administer.

NOTE Confidence: 0.98686314

00:03:16.420 --> 00:03:18.406 The Dacarbazine might have shrunk the

NOTE Confidence: 0.98686314

00:03:18.406 --> 00:03:20.320 tumors temporarily for a few weeks,

NOTE Confidence: 0.98686314

00:03:20.320 --> 00:03:22.025 and the high dose interleukin

NOTE Confidence: 0.98686314

00:03:22.025 --> 00:03:23.048 two would result

NOTE Confidence: 0.98686314

00:03:23.050 --> 00:03:24.061 in actual cure,

NOTE Confidence: 0.98686314

00:03:24.061 --> 00:03:27.110 but in a very small percentage of patients,

NOTE Confidence: 0.98686314

00:03:27.110 --> 00:03:28.578 perhaps 4 or 5%.

NOTE Confidence: 0.98686314

00:03:28.578 --> 00:03:30.046 Newer therapies were then

NOTE Confidence: 0.98686314

00:03:30.046 --> 00:03:31.170 developed after that,

NOTE Confidence: 0.98686314

00:03:31.170 --> 00:03:33.722 and by 2005 or 2006 we were seeing

NOTE Confidence: 0.98686314

00:03:33.722 --> 00:03:35.672 that the median survival was

NOTE Confidence: 0.98686314

00:03:35.672 --> 00:03:38.542 actually in the order of one year.

NOTE Confidence: 0.98686314

00:03:38.550 --> 00:03:40.692 At present we don't actually even

NOTE Confidence: 0.98686314

00:03:40.692 --> 00:03:42.979 know what the median survival is,

NOTE Confidence: 0.98686314

00:03:42.980 --> 00:03:45.032 and when a patient comes in

NOTE Confidence: 0.98686314

00:03:45.032 --> 00:03:47.400 and asks what the prognosis is,

NOTE Confidence: 0.98686314

00:03:47.400 --> 00:03:49.950 I say at least 50% chance that

NOTE Confidence: 0.98686314

00:03:49.950 --> 00:03:51.700 we're going to have prolonged

NOTE Confidence: 0.98686314

00:03:51.700 --> 00:03:53.430 survival and if prolonged,

NOTE Confidence: 0.98686314

00:03:53.430 --> 00:03:54.388 disease free.

00:03:54.867 --> 00:03:58.220 But I can't actually tell people if

NOTE Confidence: 0.98686314

00:03:58.306 --> 00:04:01.498 the cancer is ever going to come back.

NOTE Confidence: 0.98686314

00:04:01.500 --> 00:04:03.460 We do believe that we are actually

NOTE Confidence: 0.98686314

00:04:03.460 --> 00:04:05.126 curing a subset of patients

NOTE Confidence: 0.98686314

00:04:05.126 --> 00:04:06.658 who have metastatic Melanoma,

NOTE Confidence: 0.98686314

00:04:06.660 --> 00:04:08.774 including people who've had a lot

NOTE Confidence: 0.98686314

00:04:08.774 --> 00:04:11.187 of disease and disease

NOTE Confidence: 0.98686314

00:04:11.190 --> 00:04:14.088 that's gone to vital organs such as the liver,

NOTE Confidence: 0.98686314

00:04:14.090 --> 00:04:14.740 the lungs,

NOTE Confidence: 0.9739811

00:04:14.740 --> 00:04:17.140 and the brain.

NOTE Confidence: 0.9739811

00:04:17.140 --> 00:04:18.609 When you say prolonged disease free survival,

NOTE Confidence: 0.9739811

00:04:18.610 --> 00:04:20.913 I'm assuming that you mean

NOTE Confidence: 0.9739811

00:04:20.913 --> 00:04:23.520 more than days or weeks and maybe even

NOTE Confidence: 0.9739811

00:04:23.520 --> 00:04:26.039 more than a few years. Is that right?

NOTE Confidence: 0.94539994

00:04:26.710 --> 00:04:28.420 Absolutely. So when we started using

NOTE Confidence: 0.94539994

00:04:28.420 --> 00:04:30.859 the first of the newer immune therapies,

NOTE Confidence: 0.94539994

00:04:30.860 --> 00:04:33.065 a drug called ipilimumab

00:04:37.240 --> 00:04:38.956 we still have patients who were

NOTE Confidence: 0.94539994

00:04:38.956 --> 00:04:41.197 treated in those years who have never

NOTE Confidence: 0.94539994

00:04:41.197 --> 00:04:42.922 required additional treatment and are

NOTE Confidence: 0.94539994

00:04:42.922 --> 00:04:44.888 disease free and living their lives.

NOTE Confidence: 0.94539994

00:04:44.890 --> 00:04:47.186 Now I can't say for sure that

NOTE Confidence: 0.94539994

00:04:47.186 --> 00:04:49.359 it's never going to be a problem,

NOTE Confidence: 0.94539994

00:04:49.360 --> 00:04:51.776 but the chances are that it's not going

NOTE Confidence: 0.94539994

00:04:51.776 --> 00:04:54.457 to be a problem over a decade later.

NOTE Confidence: 0.94539994

00:04:54.460 --> 00:04:56.380 So yes, we're talking about years.

NOTE Confidence: 0.98663855

00:04:56.820 --> 00:04:58.746 We've talked a little

NOTE Confidence: 0.98663855

00:04:58.746 --> 00:05:00.876 bit on this show about immune

NOTE Confidence: 0.98663855

00:05:00.876 --> 00:05:03.186 therapy for a variety of cancers,

NOTE Confidence: 0.98663855

00:05:03.190 --> 00:05:05.170 but it seems that in metastatic

NOTE Confidence: 0.98663855

00:05:05.170 --> 00:05:06.954 Melanoma it really seems to

NOTE Confidence: 0.98663855

00:05:06.954 --> 00:05:08.148 be incredibly effective,

NOTE Confidence: 0.98663855

00:05:08.150 --> 00:05:09.562 especially when you look

NOTE Confidence: 0.98663855

00:05:09.562 --> 00:05:11.327 at how far we've come

00:05:13.598 --> 00:05:15.490 in 2001 telling people that

NOTE Confidence: 0.98663855

00:05:15.490 --> 00:05:17.350 they had less than a year,

NOTE Confidence: 0.98663855

00:05:17.350 --> 00:05:19.828 and to get their affairs in order,

NOTE Confidence: 0.98663855

00:05:19.830 --> 00:05:21.948 why is it that immunotherapy seems

NOTE Confidence: 0.98663855

00:05:21.948 --> 00:05:24.711 to work so well in Melanoma but may

NOTE Confidence: 0.98663855

00:05:24.711 --> 00:05:27.260 not work as well in other cancers?

NOTE Confidence: 0.95165044

00:05:27.790 --> 00:05:29.790 That's an excellent question.

NOTE Confidence: 0.95165044

00:05:29.790 --> 00:05:32.492 Melanoma by nature tends to have

NOTE Confidence: 0.95165044

00:05:32.492 --> 00:05:34.988 more mutations than many other tumors.

NOTE Confidence: 0.95165044

00:05:34.990 --> 00:05:37.390 It's for the most part a

NOTE Confidence: 0.95165044

00:05:37.390 --> 00:05:38.978 sun exposed malignancy.

NOTE Confidence: 0.95165044

00:05:38.978 --> 00:05:42.589 So the sun will cause damage in many,

NOTE Confidence: 0.95165044

00:05:42.590 --> 00:05:45.579 many genes and because of the multiple

NOTE Confidence: 0.95165044

00:05:45.579 --> 00:05:48.550 mutations there are a lot of immune

NOTE Confidence: 0.95165044

00:05:48.550 --> 00:05:50.570 cells that recognize these

NOTE Confidence: 0.95165044

00:05:50.570 --> 00:05:53.174 cancer cells as foreign or bad and

NOTE Confidence: 0.95165044

00:05:53.174 --> 00:05:55.970 with time they get exhausted and

NOTE Confidence: 0.95165044

00:05:55.970 --> 00:05:58.730 these newer drugs will stimulate them.

NOTE Confidence: 0.95165044

00:05:58.730 --> 00:06:00.944 But we probably have a larger

NOTE Confidence: 0.95165044

00:06:00.944 --> 00:06:02.882 repertoire of immune cells in

NOTE Confidence: 0.95165044

00:06:02.882 --> 00:06:04.857 Melanoma than most other cancers,

NOTE Confidence: 0.95165044

00:06:04.860 --> 00:06:07.158 and that's why they respond better.

NOTE Confidence: 0.95165044

00:06:07.160 --> 00:06:09.542 And I think another interesting point

NOTE Confidence: 0.95165044

00:06:09.542 --> 00:06:12.651 to make is that there are

NOTE Confidence: 0.95165044

00:06:12.651 --> 00:06:14.817 two other types of skin cancers.

NOTE Confidence: 0.95165044

00:06:14.820 --> 00:06:17.118 There's a fairly rare skin cancer

NOTE Confidence: 0.95165044

00:06:17.118 --> 00:06:18.650 called Merkel cell carcinoma,

NOTE Confidence: 0.95165044

00:06:18.650 --> 00:06:20.841 which also has a fair number of

NOTE Confidence: 0.95165044

00:06:20.841 --> 00:06:23.264 mutations and also some related and

NOTE Confidence: 0.95165044

00:06:23.264 --> 00:06:25.160 metastatic squamous cell carcinomas and

NOTE Confidence: 0.95165044

00:06:25.160 --> 00:06:27.834 also will respond very well to immunotherapy,

NOTE Confidence: 0.95165044

00:06:27.840 --> 00:06:30.420 better than many other tumor types

NOTE Confidence: 0.95165044

00:06:30.420 --> 00:06:34.119 where we might see response but not for many,

NOTE Confidence: 0.95165044

00:06:34.120 --> 00:06:36.997 many years as we see in Melanoma.

NOTE Confidence: 0.95165044

00:06:37.000 --> 00:06:39.919 But we do think it's related to

NOTE Confidence: 0.95165044

00:06:39.919 --> 00:06:42.338 the tumor mutation burden or the

NOTE Confidence: 0.9840308

00:06:42.340 --> 00:06:45.217 number of mutations that these cells have.

NOTE Confidence: 0.9840308

00:06:45.220 --> 00:06:48.090 And so as you think about immunotherapy,

NOTE Confidence: 0.9840308

00:06:48.090 --> 00:06:50.806 you mentioned that the first

NOTE Confidence: 0.9840308

00:06:50.806 --> 00:06:52.910 generation of these was actually

NOTE Confidence: 0.9840308

00:06:52.910 --> 00:06:55.491 brought into practice in 2005, 2006.

NOTE Confidence: 0.9840308

00:06:55.491 --> 00:06:57.546 Have we developed newer forms

NOTE Confidence: 0.9840308

00:06:57.546 --> 00:06:59.190 of immunotherapy since then?

NOTE Confidence: 0.9840308

00:06:59.190 --> 00:07:01.340 And what's the prognosis?

NOTE Confidence: 0.9840308

00:07:01.340 --> 00:07:03.764 What are some of

NOTE Confidence: 0.9840308

00:07:03.764 --> 00:07:05.380 the exciting developments that

NOTE Confidence: 0.9840308

00:07:05.456 --> 00:07:07.340 have happened over the more

NOTE Confidence: 0.9641474

00:07:07.340 --> 00:07:08.540 recent time?

NOTE Confidence: 0.9641474

00:07:08.540 --> 00:07:10.940 So there are many exciting developments,

NOTE Confidence: 0.9641474

00:07:10.940 --> 00:07:13.286 the first drug Ipilimumab

NOTE Confidence: 0.9641474

00:07:13.286 --> 00:07:15.733 was brought into

NOTE Confidence: 0.9641474

00:07:15.733 --> 00:07:18.139 clinical trials in those years.

NOTE Confidence: 0.9641474

00:07:18.140 --> 00:07:20.140 But it actually took many

NOTE Confidence: 0.9641474

00:07:20.140 --> 00:07:22.140 years to achieve FDA approval.

NOTE Confidence: 0.9641474

00:07:22.140 --> 00:07:24.540 It was only FDA approved for

NOTE Confidence: 0.9641474

00:07:24.540 --> 00:07:26.140 metastatic Melanoma in 2011,

NOTE Confidence: 0.9641474

00:07:26.140 --> 00:07:28.140 so the first Ipilimumab,

NOTE Confidence: 0.9641474

00:07:28.140 --> 00:07:30.140 results in nice tumor regression,

NOTE Confidence: 0.9641474

00:07:30.140 --> 00:07:32.516 in maybe 10% of

NOTE Confidence: 0.9641474

00:07:32.516 --> 00:07:34.880 patient's, but the second generation drug is

NOTE Confidence: 0.9641474

00:07:34.953 --> 00:07:37.833 a drug that targets a molecule called PD1,

NOTE Confidence: 0.9641474

00:07:37.840 --> 00:07:40.430 which stands for programmed death one.

NOTE Confidence: 0.9641474

00:07:40.430 --> 00:07:42.482 There were two that were first

NOTE Confidence: 0.9641474

00:07:42.482 --> 00:07:44.500 given to patients with Melanoma.

NOTE Confidence: 0.9641474

00:07:44.500 --> 00:07:45.610 Nivolumab and pembrolizumab,

NOTE Confidence: 0.9641474

00:07:45.610 --> 00:07:48.200 also known as Opdivo and Keytruda.

NOTE Confidence: 0.9641474

00:07:48.200 --> 00:07:48.625 Subsequently,

NOTE Confidence: 0.9641474

00:07:48.625 --> 00:07:50.750 many other companies have developed

NOTE Confidence: 0.9641474

00:07:50.750 --> 00:07:53.077 drugs that inhibit PD one and

NOTE Confidence: 0.9641474

00:07:53.077 --> 00:07:55.044 this one seemed to be the better

NOTE Confidence: 0.9641474

00:07:55.044 --> 00:07:56.709 target for the immunotherapy.

NOTE Confidence: 0.9641474

00:07:56.710 --> 00:07:59.670 So when we give this to Melanoma patients,

NOTE Confidence: 0.9641474

00:07:59.670 --> 00:08:02.726 instead of seeing nice responses in maybe 10

NOTE Confidence: 0.9641474

00:08:02.730 --> 00:08:05.214 percent of patients we will see good

NOTE Confidence: 0.9641474

00:08:05.214 --> 00:08:08.000 responses in 30 to 40% of patients,

NOTE Confidence: 0.9641474

00:08:08.000 --> 00:08:08.810 and interestingly,

NOTE Confidence: 0.9641474

00:08:08.810 --> 00:08:10.430 this is less toxic,

NOTE Confidence: 0.9641474

00:08:10.430 --> 00:08:12.734 so the second generation was both

NOTE Confidence: 0.9641474

00:08:12.734 --> 00:08:14.773 more effective and less toxic

NOTE Confidence: 0.9641474

00:08:14.773 --> 00:08:16.497 than the first generation.

NOTE Confidence: 0.9641474

00:08:16.500 --> 00:08:19.335 Then the question asked in around 2009,

NOTE Confidence: 0.9641474

00:08:19.340 --> 00:08:21.776 when we already had a little

NOTE Confidence: 0.9641474

00:08:21.776 --> 00:08:24.199 bit of experience with these PD one

NOTE Confidence: 0.9641474

00:08:24.200 --> 00:08:26.462 inhibitors was what would happen

NOTE Confidence: 0.9641474

00:08:26.462 --> 00:08:29.459 if we give the two drugs together.

NOTE Confidence: 0.9641474

00:08:29.460 --> 00:08:31.956 So these two classes of drugs

NOTE Confidence: 0.9641474

00:08:31.956 --> 00:08:32.788 target non redundant pathways

NOTE Confidence: 0.9641474

00:08:32.790 --> 00:08:34.848 in the immune cell and

NOTE Confidence: 0.9641474

00:08:34.848 --> 00:08:36.630 its interaction with cancer cells.

NOTE Confidence: 0.9641474

00:08:36.630 --> 00:08:39.062 So if we inhibited two different

NOTE Confidence: 0.9641474

00:08:39.062 --> 00:08:41.287 places in theory we will get enhanced

NOTE Confidence: 0.9641474

00:08:41.287 --> 00:08:43.609 activation of our chief immune cell,

NOTE Confidence: 0.9641474

00:08:43.610 --> 00:08:45.350 which is called a T cell.

NOTE Confidence: 0.9641474

00:08:45.350 --> 00:08:47.822 And indeed this was the case, when we

NOTE Confidence: 0.9641474

00:08:47.822 --> 00:08:50.238 give the two together in Melanoma,

NOTE Confidence: 0.9641474

00:08:50.240 --> 00:08:52.334 we now see very nice responses

NOTE Confidence: 0.9641474

00:08:52.334 --> 00:08:54.540 in excess of 55% of patients.

NOTE Confidence: 0.9641474

00:08:54.540 --> 00:08:56.970 So the two together is better

NOTE Confidence: 0.9641474

00:08:56.970 --> 00:08:57.780 than either one alone.

NOTE Confidence: 0.9221058

00:08:57.780 --> 00:08:59.796 Just to clarify,

NOTE Confidence: 0.9221058

00:08:59.800 --> 00:09:01.876 when you say the two together

NOTE Confidence: 0.9221058

00:09:01.876 --> 00:09:03.839 you mean Ipilimumab and

NOTE Confidence: 0.9221058

00:09:03.840 --> 00:09:05.530 pembrolizumab.

NOTE Confidence: 0.9221058

00:09:05.530 --> 00:09:07.582 The studies have used Ipilimumab

NOTE Confidence: 0.9221058

00:09:07.582 --> 00:09:09.668 and nivolumab simply because both of

NOTE Confidence: 0.9221058

00:09:09.668 --> 00:09:11.618 these drugs were developed by the

NOTE Confidence: 0.9221058

00:09:11.618 --> 00:09:13.618 same company. But yes, it's been

NOTE Confidence: 0.9221058

00:09:13.620 --> 00:09:15.300 given with pembrolizumab as well,

NOTE Confidence: 0.9221058

00:09:15.300 --> 00:09:16.652 but not Ipilimumab and

NOTE Confidence: 0.9221058

00:09:16.652 --> 00:09:17.998 pembrolizumab, which both target

NOTE Confidence: 0.9221058

00:09:18.000 --> 00:09:19.734 PD 1 correct. There's no point

NOTE Confidence: 0.9221058

00:09:19.734 --> 00:09:21.766 in giving two drugs that inhibit

NOTE Confidence: 0.9221058

00:09:21.766 --> 00:09:23.386 the same target concurrently,

NOTE Confidence: 0.9221058

00:09:23.390 --> 00:09:25.790 so by that point, did we switch all

NOTE Confidence: 0.9221058

00:09:25.790 --> 00:09:28.247 of our patients to dual therapy?

NOTE Confidence: 0.9221058

00:09:28.250 --> 00:09:29.330 Actually no, because

NOTE Confidence: 0.9675461

00:09:29.330 --> 00:09:31.130 remember, some of the patients

NOTE Confidence: 0.9675461

00:09:31.130 --> 00:09:32.930 do very well with monotherapy.

NOTE Confidence: 0.9675461

00:09:32.930 --> 00:09:36.170 30-40% will do well with the one drug,

NOTE Confidence: 0.9675461

00:09:36.170 --> 00:09:37.562 the PD one inhibitor.

NOTE Confidence: 0.9675461

00:09:37.562 --> 00:09:40.107 So we're trying very hard to select

NOTE Confidence: 0.9675461

00:09:40.107 --> 00:09:42.405 those patients who are more likely

NOTE Confidence: 0.9675461

00:09:42.405 --> 00:09:44.961 to respond to one drug and also

NOTE Confidence: 0.9675461

00:09:44.961 --> 00:09:46.965 patients who might not be able

NOTE Confidence: 0.9675461

00:09:46.970 --> 00:09:48.562 to tolerate extensive toxicity.

NOTE Confidence: 0.9675461

00:09:48.562 --> 00:09:50.950 The toxicities are the main problem, it

NOTE Confidence: 0.9675461

00:09:51.017 --> 00:09:52.947 depends where the patient lives,

NOTE Confidence: 0.9675461

00:09:52.950 --> 00:09:54.366 how socially and economically

NOTE Confidence: 0.9675461

00:09:54.366 --> 00:09:55.428 robust they are,

NOTE Confidence: 0.9675461

00:09:55.430 --> 00:09:56.674 whether they're associated with

NOTE Confidence: 0.9675461

00:09:56.674 --> 00:09:58.540 a health care system that can

NOTE Confidence: 0.9675461

00:09:58.596 --> 00:10:00.030 support extensive toxicities,

NOTE Confidence: 0.9675461

00:10:00.030 --> 00:10:02.242 but when we have patients who've got

NOTE Confidence: 0.9675461

00:10:02.242 --> 00:10:04.037 aggressive disease and particularly young

NOTE Confidence: 0.9675461

00:10:04.037 --> 00:10:06.407 patients with no other medical problems,

NOTE Confidence: 0.9675461

00:10:06.410 --> 00:10:09.950 we do start off with the two drugs up front.

NOTE Confidence: 0.9675461

00:10:09.950 --> 00:10:12.398 There are other people in the

NOTE Confidence: 0.9675461

00:10:12.398 --> 00:10:14.786 Melanoma field who might start with

NOTE Confidence: 0.9675461

00:10:14.786 --> 00:10:17.506 one and then add the second one if

NOTE Confidence: 0.9675461

00:10:17.581 --> 00:10:20.150 the first one alone does not work.

NOTE Confidence: 0.9675461

00:10:20.150 --> 00:10:22.488 So a lot of refinement of these

NOTE Confidence: 0.9675461

00:10:22.488 --> 00:10:24.249 regimens still needs to be done,

NOTE Confidence: 0.9675461

00:10:24.250 --> 00:10:26.658 and there are many studies looking at how

NOTE Confidence: 0.9675461

00:10:26.658 --> 00:10:29.285 much to give, when to give, what sequence, etc.

00:10:29.769 --> 00:10:34.080 It takes years to sort all of this out.

NOTE Confidence: 0.9675461

00:10:34.080 --> 00:10:37.762 I also want to add that we now have a third

NOTE Confidence: 0.9675461

00:10:37.762 --> 00:10:40.894 target that is looking very promising

NOTE Confidence: 0.9675461

00:10:40.900 --> 00:10:41.700 in Melanoma,

NOTE Confidence: 0.9675461

00:10:41.700 --> 00:10:44.100 there's a target called LAG-3.

NOTE Confidence: 0.9675461

00:10:44.100 --> 00:10:46.963 It's an antigen that's expressed

NOTE Confidence: 0.9675461

00:10:46.963 --> 00:10:50.118 on these same immune cells or T cells,

NOTE Confidence: 0.9675461

00:10:50.120 --> 00:10:53.144 and when you give inhibitors of LAG-3

NOTE Confidence: 0.9675461

00:10:53.144 --> 00:10:55.940 together with PD one inhibitors,

NOTE Confidence: 0.9675461

00:10:55.940 --> 00:10:58.332 it does appear that it's going to be

NOTE Confidence: 0.9675461

00:10:58.332 --> 00:11:00.497 better than PD one inhibitors alone.

NOTE Confidence: 0.9675461

00:11:00.500 --> 00:11:03.092 The data are still very new and more

NOTE Confidence: 0.9675461

00:11:03.092 --> 00:11:06.049 maturity of the data is going to be required.

NOTE Confidence: 0.9675461

00:11:06.050 --> 00:11:07.028 In other words,

NOTE Confidence: 0.9675461

00:11:07.028 --> 00:11:09.310 we need to follow patients for much

NOTE Confidence: 0.9611162

00:11:09.310 --> 00:11:11.266 longer to make sure that it

NOTE Confidence: 0.9611162

00:11:11.266 --> 00:11:13.220 actually holds up.

NOTE Confidence: 0.9611162

00:11:13.220 --> 00:11:15.170 Clinical trials for that drug are

NOTE Confidence: 0.9611162

00:11:15.170 --> 00:11:15.822 currently ongoing.

00:11:17.117 --> 00:11:19.019 It's already in a phase three

NOTE Confidence: 0.9611162

00:11:19.019 --> 00:11:20.703 study which is completed accrual

NOTE Confidence: 0.9611162

00:11:20.703 --> 00:11:22.713 and the first data do suggest

NOTE Confidence: 0.9611162

00:11:22.713 --> 00:11:24.694 that the two drugs are better

NOTE Confidence: 0.9611162

00:11:24.694 --> 00:11:26.254 than the nivolumab alone.

NOTE Confidence: 0.9677876

00:11:26.610 --> 00:11:28.242 And has anybody thought

NOTE Confidence: 0.9677876

00:11:28.242 --> 00:11:29.880 about adding Ipilimumab?

NOTE Confidence: 0.9677876

00:11:29.880 --> 00:11:32.718 Yes, there we again will run into

NOTE Confidence: 0.9677876

00:11:32.718 --> 00:11:35.426 problems with side effects and we

NOTE Confidence: 0.9677876

00:11:35.426 --> 00:11:37.953 have to be very careful when we

NOTE Confidence: 0.9677876

00:11:37.953 --> 00:11:40.930 mix 3 drugs and this takes a

NOTE Confidence: 0.9677876

00:11:40.930 --> 00:11:42.262 long time to work all of this out.

00:11:45.461 --> 00:11:48.072 It sounds like with now the three

NOTE Confidence: 0.9677876

00:11:48.160 --> 00:11:50.730 kind of tiers of immunotherapy

NOTE Confidence: 0.9677876

00:11:50.730 --> 00:11:52.786 that you're talking about,

NOTE Confidence: 0.9677876

00:11:52.790 --> 00:11:54.830 upwards of 55, maybe even

NOTE Confidence: 0.9677876

00:11:54.830 --> 00:11:57.096 close to 65-75% of patients

NOTE Confidence: 0.9677876

00:11:57.096 --> 00:11:58.650 might have prolonged

NOTE Confidence: 0.9677876

00:11:58.650 --> 00:12:00.510 disease free survival.

NOTE Confidence: 0.98488665

00:12:00.510 --> 00:12:02.624 We don't know yet about the 65-75%.

NOTE Confidence: 0.98488665

00:12:03.533 --> 00:12:05.038 That's what we're shooting for,

NOTE Confidence: 0.98488665

00:12:05.040 --> 00:12:05.896 and ultimately,

NOTE Confidence: 0.98488665

00:12:05.896 --> 00:12:08.464 we're going to shoot for 100%.

NOTE Confidence: 0.98488665

00:12:08.470 --> 00:12:11.302 I also want to add that this is

NOTE Confidence: 0.98488665

00:12:11.302 --> 00:12:14.138 just one type of immune therapy.

NOTE Confidence: 0.98488665

00:12:14.140 --> 00:12:16.570 We call it immune checkpoint inhibitors,

NOTE Confidence: 0.98488665

00:12:16.570 --> 00:12:19.279 so the checkpoint refers to a negative

NOTE Confidence: 0.98488665

00:12:19.279 --> 00:12:21.430 regulator of the immune cells,

NOTE Confidence: 0.98488665

00:12:21.430 --> 00:12:23.924 and that's what these drugs target.

NOTE Confidence: 0.98488665

00:12:23.924 --> 00:12:26.546 The various other types of cellular

NOTE Confidence: 0.98488665

00:12:26.546 --> 00:12:28.950 manipulations that we can give to

NOTE Confidence: 0.98488665

00:12:28.950 --> 00:12:31.146 activate the immune system against cancer,

NOTE Confidence: 0.98488665

00:12:31.150 --> 00:12:32.874 but the immune checkpoint

NOTE Confidence: 0.98488665

00:12:32.874 --> 00:12:34.167 inhibitors specifically refers

NOTE Confidence: 0.98488665

00:12:34.167 --> 00:12:36.646 to molecules on immune cells and

NOTE Confidence: 0.98488665

00:12:36.646 --> 00:12:38.516 cancer cells that have crosstalk.

NOTE Confidence: 0.98488665

00:12:38.520 --> 00:12:41.088 They talk to each other and the cancer

NOTE Confidence: 0.98488665

00:12:41.088 --> 00:12:43.311 cell will suppress an immune cell so

NOTE Confidence: 0.98488665

00:12:43.311 --> 00:12:45.829 that it remains alive.

NOTE Confidence: 0.98488665

00:12:45.830 --> 00:12:48.609 And so this is just one approach

NOTE Confidence: 0.98488665

00:12:48.609 --> 00:12:50.400 to immunotherapy for cancer.

NOTE Confidence: 0.9878226

00:12:51.060 --> 00:12:52.620 Well, we certainly want to

NOTE Confidence: 0.9878226

00:12:52.620 --> 00:12:54.682 find out more about the other

NOTE Confidence: 0.9878226

00:12:54.682 --> 00:12:56.430 approaches to immune therapy.

NOTE Confidence: 0.9878226

00:12:56.430 --> 00:12:58.966 We talk a lot on this show about

NOTE Confidence: 0.9878226

00:12:58.966 --> 00:13:00.370 immune checkpoint inhibitors,

NOTE Confidence: 0.9878226

00:13:00.370 --> 00:13:02.350 but certainly thinking about other ways

NOTE Confidence: 0.9878226

00:13:02.350 --> 00:13:05.318 that we can use and manipulate the immune

NOTE Confidence: 0.9878226

00:13:05.318 --> 00:13:07.298 system to fight metastatic Melanoma

NOTE Confidence: 0.9878226

00:13:07.298 --> 00:13:09.678 will be very exciting to learn about,

NOTE Confidence: 0.9878226

00:13:09.680 --> 00:13:12.032 but first we're going to take a

NOTE Confidence: 0.9878226

00:13:12.032 --> 00:13:14.329 short break for a medical minute,

NOTE Confidence: 0.9878226

00:13:14.330 --> 00:13:16.352 so please stay tuned to learn

NOTE Confidence: 0.9878226

00:13:16.352 --> 00:13:18.151 more about Melanoma with my

NOTE Confidence: 0.9878226

00:13:18.151 --> 00:13:19.699 guest Doctor Harriet Kluger.

NOTE Confidence: 0.9530473

00:13:20.480 --> 00:13:22.580 Funding for Yale Cancer Answers

NOTE Confidence: 0.9530473

00:13:22.580 --> 00:13:24.680 comes from Smilow Cancer Hospital.

NOTE Confidence: 0.9530473

00:13:24.680 --> 00:13:26.996 15 care centers offer access to

NOTE Confidence: 0.9530473

00:13:26.996 --> 00:13:28.540 oncologists committed to providing

NOTE Confidence: 0.9530473

00:13:28.601 --> 00:13:31.355 patients with cancer and blood diseases

NOTE Confidence: 0.9530473

00:13:31.355 --> 00:13:32.660 individualized, innovative care.

NOTE Confidence: 0.9530473

00:13:32.660 --> 00:13:35.600 Find a Smilow Care Center near

NOTE Confidence: 0.9530473

00:13:35.600 --> 00:13:38.118 you at YaleCancerCenter.org.

NOTE Confidence: 0.986256300000001

00:13:40.410 --> 00:13:42.250 The American Cancer Society

NOTE Confidence: 0.986256300000001

00:13:42.250 --> 00:13:44.550 estimates that more than 65,000

NOTE Confidence: 0.986256300000001

00:13:44.550 --> 00:13:46.524 Americans will be diagnosed with

NOTE Confidence: 0.986256300000001

00:13:46.524 --> 00:13:48.684 head and neck cancer this year,

NOTE Confidence: 0.986256300000001

00:13:48.690 --> 00:13:51.525 making up about 4% of all cancers.

NOTE Confidence: 0.986256300000001

00:13:51.525 --> 00:13:53.240 When detected early,

NOTE Confidence: 0.986256300000001

00:13:53.240 --> 00:13:55.616 however, head and neck cancers are

NOTE Confidence: 0.986256300000001

00:13:55.616 --> 00:13:57.800 easily treated and highly curable.

NOTE Confidence: 0.986256300000001

00:13:57.800 --> 00:13:59.860 Clinical trials are currently

NOTE Confidence: 0.986256300000001

00:13:59.860 --> 00:14:01.920 underway at federally designated

NOTE Confidence: 0.986256300000001

00:14:01.920 --> 00:14:03.698 Comprehensive cancer centers such

NOTE Confidence: 0.986256300000001

00:14:03.698 --> 00:14:06.085 as Yale Cancer Center and at Smilow

NOTE Confidence: 0.986256300000001

00:14:06.085 --> 00:14:08.354 Cancer Hospital to test innovative new

NOTE Confidence: 0.986256300000001

00:14:08.354 --> 00:14:10.681 treatments for head and neck cancers.

NOTE Confidence: 0.986256300000001

00:14:10.681 --> 00:14:13.447 Yale Cancer Center was recently awarded

NOTE Confidence: 0.986256300000001

00:14:13.447 --> 00:14:15.701 grants from the National Institutes

NOTE Confidence: 0.986256300000001

00:14:15.701 --> 00:14:18.473 of Health to fund the Yale Head

NOTE Confidence: 0.986256300000001

00:14:18.473 --> 00:14:20.853 and Neck Cancer Specialized Program

NOTE Confidence: 0.986256300000001

00:14:20.853 --> 00:14:23.709 of Research Excellence or SPORE to

NOTE Confidence: 0.986256300000001

00:14:23.710 --> 00:14:25.845 address critical barriers to treatment

NOTE Confidence: 0.986256300000001

00:14:25.845 --> 00:14:28.442 of head and neck squamous cell

NOTE Confidence: 0.986256300000001

00:14:28.442 --> 00:14:30.800 carcinoma due to resistance to immune

NOTE Confidence: 0.986256300000001

00:14:30.800 --> 00:14:33.189 DNA damage and targeted therapy.

NOTE Confidence: 0.986256300000001

00:14:33.190 --> 00:14:35.405 More information is available at

NOTE Confidence: 0.986256300000001

00:14:35.405 --> 00:14:36.734 yalecancercenter.org. You're listening

NOTE Confidence: 0.986256300000001

00:14:36.734 --> 00:14:38.359 to Connecticut Public Radio.

NOTE Confidence: 0.97392863

00:14:39.390 --> 00:14:41.766 Welcome back to Yale Cancer Answers.

NOTE Confidence: 0.97392863

00:14:41.770 --> 00:14:43.326 This is doctor Anees Chagpar

NOTE Confidence: 0.97392863

00:14:43.326 --> 00:14:45.660 and I'm joined tonight

NOTE Confidence: 0.97392863

00:14:45.735 --> 00:14:48.099 by my guest Doctor Harriet Kluger.

NOTE Confidence: 0.97392863

00:14:48.100 --> 00:14:50.648 We're talking about Melanoma and T cells

NOTE Confidence: 0.97392863

00:14:50.648 --> 00:14:53.408 and Harriet right before the break we

NOTE Confidence: 0.97392863

00:14:53.408 --> 00:14:55.413 were talking about these tremendous

NOTE Confidence: 0.97392863

00:14:55.413 --> 00:14:57.941 advances that have happened in the

NOTE Confidence: 0.97392863

00:14:57.941 --> 00:14:59.585 treatment of metastatic Melanoma.

NOTE Confidence: 0.97392863

00:14:59.590 --> 00:15:01.960 For anyone who just joined us,

NOTE Confidence: 0.97392863

00:15:01.960 --> 00:15:04.438 Harriet was mentioning that when

NOTE Confidence: 0.97392863

00:15:04.438 --> 00:15:06.090 she started treating metastatic

NOTE Confidence: 0.97392863

00:15:06.153 --> 00:15:07.509 Melanoma back in 2001,

NOTE Confidence: 0.97392863

00:15:07.510 --> 00:15:09.550 prognosis wasn't great. Six months.

NOTE Confidence: 0.97392863

00:15:09.550 --> 00:15:11.884 12 months, but we've now had

NOTE Confidence: 0.97392863

00:15:11.884 --> 00:15:14.350 a series of immune therapies,

NOTE Confidence: 0.97392863

00:15:14.350 --> 00:15:16.094 particularly with checkpoint inhibitors

NOTE Confidence: 0.97392863

00:15:16.094 --> 00:15:18.710 that have really improved the disease

NOTE Confidence: 0.97392863

00:15:18.710 --> 00:15:20.885 free survival now getting prolonged

NOTE Confidence: 0.97392863

00:15:20.885 --> 00:15:23.550 survival in over 50% of patients.

NOTE Confidence: 0.97392863

00:15:23.550 --> 00:15:26.310 But Harriet right before the break

NOTE Confidence: 0.97392863

00:15:26.310 --> 00:15:28.736 you left us with this little

NOTE Confidence: 0.97392863

00:15:28.736 --> 00:15:31.650 teaser that there may be other ways

NOTE Confidence: 0.97392863

00:15:31.650 --> 00:15:33.690 to manipulate the immune system

NOTE Confidence: 0.97392863

00:15:33.772 --> 00:15:36.147 that are now being investigated.

NOTE Confidence: 0.97392863

00:15:36.150 --> 00:15:39.066 That might hold promise in metastatic melanoma.

NOTE Confidence: 0.97392863

00:15:39.066 --> 00:15:41.129 Tell us more.

NOTE Confidence: 0.9863214

00:15:41.130 --> 00:15:42.582 Thank you and

NOTE Confidence: 0.9863214

00:15:42.582 --> 00:15:43.663 yes, absolutely.

NOTE Confidence: 0.9863214

00:15:43.663 --> 00:15:46.134 We have a few teasers and that's

NOTE Confidence: 0.9863214

00:15:46.134 --> 00:15:48.387 what makes this field so exciting.

NOTE Confidence: 0.9863214

00:15:48.390 --> 00:15:50.714 So one of the additional classes of

NOTE Confidence: 0.9863214

00:15:50.714 --> 00:15:53.469 therapies that we give is cellular therapies.

NOTE Confidence: 0.9863214

00:15:53.470 --> 00:15:55.808 So for Melanoma or solid tumors we

NOTE Confidence: 0.9863214

00:15:55.808 --> 00:15:58.420 know that we have these immune cells

NOTE Confidence: 0.9863214

00:15:58.420 --> 00:16:01.150 that live within the tumor but

NOTE Confidence: 0.9863214

00:16:01.150 --> 00:16:03.635 they keep trying to fight the tumor.

NOTE Confidence: 0.9863214

00:16:03.640 --> 00:16:06.160 But at some point they get exhausted

NOTE Confidence: 0.9863214

00:16:06.160 --> 00:16:08.112 and they're no longer capable

NOTE Confidence: 0.9863214

00:16:08.112 --> 00:16:10.494 of getting rid of tumor cells.

NOTE Confidence: 0.9863214

00:16:10.500 --> 00:16:12.775 So many years ago at the National

NOTE Confidence: 0.9863214

00:16:12.775 --> 00:16:14.380 Cancer Institute doctor Rosenberg,

NOTE Confidence: 0.9863214

00:16:14.380 --> 00:16:16.260 Steve Rosenberg pioneered a treatment

NOTE Confidence: 0.9863214

00:16:16.260 --> 00:16:18.140 modality whereby he would resect

NOTE Confidence: 0.9863214

00:16:18.198 --> 00:16:20.466 tumor and then break up all the

NOTE Confidence: 0.9863214

00:16:20.466 --> 00:16:21.438 different cellular components,

00:16:22.086 --> 00:16:24.670 and take the T cells that

NOTE Confidence: 0.9863214

00:16:24.741 --> 00:16:26.456 originated from within the tumor

NOTE Confidence: 0.9863214

00:16:26.456 --> 00:16:29.387 and grow them in a Petri dish and

NOTE Confidence: 0.9863214

00:16:29.387 --> 00:16:31.673 make billions and billions of cells.

NOTE Confidence: 0.9863214

00:16:31.680 --> 00:16:33.032 Then, in the meanwhile,

NOTE Confidence: 0.9863214

00:16:33.032 --> 00:16:35.855 he'd bring a patient back and give them

NOTE Confidence: 0.9863214

00:16:35.855 --> 00:16:38.389 high doses of chemotherapy to make space,

NOTE Confidence: 0.9863214

00:16:38.390 --> 00:16:40.350 if you will, for these

NOTE Confidence: 0.9863214

00:16:40.350 --> 00:16:42.054 newest cells that were growing in

NOTE Confidence: 0.9863214

00:16:42.054 --> 00:16:43.958 the Petri dish and actually are

NOTE Confidence: 0.9863214

00:16:43.958 --> 00:16:45.718 educated to recognize the tumor.

NOTE Confidence: 0.9863214

00:16:45.720 --> 00:16:47.750 Then he would infuse those into the

NOTE Confidence: 0.9863214

00:16:47.750 --> 00:16:49.281 patient after the chemotherapy and

NOTE Confidence: 0.9863214

00:16:49.281 --> 00:16:51.689 after the space was made and then give

NOTE Confidence: 0.9863214

00:16:51.748 --> 00:16:53.473 some growth factor called Interleukin

NOTE Confidence: 0.9863214

00:16:53.473 --> 00:16:55.485 two and then cells within patients

NOTE Confidence: 0.9863214

00:16:55.485 --> 00:16:57.480 would recover and go home and there

NOTE Confidence: 0.9863214

00:16:57.480 --> 00:16:59.797 is a subset of patients who were actually

NOTE Confidence: 0.9863214

00:16:59.797 --> 00:17:01.840 cured from this therapy as well.

NOTE Confidence: 0.9863214

00:17:01.840 --> 00:17:04.090 It's similar to having a bone

NOTE Confidence: 0.9863214

00:17:04.090 --> 00:17:06.185 marrow transplant you go in for

NOTE Confidence: 0.9863214

00:17:06.185 --> 00:17:08.289 a one time shot for a few weeks

NOTE Confidence: 0.9863214

00:17:08.367 --> 00:17:10.446 and then you go home and live your life.

00:17:11.222 --> 00:17:13.538 The initial response rates at the

NOTE Confidence: 0.9863214

00:17:13.538 --> 00:17:15.316 National Cancer Institute were in

NOTE Confidence: 0.9863214

00:17:15.316 --> 00:17:18.082 the order of 50%, now with the immune

NOTE Confidence: 0.9863214

00:17:18.082 --> 00:17:19.594 checkpoint inhibitors we're seeing

NOTE Confidence: 0.9863214

00:17:19.594 --> 00:17:21.410 lower response rates simply because

NOTE Confidence: 0.9863214

00:17:21.410 --> 00:17:23.414 many of the patients whose tumors

NOTE Confidence: 0.9863214

00:17:23.414 --> 00:17:25.231 immune sensitive are actually cured

NOTE Confidence: 0.9863214

00:17:25.231 --> 00:17:27.367 by the checkpoints that we discussed

NOTE Confidence: 0.9863214

00:17:27.370 --> 00:17:29.530 in the previous session over here,

NOTE Confidence: 0.9863214

00:17:29.530 --> 00:17:31.749 but still they work and we have

NOTE Confidence: 0.9863214

00:17:31.749 --> 00:17:34.031 patients who are cured now from

NOTE Confidence: 0.9863214

00:17:34.031 --> 00:17:35.288 the cellular therapies.

00:17:35.958 --> 00:17:37.628 After they haven't responded to

NOTE Confidence: 0.9863214

00:17:37.628 --> 00:17:39.250 the immune checkpoint inhibitors,

NOTE Confidence: 0.9863214

00:17:39.250 --> 00:17:40.770 that gives patients

NOTE Confidence: 0.9863214

00:17:40.770 --> 00:17:42.535 another option.

NOTE Confidence: 0.9863214

00:17:42.535 --> 00:17:44.210 This treatment is now being

NOTE Confidence: 0.9863214

00:17:44.210 --> 00:17:46.429 studied in other cancers as well.

NOTE Confidence: 0.9863214

00:17:46.430 --> 00:17:48.180 Lung cancer, head neck cancer,

NOTE Confidence: 0.9863214

00:17:48.180 --> 00:17:49.930 cervical cancer, and so on,

NOTE Confidence: 0.9863214

00:17:49.930 --> 00:17:52.380 and responses are being seen there too.

NOTE Confidence: 0.9863214

00:17:52.380 --> 00:17:54.318 In the meanwhile the field

NOTE Confidence: 0.9863214

00:17:54.318 --> 00:17:56.295 has moved forward and the cellular

NOTE Confidence: 0.9863214

00:17:56.295 --> 00:17:58.161 therapy is no longer only given

NOTE Confidence: 0.9863214

00:17:58.161 --> 00:18:00.428 at the National Cancer Institute.

NOTE Confidence: 0.9863214

00:18:00.430 --> 00:18:00.984 In fact,

NOTE Confidence: 0.9863214

00:18:00.984 --> 00:18:02.923 at Yale we have a lab that

NOTE Confidence: 0.9863214

00:18:02.923 --> 00:18:04.978 can manufacture these cells.

NOTE Confidence: 0.9863214

00:18:04.980 --> 00:18:07.032 There are also companies that are

NOTE Confidence: 0.9863214

00:18:07.032 --> 00:18:08.817 trying to commercialize this

NOTE Confidence: 0.9863214

00:18:08.817 --> 00:18:11.040 modality. So you send the tumor

NOTE Confidence: 0.9863214

00:18:11.040 --> 00:18:14.343 to the company, they grow the cells for you.

NOTE Confidence: 0.9863214

00:18:14.350 --> 00:18:16.744 They send them back and we give

NOTE Confidence: 0.9863214

00:18:16.744 --> 00:18:18.769 the treatment in the hospital.

NOTE Confidence: 0.9863214

00:18:18.770 --> 00:18:21.032 So that is something that likely

NOTE Confidence: 0.9863214

00:18:21.032 --> 00:18:23.665 will also be on the menu of

NOTE Confidence: 0.9863214

00:18:23.665 --> 00:18:25.759 options within a year or so

NOTE Confidence: 0.9863214

00:18:25.760 --> 00:18:27.968 for metastatic Melanoma and in the

NOTE Confidence: 0.98175156

00:18:27.970 --> 00:18:29.810 future, for other tumor types.

NOTE Confidence: 0.98175156

00:18:29.810 --> 00:18:31.958 So Harriet just picking up on

NOTE Confidence: 0.98175156

00:18:31.958 --> 00:18:34.219 that when we think about

NOTE Confidence: 0.98175156

00:18:34.220 --> 00:18:36.060 things like bone marrow

NOTE Confidence: 0.98175156

00:18:36.060 --> 00:18:37.532 transplant or other transplants,

NOTE Confidence: 0.98175156

00:18:37.540 --> 00:18:39.375 anytime we're thinking about putting

NOTE Confidence: 0.98175156

00:18:39.375 --> 00:18:41.292 cells into somebody, we always

NOTE Confidence: 0.98175156

00:18:41.292 --> 00:18:42.510 worry about rejection.

NOTE Confidence: 0.98175156

00:18:42.510 --> 00:18:45.446 So do I have it correct that, what

NOTE Confidence: 0.98175156

00:18:45.446 --> 00:18:47.946 we're actually doing in this cellular

NOTE Confidence: 0.98175156

00:18:47.946 --> 00:18:51.010 therapy is taking a patients own tumor?

NOTE Confidence: 0.98175156

00:18:51.010 --> 00:18:53.452 Taking finding their own T cells

NOTE Confidence: 0.98175156

00:18:53.452 --> 00:18:56.458 and getting those T cells to grow

NOTE Confidence: 0.98175156

00:18:56.458 --> 00:18:59.044 and replicate and giving the patient

NOTE Confidence: 0.98175156

00:18:59.044 --> 00:19:01.714 back their own T cells so that

NOTE Confidence: 0.98175156

00:19:01.714 --> 00:19:03.565 there's less risk of rejection?

NOTE Confidence: 0.98175156

00:19:03.565 --> 00:19:04.780 Is that right?

NOTE Confidence: 0.98175156

00:19:04.780 --> 00:19:06.000 That's right, there's

NOTE Confidence: 0.98592633

00:19:06.000 --> 00:19:08.020 actually no risk of rejection.

NOTE Confidence: 0.98592633

00:19:08.020 --> 00:19:10.090 The rejection only happens when

NOTE Confidence: 0.98592633

00:19:10.090 --> 00:19:12.160 you give somebody another person's

NOTE Confidence: 0.98592633

00:19:12.160 --> 00:19:14.476 immune cells, but in this case

NOTE Confidence: 0.98592633

00:19:14.476 --> 00:19:16.440 we're talking about giving a

NOTE Confidence: 0.98592633

00:19:16.440 --> 00:19:18.190 patient back their own cells,

NOTE Confidence: 0.98592633

00:19:18.190 --> 00:19:20.612 just amplified to the tune

NOTE Confidence: 0.98592633

00:19:20.612 --> 00:19:23.344 of billions of cells so that these

NOTE Confidence: 0.98592633

00:19:23.344 --> 00:19:25.768 are the special cells that recognize

NOTE Confidence: 0.98592633

00:19:25.843 --> 00:19:28.370 the tumor and can then work against

NOTE Confidence: 0.95115936

00:19:28.370 --> 00:19:31.350 the tumor.

NOTE Confidence: 0.95115936

00:19:31.350 --> 00:19:34.707 And one would think that if some

NOTE Confidence: 0.95115936

00:19:34.707 --> 00:19:37.470 people think that your immune system

NOTE Confidence: 0.95115936

00:19:37.470 --> 00:19:40.569 is fighting off cancer all the time,

NOTE Confidence: 0.95115936

00:19:40.570 --> 00:19:43.078 and that people have

NOTE Confidence: 0.95115936

00:19:43.080 --> 00:19:46.020 quote cancer floating around in them,

NOTE Confidence: 0.95115936

00:19:46.020 --> 00:19:48.264 and that your immune system kind

NOTE Confidence: 0.95115936

00:19:48.264 --> 00:19:50.727 of fights all of these little

NOTE Confidence: 0.95115936

00:19:50.727 --> 00:19:53.385 deformed cells off so that you

NOTE Confidence: 0.95115936

00:19:53.385 --> 00:19:55.650 don't actually develop a cancer,

NOTE Confidence: 0.95115936

00:19:55.650 --> 00:19:57.354 if that was true,

NOTE Confidence: 0.95115936

00:19:57.354 --> 00:19:59.484 then why wouldn't this therapy

NOTE Confidence: 0.95115936

00:19:59.484 --> 00:20:01.850 work for everybody? Why

NOTE Confidence: 0.95115936

00:20:01.850 --> 00:20:03.830 do we need the checkpoint inhibitors?

00:20:06.200 --> 00:20:08.965 I think the problem is that when

NOTE Confidence: 0.98770815

00:20:08.965 --> 00:20:10.940 we give the cellular therapy,

NOTE Confidence: 0.98770815

00:20:10.940 --> 00:20:13.000 sometimes patients have many different

NOTE Confidence: 0.98770815

00:20:13.000 --> 00:20:15.856 tumors in different locations and we already

NOTE Confidence: 0.98770815

00:20:15.856 --> 00:20:18.046 know now that melanomas can metastasize.

NOTE Confidence: 0.98770815

00:20:18.050 --> 00:20:21.362 So it is correct that they all start from

NOTE Confidence: 0.98770815

00:20:21.362 --> 00:20:24.754 the same clone of cells within the skin,

NOTE Confidence: 0.98770815

00:20:24.760 --> 00:20:26.805 then they metastasize internally and

NOTE Confidence: 0.98770815

00:20:26.805 --> 00:20:29.280 you get subclones and daughter clones

NOTE Confidence: 0.98770815

00:20:29.280 --> 00:20:31.476 and granddaughter clones and so on.

NOTE Confidence: 0.98770815

00:20:31.480 --> 00:20:33.068 And those next generation

NOTE Confidence: 0.98770815

00:20:33.068 --> 00:20:35.053 clones might have different mutations.

NOTE Confidence: 0.98770815

00:20:35.060 --> 00:20:38.219 Now if we remove a tumor to generate the

NOTE Confidence: 0.98770815

00:20:38.219 --> 00:20:41.168 immune cells from one location,

NOTE Confidence: 0.98770815

00:20:41.168 --> 00:20:43.681 these cells might not be active against

NOTE Confidence: 0.98770815

00:20:43.681 --> 00:20:46.216 the tumors in a different location,

NOTE Confidence: 0.98770815

00:20:46.220 --> 00:20:49.685 so that's one reason that it might not work.

NOTE Confidence: 0.98770815

00:20:49.690 --> 00:20:51.710 Other reasons for failure are

NOTE Confidence: 0.98770815

00:20:51.710 --> 00:20:54.507 inability to grow the cells in the

NOTE Confidence: 0.98770815

00:20:54.507 --> 00:20:56.613 lab so not every cell grows.

NOTE Confidence: 0.98770815

00:20:56.620 --> 00:20:58.160 The vast majority do,

NOTE Confidence: 0.98770815

00:20:58.160 --> 00:21:01.284 but there's about 10-15% that do not grow,

NOTE Confidence: 0.98770815

00:21:01.284 --> 00:21:03.264 and sometimes they just don't

NOTE Confidence: 0.98770815

00:21:03.270 --> 00:21:05.200 grow enough to substantial quantities

NOTE Confidence: 0.98770815

00:21:05.200 --> 00:21:07.546 and it's just insufficient to overcome

NOTE Confidence: 0.98770815

00:21:07.546 --> 00:21:10.017 the tumor cells that are actually there.

NOTE Confidence: 0.8992716

00:21:11.140 --> 00:21:14.059 And this whole concept of

NOTE Confidence: 0.8992716

00:21:14.060 --> 00:21:16.979 taking cells, sorting them out,

NOTE Confidence: 0.8992716

00:21:16.980 --> 00:21:18.608 finding the T cells,

NOTE Confidence: 0.8992716

00:21:18.608 --> 00:21:21.570 growing them up in a Petri dish,

NOTE Confidence: 0.8992716

00:21:21.570 --> 00:21:24.066 giving them back to the patient,

NOTE Confidence: 0.8992716

00:21:24.070 --> 00:21:26.989 it sounds really like a major production,

NOTE Confidence: 0.8992716

00:21:26.990 --> 00:21:29.492 and so whenever we think about

NOTE Confidence: 0.8992716

00:21:29.492 --> 00:21:31.160 major productions in medicine,

NOTE Confidence: 0.8992716

00:21:31.160 --> 00:21:34.224 I always think about how much does that

NOTE Confidence: 0.8992716

00:21:34.224 --> 00:21:37.410 cost and does insurance cover it?

NOTE Confidence: 0.8992716

00:21:37.410 --> 00:21:39.114 That's an excellent question.

NOTE Confidence: 0.8992716

00:21:39.114 --> 00:21:41.670 So at present it's still experimental.

NOTE Confidence: 0.8992716

00:21:41.670 --> 00:21:43.488 So the company that's making the

NOTE Confidence: 0.8992716

00:21:43.488 --> 00:21:45.794 cells for us in our current clinical

NOTE Confidence: 0.8992716

00:21:45.794 --> 00:21:47.852 trial covers the cost of it.

NOTE Confidence: 0.8992716

00:21:47.860 --> 00:21:49.340 The National Cancer Institute,

NOTE Confidence: 0.8992716

00:21:49.340 --> 00:21:51.116 when they used to do it,

NOTE Confidence: 0.8992716

00:21:51.120 --> 00:21:52.940 it was free, but with some it

NOTE Confidence: 0.8992716

00:21:52.940 --> 00:21:54.669 was covered by the government,

NOTE Confidence: 0.8992716

00:21:54.670 --> 00:21:55.555 essentially the taxpayer.

NOTE Confidence: 0.8992716

00:21:55.555 --> 00:21:57.796 But you are right, it is very expensive.

NOTE Confidence: 0.8992716

00:21:57.796 --> 00:22:00.189 I think we also need to keep in

NOTE Confidence: 0.8992716

00:22:00.189 --> 00:22:02.064 mind that the immune checkpoint

NOTE Confidence: 0.8992716

00:22:02.064 --> 00:22:03.840 inhibitors are similarly expensive.

NOTE Confidence: 0.8992716

00:22:03.840 --> 00:22:05.961 And those can also cost hundreds of

NOTE Confidence: 0.8992716

00:22:05.961 --> 00:22:07.580 thousands of dollars per patient.

NOTE Confidence: 0.8992716

00:22:07.580 --> 00:22:09.806 So if you start adding up the

NOTE Confidence: 0.8992716

00:22:09.806 --> 00:22:11.422 hundreds of thousands of dollars

NOTE Confidence: 0.8992716

00:22:11.422 --> 00:22:13.508 and you compare it to maybe 200,

NOTE Confidence: 0.8992716

00:22:13.510 --> 00:22:15.274 $300,000 for a one time

NOTE Confidence: 0.8992716

00:22:15.274 --> 00:22:16.940 therapy such as cellular therapy,

NOTE Confidence: 0.8992716

00:22:16.940 --> 00:22:18.879 it's not all that different in terms

NOTE Confidence: 0.8992716

00:22:18.879 --> 00:22:20.791 of order of magnitude is actually

NOTE Confidence: 0.8992716

00:22:20.791 --> 00:22:23.171 might be a little bit less expensive,

NOTE Confidence: 0.8992716

00:22:23.180 --> 00:22:23.810 if anything.

NOTE Confidence: 0.96757966

00:22:25.080 --> 00:22:27.824 And so getting back to the checkpoint

NOTE Confidence: 0.96757966

00:22:27.824 --> 00:22:29.399 inhibitors, those are generally

NOTE Confidence: 0.96757966

00:22:29.399 --> 00:22:31.364 covered by insurance now aren't they?

NOTE Confidence: 0.96757966

00:22:31.370 --> 00:22:33.330 They are yes, correct.

NOTE Confidence: 0.96757966

00:22:33.330 --> 00:22:34.906 Other than the experimental

NOTE Confidence: 0.96757966

00:22:34.906 --> 00:22:36.868 ones, the ones that are

NOTE Confidence: 0.96757966

00:22:36.870 --> 00:22:39.228 approved are covered.

NOTE Confidence: 0.96757966

00:22:39.230 --> 00:22:42.366 So it sounds to me like

NOTE Confidence: 0.96757966

00:22:42.370 --> 00:22:44.335 when you have a patient

NOTE Confidence: 0.96757966

00:22:44.335 --> 00:22:45.514 with metastatic Melanoma,

NOTE Confidence: 0.96757966

00:22:45.520 --> 00:22:48.271 your first line of therapy is the

NOTE Confidence: 0.96757966

00:22:48.271 --> 00:22:49.450 immune checkpoint inhibitors.

NOTE Confidence: 0.96757966

00:22:49.450 --> 00:22:51.410 If they fail, that cellular

NOTE Confidence: 0.96757966

00:22:51.410 --> 00:22:52.978 therapy is another option.

NOTE Confidence: 0.96757966

00:22:52.980 --> 00:22:54.950 What if they fail that?

NOTE Confidence: 0.9806514

00:22:55.600 --> 00:22:58.948 So if they fail that or sometimes by choice,

NOTE Confidence: 0.9806514

00:22:58.950 --> 00:23:00.434 we actually have additional

NOTE Confidence: 0.9806514

00:23:00.434 --> 00:23:01.918 experimental options for patients.

NOTE Confidence: 0.9806514

00:23:01.920 --> 00:23:04.888 So I had talked about the T

NOTE Confidence: 0.9806514

00:23:04.888 --> 00:23:07.139 cells that recognize the tumor.

NOTE Confidence: 0.9806514

00:23:07.140 --> 00:23:09.480 Those are called adaptive immune cells.

NOTE Confidence: 0.9806514

00:23:09.480 --> 00:23:10.650 In other words,

NOTE Confidence: 0.9806514

00:23:10.650 --> 00:23:12.600 they've adapted to the cancer.

NOTE Confidence: 0.9806514

00:23:12.600 --> 00:23:14.152 They have special specific

NOTE Confidence: 0.9806514

00:23:14.152 --> 00:23:16.092 qualities that recognize that we

NOTE Confidence: 0.9806514

00:23:16.092 --> 00:23:18.059 also have innate immune cells.

NOTE Confidence: 0.9806514

00:23:18.060 --> 00:23:20.106 Those are generalized cells that are

NOTE Confidence: 0.9806514

00:23:20.106 --> 00:23:22.885 floating around in our bodies that have

NOTE Confidence: 0.9806514

00:23:22.885 --> 00:23:25.140 not developed receptors that recognize

NOTE Confidence: 0.9806514

00:23:25.140 --> 00:23:27.028 specific abnormalities in cancer cells.

NOTE Confidence: 0.9806514

00:23:27.030 --> 00:23:29.418 Now those innate immune cells are

NOTE Confidence: 0.9806514

00:23:29.418 --> 00:23:32.509 another whole army of cells that we can

NOTE Confidence: 0.9806514

00:23:32.509 --> 00:23:35.220 activate in order to target the cancer,

NOTE Confidence: 0.9806514

00:23:35.220 --> 00:23:37.566 and sometimes we can co-activate

NOTE Confidence: 0.9806514

00:23:37.566 --> 00:23:39.150 the innate immune cells

NOTE Confidence: 0.9806514

00:23:39.150 --> 00:23:40.734 and the adaptive cells,

NOTE Confidence: 0.9806514

00:23:40.740 --> 00:23:43.218 so we can combine additional drugs to

NOTE Confidence: 0.9806514

00:23:43.218 --> 00:23:44.980 these immune checkpoint inhibitors.

NOTE Confidence: 0.9806514

00:23:44.980 --> 00:23:47.170 There are many approaches that are

NOTE Confidence: 0.9806514

00:23:47.170 --> 00:23:49.210 being taken across the country.

NOTE Confidence: 0.9806514

00:23:49.210 --> 00:23:51.364 One of the approaches that we're

NOTE Confidence: 0.9806514

00:23:51.364 --> 00:23:54.088 doing over here is to activate a

NOTE Confidence: 0.9806514

00:23:54.088 --> 00:23:56.524 group of cells called dendritic cells,

NOTE Confidence: 0.9806514

00:23:56.530 --> 00:23:58.840 that actually present the

NOTE Confidence: 0.9806514

00:23:58.840 --> 00:24:01.682 tumor antigen to the T cells

NOTE Confidence: 0.9806514

00:24:01.682 --> 00:24:04.552 as foreign and then make them

NOTE Confidence: 0.9806514

00:24:04.552 --> 00:24:06.628 become educated or adapted.

NOTE Confidence: 0.9806514

00:24:06.630 --> 00:24:09.178 So if we give those two together,

NOTE Confidence: 0.9806514

00:24:09.180 --> 00:24:11.352 we might have better responses than

NOTE Confidence: 0.9806514

00:24:11.352 --> 00:24:13.180 using the checkpoint inhibitors alone,

NOTE Confidence: 0.9806514

00:24:13.180 --> 00:24:15.728 so that's one example of an approach.

NOTE Confidence: 0.9806514

00:24:15.730 --> 00:24:17.949 There are groups that are targeting a

NOTE Confidence: 0.9806514

00:24:17.949 --> 00:24:20.099 subset of cells called macrophages,

NOTE Confidence: 0.9806514

00:24:20.100 --> 00:24:23.088 which are also innate immune cells.

NOTE Confidence: 0.9806514

00:24:23.090 --> 00:24:25.982 Then we need to think about

NOTE Confidence: 0.9806514

00:24:25.982 --> 00:24:27.910 what these cells do,

NOTE Confidence: 0.9806514

00:24:27.910 --> 00:24:31.738 so they secrete substances called cytokines.

NOTE Confidence: 0.9806514

00:24:31.740 --> 00:24:34.666 Interleukin two, that early drug that I

NOTE Confidence: 0.9806514

00:24:34.666 --> 00:24:37.006 had mentioned that was approved already

NOTE Confidence: 0.9806514

00:24:37.006 --> 00:24:40.249 in the 1990s is a type of a cytokine.

NOTE Confidence: 0.9806514

00:24:40.250 --> 00:24:42.185 Many companies are now developing

NOTE Confidence: 0.9806514

00:24:42.185 --> 00:24:42.959 novel cytokines,

NOTE Confidence: 0.9806514

00:24:42.960 --> 00:24:45.084 so either better versions of interleukin

NOTE Confidence: 0.9806514

00:24:45.084 --> 00:24:47.829 two that bind to the interleukin two

NOTE Confidence: 0.9806514

00:24:47.829 --> 00:24:49.929 receptors that are more important,

NOTE Confidence: 0.9806514

00:24:49.930 --> 00:24:52.422 or that bind with a

NOTE Confidence: 0.9806514

00:24:52.422 --> 00:24:54.569 stronger affinity to the receptors.

NOTE Confidence: 0.9806514

00:24:54.570 --> 00:24:56.898 And then there are other interleukins,

NOTE Confidence: 0.9806514

00:24:56.900 --> 00:24:59.216 interleukins that are made by

NOTE Confidence: 0.9806514

00:24:59.216 --> 00:25:01.940 our cells. So you could have

NOTE Confidence: 0.9806514

00:25:01.940 --> 00:25:03.504 Interleukin 12, interleukin 18,

NOTE Confidence: 0.9806514

00:25:03.504 --> 00:25:04.288 interleukin 15,

NOTE Confidence: 0.9806514

00:25:04.288 --> 00:25:06.640 all of these are being looked

NOTE Confidence: 0.9806514

00:25:06.708 --> 00:25:07.928 at as drug targets,

NOTE Confidence: 0.9806514

00:25:07.930 --> 00:25:10.611 and in fact there's a researcher at

NOTE Confidence: 0.9806514

00:25:10.611 --> 00:25:12.926 Yale who has developed a

NOTE Confidence: 0.9806514

00:25:12.926 --> 00:25:15.460 drug that is a mimic of interleukin

NOTE Confidence: 0.9806514

00:25:15.536 --> 00:25:17.666 18 that doesn't get sucked up

NOTE Confidence: 0.9806514

00:25:17.666 --> 00:25:19.802 by decoy proteins in the body,

NOTE Confidence: 0.9806514

00:25:19.802 --> 00:25:22.294 so should be more potent and we

NOTE Confidence: 0.9806514

00:25:22.294 --> 00:25:24.821 will be excited to study that in

NOTE Confidence: 0.9806514

00:25:24.821 --> 00:25:27.878 the next month or two in the clinic.

NOTE Confidence: 0.9806514

00:25:27.878 --> 00:25:29.853 There's a trial that's opening

NOTE Confidence: 0.9806514

00:25:29.853 --> 00:25:32.240 up and we will be administering

NOTE Confidence: 0.9806514

00:25:32.240 --> 00:25:34.298 that drug to patients who have not

NOTE Confidence: 0.9806514

00:25:34.298 --> 00:25:36.096 responded to the immune checkpoint

NOTE Confidence: 0.9806514

00:25:36.096 --> 00:25:37.812 inhibitors both with Melanoma

NOTE Confidence: 0.9806514

00:25:37.812 --> 00:25:39.099 and other diseases.

NOTE Confidence: 0.9238917

00:25:39.770 --> 00:25:42.322 So Harriet just to unpack a couple

NOTE Confidence: 0.9238917

00:25:42.322 --> 00:25:45.119 of the concepts that you mentioned.

NOTE Confidence: 0.9238917

00:25:45.120 --> 00:25:47.373 It sounds to me like

NOTE Confidence: 0.9238917

00:25:47.373 --> 00:25:49.431 the activation of both the innate

NOTE Confidence: 0.9238917

00:25:49.431 --> 00:25:51.399 and the adaptive immune system

NOTE Confidence: 0.9238917

00:25:51.399 --> 00:25:53.135 just makes intuitive sense.

NOTE Confidence: 0.9238917

00:25:53.140 --> 00:25:55.050 If you have more

NOTE Confidence: 0.9238917

00:25:55.050 --> 00:25:56.940 adaptive immune cells and

NOTE Confidence: 0.9238917

00:25:56.940 --> 00:25:59.309 you pair that with more cells

NOTE Confidence: 0.9238917

00:25:59.309 --> 00:26:01.709 that are presenting to them the

NOTE Confidence: 0.9238917

00:26:01.709 --> 00:26:03.840 antigens they need to go after,

NOTE Confidence: 0.9238917

00:26:03.840 --> 00:26:05.745 it seems like that would

NOTE Confidence: 0.9238917

00:26:05.745 --> 00:26:07.269 be a better approach.

NOTE Confidence: 0.9238917

00:26:07.270 --> 00:26:10.049 So is that something that is routinely

NOTE Confidence: 0.9238917

00:26:10.050 --> 00:26:11.946 being done or is the cellular

NOTE Confidence: 0.9238917

00:26:11.946 --> 00:26:13.656 therapies that we were talking

NOTE Confidence: 0.9238917

00:26:13.656 --> 00:26:15.571 about earlier really going after

NOTE Confidence: 0.9238917

00:26:15.571 --> 00:26:17.530 more of those adaptive cells?

NOTE Confidence: 0.9238917

00:26:17.530 --> 00:26:20.176 And wouldn't it be better if they

NOTE Confidence: 0.9238917

00:26:20.176 --> 00:26:22.968 could also grow up in a Petri dish

NOTE Confidence: 0.9238917

00:26:22.968 --> 00:26:25.710 of patients innate T cells as well?

NOTE Confidence: 0.98698205

00:26:27.220 --> 00:26:29.484 Well, we can grow it up in a

NOTE Confidence: 0.98698205

00:26:29.484 --> 00:26:31.217 Petri dish or in the body,

NOTE Confidence: 0.98698205

00:26:31.220 --> 00:26:32.640 so the whole concept behind

NOTE Confidence: 0.98698205

00:26:32.640 --> 00:26:34.370 giving cytokines is to grow them

NOTE Confidence: 0.98698205

00:26:34.370 --> 00:26:35.390 actually in the human.

NOTE Confidence: 0.98698205

00:26:35.390 --> 00:26:37.278 So we give more of the cytokines

NOTE Confidence: 0.98698205

00:26:37.278 --> 00:26:39.078 and we grow up both innate

NOTE Confidence: 0.98698205

00:26:39.078 --> 00:26:40.380 and the adaptive cells.

NOTE Confidence: 0.98698205

00:26:40.380 --> 00:26:41.805 So these are like growth

NOTE Confidence: 0.98698205

00:26:41.805 --> 00:26:42.945 factors for these cells.

NOTE Confidence: 0.98698205

00:26:42.950 --> 00:26:43.808 They should make

NOTE Confidence: 0.98698205

00:26:43.810 --> 00:26:44.602 them propagate.

NOTE Confidence: 0.98698205

00:26:44.602 --> 00:26:46.450 So that was going to be my

NOTE Confidence: 0.98698205

00:26:46.505 --> 00:26:48.015 next question is you talk

NOTE Confidence: 0.98698205

00:26:48.015 --> 00:26:49.525 about all of these cytokines?

NOTE Confidence: 0.98698205

00:26:49.530 --> 00:26:51.570 These interleukins with various numbers?

NOTE Confidence: 0.98698205

00:26:51.570 --> 00:26:54.685 How exactly do they work?

NOTE Confidence: 0.98698205

00:26:54.690 --> 00:26:57.906 It's sounds now like they just

NOTE Confidence: 0.98698205

00:26:57.906 --> 00:27:00.490 stimulate the innate immune system.

NOTE Confidence: 0.98698205

00:27:00.490 --> 00:27:01.828 Is that right?

NOTE Confidence: 0.97825295

00:27:01.830 --> 00:27:04.060 Both innate and adaptive actually?

NOTE Confidence: 0.97825295

00:27:04.060 --> 00:27:05.504 So they stimulate both.

NOTE Confidence: 0.97825295

00:27:05.504 --> 00:27:07.670 So all of those different

NOTE Confidence: 0.97825295

00:27:07.748 --> 00:27:09.972 numbers reflect molecules that

NOTE Confidence: 0.97825295

00:27:09.972 --> 00:27:11.640 have different activities.

NOTE Confidence: 0.97825295

00:27:11.640 --> 00:27:15.208 So some of them will stimulate innate cells

NOTE Confidence: 0.97825295

00:27:15.210 --> 00:27:17.440 and some stimulate the adaptive cells,

NOTE Confidence: 0.97825295

00:27:17.440 --> 00:27:19.332 some stimulates suppressor cells.

NOTE Confidence: 0.97825295

00:27:19.332 --> 00:27:21.224 The biology is getting

NOTE Confidence: 0.97825295

00:27:21.224 --> 00:27:23.489 more and more complicated.

NOTE Confidence: 0.97825295

00:27:23.490 --> 00:27:24.850 Well, it's always been complicated.

NOTE Confidence: 0.97825295

00:27:24.850 --> 00:27:25.934 We're just learning now

NOTE Confidence: 0.97825295

00:27:25.934 --> 00:27:27.024 how complicated it is,

NOTE Confidence: 0.97825295

00:27:27.024 --> 00:27:28.386 and every time we look,

NOTE Confidence: 0.97825295

00:27:28.386 --> 00:27:30.018 we discover that we knew nothing.

NOTE Confidence: 0.96022385

00:27:31.520 --> 00:27:33.963 And so it sounds like we're

NOTE Confidence: 0.96022385

00:27:33.963 --> 00:27:35.590 almost coming full circle,

NOTE Confidence: 0.96022385

00:27:35.590 --> 00:27:37.174 though, because interleukin two

NOTE Confidence: 0.96022385

00:27:37.174 --> 00:27:39.550 was something that you had talked

NOTE Confidence: 0.96022385

00:27:39.615 --> 00:27:41.664 about at the very outset, which

NOTE Confidence: 0.96022385

00:27:41.664 --> 00:27:44.808 really wasn't terribly effective back then.

NOTE Confidence: 0.96022385

00:27:44.810 --> 00:27:47.468 Why would we think that now

NOTE Confidence: 0.96022385

00:27:47.470 --> 00:27:49.238 these other interleukins will

NOTE Confidence: 0.96022385

00:27:49.238 --> 00:27:51.899 be more effective?

NOTE Confidence: 0.9906297

00:27:51.900 --> 00:27:55.062 Now we have

NOTE Confidence: 0.9906297

00:27:55.062 --> 00:27:57.979 other bullets to administer with it.

NOTE Confidence: 0.9906297

00:27:57.980 --> 00:28:00.700 And we understand better how to engineer

NOTE Confidence: 0.9906297

00:28:00.700 --> 00:28:03.949 them so that they can be more effective.

NOTE Confidence: 0.9767311

00:28:05.120 --> 00:28:07.256 So the idea is that you would use

NOTE Confidence: 0.9767311

00:28:07.256 --> 00:28:08.940 these interleukins along with cellular

NOTE Confidence: 0.9767311

00:28:08.940 --> 00:28:10.770 therapy and or checkpoint inhibitors.

NOTE Confidence: 0.9767311

00:28:10.770 --> 00:28:13.274 Yes, or if they're so good we might

NOTE Confidence: 0.9767311

00:28:13.280 --> 00:28:15.170 be able to use them alone.

NOTE Confidence: 0.9767311

00:28:15.170 --> 00:28:17.418 Time will tell when you have a new

NOTE Confidence: 0.9767311

00:28:17.418 --> 00:28:19.878 drug you start studying it by itself,

NOTE Confidence: 0.9767311

00:28:19.880 --> 00:28:21.450 mainly because you want to

NOTE Confidence: 0.9767311

00:28:21.450 --> 00:28:23.020 look at whether it's toxic,

NOTE Confidence: 0.9767311

00:28:23.020 --> 00:28:25.508 but you also look a little bit at

NOTE Confidence: 0.9767311

00:28:25.508 --> 00:28:27.694 the activity so some of them might

NOTE Confidence: 0.9767311

00:28:27.694 --> 00:28:29.929 end up being active on their own.

NOTE Confidence: 0.9767311

00:28:29.930 --> 00:28:30.869 We will see.

NOTE Confidence: 0.9274463

00:28:31.710 --> 00:28:33.816 Doctor Harriet Kluger is a professor

NOTE Confidence: 0.9274463

00:28:33.816 --> 00:28:35.620 of medicine and medical oncology

NOTE Confidence: 0.9274463

00:28:35.620 --> 00:28:37.630 at the Yale School of Medicine.

NOTE Confidence: 0.9274463

00:28:37.630 --> 00:28:39.862 If you have questions the addresses

NOTE Confidence: 0.9274463

00:28:39.862 --> 00:28:41.748 cancer answers at yale.edu and

NOTE Confidence: 0.9274463

00:28:41.748 --> 00:28:43.728 past editions of the program are

NOTE Confidence: 0.9274463

00:28:43.728 --> 00:28:45.431 available in audio and written

NOTE Confidence: 0.9274463

00:28:45.431 --> 00:28:47.369 form at yalecancercenter.org.

NOTE Confidence: 0.9274463

00:28:47.370 --> 00:28:49.610 We hope you'll join us next week to

NOTE Confidence: 0.9274463

00:28:49.610 --> 00:28:51.775 learn more about the fight against

NOTE Confidence: 0.9274463

00:28:51.775 --> 00:28:53.695 cancer here on Connecticut Public

NOTE Confidence: 0.9274463

00:28:53.695 --> 00:28:55.611 radio funding for Yale Cancer

NOTE Confidence: 0.9274463

00:28:55.611 --> 00:28:57.441 Answers is provided by Smilow

NOTE Confidence: 0.9274463

00:28:57.441 --> 00:29:00.070 Cancer Hospital and AstraZeneca.