WEBVTT

NOTE duration:"01:01:42"

NOTE recognizability:0.527

NOTE language:en-us

NOTE Confidence: 0.74346846

00:00:00.000 --> 00:00:03.036 Real pleasure to introduce Roy Herbst.

NOTE Confidence: 0.74346846

00:00:03.040 --> 00:00:05.420 Roy of course needs no

NOTE Confidence: 0.74346846

00:00:05.420 --> 00:00:07.800 introduction to all of you.

NOTE Confidence: 0.74346846

00:00:07.800 --> 00:00:10.419 You can see his title on the screen Moving

NOTE Confidence: 0.74346846

00:00:10.419 --> 00:00:12.905 from Palliation to Cure Progress in the

NOTE Confidence: 0.74346846

00:00:12.905 --> 00:00:15.440 treatment of non small cell lung cancer.

NOTE Confidence: 0.74346846

00:00:15.440 --> 00:00:18.032 But let me just make a couple of comments.

NOTE Confidence: 0.74346846

00:00:18.040 --> 00:00:22.688 So Roy has really witnessed over the

NOTE Confidence: 0.74346846

00:00:22.688 --> 00:00:28.628 course of his 25 year career or so since

NOTE Confidence: 0.74346846

00:00:28.628 --> 00:00:31.256 completing training of has has witnessed

NOTE Confidence: 0.74346846

00:00:31.256 --> 00:00:33.669 a real revolution in lung cancer.

NOTE Confidence: 0.74346846

00:00:33.670 --> 00:00:37.637 And I remember when I was a fellow

NOTE Confidence: 0.74346846

00:00:37.637 --> 00:00:39.575 and nobody was interested in lung

NOTE Confidence: 0.74346846

00:00:39.575 --> 00:00:41.976 cancer and there seemed to be little

NOTE Confidence: 0.74346846

00:00:42.047 --> 00:00:44.105 hope for progress in lung cancer.

NOTE Confidence: 0.74346846

00:00:44.110 --> 00:00:48.170 And that has really changed so very

NOTE Confidence: 0.74346846

00:00:48.170 --> 00:00:51.300 dramatically And as Roy has witnessed

NOTE Confidence: 0.74346846

00:00:51.300 --> 00:00:54.343 that he's also participated in it

NOTE Confidence: 0.74346846

00:00:54.343 --> 00:00:58.450 and he has been involved in the vast

NOTE Confidence: 0.74346846

00:00:58.450 --> 00:01:01.326 majority of clinical trials that have

NOTE Confidence: 0.74346846

00:01:01.326 --> 00:01:03.490 led to major changes in lung cancer,

NOTE Confidence: 0.74346846

00:01:03.490 --> 00:01:06.770 whether that's related to EGFR,

NOTE Confidence: 0.74346846

00:01:06.770 --> 00:01:08.720 associated lung cancer or for

NOTE Confidence: 0.74346846

00:01:08.720 --> 00:01:10.670 that matter trials focused on

NOTE Confidence: 0.74346846

00:01:10.736 --> 00:01:13.048 immunotherapy and other treatments.

NOTE Confidence: 0.74346846

00:01:13.050 --> 00:01:15.726 So great pleasure to introduce Roy.

NOTE Confidence: 0.74346846

00:01:15.730 --> 00:01:18.495 He will take us through this talk

NOTE Confidence: 0.74346846

00:01:18.495 --> 00:01:22.039 and is a great inaugural speaker.

NOTE Confidence: 0.74346846

00:01:22.040 --> 00:01:22.904 Thank you, Eric.

NOTE Confidence: 0.74346846

00:01:22.904 --> 00:01:26.360 And it's great to be back here in person in

NOTE Confidence: 0.74346846

00:01:26.360 --> 00:01:28.817 the auditorium and happy Friday everyone.

NOTE Confidence: 0.74346846

00:01:28.817 --> 00:01:31.531 And what I'm going to do in the

NOTE Confidence: 0.74346846

00:01:31.531 --> 00:01:33.940 next 45 to 50 minutes is give you a

NOTE Confidence: 0.74346846

00:01:33.940 --> 00:01:36.542 little bit of a tour of lung cancer.

NOTE Confidence: 0.74346846

00:01:36.542 --> 00:01:39.146 So actually my journey began here

NOTE Confidence: 0.74346846

00:01:39.146 --> 00:01:41.800 at Yale 44 years ago and my Pecam

NOTE Confidence: 0.74346846

00:01:41.800 --> 00:01:43.400 professor's in the front row,

NOTE Confidence: 0.74346846

00:01:43.400 --> 00:01:45.146 Don Engleman and and it's amazing

NOTE Confidence: 0.74346846

00:01:45.146 --> 00:01:46.920 to see you and you know,

NOTE Confidence: 0.74346846

00:01:46.920 --> 00:01:48.150 and I I actually wasn't his

NOTE Confidence: 0.74346846

00:01:48.150 --> 00:01:49.360 course like he would probably

NOTE Confidence: 0.46130416

00:01:51.760 --> 00:01:52.772 but it's you know,

NOTE Confidence: 0.46130416

00:01:52.772 --> 00:01:54.037 Yale's just a phenomenal place.

NOTE Confidence: 0.46130416

00:01:54.040 --> 00:01:55.342 So it's just so amazing for

NOTE Confidence: 0.46130416

00:01:55.342 --> 00:01:57.442 me to be to be here and I gave

NOTE Confidence: 0.46130416

00:01:57.442 --> 00:01:58.959 a grand rounds about 12 years

NOTE Confidence: 0.46130416

00:01:58.959 --> 00:02:00.399 ago when I first arrived.

NOTE Confidence: 0.46130416

00:02:00.400 --> 00:02:02.200 So a little bit of progress

NOTE Confidence: 0.46130416

00:02:02.200 --> 00:02:04.016 since then and I'll show you

NOTE Confidence: 0.46130416

00:02:04.016 --> 00:02:05.680 that now my disclosures.

NOTE Confidence: 0.46130416

00:02:07.760 --> 00:02:11.915 So we're back. This was last week at

NOTE Confidence: 0.46130416

00:02:14.080 --> 00:02:16.352 East Haven. We had our ASCO review and

NOTE Confidence: 0.46130416

00:02:16.352 --> 00:02:18.997 and a dinner for some of the faculty.

NOTE Confidence: 0.46130416

00:02:19.000 --> 00:02:20.944 It was just great to see so many

NOTE Confidence: 0.46130416

00:02:20.944 --> 00:02:22.558 people there and the spirits there.

NOTE Confidence: 0.46130416

00:02:22.558 --> 00:02:24.250 We had a great day discussing

NOTE Confidence: 0.46130416

00:02:24.305 --> 00:02:26.078 all of our different divisions,

NOTE Confidence: 0.46130416

00:02:26.078 --> 00:02:29.685 both solid and liquid advances in the

NOTE Confidence: 0.46130416

00:02:29.685 --> 00:02:32.043 field and it's good to see so many

NOTE Confidence: 0.46130416

00:02:32.043 --> 00:02:34.143 of those being done here at Yale.

NOTE Confidence: 0.46130416

00:02:34.150 --> 00:02:37.130 And then of course we we had many of

NOTE Confidence: 0.46130416

00:02:37.130 --> 00:02:39.112 our fellows and actually we're we're

NOTE Confidence: 0.46130416

00:02:39.112 --> 00:02:40.448 really multidisciplinary of course

NOTE Confidence: 0.46130416

00:02:40.448 --> 00:02:42.747 we have our hospitals team was there,

NOTE Confidence: 0.46130416

00:02:42.750 --> 00:02:43.986 many of our fellows were there,

NOTE Confidence: 0.46130416

00:02:43.990 --> 00:02:45.234 we had surgeons there,

NOTE Confidence: 0.46130416

00:02:45.234 --> 00:02:47.520 we'd love to have our surgeons there,

NOTE Confidence: 0.46130416

00:02:47.520 --> 00:02:48.038 radiation oncology.

NOTE Confidence: 0.46130416

00:02:48.038 --> 00:02:50.110 One thing that I want to get across

NOTE Confidence: 0.46130416

00:02:50.163 --> 00:02:51.913 today is the way we're making progress

NOTE Confidence: 0.46130416

00:02:51.913 --> 00:02:53.560 in lung cancer and many diseases.

NOTE Confidence: 0.46130416

00:02:53.560 --> 00:02:56.504 This is in a in a multi modality

NOTE Confidence: 0.46130416

00:02:56.504 --> 00:02:58.140 fashion and you know the the

NOTE Confidence: 0.46130416

00:02:58.140 --> 00:02:59.960 burden of lung cancer is is great.

NOTE Confidence: 0.46130416

00:02:59.960 --> 00:03:02.200 I think most of this group is aware of that,

NOTE Confidence: 0.46130416

00:03:02.200 --> 00:03:03.835 but it's the leading cause

NOTE Confidence: 0.46130416

00:03:03.835 --> 00:03:05.143 of cancer death worldwide.

NOTE Confidence: 0.46130416

00:03:05.150 --> 00:03:07.070 You know, more, more cases,

NOTE Confidence: 0.46130416

00:03:07.070 --> 00:03:08.750 probably a skin cancer diagnosed of course,

NOTE Confidence: 0.46130416

00:03:08.750 --> 00:03:10.550 but for you know, more,

NOTE Confidence: 0.46130416

00:03:10.550 --> 00:03:11.426 more, you know,

NOTE Confidence: 0.46130416

00:03:11.426 --> 00:03:13.178 it's more breast cancer in women

NOTE Confidence: 0.46130416

00:03:13.178 --> 00:03:14.827 and prostate cancer in men.

NOTE Confidence: 0.46130416

00:03:14.830 --> 00:03:16.902 But lung cancer is the number one

NOTE Confidence: 0.46130416

00:03:16.902 --> 00:03:18.653 killer with over 2 million deaths

NOTE Confidence: 0.46130416

00:03:18.653 --> 00:03:20.780 a year in the world with over

NOTE Confidence: 0.46130416

00:03:20.780 --> 00:03:23.150 200,000 deaths in the United case,

NOTE Confidence: 0.46130416

00:03:23.150 --> 00:03:24.800 200,000 new cases in the US

NOTE Confidence: 0.46130416

00:03:24.800 --> 00:03:26.056 with over 130,000 deaths.

NOTE Confidence: 0.46130416

00:03:26.056 --> 00:03:28.384 So this is the reason there's so

NOTE Confidence: 0.46130416

00:03:28.384 --> 00:03:29.932 much research and pharmaceutical

NOTE Confidence: 0.46130416

00:03:29.932 --> 00:03:31.480 development in this area.

NOTE Confidence: 0.46130416

00:03:31.480 --> 00:03:32.968 84% of lung cancer is non

NOTE Confidence: 0.46130416

00:03:32.968 --> 00:03:33.960 small cell lung cancer.

NOTE Confidence: 0.46130416

00:03:33.960 --> 00:03:35.936 A a great effort now still with small

NOTE Confidence: 0.46130416

00:03:35.936 --> 00:03:37.964 cell lung cancer used to be that

NOTE Confidence: 0.46130416

00:03:37.964 --> 00:03:39.439 was only associated with smokers.

NOTE Confidence: 0.46130416

00:03:39.440 --> 00:03:40.840 It's still mostly with smokers.

NOTE Confidence: 0.46130416

00:03:40.840 --> 00:03:42.560 But now we know that EGFR mutated lung

NOTE Confidence: 0.46130416

00:03:42.560 --> 00:03:43.988 cancer can develop into small cell

NOTE Confidence: 0.46130416

00:03:43.988 --> 00:03:45.658 lung cancer and Sheng lives in the

NOTE Confidence: 0.46130416

00:03:45.658 --> 00:03:47.242 2nd row sort of leads to that effort

NOTE Confidence: 0.46130416

00:03:47.242 --> 00:03:49.960 here and she'll probably give a grand round.

NOTE Confidence: 0.46130416

00:03:49.960 --> 00:03:50.560 Oh yeah,

NOTE Confidence: 0.46130416

00:03:50.560 --> 00:03:50.860 please.

NOTE Confidence: 0.46130416

00:03:50.860 --> 00:03:52.360 It is a little distracting

NOTE Confidence: 0.61711353

00:03:59.620 --> 00:03:59.940 thank you

NOTE Confidence: 0.61711353

00:04:04.700 --> 00:04:06.646 and and we'll hear from Ann hopefully

NOTE Confidence: 0.61711353

00:04:06.646 --> 00:04:09.042 in in this series later this year Well

NOTE Confidence: 0.61711353

00:04:09.042 --> 00:04:10.840 when I started out you know as after

NOTE Confidence: 0.61711353

00:04:10.840 --> 00:04:13.390 I I left Yale and I spent some time in

NOTE Confidence: 0.61711353

00:04:13.390 --> 00:04:15.334 New York at Cornell and Rockefeller.

NOTE Confidence: 0.61711353

00:04:15.340 --> 00:04:18.700 I went up to Boston and I I was working

NOTE Confidence: 0.61711353

00:04:18.788 --> 00:04:21.804 at Dana Farber and I I I said this last

NOTE Confidence: 0.61711353

00:04:21.804 --> 00:04:24.250 week at the to some of the fellows.

NOTE Confidence: 0.61711353

00:04:24.250 --> 00:04:25.727 I got the job in lung cancer

NOTE Confidence: 0.61711353

00:04:25.727 --> 00:04:26.730 because that's all it was.

NOTE Confidence: 0.61711353

00:04:26.730 --> 00:04:28.170 You know the breast cancer

NOTE Confidence: 0.61711353

00:04:28.170 --> 00:04:29.322 jobs were all filled.

NOTE Confidence: 0.61711353

00:04:29.330 --> 00:04:31.346 The leukemia and lymphoma jobs actually liked

NOTE Confidence: 0.61711353

00:04:31.346 --> 00:04:33.486 lung cancer and was very interested in it.

NOTE Confidence: 0.61711353

00:04:33.490 --> 00:04:34.610 I had a wonderful mentor,

NOTE Confidence: 0.61711353

00:04:34.610 --> 00:04:37.940 Emil Fry, also a Yale graduate,

NOTE Confidence: 0.61711353

00:04:37.940 --> 00:04:40.952 But it was pretty dismal and it's very hard,

NOTE Confidence: 0.61711353

00:04:40.952 --> 00:04:41.826 you know, you know,

NOTE Confidence: 0.61711353

00:04:41.826 --> 00:04:43.387 as oncologists to work in the clinic

NOTE Confidence: 0.61711353

00:04:43.387 --> 00:04:44.977 when you don't have tools to offer.

NOTE Confidence: 0.61711353

00:04:44.980 --> 00:04:46.740 We had tools of chemotherapy,

NOTE Confidence: 0.61711353

00:04:46.740 --> 00:04:48.609 but this is what survival curves look

NOTE Confidence: 0.61711353

00:04:48.609 --> 00:04:50.807 like about 25 years ago for lung cancer.

NOTE Confidence: 0.61711353

00:04:50.807 --> 00:04:53.220 And you can see there's really none at at,

NOTE Confidence: 0.61711353

00:04:53.220 --> 00:04:55.020 you know, at at two years.

NOTE Confidence: 0.61711353

00:04:55.020 --> 00:04:57.057 There's very little survival at three years,

NOTE Confidence: 0.61711353

00:04:57.060 --> 00:04:57.756 almost nothing.

NOTE Confidence: 0.61711353

00:04:57.756 --> 00:04:59.844 And progression was quite steep and

NOTE Confidence: 0.61711353

00:04:59.844 --> 00:05:02.377 there was all this excitement about Dosi,

NOTE Confidence: 0.61711353

00:05:02.380 --> 00:05:05.996 Taxol, Packley, Taxol, Amcitabine,

NOTE Confidence: 0.61711353

00:05:05.996 --> 00:05:06.900 Carboplatinum.

NOTE Confidence: 0.61711353

00:05:06.900 --> 00:05:08.440 These drugs made a difference

NOTE Confidence: 0.61711353

00:05:08.440 --> 00:05:09.980 and they did improve survival,

NOTE Confidence: 0.61711353

00:05:09.980 --> 00:05:11.696 but to a very small extent.

NOTE Confidence: 0.61711353

00:05:11.700 --> 00:05:14.058 A median survival is of 7 to 8 months.

NOTE Confidence: 0.61711353

00:05:14.060 --> 00:05:16.112 So the question was a paradigm

NOTE Confidence: 0.61711353

00:05:16.112 --> 00:05:17.138 shift was needed.

NOTE Confidence: 0.61711353

00:05:17.140 --> 00:05:18.245 And you know, you're you're

NOTE Confidence: 0.61711353

00:05:18.245 --> 00:05:19.740 really a product of your mentors.

NOTE Confidence: 0.61711353

00:05:19.740 --> 00:05:22.053 And I was very fortunate at at Dana Farber,

NOTE Confidence: 0.61711353

00:05:22.060 --> 00:05:22.780 Tom Fry.

NOTE Confidence: 0.61711353

00:05:22.780 --> 00:05:25.300 In the later years of his career,

NOTE Confidence: 0.61711353

00:05:25.300 --> 00:05:27.100 I became his mentee and we we met,

NOTE Confidence: 0.61711353

00:05:27.100 --> 00:05:27.372 you know,

NOTE Confidence: 0.61711353

00:05:27.372 --> 00:05:28.460 at least two or three times a week.

NOTE Confidence: 0.61711353

00:05:28.460 --> 00:05:31.057 And he always said take your best

NOTE Confidence: 0.61711353

00:05:31.057 --> 00:05:32.977 drugs and use them early use them you

NOTE Confidence: 0.61711353

00:05:32.977 --> 00:05:34.696 know in the multi modality setting

NOTE Confidence: 0.61711353

00:05:34.696 --> 00:05:36.700 with surgery with radiation and we

NOTE Confidence: 0.61711353

00:05:36.700 --> 00:05:38.537 already had seen that in lung cancer

NOTE Confidence: 0.61711353

00:05:38.537 --> 00:05:40.132 back in those days because chemo

NOTE Confidence: 0.61711353

00:05:40.132 --> 00:05:42.309 radiation it was a study done by

NOTE Confidence: 0.61711353

00:05:42.309 --> 00:05:44.627 Doctor Dillman back in the the late 80s,

NOTE Confidence: 0.61711353

00:05:44.630 --> 00:05:47.054 early 90s had shown that there was a

NOTE Confidence: 0.61711353

00:05:47.054 --> 00:05:49.235 benefit for chemo radiation in this

NOTE Confidence: 0.61711353

00:05:49.235 --> 00:05:51.503 disease and it did improve survival.

NOTE Confidence: 0.61711353

00:05:51.510 --> 00:05:53.750 So what causes lung cancer?

NOTE Confidence: 0.61711353

00:05:53.750 --> 00:05:55.374 I could give a whole talk on this

NOTE Confidence: 0.61711353

00:05:55.374 --> 00:05:56.763 and and tobacco cessation efforts

NOTE Confidence: 0.61711353

00:05:56.763 --> 00:05:58.611 that we're we're doing here and

NOTE Confidence: 0.61711353

00:05:58.611 --> 00:06:00.530 with the ACR and you know we have a

NOTE Confidence: 0.61711353

00:06:00.530 --> 00:06:02.098 a large tobacco grant here at Yale

NOTE Confidence: 0.61711353

00:06:02.098 --> 00:06:03.610 and that that's very important for

NOTE Confidence: 0.61711353

00:06:03.610 --> 00:06:05.380 our community cause New Haven is a

NOTE Confidence: 0.61711353

00:06:05.380 --> 00:06:06.844 community where smoking is higher than

NOTE Confidence: 0.61711353

00:06:06.844 --> 00:06:08.796 than in the rest of the United States.

NOTE Confidence: 0.61711353

00:06:08.800 --> 00:06:10.944 But as I said many of the lung

NOTE Confidence: 0.61711353

00:06:10.944 --> 00:06:12.242 cancers are non-smoking related now

NOTE Confidence: 0.61711353

00:06:12.242 --> 00:06:13.766 and you can see actual mutations

NOTE Confidence: 0.61711353

00:06:13.766 --> 00:06:15.000 and that's the excitement.

NOTE Confidence: 0.61711353

00:06:15.000 --> 00:06:16.890 This is why so many people want to work

NOTE Confidence: 0.61711353

00:06:16.890 --> 00:06:18.814 in this field because 20 years ago

NOTE Confidence: 0.61711353

00:06:18.814 --> 00:06:20.520 each GFR mutations were identified.

NOTE Confidence: 0.61711353

00:06:20.520 --> 00:06:22.194 So we actually know driver mutations

NOTE Confidence: 0.61711353

00:06:22.194 --> 00:06:23.680 so we can target those.

NOTE Confidence: 0.61711353

00:06:23.680 --> 00:06:27.856 But there are now at least ten other

NOTE Confidence: 0.61711353

00:06:27.856 --> 00:06:30.260 targetable alterations and we're

NOTE Confidence: 0.61711353

00:06:30.260 --> 00:06:32.672 seeing evidence of of benefit,

NOTE Confidence: 0.61711353

00:06:32.672 --> 00:06:33.538 you know,

NOTE Confidence: 0.7823865

00:06:33.540 --> 00:06:34.480 with a broad perspective.

NOTE Confidence: 0.7823865

00:06:34.480 --> 00:06:35.420 I can see it.

NOTE Confidence: 0.7823865

00:06:35.420 --> 00:06:36.500 Of course, to any given patient,

NOTE Confidence: 0.7823865

00:06:36.500 --> 00:06:38.180 it's still not nearly enough.

NOTE Confidence: 0.7823865

00:06:38.180 --> 00:06:40.168 And I'm sure almost everyone here has

NOTE Confidence: 0.7823865

00:06:40.168 --> 00:06:41.780 some experience either as a physician,

NOTE Confidence: 0.7823865

00:06:41.780 --> 00:06:43.938 as a, as a family member, as a friend,

NOTE Confidence: 0.7823865

00:06:43.938 --> 00:06:45.294 with someone who's had lung cancer.

NOTE Confidence: 0.7823865

00:06:45.300 --> 00:06:47.500 And while we can see that in men

NOTE Confidence: 0.7823865

00:06:47.500 --> 00:06:49.237 survival death rates are coming down

NOTE Confidence: 0.7823865

00:06:49.237 --> 00:06:51.316 and in women with a little bit of

NOTE Confidence: 0.7823865

00:06:51.316 --> 00:06:53.708 a of a lag smoking in women began

NOTE Confidence: 0.7823865

00:06:53.708 --> 00:06:55.834 later but still if you look in men

NOTE Confidence: 0.7823865

00:06:55.834 --> 00:06:58.084 the incidence is coming down a lot of

NOTE Confidence: 0.7823865

00:06:58.084 --> 00:06:59.562 that's screening and smoking cessation

NOTE Confidence: 0.7823865

00:06:59.562 --> 00:07:01.978 but the mortality is coming down even more.

NOTE Confidence: 0.7823865

00:07:01.980 --> 00:07:05.139 And in in women the same 1.2 and 3.1.

NOTE Confidence: 0.7823865

00:07:05.140 --> 00:07:06.778 So we are making a difference in these data.

NOTE Confidence: 0.7823865

00:07:06.780 --> 00:07:08.490 You know the data you get from the American

NOTE Confidence: 0.7823865

00:07:08.490 --> 00:07:09.896 Cancer Society is always two or three,

NOTE Confidence: 0.7823865

00:07:09.900 --> 00:07:10.620 four years old.

NOTE Confidence: 0.7823865

00:07:10.620 --> 00:07:11.580 So I think this,

NOTE Confidence: 0.7823865

00:07:11.580 --> 00:07:13.603 this shows some of the targeted therapies

NOTE Confidence: 0.7823865

00:07:13.603 --> 00:07:15.393 which I'll talk about in the first

NOTE Confidence: 0.7823865

00:07:15.393 --> 00:07:17.082 half of the talk and the immunotherapy

NOTE Confidence: 0.7823865

00:07:17.082 --> 00:07:19.385 benefits are are still on the horizon.

NOTE Confidence: 0.7823865

00:07:19.390 --> 00:07:22.630 Well, we've built an outstanding program.

NOTE Confidence: 0.7823865

00:07:22.630 --> 00:07:23.866 We've had retreats over the years.

NOTE Confidence: 0.7823865

00:07:23.870 --> 00:07:26.150 This is a retreat about 5-6 years ago.

NOTE Confidence: 0.7823865

00:07:26.150 --> 00:07:27.410 And I guess want to point out

NOTE Confidence: 0.7823865

00:07:27.410 --> 00:07:28.509 two things about this picture.

NOTE Confidence: 0.7823865

00:07:28.510 --> 00:07:30.046 One actually three things.

NOTE Confidence: 0.7823865

00:07:30.046 --> 00:07:32.590 One, this is a great group

NOTE Confidence: 0.7823865

00:07:32.590 --> 00:07:34.750 multidisciplinary working as a team.

NOTE Confidence: 0.7823865

00:07:34.750 --> 00:07:36.910 There's myself that's Dan Baffa,

NOTE Confidence: 0.7823865

00:07:36.910 --> 00:07:37.786 this is David Swenson.

NOTE Confidence: 0.7823865

00:07:37.786 --> 00:07:39.406 We we held this at the Business

NOTE Confidence: 0.7823865

00:07:39.406 --> 00:07:41.205 School and and David came in and

NOTE Confidence: 0.7823865

00:07:41.205 --> 00:07:43.031 inspired us with some of his you know

NOTE Confidence: 0.7823865

00:07:43.031 --> 00:07:45.235 you know go after the problem hard.

NOTE Confidence: 0.7823865

00:07:45.235 --> 00:07:47.706 He gave a very amazing speech.

NOTE Confidence: 0.7823865

00:07:47.706 --> 00:07:48.882 Of course David passed away or

NOTE Confidence: 0.7823865

00:07:48.882 --> 00:07:49.909 in the last few years,

NOTE Confidence: 0.7823865

00:07:49.910 --> 00:07:51.401 but then I also want to point

NOTE Confidence: 0.7823865

00:07:51.401 --> 00:07:52.430 out that's Roy Decker.

NOTE Confidence: 0.7823865

00:07:52.430 --> 00:07:54.962 We had one of the best

NOTE Confidence: 0.7823865

00:07:54.962 --> 00:07:56.228 radiation oncologists ever,

NOTE Confidence: 0.7823865

00:07:56.230 --> 00:07:58.126 both as a clinician,

NOTE Confidence: 0.7823865

00:07:58.126 --> 00:08:00.558 as a person in with patients and

NOTE Confidence: 0.7823865

00:08:00.558 --> 00:08:02.070 he passed away recently as well.

NOTE Confidence: 0.7823865

00:08:02.070 --> 00:08:04.149 So we lost a great member of our team.

NOTE Confidence: 0.7823865

00:08:04.150 --> 00:08:06.530 But I just wanted to just say

NOTE Confidence: 0.7823865

00:08:06.530 --> 00:08:08.549 we miss you dearly Roy.

NOTE Confidence: 0.7823865

00:08:08.550 --> 00:08:10.989 And then you know we've continued to to meet,

NOTE Confidence: 0.7823865

00:08:10.990 --> 00:08:13.468 this is a few years later

NOTE Confidence: 0.7823865

00:08:13.470 --> 00:08:15.227 and you can see it's a team.

NOTE Confidence: 0.7823865

00:08:15.230 --> 00:08:16.292 The only way we're going to

NOTE Confidence: 0.7823865

00:08:16.292 --> 00:08:17.309 make progress is as a team,

NOTE Confidence: 0.7823865

00:08:17.310 --> 00:08:18.752 as a multi modality team and this

NOTE Confidence: 0.7823865

00:08:18.752 --> 00:08:20.310 is more of a clinical meeting.

NOTE Confidence: 0.7823865

00:08:20.310 --> 00:08:21.750 I'll show you a translational

NOTE Confidence: 0.7823865

00:08:21.750 --> 00:08:22.902 meeting at the end.

NOTE Confidence: 0.7823865

00:08:22.910 --> 00:08:24.860 But you can see you know it's a it's a

NOTE Confidence: 0.7823865

00:08:24.918 --> 00:08:27.054 team approach to lung cancer and you can

NOTE Confidence: 0.7823865

00:08:27.054 --> 00:08:29.186 see there's Dan Lynn Tenui from pulmonary,

NOTE Confidence: 0.7823865

00:08:29.190 --> 00:08:29.846 Frank Getterbach,

NOTE Confidence: 0.7823865

00:08:29.846 --> 00:08:31.158 Sarah Goldberg who unfortunately

NOTE Confidence: 0.7823865

00:08:31.158 --> 00:08:32.470 can't be here today,

NOTE Confidence: 0.7823865

00:08:32.470 --> 00:08:35.366 but she sent me a nice note and this,

NOTE Confidence: 0.7823865

00:08:35.366 --> 00:08:38.082 this was over at the West campus.

NOTE Confidence: 0.7823865

00:08:38.090 --> 00:08:38.735 Now the centers,

NOTE Confidence: 0.7823865

00:08:38.735 --> 00:08:39.810 you know these disease centers,

NOTE Confidence: 0.7823865

00:08:39.810 --> 00:08:40.842 I just say thought I'd say

NOTE Confidence: 0.7823865

00:08:40.842 --> 00:08:41.770 a few words about that.

NOTE Confidence: 0.7823865

00:08:41.770 --> 00:08:43.324 We talk about it a great deal.

NOTE Confidence: 0.7823865

00:08:43.330 --> 00:08:44.308 That's the goal.

NOTE Confidence: 0.7823865

00:08:44.308 --> 00:08:45.286 Centers of excellence,

NOTE Confidence: 0.7823865

00:08:45.290 --> 00:08:47.370 multi modality centers of excellence,

NOTE Confidence: 0.7823865

00:08:47.370 --> 00:08:49.578 taking care of lung cancer throughout

NOTE Confidence: 0.7823865

00:08:49.578 --> 00:08:51.050 Connecticut throughout the network.

NOTE Confidence: 0.7823865

00:08:51.050 --> 00:08:52.890 You know we have I I lose count.

NOTE Confidence: 0.7823865

00:08:52.890 --> 00:08:54.462 What is it Eric,

NOTE Confidence: 0.7823865

00:08:54.462 --> 00:08:55.248 15 sites

NOTE Confidence: 0.6782555

00:08:55.250 --> 00:08:56.890 around We we are going to have experts

NOTE Confidence: 0.6782555

00:08:56.890 --> 00:08:58.768 at all those sites seeing lung cancer.

NOTE Confidence: 0.6782555

00:08:58.770 --> 00:08:59.970 We might not have every

NOTE Confidence: 0.6782555

00:08:59.970 --> 00:09:00.930 discipline at each center,

NOTE Confidence: 0.6782555

00:09:00.930 --> 00:09:03.066 but we will work as a team to

NOTE Confidence: 0.6782555

00:09:03.066 --> 00:09:05.129 coordinate and really build a big tent,

NOTE Confidence: 0.6782555

00:09:05.130 --> 00:09:06.918 bring the science to the patients.

NOTE Confidence: 0.6782555

00:09:06.920 --> 00:09:08.480 The only way to continue to make progress

NOTE Confidence: 0.6782555

00:09:08.480 --> 00:09:10.307 and I hope you'll see that at the end of

NOTE Confidence: 0.6782555

00:09:10.307 --> 00:09:12.235 my hour is by bringing science to the clinic.

NOTE Confidence: 0.6782555

00:09:12.240 --> 00:09:15.120 That's the theme of today's talk.

NOTE Confidence: 0.6782555

00:09:15.120 --> 00:09:16.278 And we also have a spore.

NOTE Confidence: 0.6782555

00:09:16.280 --> 00:09:18.000 So we began the spore now a God,

NOTE Confidence: 0.6782555

00:09:18.000 --> 00:09:21.480 it's hard to believe almost 10 years ago.

NOTE Confidence: 0.6782555

00:09:21.480 --> 00:09:22.828 We have three projects

NOTE Confidence: 0.6782555

00:09:22.828 --> 00:09:24.270 in the spore cyclic 15,

NOTE Confidence: 0.6782555

00:09:24.270 --> 00:09:26.600 which is and I'll tell you a lot about that,

NOTE Confidence: 0.6782555

00:09:26.600 --> 00:09:28.616 that's actually featured in the CCSG grant

NOTE Confidence: 0.6782555

00:09:28.616 --> 00:09:31.197 both in the DT and the immunology programs.

NOTE Confidence: 0.6782555

00:09:31.200 --> 00:09:33.424 And what you'll it's a new agent developed

NOTE Confidence: 0.6782555

00:09:33.424 --> 00:09:35.869 here at at at Yale and liping Shen's lab.

NOTE Confidence: 0.6782555

00:09:35.870 --> 00:09:37.466 The mechanism based approach is to

NOTE Confidence: 0.6782555

00:09:37.466 --> 00:09:39.011 targeting EGFR are very relevant to

NOTE Confidence: 0.6782555

00:09:39.011 --> 00:09:40.731 the first part of my talk and brain

NOTE Confidence: 0.6782555

00:09:40.786 --> 00:09:42.669 metastases which I'll talk about as well.

NOTE Confidence: 0.6782555

00:09:42.670 --> 00:09:44.362 And you can see we have Coors and and

NOTE Confidence: 0.6782555

00:09:44.362 --> 00:09:45.865 David and David's in the front row.

NOTE Confidence: 0.6782555

00:09:45.870 --> 00:09:48.066 We have wonderful bio statistical core,

NOTE Confidence: 0.6782555

00:09:48.070 --> 00:09:50.105 we have developmental programs and

NOTE Confidence: 0.6782555

00:09:50.105 --> 00:09:52.852 we we were first funded in 2015.

NOTE Confidence: 0.6782555

00:09:52.852 --> 00:09:56.378 So this effort began on March 1st, 2011.

NOTE Confidence: 0.6782555

00:09:56.378 --> 00:09:58.410 When I arrived here we had a number

NOTE Confidence: 0.6782555

00:09:58.470 --> 00:10:00.035 of submissions just for anyone

NOTE Confidence: 0.6782555

00:10:00.035 --> 00:10:01.280 who is getting depressed.

NOTE Confidence: 0.6782555

00:10:01.280 --> 00:10:03.140 It took three submissions to get

NOTE Confidence: 0.6782555

00:10:03.140 --> 00:10:05.080 this score and so it's not easy

NOTE Confidence: 0.6782555

00:10:05.080 --> 00:10:06.988 but it's it's been great and you're

NOTE Confidence: 0.6782555

00:10:06.988 --> 00:10:08.850 gonna see and why in a moment.

NOTE Confidence: 0.6782555

00:10:08.850 --> 00:10:11.622 And it was renewed in 2020 a lot more

NOTE Confidence: 0.6782555

00:10:11.622 --> 00:10:13.520 easily and now we're gonna renew it

NOTE Confidence: 0.6782555

00:10:13.520 --> 00:10:15.297 again because I've taken on a new

NOTE Confidence: 0.6782555

00:10:15.297 --> 00:10:16.837 MPI and Doctor Paletti who's in the

NOTE Confidence: 0.6782555

00:10:16.894 --> 00:10:18.539 front row and 2nd row and working

NOTE Confidence: 0.6782555

00:10:18.539 --> 00:10:20.570 with Lee Ping who remains the Co Pi.

NOTE Confidence: 0.6782555

00:10:20.570 --> 00:10:22.166 We're we're going back in in January.

NOTE Confidence: 0.6782555

00:10:22.170 --> 00:10:23.778 So we we wanted to wait till the

NOTE Confidence: 0.6782555

00:10:23.778 --> 00:10:25.517 core grant went in so we weren't

NOTE Confidence: 0.6782555

00:10:25.517 --> 00:10:26.802 competing for the same resources.

NOTE Confidence: 0.6782555

00:10:26.810 --> 00:10:28.798 Although there there is I guess a

NOTE Confidence: 0.6782555

00:10:28.798 --> 00:10:30.612 site visit coming up too and the

NOTE Confidence: 0.6782555

00:10:30.612 --> 00:10:32.579 beautiful thing about the Spore is we

NOTE Confidence: 0.6782555

00:10:32.579 --> 00:10:34.516 have developmental projects over 50 of

NOTE Confidence: 0.6782555

00:10:34.516 --> 00:10:37.208 them over the years and you can see

NOTE Confidence: 0.6782555

00:10:37.208 --> 00:10:38.928 these are career enhancement program,

NOTE Confidence: 0.6782555

00:10:38.930 --> 00:10:40.210 you know young investigators

NOTE Confidence: 0.6782555

00:10:40.210 --> 00:10:41.810 who aren't working lung cancer,

NOTE Confidence: 0.6782555

00:10:41.810 --> 00:10:43.476 we're getting them involved in lung cancer

NOTE Confidence: 0.6782555

00:10:43.476 --> 00:10:45.687 and this is a developmental research program.

NOTE Confidence: 0.6782555

00:10:45.690 --> 00:10:47.650 We could have 10 projects on the SPORE.

NOTE Confidence: 0.6782555

00:10:47.650 --> 00:10:49.450 The problem is you can really only have

NOTE Confidence: 0.6782555

00:10:49.450 --> 00:10:50.814 three projects on these grants because

NOTE Confidence: 0.6782555

00:10:50.814 --> 00:10:52.410 the NCI continues to cut the funds.

NOTE Confidence: 0.6782555

00:10:52.410 --> 00:10:54.144 We have developmental funds and and

NOTE Confidence: 0.6782555

00:10:54.144 --> 00:10:56.369 and donor funds we used to enhance it.

NOTE Confidence: 0.6782555

00:10:56.370 --> 00:10:57.446 But look at this,

NOTE Confidence: 0.6782555

00:10:57.446 --> 00:10:58.522 all the different departments

NOTE Confidence: 0.6782555

00:10:58.522 --> 00:10:59.540 that are involved,

NOTE Confidence: 0.6782555

00:10:59.540 --> 00:11:00.760 it's building a community of

NOTE Confidence: 0.6782555

00:11:00.760 --> 00:11:01.980 lung cancer here at Yale.

NOTE Confidence: 0.6782555

00:11:01.980 --> 00:11:06.180 And I think they're about 17 or ones.

NOTE Confidence: 0.6782555

00:11:06.180 --> 00:11:06.940 And this is the team.

NOTE Confidence: 0.6782555

00:11:06.940 --> 00:11:07.394 And again,

NOTE Confidence: 0.6782555

00:11:07.394 --> 00:11:09.500 I just want to point out Anna Esteppe here,

NOTE Confidence: 0.6782555

00:11:09.500 --> 00:11:11.040 who now Ed Cafton,

NOTE Confidence: 0.6782555

00:11:11.040 --> 00:11:12.965 actually Julie Boyer many years

NOTE Confidence: 0.6782555

00:11:12.965 --> 00:11:14.500 ago was our initial

NOTE Confidence: 0.35788172

00:11:14.500 --> 00:11:15.512 administrative leader and then

NOTE Confidence: 0.35788172

00:11:15.512 --> 00:11:16.777 Ed Cafton for many years.

NOTE Confidence: 0.35788172

00:11:16.780 --> 00:11:18.634 Now of course he's working closely

NOTE Confidence: 0.35788172

00:11:18.634 --> 00:11:20.767 on the CCSG but there's Anna

NOTE Confidence: 0.35788172

00:11:20.767 --> 00:11:22.170 Esteppe are now staff who who who

NOTE Confidence: 0.35788172

00:11:22.170 --> 00:11:23.565 just is doing a phenomenal job and

NOTE Confidence: 0.35788172

00:11:23.565 --> 00:11:24.939 actually made this slide for me.

NOTE Confidence: 0.35788172

00:11:24.940 --> 00:11:26.098 We probably need a second slide.

NOTE Confidence: 0.35788172

00:11:26.100 --> 00:11:27.524 These are all the people that are working

NOTE Confidence: 0.35788172

00:11:27.524 --> 00:11:29.178 in the community of lung Cancer Research.

NOTE Confidence: 0.35788172

00:11:29.180 --> 00:11:30.762 And then I just want to give

NOTE Confidence: 0.35788172

00:11:30.762 --> 00:11:32.180 a little shout out to Katie.

NOTE Confidence: 0.35788172

00:11:32.180 --> 00:11:33.935 So we had a little we went to New

NOTE Confidence: 0.35788172

00:11:33.935 --> 00:11:35.627 York last week and maybe two weeks

NOTE Confidence: 0.35788172

00:11:35.627 --> 00:11:37.535 ago now and Katie was honored by

NOTE Confidence: 0.35788172

00:11:37.535 --> 00:11:39.020 the Lung Cancer Research Foundation

NOTE Confidence: 0.35788172

00:11:39.020 --> 00:11:41.350 and see the multi modality in this

NOTE Confidence: 0.35788172

00:11:41.350 --> 00:11:43.575 Shen Liu of the Sheriff Pathology

NOTE Confidence: 0.35788172

00:11:43.575 --> 00:11:44.700 Valentina from genetics.

NOTE Confidence: 0.35788172

00:11:44.700 --> 00:11:47.458 Some of us really, we're a community

NOTE Confidence: 0.35788172

00:11:47.458 --> 00:11:49.270 that's tackling this disease.

NOTE Confidence: 0.35788172

00:11:49.270 --> 00:11:50.306 So now let's do a little science.

NOTE Confidence: 0.35788172

00:11:50.310 --> 00:11:51.468 I've already used 10 minutes up,

NOTE Confidence: 0.35788172

00:11:51.470 --> 00:11:53.507 but you know, I'm always taking pictures.

NOTE Confidence: 0.35788172

00:11:53.510 --> 00:11:55.748 You see why.

NOTE Confidence: 0.35788172

00:11:55.750 --> 00:11:57.388 So So what about targeted therapy?

NOTE Confidence: 0.35788172

00:11:57.390 --> 00:11:59.110 I'm going to tell you about targeted therapy,

NOTE Confidence: 0.35788172

00:11:59.110 --> 00:12:00.334 immunotherapy in the future.

NOTE Confidence: 0.35788172

00:12:00.334 --> 00:12:01.702 And I, I might skip through

NOTE Confidence: 0.35788172

00:12:01.702 --> 00:12:02.830 some slides if it's going along.

NOTE Confidence: 0.35788172

00:12:02.830 --> 00:12:04.054 So we have time for questions

NOTE Confidence: 0.35788172

00:12:04.054 --> 00:12:05.190 because you're here in person.

NOTE Confidence: 0.35788172

00:12:05.190 --> 00:12:07.014 We should be interactive.

NOTE Confidence: 0.35788172

00:12:07.014 --> 00:12:07.470 Well,

NOTE Confidence: 0.35788172

00:12:07.470 --> 00:12:11.210 I began when I when I I finished

NOTE Confidence: 0.35788172

00:12:11.210 --> 00:12:13.430 my my work at Dana Farber.

NOTE Confidence: 0.35788172

00:12:13.430 --> 00:12:13.608 I,

NOTE Confidence: 0.35788172

00:12:13.608 --> 00:12:13.786 I,

NOTE Confidence: 0.35788172

00:12:13.786 --> 00:12:15.210 I went to MD Anderson and I was

NOTE Confidence: 0.35788172

00:12:15.260 --> 00:12:16.844 telling one of the fellows yesterday

NOTE Confidence: 0.35788172

00:12:16.844 --> 00:12:18.389 when I was meeting with her,

NOTE Confidence: 0.35788172

00:12:18.390 --> 00:12:19.625 it's all about the mentors

NOTE Confidence: 0.35788172

00:12:19.625 --> 00:12:21.310 you have and I had worked,

NOTE Confidence: 0.35788172

00:12:21.310 --> 00:12:22.150 I had been at Yale,

NOTE Confidence: 0.35788172

00:12:22.150 --> 00:12:23.542 I had worked in Kim Darnell's

NOTE Confidence: 0.35788172

00:12:23.542 --> 00:12:24.470 lab at at Rockefeller.

NOTE Confidence: 0.35788172

00:12:24.470 --> 00:12:25.922 I was very interested in signal

NOTE Confidence: 0.35788172

00:12:25.922 --> 00:12:27.211 transduction and I was very

NOTE Confidence: 0.35788172

00:12:27.211 --> 00:12:28.825 interested in EGFR and EGFR receptor.

NOTE Confidence: 0.35788172

00:12:28.830 --> 00:12:30.937 And just around that time the first

NOTE Confidence: 0.35788172

00:12:30.937 --> 00:12:32.221 small molecules and antibodies

NOTE Confidence: 0.35788172

00:12:32.221 --> 00:12:33.836 had been developed against EGFR

NOTE Confidence: 0.35788172

00:12:33.836 --> 00:12:35.824 and we knew that in epithelial

NOTE Confidence: 0.35788172

00:12:35.824 --> 00:12:37.424 tumors such as lung cancer,

NOTE Confidence: 0.35788172

00:12:37.430 --> 00:12:39.030 EGFR was up regulated.

NOTE Confidence: 0.35788172

00:12:39.030 --> 00:12:41.030 So I was very fortunate.

NOTE Confidence: 0.35788172

00:12:41.030 --> 00:12:41.640 Juan Kihan,

NOTE Confidence: 0.35788172

00:12:41.640 --> 00:12:43.775 who is my mentor and who had

NOTE Confidence: 0.35788172

00:12:43.775 --> 00:12:45.734 recruited me to MD Anderson brought me

NOTE Confidence: 0.35788172

00:12:45.734 --> 00:12:47.094 upstairs to the president's office.

NOTE Confidence: 0.35788172

00:12:47.094 --> 00:12:47.638 John Mendelson,

NOTE Confidence: 0.35788172

00:12:47.638 --> 00:12:49.270 who had worked in the e.g.

NOTE Confidence: 0.35788172

00:12:49.270 --> 00:12:51.230 Fr field and these new molecules were

NOTE Confidence: 0.35788172

00:12:51.230 --> 00:12:52.845 coming through and they they offered

NOTE Confidence: 0.35788172

00:12:52.845 --> 00:12:54.830 me the project and I just said sure.

NOTE Confidence: 0.35788172

00:12:54.830 --> 00:12:55.445 And I I,

NOTE Confidence: 0.35788172

00:12:55.445 --> 00:12:56.675 I don't think I realized how

NOTE Confidence: 0.35788172

00:12:56.675 --> 00:12:57.907 good it was at that time.

NOTE Confidence: 0.35788172

00:12:57.910 --> 00:12:59.254 I knew that it was a good science

NOTE Confidence: 0.35788172

00:12:59.254 --> 00:13:00.661 and the science was evolving and and

NOTE Confidence: 0.35788172

00:13:00.661 --> 00:13:02.390 then we started to do clinical trials.

NOTE Confidence: 0.35788172

00:13:02.390 --> 00:13:04.334 But also we worked in the lab to try

NOTE Confidence: 0.35788172

00:13:04.334 --> 00:13:06.191 to identify biomarkers and I went

NOTE Confidence: 0.35788172

00:13:06.191 --> 00:13:08.088 to start my first clinical trial

NOTE Confidence: 0.35788172

00:13:08.088 --> 00:13:10.494 and a drug called ZD 1839 and the

NOTE Confidence: 0.35788172

00:13:10.494 --> 00:13:12.570 investigator meeting was in Palm Beach,

NOTE Confidence: 0.35788172

00:13:12.570 --> 00:13:13.518 FL which is nice.

NOTE Confidence: 0.35788172

00:13:13.518 --> 00:13:15.222 My parents live there and then I

NOTE Confidence: 0.35788172

00:13:15.222 --> 00:13:16.846 go to the hotel and who's sitting

NOTE Confidence: 0.35788172

00:13:16.846 --> 00:13:18.249 across from me but Pat Larusso

NOTE Confidence: 0.35788172

00:13:18.250 --> 00:13:21.081 that's when I met Pat in 1997 and we

NOTE Confidence: 0.35788172

00:13:21.081 --> 00:13:23.580 started and we were the Co leaders

NOTE Confidence: 0.35788172

00:13:23.661 --> 00:13:25.942 of this first trial of ZD 1839,

NOTE Confidence: 0.35788172

00:13:25.942 --> 00:13:27.372 which became known as confitinib

NOTE Confidence: 0.35788172

00:13:27.372 --> 00:13:29.208 and some might know it as Aressa.

NOTE Confidence: 0.35788172

00:13:29.210 --> 00:13:30.488 And we started using this drug,

NOTE Confidence: 0.27635187

00:13:30.490 --> 00:13:32.560 an oral agent against patients with

NOTE Confidence: 0.27635187

00:13:32.560 --> 00:13:34.654 lung cancer, with what we would

NOTE Confidence: 0.27635187

00:13:34.654 --> 00:13:36.058 call broncholoviral lung cancer.

NOTE Confidence: 0.27635187

00:13:36.060 --> 00:13:37.734 And in one of 10 patients we saw this,

NOTE Confidence: 0.27635187

00:13:37.740 --> 00:13:38.712 this clearing unheard of.

NOTE Confidence: 0.27635187

00:13:38.712 --> 00:13:40.700 You saw the survival curves I showed you.

NOTE Confidence: 0.27635187

00:13:40.700 --> 00:13:42.373 And these would be patients who could

NOTE Confidence: 0.27635187

00:13:42.373 --> 00:13:44.160 hardly walk into the clinic and then a

NOTE Confidence: 0.27635187

00:13:44.160 --> 00:13:45.979 week or two later they'd be feeling great.

NOTE Confidence: 0.27635187

00:13:45.980 --> 00:13:47.564 We didn't know at that time

NOTE Confidence: 0.27635187

00:13:47.564 --> 00:13:48.620 what the biomarkers were.

NOTE Confidence: 0.27635187

00:13:48.620 --> 00:13:50.460 We thought it was easy of our expression.

NOTE Confidence: 0.27635187

00:13:50.460 --> 00:13:51.468 It it wasn't.

NOTE Confidence: 0.27635187

00:13:51.468 --> 00:13:53.488 Of course, mutations were found after

NOTE Confidence: 0.27635187

00:13:53.488 --> 00:13:55.060 about 1002 thousand patients were

NOTE Confidence: 0.27635187

00:13:55.060 --> 00:13:56.740 treated and and people looked back.

NOTE Confidence: 0.27635187

00:13:56.740 --> 00:13:58.259 I'll show you that in a moment.

NOTE Confidence: 0.27635187

00:13:58.260 --> 00:13:59.780 We we knew that it was women were

NOTE Confidence: 0.27635187

00:13:59.780 --> 00:14:01.060 more likely to respond than men,

NOTE Confidence: 0.27635187

00:14:01.060 --> 00:14:02.500 but it was really people who

NOTE Confidence: 0.27635187

00:14:02.500 --> 00:14:03.676 had smoked less and smoking.

NOTE Confidence: 0.27635187

00:14:03.676 --> 00:14:04.816 You know, if you smoke,

NOTE Confidence: 0.27635187

00:14:04.820 --> 00:14:05.720 you're more likely to have

NOTE Confidence: 0.27635187

00:14:05.720 --> 00:14:06.620 other mutations like K Ras.

NOTE Confidence: 0.27635187

00:14:06.620 --> 00:14:08.576 And the never smokers did well,

NOTE Confidence: 0.27635187

00:14:08.580 --> 00:14:09.735 we did a lot of skin biopsies.

NOTE Confidence: 0.27635187

00:14:09.740 --> 00:14:11.049 That's that's when I first met Pat

NOTE Confidence: 0.27635187

00:14:11.049 --> 00:14:12.464 because we were talking at the meeting

NOTE Confidence: 0.27635187

00:14:12.464 --> 00:14:13.879 about doing skin biopsies and I was

NOTE Confidence: 0.27635187

00:14:13.879 --> 00:14:15.292 at MD Anderson at the time and I said,

NOTE Confidence: 0.27635187

00:14:15.300 --> 00:14:15.484 oh,

NOTE Confidence: 0.27635187

00:14:15.484 --> 00:14:16.772 I need to bring in my dermatologist

NOTE Confidence: 0.27635187

00:14:16.772 --> 00:14:18.188 and we need to do a contract and

NOTE Confidence: 0.27635187

00:14:18.188 --> 00:14:19.588 Pat just gets up and says I do

NOTE Confidence: 0.27635187

00:14:19.588 --> 00:14:20.747 them myself and then sew them up.

NOTE Confidence: 0.27635187

00:14:20.747 --> 00:14:22.220 And I was a little scared of her at the time.

NOTE Confidence: 0.27635187

00:14:22.220 --> 00:14:23.296 It was like pretty.

NOTE Confidence: 0.27635187

00:14:23.296 --> 00:14:25.215 She was pretty intimidating and and and

NOTE Confidence: 0.27635187

00:14:25.215 --> 00:14:27.215 now you know why she's been so successful.

NOTE Confidence: 0.27635187

00:14:27.220 --> 00:14:29.340 She does it herself.

NOTE Confidence: 0.27635187

00:14:29.340 --> 00:14:31.152 Well, then of course skipping a

NOTE Confidence: 0.27635187

00:14:31.152 --> 00:14:32.868 little ahead because it's only an

NOTE Confidence: 0.27635187

00:14:32.868 --> 00:14:34.324 hour talk about four years later,

NOTE Confidence: 0.27635187

00:14:34.324 --> 00:14:35.077 five years later.

NOTE Confidence: 0.27635187

00:14:35.080 --> 00:14:36.190 And John Mendelson and I used

NOTE Confidence: 0.27635187

00:14:36.190 --> 00:14:37.160 to always talk about that.

NOTE Confidence: 0.27635187

00:14:37.160 --> 00:14:38.080 How can we keep it?

NOTE Confidence: 0.27635187

00:14:38.080 --> 00:14:39.718 Actually it was eight years later,

NOTE Confidence: 0.27635187

00:14:39.720 --> 00:14:40.692 the mutations were discovered.

NOTE Confidence: 0.27635187

00:14:40.692 --> 00:14:42.560 How can we do this more quickly?

NOTE Confidence: 0.27635187

00:14:42.560 --> 00:14:43.904 That's why with all the work we're

NOTE Confidence: 0.27635187

00:14:43.904 --> 00:14:45.040 doing with pathology and biomarkers,

NOTE Confidence: 0.27635187

00:14:45.040 --> 00:14:46.678 we've got to be even quicker now.

NOTE Confidence: 0.27635187

00:14:46.680 --> 00:14:47.835 But back then it took a while.

NOTE Confidence: 0.27635187

00:14:47.840 --> 00:14:50.000 Sequencing techniques were still developing.

NOTE Confidence: 0.27635187

00:14:50.000 --> 00:14:51.120 You know, it wasn't long before this.

NOTE Confidence: 0.27635187

00:14:51.120 --> 00:14:52.646 We're just doing the Max and Gilbert

NOTE Confidence: 0.27635187

00:14:52.646 --> 00:14:53.950 sequencing and reading the gels, right.

NOTE Confidence: 0.27635187

00:14:53.950 --> 00:14:54.490 So but,

NOTE Confidence: 0.27635187

00:14:54.490 --> 00:14:55.840 but a couple of centers,

NOTE Confidence: 0.27635187

00:14:55.840 --> 00:14:58.272 Boston and New York took the samples from

NOTE Confidence: 0.27635187

00:14:58.272 --> 00:15:00.349 patients who were getting these drugs.

NOTE Confidence: 0.27635187

00:15:00.350 --> 00:15:02.226 These drugs went to what we call

NOTE Confidence: 0.27635187

00:15:02.226 --> 00:15:03.395 an extended access trial.

NOTE Confidence: 0.27635187

00:15:03.395 --> 00:15:05.777 People could get it off label while

NOTE Confidence: 0.27635187

00:15:05.777 --> 00:15:07.086 that while we were waiting for the

NOTE Confidence: 0.27635187

00:15:07.086 --> 00:15:08.578 drugs to be approved and many patients

NOTE Confidence: 0.27635187

00:15:08.578 --> 00:15:10.068 were treated and of course it was

NOTE Confidence: 0.27635187

00:15:10.068 --> 00:15:11.190 found that in the EGFR receptor,

NOTE Confidence: 0.27635187

00:15:11.190 --> 00:15:12.226 which of course would be a dimer.

NOTE Confidence: 0.27635187

00:15:12.230 --> 00:15:13.695 This is a simplification in

NOTE Confidence: 0.27635187

00:15:13.695 --> 00:15:14.867 the tyrosine kinase domain.

NOTE Confidence: 0.27635187

00:15:14.870 --> 00:15:17.000 There were specific mutations mostly at

NOTE Confidence: 0.27635187

00:15:17.000 --> 00:15:19.437 that time discovered in exxons 19 and 21.

NOTE Confidence: 0.27635187

00:15:19.440 --> 00:15:21.078 Now we see them in Exxon 20 as well.

NOTE Confidence: 0.27635187

00:15:21.080 --> 00:15:22.922 And these mutations of course activated

NOTE Confidence: 0.27635187

00:15:22.922 --> 00:15:24.838 and caused this to be a driver.

NOTE Confidence: 0.27635187

00:15:24.840 --> 00:15:26.574 And then these small molecules bound

NOTE Confidence: 0.27635187

00:15:26.574 --> 00:15:28.797 into the ATP binding site and we're very,

NOTE Confidence: 0.27635187

00:15:28.800 --> 00:15:29.346 very potent.

NOTE Confidence: 0.27635187

00:15:29.346 --> 00:15:30.438 They had some rash,

NOTE Confidence: 0.27635187

00:15:30.440 --> 00:15:31.292 they had some diarrhea,

NOTE Confidence: 0.27635187

00:15:31.292 --> 00:15:32.357 but they were very potent.

NOTE Confidence: 0.5602203

00:15:32.360 --> 00:15:33.920 And that led to this is actually being

NOTE Confidence: 0.5602203

00:15:33.920 --> 00:15:35.799 in a place like MD Anderson patients just

NOTE Confidence: 0.5602203

00:15:35.799 --> 00:15:38.037 flowed in and we had a big phase one clinic.

NOTE Confidence: 0.5602203

00:15:38.040 --> 00:15:40.101 I think we must have treated a couple 100

NOTE Confidence: 0.5602203

00:15:40.101 --> 00:15:41.887 patients in the first two or three years and

NOTE Confidence: 0.5602203

00:15:41.887 --> 00:15:43.920 I LED the trial and that's Cicely Harris.

NOTE Confidence: 0.5602203

00:15:43.920 --> 00:15:45.635 She was one of the first patients.

NOTE Confidence: 0.5602203

00:15:45.640 --> 00:15:46.949 And, you know, she was written up

NOTE Confidence: 0.5602203

00:15:46.949 --> 00:15:48.315 in the Wall Street Journal because

NOTE Confidence: 0.5602203

00:15:48.315 --> 00:15:49.839 the idea was we probably didn't.

NOTE Confidence: 0.5602203

00:15:49.840 --> 00:15:50.836 We didn't cure her lung cancer.

NOTE Confidence: 0.5602203

00:15:50.840 --> 00:15:52.040 She only lived for nine years,

NOTE Confidence: 0.5602203

00:15:52.040 --> 00:15:53.640 but we prolonged her survival

NOTE Confidence: 0.5602203

00:15:53.640 --> 00:15:55.240 with good quality of life.

NOTE Confidence: 0.5602203

00:15:55.240 --> 00:15:56.800 And that's why Tara Parker Pope,

NOTE Confidence: 0.5602203

00:15:56.800 --> 00:15:58.795 you know, wrote this article about her.

NOTE Confidence: 0.5602203

00:15:58.800 --> 00:16:00.910 It's like insulin for diabetes

NOTE Confidence: 0.5602203

00:16:00.910 --> 00:16:02.492 or or hypertensive medicine.

NOTE Confidence: 0.5602203

00:16:02.492 --> 00:16:03.956 But that's the problem.

NOTE Confidence: 0.5602203

00:16:03.960 --> 00:16:05.304 And it continues to be the problem

NOTE Confidence: 0.5602203

00:16:05.304 --> 00:16:06.359 with EGFR mutated lung cancer.

NOTE Confidence: 0.5602203

00:16:06.360 --> 00:16:08.280 I've been doing this for 25 plus years.

NOTE Confidence: 0.5602203

00:16:08.280 --> 00:16:09.655 No one's unfortunately in the

NOTE Confidence: 0.5602203

00:16:09.655 --> 00:16:10.755 advanced stage ever cured.

NOTE Confidence: 0.5602203

00:16:10.760 --> 00:16:11.756 That's why the work that Katie

NOTE Confidence: 0.5602203

00:16:11.756 --> 00:16:12.680 and her lab are doing.

NOTE Confidence: 0.5602203

00:16:12.680 --> 00:16:14.038 Mark Lemon, I'll show you the project.

NOTE Confidence: 0.5602203

00:16:14.040 --> 00:16:16.021 We have to find new agents because

NOTE Confidence: 0.5602203

00:16:16.021 --> 00:16:18.068 we to always stay one step ahead

NOTE Confidence: 0.5602203

00:16:18.068 --> 00:16:19.940 of the cancer and this just shows

NOTE Confidence: 0.5602203

00:16:19.940 --> 00:16:21.470 that these are the first generation

NOTE Confidence: 0.5602203

00:16:21.525 --> 00:16:22.917 drugs gafitinib and orlatinib.

NOTE Confidence: 0.5602203

00:16:22.920 --> 00:16:24.720 This was known as OSI 774.

NOTE Confidence: 0.5602203

00:16:24.720 --> 00:16:26.112 For those those interested,

NOTE Confidence: 0.5602203

00:16:26.112 --> 00:16:28.200 this was actually a Pfizer drug

NOTE Confidence: 0.5602203

00:16:28.265 --> 00:16:29.920 and Pfizer when they merged,

NOTE Confidence: 0.5602203

00:16:29.920 --> 00:16:31.600 when they took over the Pharmacia drug,

NOTE Confidence: 0.5602203

00:16:31.600 --> 00:16:32.944 they they went with the Pharmacia

NOTE Confidence: 0.5602203

00:16:32.944 --> 00:16:34.836 product and made a bit of a mistake

NOTE Confidence: 0.5602203

00:16:34.836 --> 00:16:36.021 because this drugs actually became

NOTE Confidence: 0.5602203

00:16:36.021 --> 00:16:37.600 the the number one ETFR inhibitor.

NOTE Confidence: 0.5602203

00:16:37.600 --> 00:16:39.400 These are, these are reversible inhibitors.

NOTE Confidence: 0.5602203

00:16:39.400 --> 00:16:41.410 They're non specific for mutated cells

NOTE Confidence: 0.5602203

00:16:41.410 --> 00:16:44.168 that get both wild type and mutated cells.

NOTE Confidence: 0.5602203

00:16:44.170 --> 00:16:45.689 Then there was a second generation drug,

NOTE Confidence: 0.5602203

00:16:45.690 --> 00:16:46.704 a fat nib,

NOTE Confidence: 0.5602203

00:16:46.704 --> 00:16:49.530 which also blocked her two and her four.

NOTE Confidence: 0.5602203

00:16:49.530 --> 00:16:51.210 You add more TKI activity,

NOTE Confidence: 0.5602203

00:16:51.210 --> 00:16:52.562 you get more toxicity.

NOTE Confidence: 0.5602203

00:16:52.562 --> 00:16:55.050 We actually did a big trial of

NOTE Confidence: 0.5602203

00:16:55.050 --> 00:16:56.970 this with cetuximab showed some

NOTE Confidence: 0.5602203

00:16:56.970 --> 00:16:58.750 increased activity but not enough.

NOTE Confidence: 0.5602203

00:16:58.750 --> 00:17:00.731 And then of course the the third

NOTE Confidence: 0.5602203

00:17:00.731 --> 00:17:01.948 generation drug asimertinib which

NOTE Confidence: 0.5602203

00:17:01.948 --> 00:17:03.528 is an irreversible inhibitor which

NOTE Confidence: 0.5602203

00:17:03.528 --> 00:17:05.411 has good brain penetration and it's

NOTE Confidence: 0.5602203

00:17:05.411 --> 00:17:06.826 easier for our mutation specific.

NOTE Confidence: 0.5602203

00:17:06.830 --> 00:17:09.147 So they'll there's less rash and diarrhea.

NOTE Confidence: 0.5602203

00:17:09.150 --> 00:17:11.046 It can be given to patients for longer

NOTE Confidence: 0.5602203

00:17:11.046 --> 00:17:12.326 periods of time without toxicity

NOTE Confidence: 0.5602203

00:17:12.326 --> 00:17:14.376 and that's how it we were able to

NOTE Confidence: 0.5602203

00:17:14.376 --> 00:17:16.028 move this drug to the earlier stage.

NOTE Confidence: 0.5602203

00:17:16.030 --> 00:17:17.955 And this is just an example and

NOTE Confidence: 0.5602203

00:17:17.955 --> 00:17:19.214 again I'm just giving you a bit

NOTE Confidence: 0.5602203

00:17:19.214 --> 00:17:19.870 of an overview today,

NOTE Confidence: 0.5602203

00:17:19.870 --> 00:17:21.952 but the most common mutation for

NOTE Confidence: 0.5602203

00:17:21.952 --> 00:17:24.360 resistance is known as T790M And the

NOTE Confidence: 0.5602203

00:17:24.360 --> 00:17:26.400 patients that have that this drug

NOTE Confidence: 0.5602203

00:17:26.400 --> 00:17:28.355 lasimertinib you know was first studied

NOTE Confidence: 0.5602203

00:17:28.355 --> 00:17:29.970 to target that resistance mutation

NOTE Confidence: 0.5602203

00:17:30.026 --> 00:17:31.721 which is about 50% of the resistance

NOTE Confidence: 0.5602203

00:17:31.721 --> 00:17:33.450 and you can see the activity that

NOTE Confidence: 0.5602203

00:17:33.499 --> 00:17:35.024 was seen there over 6070% response.

NOTE Confidence: 0.5602203

00:17:35.024 --> 00:17:36.534 And this quickly became the

NOTE Confidence: 0.5602203

00:17:36.534 --> 00:17:38.270 front line agent again bring your

NOTE Confidence: 0.5602203

00:17:38.270 --> 00:17:39.812 best drugs to the front line.

NOTE Confidence: 0.5602203

00:17:39.820 --> 00:17:41.899 But again few if any are cured.

NOTE Confidence: 0.5602203

00:17:41.900 --> 00:17:42.716 That's the problem.

NOTE Confidence: 0.5602203

00:17:42.716 --> 00:17:44.620 That's what I'm gonna talk to you

NOTE Confidence: 0.5602203

00:17:44.677 --> 00:17:46.765 about now I was at MD Anderson

NOTE Confidence: 0.5602203

00:17:46.765 --> 00:17:48.960 and you know when you you know

NOTE Confidence: 0.5602203

00:17:48.960 --> 00:17:50.500 here we put about 100

NOTE Confidence: 0.27161515

00:17:50.579 --> 00:17:52.740 and 10120 patients on lung trials

NOTE Confidence: 0.27161515

00:17:52.740 --> 00:17:54.630 in a Goodyear there we're putting

NOTE Confidence: 0.27161515

00:17:54.630 --> 00:17:56.310 with three or 400 patients on trial.

NOTE Confidence: 0.27161515

00:17:56.310 --> 00:17:57.920 But what I noticed I was leading

NOTE Confidence: 0.27161515

00:17:57.920 --> 00:17:59.707 the group lung group there is we're

NOTE Confidence: 0.27161515

00:17:59.707 --> 00:18:01.267 doing it on 20 different trials.

NOTE Confidence: 0.27161515

00:18:01.270 --> 00:18:03.664 So we we said can we do one trial

NOTE Confidence: 0.27161515

00:18:03.670 --> 00:18:06.274 and and and use biomarkers to

NOTE Confidence: 0.27161515

00:18:06.274 --> 00:18:08.950 decide who should get which drug

NOTE Confidence: 0.27161515

00:18:08.950 --> 00:18:10.525 and wasn't easy 'cause you know if

NOTE Confidence: 0.27161515

00:18:10.525 --> 00:18:12.463 you have a group that's 20 people

NOTE Confidence: 0.27161515

00:18:12.463 --> 00:18:14.269 everyone has their own favorite drug.

NOTE Confidence: 0.27161515

00:18:14.270 --> 00:18:16.252 It it really is a a sociology project

NOTE Confidence: 0.27161515

00:18:16.252 --> 00:18:18.906 and we didn't have a sociology department

NOTE Confidence: 0.27161515

00:18:18.906 --> 00:18:21.354 there like we have here or or psychology.

NOTE Confidence: 0.27161515

00:18:21.360 --> 00:18:23.096 But what we did is we actually

NOTE Confidence: 0.27161515

00:18:23.096 --> 00:18:24.704 convinced the team that it would be

NOTE Confidence: 0.27161515

00:18:24.704 --> 00:18:26.452 better for all of us to work together

NOTE Confidence: 0.27161515

00:18:26.452 --> 00:18:28.356 on one trial and we used a little

NOTE Confidence: 0.27161515

00:18:28.360 --> 00:18:30.208 bit of push and and and and and

NOTE Confidence: 0.27161515

00:18:30.208 --> 00:18:32.231 there was a pull though because the

NOTE Confidence: 0.27161515

00:18:32.231 --> 00:18:34.343 science was exciting and at that time

NOTE Confidence: 0.27161515

00:18:34.343 --> 00:18:36.275 and and David Meta who's here now,

NOTE Confidence: 0.27161515

00:18:36.280 --> 00:18:38.192 I work with him at that time we

NOTE Confidence: 0.27161515

00:18:38.192 --> 00:18:40.157 we we we could get biopsies.

NOTE Confidence: 0.27161515

00:18:40.160 --> 00:18:44.130 Core biopsies, prior to 2004,

NOTE Confidence: 0.27161515

00:18:44.130 --> 00:18:45.630 2005, most lung cancer biopsies

NOTE Confidence: 0.27161515

00:18:45.630 --> 00:18:46.830 were fine needle aspirations.

NOTE Confidence: 0.27161515

00:18:46.830 --> 00:18:48.430 You had a little bit of few cells,

NOTE Confidence: 0.27161515

00:18:48.430 --> 00:18:49.270 maybe you made a cell block,

NOTE Confidence: 0.27161515

00:18:49.270 --> 00:18:50.555 but you didn't have really

NOTE Confidence: 0.27161515

00:18:50.555 --> 00:18:51.583 enough tissue for sequencing.

NOTE Confidence: 0.27161515

00:18:51.590 --> 00:18:52.674 But now that sequencing

NOTE Confidence: 0.27161515

00:18:52.674 --> 00:18:54.029 was coming to to bear.

NOTE Confidence: 0.27161515

00:18:54.030 --> 00:18:56.343 We said can we do a trial called Battle

NOTE Confidence: 0.27161515

00:18:56.350 --> 00:18:57.628 and we worked with a pathologist,

NOTE Confidence: 0.27161515

00:18:57.630 --> 00:19:00.856 Ignacio Astuba Jack Lee,

NOTE Confidence: 0.27161515

00:19:00.856 --> 00:19:01.762 a biostatistician,

NOTE Confidence: 0.27161515

00:19:01.762 --> 00:19:04.152 Ed Kim now at City of Hope and

NOTE Confidence: 0.27161515

00:19:04.152 --> 00:19:05.589 with our mentor Wang Ki Han.

NOTE Confidence: 0.27161515

00:19:05.590 --> 00:19:08.187 We developed a trial we called Battle

NOTE Confidence: 0.27161515

00:19:08.190 --> 00:19:10.045 and what we called it is biomarker

NOTE Confidence: 0.27161515

00:19:10.045 --> 00:19:11.242 integrated approach of targeted

NOTE Confidence: 0.27161515

00:19:11.242 --> 00:19:12.987 therapy for lung cancer elimination.

NOTE Confidence: 0.27161515

00:19:12.990 --> 00:19:14.678 So what we did is we had four

NOTE Confidence: 0.27161515

00:19:14.678 --> 00:19:16.069 or five different drugs.

NOTE Confidence: 0.27161515

00:19:16.070 --> 00:19:16.942 We did a biopsy.

NOTE Confidence: 0.27161515

00:19:16.942 --> 00:19:18.528 We got the result within 14 days

NOTE Confidence: 0.27161515

00:19:18.528 --> 00:19:20.312 and then we used that result to say

NOTE Confidence: 0.27161515

00:19:20.312 --> 00:19:22.030 this patient has an EGFR mutation,

NOTE Confidence: 0.27161515

00:19:22.030 --> 00:19:23.310 they should go on herlatinib.

NOTE Confidence: 0.27161515

00:19:23.310 --> 00:19:24.990 This patient has a VEGF up regulation,

NOTE Confidence: 0.27161515

00:19:24.990 --> 00:19:26.873 they should go on VET detonib and

NOTE Confidence: 0.27161515

00:19:26.873 --> 00:19:28.898 I actually think it's and we used

NOTE Confidence: 0.27161515

00:19:28.898 --> 00:19:30.478 an adaptive statistical design and

NOTE Confidence: 0.27161515

00:19:30.478 --> 00:19:32.429 I've talked about that here before.

NOTE Confidence: 0.27161515

00:19:32.430 --> 00:19:34.230 The results did pan out.

NOTE Confidence: 0.27161515

00:19:34.230 --> 00:19:34.601 We,

NOTE Confidence: 0.27161515

00:19:34.601 --> 00:19:37.198 we found new biomarkers for VEGF inhibitors.

NOTE Confidence: 0.27161515

00:19:37.200 --> 00:19:39.760 The EGFR mutation came out of the story.

NOTE Confidence: 0.27161515

00:19:39.760 --> 00:19:40.993 Now of course you say we knew that already,

NOTE Confidence: 0.27161515

00:19:41.000 --> 00:19:41.777 but we didn't.

NOTE Confidence: 0.27161515

00:19:41.777 --> 00:19:43.590 This was before the mutation was fully

NOTE Confidence: 0.27161515

00:19:43.648 --> 00:19:45.412 validated and we showed that core

NOTE Confidence: 0.27161515

00:19:45.412 --> 00:19:47.079 biopsies were feasible and and safe.

NOTE Confidence: 0.27161515

00:19:47.080 --> 00:19:49.114 And this is about when I came to Yale.

NOTE Confidence: 0.27161515

00:19:49.120 --> 00:19:49.996 So when I came to Yale,

NOTE Confidence: 0.27161515

00:19:50.000 --> 00:19:51.476 I said let's let's do a battle trial here.

NOTE Confidence: 0.27161515

00:19:51.480 --> 00:19:52.894 And David RIM, my friend in the

NOTE Confidence: 0.27161515

00:19:52.894 --> 00:19:54.360 front row and that's Jeff Sklar.

NOTE Confidence: 0.27161515

00:19:54.360 --> 00:19:55.790 I miss good old Jeff.

NOTE Confidence: 0.27161515

00:19:55.790 --> 00:19:56.136 You know,

NOTE Confidence: 0.27161515

00:19:56.136 --> 00:19:57.734 he used to always be in the front row

NOTE Confidence: 0.27161515

00:19:57.734 --> 00:19:59.086 at the grand rounds he'd be here and

NOTE Confidence: 0.27161515

00:19:59.086 --> 00:20:00.627 I I said can we do a core biopsies?

NOTE Confidence: 0.27161515

00:20:00.630 --> 00:20:01.673 And they told me we had one

NOTE Confidence: 0.27161515

00:20:01.673 --> 00:20:02.588 table where we could do it.

NOTE Confidence: 0.27161515

00:20:02.590 --> 00:20:04.510 You know, there's no, no capacity.

NOTE Confidence: 0.27161515

00:20:04.510 --> 00:20:07.150 I was saying I should go back home and then

NOTE Confidence: 0.80064046

00:20:07.150 --> 00:20:09.088 that that was Rocco who was

NOTE Confidence: 0.80064046

00:20:09.088 --> 00:20:10.989 working with us from the CTO.

NOTE Confidence: 0.80064046

00:20:10.990 --> 00:20:12.262 And that's Julie Boyer,

NOTE Confidence: 0.80064046

00:20:12.262 --> 00:20:14.710 that's Emily who now works as an APRN.

NOTE Confidence: 0.80064046

00:20:14.710 --> 00:20:16.390 She was a researcher nurse at the time.

NOTE Confidence: 0.80064046

00:20:16.390 --> 00:20:17.741 We put a little team together and

NOTE Confidence: 0.80064046

00:20:17.741 --> 00:20:19.335 we ended up putting about 40 or 50

NOTE Confidence: 0.80064046

00:20:19.335 --> 00:20:20.910 patients on the on the battle trial.

NOTE Confidence: 0.80064046

00:20:20.910 --> 00:20:22.686 Now it wasn't as many as a 300

NOTE Confidence: 0.80064046

00:20:22.686 --> 00:20:24.284 MD Anderson but we started doing

NOTE Confidence: 0.80064046

00:20:24.284 --> 00:20:25.934 a tissue based approach and and

NOTE Confidence: 0.80064046

00:20:25.987 --> 00:20:27.667 the team started to work together

NOTE Confidence: 0.80064046

00:20:27.667 --> 00:20:29.573 and and that that's how that was

NOTE Confidence: 0.80064046

00:20:29.573 --> 00:20:31.400 we were doing that and that was

NOTE Confidence: 0.80064046

00:20:31.459 --> 00:20:33.731 actually funded by an RO one that I

NOTE Confidence: 0.80064046

00:20:33.731 --> 00:20:35.669 brought with me from from Anderson.

NOTE Confidence: 0.80064046

00:20:35.670 --> 00:20:37.389 But moving to the what I want to tell

NOTE Confidence: 0.80064046

00:20:37.389 --> 00:20:38.932 you about it in my first story is

NOTE Confidence: 0.80064046

00:20:38.932 --> 00:20:40.708 how can we do better in lung cancer.

NOTE Confidence: 0.80064046

00:20:40.710 --> 00:20:42.131 We're not going to do better by

NOTE Confidence: 0.80064046

00:20:42.131 --> 00:20:43.055 using these targeted therapies

NOTE Confidence: 0.80064046

00:20:43.055 --> 00:20:44.147 just in advanced disease.

NOTE Confidence: 0.80064046

00:20:44.150 --> 00:20:45.837 We have to find the disease earlier

NOTE Confidence: 0.80064046

00:20:45.837 --> 00:20:47.231 and we're finding disease early

NOTE Confidence: 0.80064046

00:20:47.231 --> 00:20:49.091 because of screening and because of

NOTE Confidence: 0.80064046

00:20:49.091 --> 00:20:50.649 smoking prevention and at the time

NOTE Confidence: 0.80064046

00:20:50.649 --> 00:20:51.987 that someone comes in for smoking

NOTE Confidence: 0.80064046

00:20:51.990 --> 00:20:53.710 prevention that's a teachable moment.

NOTE Confidence: 0.80064046

00:20:53.710 --> 00:20:55.152 But we know that even in lung

NOTE Confidence: 0.80064046

00:20:55.152 --> 00:20:56.647 cancer when you find it early you

NOTE Confidence: 0.80064046

00:20:56.647 --> 00:20:58.172 know and so often they find it

NOTE Confidence: 0.80064046

00:20:58.172 --> 00:20:59.588 in the emergency room these days,

NOTE Confidence: 0.80064046

00:20:59.590 --> 00:21:00.610 right they're doing a cardiac

NOTE Confidence: 0.80064046

00:21:00.610 --> 00:21:01.630 scan or some other scan.

NOTE Confidence: 0.80064046

00:21:01.630 --> 00:21:03.310 Someone has a small nodule,

NOTE Confidence: 0.80064046

00:21:03.310 --> 00:21:04.960 the five year old survival even

NOTE Confidence: 0.80064046

00:21:04.960 --> 00:21:07.052 even there is only 60 to 74% that's

NOTE Confidence: 0.80064046

00:21:07.052 --> 00:21:08.707 how metastatic lung cancer is.

NOTE Confidence: 0.80064046

00:21:08.710 --> 00:21:11.230 And if it's stage 2 with a few other nodes,

NOTE Confidence: 0.80064046

00:21:11.230 --> 00:21:13.718 47 to 55% and it happens to be

NOTE Confidence: 0.80064046

00:21:13.718 --> 00:21:16.190 stage 3 with N2 lymph nodes or

NOTE Confidence: 0.80064046

00:21:16.190 --> 00:21:18.470 stage 3 B 38% five year survival.

NOTE Confidence: 0.80064046

00:21:18.470 --> 00:21:21.186 So even early disease even with chemotherapy

NOTE Confidence: 0.80064046

00:21:21.186 --> 00:21:24.230 is not as curable as we would like.

NOTE Confidence: 0.80064046

00:21:24.230 --> 00:21:26.278 So if someone has an EGFR mutation which

NOTE Confidence: 0.80064046

00:21:26.278 --> 00:21:28.272 are about 1015% of the patients in the

NOTE Confidence: 0.80064046

00:21:28.272 --> 00:21:31.160 Western world and as many as 40% in the East,

NOTE Confidence: 0.80064046

00:21:31.160 --> 00:21:31.590 Asia,

NOTE Confidence: 0.80064046

00:21:31.590 --> 00:21:32.020 China,

NOTE Confidence: 0.80064046

00:21:32.020 --> 00:21:33.315 wouldn't it be nice if we could

NOTE Confidence: 0.80064046

00:21:33.315 --> 00:21:34.670 and we know that the percentage

NOTE Confidence: 0.80064046

00:21:34.670 --> 00:21:36.170 of mutations are about the same

NOTE Confidence: 0.80064046

00:21:36.170 --> 00:21:37.459 across the spectrum of stages.

NOTE Confidence: 0.80064046

00:21:37.460 --> 00:21:38.930 Wouldn't it be nice if we could

NOTE Confidence: 0.80064046

00:21:38.930 --> 00:21:40.460 give the EGFR inhibitor earlier.

NOTE Confidence: 0.80064046

00:21:40.460 --> 00:21:42.948 So that's that we we sat down about

NOTE Confidence: 0.80064046

00:21:42.948 --> 00:21:45.167 10 years ago now a group of us

NOTE Confidence: 0.80064046

00:21:45.167 --> 00:21:47.472 and I had a colleague Masa Hara

NOTE Confidence: 0.80064046

00:21:47.472 --> 00:21:50.262 Suboi from Japan and Ylan Wu from

NOTE Confidence: 0.80064046

00:21:50.262 --> 00:21:52.054 China working with AstraZeneca.

NOTE Confidence: 0.80064046

00:21:52.060 --> 00:21:53.776 We said let's let's design this

NOTE Confidence: 0.80064046

00:21:53.776 --> 00:21:55.500 trial now and they were very

NOTE Confidence: 0.80064046

00:21:55.500 --> 00:21:56.940 proactive and and and they said,

NOTE Confidence: 0.80064046

00:21:56.940 --> 00:21:57.166 yeah,

NOTE Confidence: 0.80064046

00:21:57.166 --> 00:21:58.974 let's do it because they we knew an

NOTE Confidence: 0.80064046

00:21:58.974 --> 00:22:00.794 active and trial would take a long time.

NOTE Confidence: 0.80064046

00:22:00.800 --> 00:22:02.920 So that's the Adura trial and the idea

NOTE Confidence: 0.80064046

00:22:02.920 --> 00:22:05.334 was to take patients who had been

NOTE Confidence: 0.80064046

00:22:05.334 --> 00:22:07.159 completely resected for lung cancer

NOTE Confidence: 0.80064046

00:22:07.160 --> 00:22:09.680 and you can see the eligibility here.

NOTE Confidence: 0.80064046

00:22:09.680 --> 00:22:11.624 And then we stratified them by

NOTE Confidence: 0.80064046

00:22:11.624 --> 00:22:13.360 their their stage 1B2 or 3A,

NOTE Confidence: 0.80064046

00:22:13.360 --> 00:22:15.280 they all had R0 resections,

NOTE Confidence: 0.80064046

00:22:15.280 --> 00:22:17.170 meaning all the tumor was removed

NOTE Confidence: 0.80064046

00:22:17.170 --> 00:22:18.115 with clean margins.

NOTE Confidence: 0.80064046

00:22:18.120 --> 00:22:19.770 We only took the two most

NOTE Confidence: 0.80064046

00:22:19.770 --> 00:22:20.595 canonical EGFR mutations,

NOTE Confidence: 0.80064046

00:22:20.600 --> 00:22:23.720 19 and 21 and we we did stratify by race.

NOTE Confidence: 0.80064046

00:22:23.720 --> 00:22:25.435 About 2/3 of these patients were Asia.

NOTE Confidence: 0.5931603

00:22:25.440 --> 00:22:26.372 You can imagine it.

NOTE Confidence: 0.5931603

00:22:26.372 --> 00:22:28.159 There were more of these mutations in Asia,

NOTE Confidence: 0.5931603

00:22:28.160 --> 00:22:30.218 so more patients went on there and

NOTE Confidence: 0.5931603

00:22:30.218 --> 00:22:31.646 then the patients were randomized to

NOTE Confidence: 0.5931603

00:22:31.646 --> 00:22:32.896 firstly they could get chemotherapy

NOTE Confidence: 0.5931603

00:22:32.896 --> 00:22:34.378 if if it was deemed appropriate.

NOTE Confidence: 0.5931603

00:22:34.380 --> 00:22:35.717 Most of this takes two and three

NOTE Confidence: 0.5931603

00:22:35.717 --> 00:22:36.728 lung cancers, get chemotherapy,

NOTE Confidence: 0.5931603

00:22:36.728 --> 00:22:38.298 platinum based chemotherapy and it's

NOTE Confidence: 0.5931603

00:22:38.298 --> 00:22:40.317 about a 5 to 6% improvement in survival.

NOTE Confidence: 0.5931603

00:22:40.317 --> 00:22:42.620 Not a lot but it does improve survival.

NOTE Confidence: 0.5931603

00:22:42.620 --> 00:22:44.996 I I would use it because it's something but

NOTE Confidence: 0.5931603

00:22:44.996 --> 00:22:46.948 then we randomized to either acimertinib

NOTE Confidence: 0.5931603

00:22:46.948 --> 00:22:49.458 at 80 milligrams once a day or placebo.

NOTE Confidence: 0.5931603

00:22:49.460 --> 00:22:51.245 I'm often criticized how could you do

NOTE Confidence: 0.5931603

00:22:51.245 --> 00:22:52.560 a placebo, but there were no data.

NOTE Confidence: 0.5931603

00:22:52.560 --> 00:22:54.121 There were plenty of trials before this

NOTE Confidence: 0.5931603

00:22:54.121 --> 00:22:55.820 that had tried other EKFR inhibitors and

NOTE Confidence: 0.5931603

00:22:55.820 --> 00:22:57.640 looked in this setting and nothing worked.

NOTE Confidence: 0.5931603

00:22:57.640 --> 00:22:58.576 They're all too toxic.

NOTE Confidence: 0.5931603

00:22:58.576 --> 00:23:00.760 But we figured this drug was brain penetrant,

NOTE Confidence: 0.5931603

00:23:00.760 --> 00:23:02.640 it was EKFR mutation specific,

NOTE Confidence: 0.5931603

00:23:02.640 --> 00:23:03.912 it could be used and it

NOTE Confidence: 0.5931603

00:23:03.912 --> 00:23:04.760 would be safely administered.

NOTE Confidence: 0.5931603

00:23:04.760 --> 00:23:06.545 So we used OSTEO Mertini versus placebo

NOTE Confidence: 0.5931603

00:23:06.545 --> 00:23:08.119 and we treated for three years.

NOTE Confidence: 0.5931603

00:23:08.120 --> 00:23:09.440 But the primary endpoint of this

NOTE Confidence: 0.5931603

00:23:09.440 --> 00:23:10.720 trial was disease free survival,

NOTE Confidence: 0.5931603

00:23:10.720 --> 00:23:11.491 no disease recurring.

NOTE Confidence: 0.5931603

00:23:11.491 --> 00:23:13.033 Remember they started with no disease.

NOTE Confidence: 0.5931603

00:23:13.040 --> 00:23:15.200 So we're seeing if anything recurs and the

NOTE Confidence: 0.5931603

00:23:15.200 --> 00:23:17.516 trial was powered for a hazard ratio of .7,

NOTE Confidence: 0.5931603

00:23:17.520 --> 00:23:19.552 meaning a 30% improvement.

NOTE Confidence: 0.5931603

00:23:19.552 --> 00:23:22.210 So about I guess it's almost four

NOTE Confidence: 0.5931603

00:23:22.210 --> 00:23:24.402 years ago now in April there was a

NOTE Confidence: 0.5931603

00:23:24.402 --> 00:23:25.690 safety review of the trial going on.

NOTE Confidence: 0.5931603

00:23:25.690 --> 00:23:27.322 We no efficacy but the cure

NOTE Confidence: 0.5931603

00:23:27.322 --> 00:23:28.410 of that safety committee.

NOTE Confidence: 0.5931603

00:23:28.410 --> 00:23:29.446 I don't know if anyone here has

NOTE Confidence: 0.5931603

00:23:29.446 --> 00:23:30.568 ever been on a safety committee.

NOTE Confidence: 0.5931603

00:23:30.570 --> 00:23:32.250 He said something's wrong here.

NOTE Confidence: 0.5931603

00:23:32.250 --> 00:23:33.730 It looks like one of the groups is

NOTE Confidence: 0.5931603

00:23:33.730 --> 00:23:34.981 doing better than the other and

NOTE Confidence: 0.5931603

00:23:34.981 --> 00:23:36.026 normally it's the control group

NOTE Confidence: 0.5931603

00:23:36.026 --> 00:23:37.556 is doing better and they stop the

NOTE Confidence: 0.5931603

00:23:37.556 --> 00:23:38.772 trial but they actually looked at

NOTE Confidence: 0.5931603

00:23:38.772 --> 00:23:40.039 it and said the the treatment group

NOTE Confidence: 0.5931603

00:23:40.039 --> 00:23:41.050 is doing so much better,

NOTE Confidence: 0.5931603

00:23:41.050 --> 00:23:43.570 it's unethical to keep the trial going.

NOTE Confidence: 0.5931603

00:23:43.570 --> 00:23:43.970 So,

NOTE Confidence: 0.5931603

00:23:43.970 --> 00:23:47.534 so we actually got a call it was in April.

NOTE Confidence: 0.5931603

00:23:47.534 --> 00:23:49.850 We we looked at the data and and

NOTE Confidence: 0.5931603

00:23:49.850 --> 00:23:51.845 actually the hazard ratio I'll show you

NOTE Confidence: 0.5931603

00:23:51.845 --> 00:23:54.145 in a moment was so good that you'll

NOTE Confidence: 0.5931603

00:23:54.145 --> 00:23:56.359 you'll see where things went after that.

NOTE Confidence: 0.5931603

00:23:56.360 --> 00:23:57.356 So this is what we saw.

NOTE Confidence: 0.5931603

00:23:57.360 --> 00:23:59.957 So this was depending on your religion,

NOTE Confidence: 0.5931603

00:23:59.960 --> 00:24:01.196 it was Good Friday and Passover,

NOTE Confidence: 0.5931603

00:24:01.200 --> 00:24:02.680 I I'll go with Passover,

NOTE Confidence: 0.5931603

00:24:02.680 --> 00:24:03.720 but you can see here,

NOTE Confidence: 0.5931603

00:24:03.720 --> 00:24:05.475 here it was in in in that year the

NOTE Confidence: 0.5931603

00:24:05.475 --> 00:24:07.101 stakes 1B and 3A patients here are

NOTE Confidence: 0.5931603

00:24:07.101 --> 00:24:08.574 patients who got the acid mertinib

NOTE Confidence: 0.5931603

00:24:08.574 --> 00:24:10.092 in the adjuvant setting and here

NOTE Confidence: 0.5931603

00:24:10.092 --> 00:24:12.220 is the control and the hazard ratio

NOTE Confidence: 0.5931603

00:24:12.220 --> 00:24:14.350 was .2 or an 80% improvement.

NOTE Confidence: 0.5931603

00:24:14.350 --> 00:24:16.900 So that that was phenomenal,

NOTE Confidence: 0.5931603

00:24:16.900 --> 00:24:17.668 better than expected.

NOTE Confidence: 0.5931603

00:24:17.668 --> 00:24:18.180 Of course,

NOTE Confidence: 0.5931603

00:24:18.180 --> 00:24:19.615 you would expect that this would work,

NOTE Confidence: 0.5931603

00:24:19.620 --> 00:24:21.363 but with this sort of separation and

NOTE Confidence: 0.5931603

00:24:21.363 --> 00:24:23.181 this sort of result and it actually

NOTE Confidence: 0.5931603

00:24:23.181 --> 00:24:24.991 made a plenary talk at ASCO that

NOTE Confidence: 0.5931603

00:24:24.991 --> 00:24:26.685 year and then we've updated it

NOTE Confidence: 0.5931603

00:24:26.685 --> 00:24:27.857 just earlier this year.

NOTE Confidence: 0.5931603

00:24:27.860 --> 00:24:28.799 This is the,

NOTE Confidence: 0.5931603

00:24:28.799 --> 00:24:30.896 this is actually the review at the

NOTE Confidence: 0.5931603

00:24:30.896 --> 00:24:32.630 time when it would have normally

NOTE Confidence: 0.5931603

00:24:32.697 --> 00:24:34.988 been been analyzed and it's still

NOTE Confidence: 0.5931603

00:24:34.988 --> 00:24:36.504 .27 or 73% improvement.

NOTE Confidence: 0.5931603

00:24:36.504 --> 00:24:39.240 So using a drug early keeps the disease

NOTE Confidence: 0.5093791

00:24:39.303 --> 00:24:41.560 from recurring. Now where do you think

NOTE Confidence: 0.5093791

00:24:41.560 --> 00:24:43.580 the disease is kept from recurring from?

NOTE Confidence: 0.5093791

00:24:43.580 --> 00:24:46.012 Well, the first, I guess we'll show you

NOTE Confidence: 0.5093791

00:24:46.012 --> 00:24:49.800 that all all parameters benefited sex,

NOTE Confidence: 0.5093791

00:24:49.800 --> 00:24:51.452 age, whether or not the patient was

NOTE Confidence: 0.5093791

00:24:51.452 --> 00:24:53.896 a prior smoker, Asian or non Asian,

NOTE Confidence: 0.5093791

00:24:53.896 --> 00:24:55.660 all three stages, both mutations.

NOTE Confidence: 0.5093791

00:24:55.660 --> 00:24:57.960 So you always do better with XN 19 deletion,

NOTE Confidence: 0.5093791

00:24:57.960 --> 00:24:59.769 it's a loss of it's a deletion versus the

NOTE Confidence: 0.5093791

00:24:59.769 --> 00:25:01.299 point mutation which can revert a bit

NOTE Confidence: 0.5093791

00:25:01.299 --> 00:25:03.283 easier and you can see whether or not

NOTE Confidence: 0.5093791

00:25:03.283 --> 00:25:04.638 the patient got adjuvant chemotherapy.

NOTE Confidence: 0.5093791

00:25:04.640 --> 00:25:05.954 When you look at a forest pot like that,

NOTE Confidence: 0.5093791

00:25:05.960 --> 00:25:07.318 for those who aren't used to it,

NOTE Confidence: 0.5093791

00:25:07.320 --> 00:25:10.440 anything to the left of 1 is good.

NOTE Confidence: 0.5093791

00:25:10.440 --> 00:25:13.223 And then if you look what happened is in

NOTE Confidence: 0.5093791

00:25:13.223 --> 00:25:15.904 the patients who got out to Mercenib,

NOTE Confidence: 0.5093791

00:25:15.910 --> 00:25:17.506 you can see actually let's start here,

NOTE Confidence: 0.5093791

00:25:17.510 --> 00:25:19.647 here the patients got placebo 46%

NOTE Confidence: 0.5093791

00:25:19.647 --> 00:25:20.241 who recurred.

NOTE Confidence: 0.5093791

00:25:20.241 --> 00:25:22.320 You can see that many of those

NOTE Confidence: 0.5093791

00:25:22.384 --> 00:25:23.869 are distant recurrences.

NOTE Confidence: 0.5093791

00:25:23.870 --> 00:25:25.340 Whereas in the small number of

NOTE Confidence: 0.5093791

00:25:25.340 --> 00:25:27.047 patients in the early data who who

NOTE Confidence: 0.5093791

00:25:27.047 --> 00:25:28.403 who recurred on the ASA emergent

NOTE Confidence: 0.5093791

00:25:28.403 --> 00:25:30.066 of on the treatment job drug only

NOTE Confidence: 0.5093791

00:25:30.066 --> 00:25:31.640 about half as many were distant.

NOTE Confidence: 0.5093791

00:25:31.640 --> 00:25:33.265 The drug is keeping patients

NOTE Confidence: 0.5093791

00:25:33.265 --> 00:25:34.870 from getting distant metastases.

NOTE Confidence: 0.5093791

00:25:34.870 --> 00:25:36.510 That's what causes patients to

NOTE Confidence: 0.5093791

00:25:36.510 --> 00:25:38.150 die metastases to other organs,

NOTE Confidence: 0.5093791

00:25:38.150 --> 00:25:39.082 brain, liver and bone.

NOTE Confidence: 0.5093791

00:25:39.082 --> 00:25:40.480 And actually we looked at that

NOTE Confidence: 0.5093791

00:25:40.529 --> 00:25:41.849 and this is pretty phenomenal.

NOTE Confidence: 0.5093791

00:25:41.850 --> 00:25:43.264 This is looking at the brain as

NOTE Confidence: 0.5093791

00:25:43.264 --> 00:25:44.529 the first site of recurrence,

NOTE Confidence: 0.5093791

00:25:44.530 --> 00:25:45.570 which is a major issue.

NOTE Confidence: 0.5093791

00:25:45.570 --> 00:25:47.604 If if you ask a patient with lung cancer,

NOTE Confidence: 0.5093791

00:25:47.610 --> 00:25:48.842 he or she will tell you I'm

NOTE Confidence: 0.5093791

00:25:48.842 --> 00:25:49.650 worried about my brain.

NOTE Confidence: 0.5093791

00:25:49.650 --> 00:25:52.404 We just had AEAB for our spore last Monday.

NOTE Confidence: 0.5093791

00:25:52.410 --> 00:25:53.450 That's exactly what our

NOTE Confidence: 0.5093791

00:25:53.450 --> 00:25:54.490 patient advocate told us.

NOTE Confidence: 0.5093791

00:25:54.490 --> 00:25:57.140 But you can see here's patients adjuvant

NOTE Confidence: 0.5093791

00:25:57.140 --> 00:25:58.790 disease who got last Emergenib.

NOTE Confidence: 0.5093791

00:25:58.790 --> 00:26:00.350 Here's the control group hazard

NOTE Confidence: 0.5093791

00:26:00.350 --> 00:26:02.230 ratio for recurrence in the brain

NOTE Confidence: 0.5093791

00:26:02.230 --> 00:26:04.966 .24 meaning a 76% decrease in in the

NOTE Confidence: 0.5093791

00:26:04.966 --> 00:26:06.950 first recurrence being in the brain.

NOTE Confidence: 0.5093791

00:26:06.950 --> 00:26:08.870 So it's keeping the tumor from the brain.

NOTE Confidence: 0.5093791

00:26:08.870 --> 00:26:10.823 We'll we'll do this forever probably not

NOTE Confidence: 0.5093791

00:26:10.823 --> 00:26:13.390 but but it did it for a long period of time.

NOTE Confidence: 0.5093791

00:26:13.390 --> 00:26:15.720 We treated for three years and

NOTE Confidence: 0.5093791

00:26:15.720 --> 00:26:17.750 here you can see now now everyone

NOTE Confidence: 0.5093791

00:26:17.750 --> 00:26:19.437 was sceptical you know I don't I

NOTE Confidence: 0.5093791

00:26:19.437 --> 00:26:21.230 I never used to do the Twitter.

NOTE Confidence: 0.5093791

00:26:21.230 --> 00:26:22.454 Then I started doing the Twitter

NOTE Confidence: 0.5093791

00:26:22.454 --> 00:26:23.740 because people said you have to

NOTE Confidence: 0.5093791

00:26:23.740 --> 00:26:24.800 read the Twitter because people

NOTE Confidence: 0.5093791

00:26:24.800 --> 00:26:25.948 are being critical of your data.

NOTE Confidence: 0.5093791

00:26:25.950 --> 00:26:27.570 And now now and I don't know how to

NOTE Confidence: 0.5093791

00:26:27.570 --> 00:26:29.388 do Twitter because it's called X and

NOTE Confidence: 0.5093791

00:26:29.388 --> 00:26:31.077 I haven't figured that out yet but

NOTE Confidence: 0.5093791

00:26:31.077 --> 00:26:32.806 there were all these people that said

NOTE Confidence: 0.5093791

00:26:32.806 --> 00:26:34.268 well there's no survival benefit.

NOTE Confidence: 0.5093791

00:26:34.270 --> 00:26:35.758 Now the drug got approved based

NOTE Confidence: 0.5093791

00:26:35.758 --> 00:26:36.750 on disease free survival,

NOTE Confidence: 0.5093791

00:26:36.750 --> 00:26:38.184 but there hadn't been a survival

NOTE Confidence: 0.5093791

00:26:38.184 --> 00:26:39.956 benefit and we had to wait for a

NOTE Confidence: 0.5093791

00:26:39.956 --> 00:26:41.652 number of years to have 20% of the

NOTE Confidence: 0.5093791

00:26:41.652 --> 00:26:42.736 patients unfortunately die because

NOTE Confidence: 0.5093791

00:26:42.736 --> 00:26:44.868 that was the end point that had been

NOTE Confidence: 0.5093791

00:26:44.868 --> 00:26:46.356 pre specified to look at survival

NOTE Confidence: 0.5093791

00:26:46.407 --> 00:26:48.055 and it's API you hate for that to

NOTE Confidence: 0.5093791

00:26:48.055 --> 00:26:49.282 happen you know because I'd rather

NOTE Confidence: 0.5093791

00:26:49.282 --> 00:26:50.776 there never be an end point because

NOTE Confidence: 0.5093791

00:26:50.776 --> 00:26:52.162 you don't want anyone to succumb

NOTE Confidence: 0.5093791

00:26:52.162 --> 00:26:52.855 to their disease.

NOTE Confidence: 0.5093791

00:26:52.860 --> 00:26:54.220 But I got a call

NOTE Confidence: 0.60456246

00:26:54.220 --> 00:26:56.082 last November that the trial was nearing

NOTE Confidence: 0.60456246

00:26:56.082 --> 00:26:58.312 the end and it was very you'll see

NOTE Confidence: 0.60456246

00:26:58.312 --> 00:26:59.900 a very interesting because Eric was

NOTE Confidence: 0.60456246

00:26:59.900 --> 00:27:02.014 you know here and the ASCO President.

NOTE Confidence: 0.60456246

00:27:02.020 --> 00:27:03.195 I'm thinking well this could

NOTE Confidence: 0.60456246

00:27:03.195 --> 00:27:04.135 be an ASCO presentation.

NOTE Confidence: 0.60456246

00:27:04.140 --> 00:27:05.202 So we're waiting for the data

NOTE Confidence: 0.60456246

00:27:05.202 --> 00:27:06.900 to make sure over the, over the,

NOTE Confidence: 0.60456246

00:27:06.900 --> 00:27:09.700 over the winter and and then about

NOTE Confidence: 0.60456246

00:27:09.700 --> 00:27:11.720 March saw this curve and this

NOTE Confidence: 0.60456246

00:27:11.720 --> 00:27:13.740 is the survival curve and again

NOTE Confidence: 0.60456246

00:27:13.740 --> 00:27:15.259 it was a very big DFS benefit.

NOTE Confidence: 0.60456246

00:27:15.260 --> 00:27:17.842 But in survival the hazard ratio is .49.

NOTE Confidence: 0.60456246

00:27:17.842 --> 00:27:19.894 So here's the patients who got

NOTE Confidence: 0.60456246

00:27:19.894 --> 00:27:21.494 osteomertinib and here's the control

NOTE Confidence: 0.60456246

00:27:21.494 --> 00:27:23.542 and you can see at at five years,

NOTE Confidence: 0.60456246

00:27:23.550 --> 00:27:24.702 88% versus 78%,

NOTE Confidence: 0.60456246

00:27:24.702 --> 00:27:26.790 so 10% improvement in survival,

NOTE Confidence: 0.60456246

00:27:26.790 --> 00:27:28.458 the hazard ratio .49,

NOTE Confidence: 0.60456246

00:27:28.458 --> 00:27:30.546 so a 51% improvement in survival.

NOTE Confidence: 0.60456246

00:27:30.550 --> 00:27:31.660 And remember the drug stopped

NOTE Confidence: 0.60456246

00:27:31.660 --> 00:27:32.548 here at three years.

NOTE Confidence: 0.60456246

00:27:32.550 --> 00:27:33.630 We only treated for three years.

NOTE Confidence: 0.60456246

00:27:33.630 --> 00:27:34.806 So now we have to continue

NOTE Confidence: 0.60456246

00:27:34.806 --> 00:27:35.590 to watch these patients.

NOTE Confidence: 0.60456246

00:27:35.590 --> 00:27:37.390 We have liquid biopsy samples.

NOTE Confidence: 0.60456246

00:27:37.390 --> 00:27:38.390 Hopefully next year I'll give

NOTE Confidence: 0.60456246

00:27:38.390 --> 00:27:38.990 another grand rounds.

NOTE Confidence: 0.60456246

00:27:38.990 --> 00:27:39.930 I have those samples.

NOTE Confidence: 0.60456246

00:27:39.930 --> 00:27:40.870 I'm analyzing them now,

NOTE Confidence: 0.60456246

00:27:40.870 --> 00:27:42.532 but we're not ready to talk

NOTE Confidence: 0.60456246

00:27:42.532 --> 00:27:43.640 about them unfortunately yet.

NOTE Confidence: 0.60456246

00:27:43.640 --> 00:27:44.756 And then it was pretty cool.

NOTE Confidence: 0.60456246

00:27:44.760 --> 00:27:45.972 So who knew that Eric was

NOTE Confidence: 0.60456246

00:27:45.972 --> 00:27:47.520 going to be the director here?

NOTE Confidence: 0.60456246

00:27:47.520 --> 00:27:48.480 It's just like,

NOTE Confidence: 0.60456246

00:27:48.480 --> 00:27:50.400 it's almost like an amazing coincidence.

NOTE Confidence: 0.60456246

00:27:50.400 --> 00:27:51.415 He's the ASCO president and

NOTE Confidence: 0.60456246

00:27:51.415 --> 00:27:52.864 there I am presenting it to the

NOTE Confidence: 0.60456246

00:27:52.864 --> 00:27:54.034 plenary beside him and Kimi Ying.

NOTE Confidence: 0.60456246

00:27:54.040 --> 00:27:55.200 It was really pretty cool.

NOTE Confidence: 0.60456246

00:27:55.200 --> 00:27:56.840 And you little can't make this stuff up.

NOTE Confidence: 0.60456246

00:27:56.840 --> 00:27:58.074 It just sort of happened, right Eric,

NOTE Confidence: 0.60456246

00:27:58.074 --> 00:27:59.359 it's who would have known?

NOTE Confidence: 0.60456246

00:27:59.360 --> 00:28:02.118 So it was really, that was phenomenal.

NOTE Confidence: 0.60456246

00:28:02.120 --> 00:28:03.144 I was pretty nervous.

NOTE Confidence: 0.60456246

00:28:03.144 --> 00:28:04.680 The only the best thing about,

NOTE Confidence: 0.60456246

00:28:04.680 --> 00:28:06.035 best thing about the plenary

NOTE Confidence: 0.60456246

00:28:06.035 --> 00:28:07.119 is the green room,

NOTE Confidence: 0.60456246

00:28:07.120 --> 00:28:08.359 the drinks and the food in there.

NOTE Confidence: 0.60456246

00:28:08.360 --> 00:28:08.644 Phenomenal.

NOTE Confidence: 0.60456246

00:28:08.644 --> 00:28:10.916 See, that's that's the secret of the ASCO.

NOTE Confidence: 0.60456246

00:28:10.920 --> 00:28:12.360 OK.

NOTE Confidence: 0.60456246

00:28:12.360 --> 00:28:14.718 Now you you see the overall

NOTE Confidence: 0.60456246

00:28:14.718 --> 00:28:16.284 survival both if patients got

NOTE Confidence: 0.60456246

00:28:16.284 --> 00:28:17.316 actually in chemotherapy or

NOTE Confidence: 0.60456246

00:28:17.316 --> 00:28:18.670 without actually in chemotherapy.

NOTE Confidence: 0.60456246

00:28:18.670 --> 00:28:21.925 So you give it if you know sometimes

NOTE Confidence: 0.60456246

00:28:21.925 --> 00:28:23.155 patients don't want it and there's

NOTE Confidence: 0.60456246

00:28:23.155 --> 00:28:24.621 a big push now to avoid the

NOTE Confidence: 0.60456246

00:28:24.621 --> 00:28:25.670 chemotherapy we're looking at that.

NOTE Confidence: 0.60456246

00:28:25.670 --> 00:28:27.740 But right now we we we we we we

NOTE Confidence: 0.60456246

00:28:27.740 --> 00:28:30.030 we we suggest that patients get

NOTE Confidence: 0.60456246

00:28:30.030 --> 00:28:31.968 chemotherapy if they can And then

NOTE Confidence: 0.60456246

00:28:31.968 --> 00:28:32.982 you know the the big critique

NOTE Confidence: 0.60456246

00:28:32.982 --> 00:28:34.361 of this trial and for those that

NOTE Confidence: 0.60456246

00:28:34.361 --> 00:28:35.356 read the New England Journal,

NOTE Confidence: 0.60456246

00:28:35.360 --> 00:28:37.028 there's there's a letter I I

NOTE Confidence: 0.60456246

00:28:37.028 --> 00:28:38.759 responded to a letter today from

NOTE Confidence: 0.60456246

00:28:38.760 --> 00:28:39.865 an investigator in Italy who

NOTE Confidence: 0.60456246

00:28:39.865 --> 00:28:41.309 said well you didn't not all

NOTE Confidence: 0.60456246

00:28:41.309 --> 00:28:42.477 your patients got ostomertinib.

NOTE Confidence: 0.60456246

00:28:42.480 --> 00:28:44.272 So it's not really a fair trial

NOTE Confidence: 0.60456246

00:28:44.272 --> 00:28:45.040 and they're right.

NOTE Confidence: 0.60456246

00:28:45.040 --> 00:28:46.960 Not everyone could get ostomertinib.

NOTE Confidence: 0.60456246

00:28:46.960 --> 00:28:48.470 But look in the ostomertinib

NOTE Confidence: 0.60456246

00:28:48.470 --> 00:28:50.308 group and in the placebo group

NOTE Confidence: 0.60456246

00:28:50.308 --> 00:28:52.407 about 8080 to 90% got an EGFR

NOTE Confidence: 0.60456246

00:28:52.407 --> 00:28:54.501 inhibitor in a second line setting

NOTE Confidence: 0.60456246

00:28:54.501 --> 00:28:55.916 did only 43% got ostomertinib.

NOTE Confidence: 0.60456246

00:28:55.916 --> 00:28:57.224 But the drug wasn't even improved

NOTE Confidence: 0.60456246

00:28:57.224 --> 00:28:58.340 in the front line setting

NOTE Confidence: 0.60456246

00:28:58.340 --> 00:28:59.400 when we started the trial.

NOTE Confidence: 0.60456246

00:28:59.400 --> 00:29:00.680 So well it's not perfect,

NOTE Confidence: 0.60456246

00:29:00.680 --> 00:29:02.144 it's not a perfect would would

NOTE Confidence: 0.60456246

00:29:02.144 --> 00:29:03.709 patients have done better if they

NOTE Confidence: 0.60456246

00:29:03.709 --> 00:29:05.074 got an osteomordinib early probably.

NOTE Confidence: 0.60456246

00:29:05.080 --> 00:29:07.600 But I I would what we said in this

NOTE Confidence: 0.60456246

00:29:07.600 --> 00:29:10.960 reply is the difference is so great.

NOTE Confidence: 0.60456246

00:29:10.960 --> 00:29:14.160 I think use your best drugs earlier and

NOTE Confidence: 0.29164207

00:29:14.160 --> 00:29:17.196 I think this these data hold hold water and

NOTE Confidence: 0.29164207

00:29:17.196 --> 00:29:19.520 then you know it's not without toxicity.

NOTE Confidence: 0.29164207

00:29:19.520 --> 00:29:20.664 Be careful as physicians,

NOTE Confidence: 0.29164207

00:29:20.664 --> 00:29:22.060 as nurses, as caregivers, you know,

NOTE Confidence: 0.29164207

00:29:22.060 --> 00:29:23.997 it's easy for you to say there's no problem

NOTE Confidence: 0.29164207

00:29:23.997 --> 00:29:25.930 when you're giving a drug versus a placebo,

NOTE Confidence: 0.29164207

00:29:25.930 --> 00:29:27.508 there's always going to be added

NOTE Confidence: 0.29164207

00:29:27.508 --> 00:29:29.353 toxicity and this drug does cause some

NOTE Confidence: 0.29164207

00:29:29.353 --> 00:29:31.089 rack and it does cause some diarrhea

NOTE Confidence: 0.29164207

00:29:31.144 --> 00:29:33.006 and it is debilitating for patients in,

NOTE Confidence: 0.29164207

00:29:33.010 --> 00:29:34.998 in about 4 to 5% of the cases.

NOTE Confidence: 0.29164207

00:29:34.998 --> 00:29:36.370 We have to be sensitive to that.

NOTE Confidence: 0.29164207

00:29:36.370 --> 00:29:37.450 Some patients need breaks,

NOTE Confidence: 0.29164207

00:29:37.450 --> 00:29:38.530 some need dose reductions.

NOTE Confidence: 0.29164207

00:29:38.530 --> 00:29:40.960 But for the most part, if you look

NOTE Confidence: 0.29164207

00:29:40.960 --> 00:29:42.610 at discontinuations and serious AE,

NOTE Confidence: 0.29164207

00:29:42.610 --> 00:29:45.088 there were 14% on placebo versus 20%

NOTE Confidence: 0.29164207

00:29:45.090 --> 00:29:47.169 on the drug which is pretty low.

NOTE Confidence: 0.29164207

00:29:47.170 --> 00:29:48.871 But again there is toxicity and this

NOTE Confidence: 0.29164207

00:29:48.871 --> 00:29:50.939 is where quality of life and you know

NOTE Confidence: 0.29164207

00:29:50.939 --> 00:29:52.224 the survivorship clinic and others,

NOTE Confidence: 0.29164207

00:29:52.230 --> 00:29:53.902 you know we need to look at this

NOTE Confidence: 0.29164207

00:29:53.902 --> 00:29:54.830 and help patients.

NOTE Confidence: 0.29164207

00:29:54.830 --> 00:29:57.070 So what's in the future,

NOTE Confidence: 0.29164207

00:29:57.070 --> 00:29:58.984 we're continuing to file the overall

NOTE Confidence: 0.29164207

00:29:58.984 --> 00:30:00.541 survival because what's going to

NOTE Confidence: 0.29164207

00:30:00.541 --> 00:30:02.109 happen in five years and 10 years,

NOTE Confidence: 0.29164207

00:30:02.110 --> 00:30:03.595 we're doing a bunch of

NOTE Confidence: 0.29164207

00:30:03.595 --> 00:30:04.189 translational analysis.

NOTE Confidence: 0.29164207

00:30:04.190 --> 00:30:06.926 We're going to have Pasayani here for the

NOTE Confidence: 0.29164207

00:30:06.926 --> 00:30:08.790 Calabrese lecture this year and he's going

NOTE Confidence: 0.29164207

00:30:08.790 --> 00:30:10.190 to tell us about procester Tri cells,

NOTE Confidence: 0.29164207

00:30:10.190 --> 00:30:11.630 which he studies and Katie

NOTE Confidence: 0.29164207

00:30:11.630 --> 00:30:12.782 studies these as well.

NOTE Confidence: 0.29164207

00:30:12.790 --> 00:30:14.995 There are still cells that remain that

NOTE Confidence: 0.29164207

00:30:14.995 --> 00:30:16.746 remain resistant to to EGFR inhibitors.

NOTE Confidence: 0.29164207

00:30:16.746 --> 00:30:18.141 We actually have blood from

NOTE Confidence: 0.29164207

00:30:18.141 --> 00:30:19.469 about 1/3 of the patients.

NOTE Confidence: 0.29164207

00:30:19.470 --> 00:30:22.574 It's very hard to get samples out of China,

NOTE Confidence: 0.29164207

00:30:22.574 --> 00:30:25.306 but from the Western world and from Japan,

NOTE Confidence: 0.29164207

00:30:25.310 --> 00:30:27.270 we do have blood samples and tissue samples.

NOTE Confidence: 0.29164207

00:30:27.270 --> 00:30:29.270 So we're looking at at at at that.

NOTE Confidence: 0.29164207

00:30:29.270 --> 00:30:30.590 We're also looking at, you know,

NOTE Confidence: 0.29164207

00:30:30.590 --> 00:30:32.275 there are trials looking at

NOTE Confidence: 0.29164207

00:30:32.275 --> 00:30:32.949 neoactuvent osteomerotradium.

NOTE Confidence: 0.29164207

00:30:32.950 --> 00:30:34.385 Now that's all the rage right now.

NOTE Confidence: 0.29164207

00:30:34.390 --> 00:30:36.890 We're looking at earlier disease.

NOTE Confidence: 0.29164207

00:30:36.890 --> 00:30:38.510 Adura 2 is looking at this

NOTE Confidence: 0.29164207

00:30:38.510 --> 00:30:39.670 was stage 1B disease,

NOTE Confidence: 0.29164207

00:30:39.670 --> 00:30:41.110 so more than 3 centimeters.

NOTE Confidence: 0.29164207

00:30:41.110 --> 00:30:42.014 Everyone always calls me

NOTE Confidence: 0.29164207

00:30:42.014 --> 00:30:43.144 what about the small tumors,

NOTE Confidence: 0.29164207

00:30:43.150 --> 00:30:44.788 I think it'll probably work there too.

NOTE Confidence: 0.29164207

00:30:44.790 --> 00:30:45.982 But we need to do the trial and

NOTE Confidence: 0.29164207

00:30:45.982 --> 00:30:46.967 we're actually doing a trial where

NOTE Confidence: 0.29164207

00:30:46.967 --> 00:30:48.147 we're giving the drug for five more

NOTE Confidence: 0.29164207

00:30:48.147 --> 00:30:49.161 years because there is some sense

NOTE Confidence: 0.29164207

00:30:49.161 --> 00:30:50.990 when you stop the drug that the the

NOTE Confidence: 0.29164207

00:30:50.990 --> 00:30:52.310 brain metastasis started to increase.

NOTE Confidence: 0.29164207

00:30:52.310 --> 00:30:53.690 So there might be some patients

NOTE Confidence: 0.29164207

00:30:53.690 --> 00:30:55.190 who are cured in my opinion,

NOTE Confidence: 0.29164207

00:30:55.190 --> 00:30:57.381 but some who are just having cytostatic

NOTE Confidence: 0.29164207

00:30:57.381 --> 00:30:58.935 stability of disease and that's

NOTE Confidence: 0.29164207

00:30:58.935 --> 00:31:00.615 something we have to figure out.

NOTE Confidence: 0.29164207

00:31:00.620 --> 00:31:01.682 So I'll just end this portion

NOTE Confidence: 0.29164207

00:31:01.682 --> 00:31:02.859 of the talk with this slide.

NOTE Confidence: 0.29164207

00:31:02.860 --> 00:31:03.780 So another mentor of mine,

NOTE Confidence: 0.29164207

00:31:03.780 --> 00:31:05.700 I don't know if anyone knew Josh Fiddler,

NOTE Confidence: 0.29164207

00:31:05.700 --> 00:31:06.216 but I I,

NOTE Confidence: 0.29164207

00:31:06.216 --> 00:31:07.900 I actually when I was at MD Anderson,

NOTE Confidence: 0.29164207

00:31:07.900 --> 00:31:10.800 I had a small lab with him and and Josh

NOTE Confidence: 0.29164207

00:31:10.882 --> 00:31:12.794 used to always say metastases are are

NOTE Confidence: 0.29164207

00:31:12.794 --> 00:31:14.934 are what would kill patients and he

NOTE Confidence: 0.29164207

00:31:14.934 --> 00:31:16.614 talked about the metastasis cascade.

NOTE Confidence: 0.29164207

00:31:16.620 --> 00:31:18.202 So I think what we've really shown

NOTE Confidence: 0.29164207

00:31:18.202 --> 00:31:20.132 here is we've taken our best surgery

NOTE Confidence: 0.29164207

00:31:20.132 --> 00:31:21.637 and chemotherapy and we've added

NOTE Confidence: 0.29164207

00:31:21.637 --> 00:31:23.137 targeted therapy to keep patients

NOTE Confidence: 0.29164207

00:31:23.137 --> 00:31:24.572 from progressing in the brain,

NOTE Confidence: 0.29164207

00:31:24.580 --> 00:31:25.189 liver and bone.

NOTE Confidence: 0.29164207

00:31:25.189 --> 00:31:26.610 And I think this is a paradigm

NOTE Confidence: 0.29164207

00:31:26.655 --> 00:31:27.978 now we're going to see more of

NOTE Confidence: 0.5511806

00:31:27.980 --> 00:31:30.644 the drug was approved as I said in 2020.

NOTE Confidence: 0.5511806

00:31:30.650 --> 00:31:32.450 There are a whole host of other mutations.

NOTE Confidence: 0.5511806

00:31:32.450 --> 00:31:33.077 As I mentioned,

NOTE Confidence: 0.5511806

00:31:33.077 --> 00:31:34.540 there's a trial called Alina that will

NOTE Confidence: 0.5511806

00:31:34.580 --> 00:31:36.083 be in the news in two weeks from today,

NOTE Confidence: 0.5511806

00:31:36.090 --> 00:31:37.966 you'll hear about Alina, this is electinib,

NOTE Confidence: 0.5511806

00:31:37.970 --> 00:31:39.848 it's the Roche drug for ALC.

NOTE Confidence: 0.5511806

00:31:39.850 --> 00:31:42.684 And we, we have a press release that

NOTE Confidence: 0.5511806

00:31:42.684 --> 00:31:44.808 that trial is positive for disease,

NOTE Confidence: 0.5511806

00:31:44.810 --> 00:31:45.838 for disease free survival.

NOTE Confidence: 0.5511806

00:31:45.838 --> 00:31:47.697 And I bet they're not going to

NOTE Confidence: 0.5511806

00:31:47.697 --> 00:31:49.007 say wait for overall survival.

NOTE Confidence: 0.5511806

00:31:49.010 --> 00:31:51.096 I think based on the Adura results

NOTE Confidence: 0.5511806

00:31:51.100 --> 00:31:52.628 and actually Anne and I are going to

NOTE Confidence: 0.5511806

00:31:52.628 --> 00:31:53.791 the American Medical Association next

NOTE Confidence: 0.5511806

00:31:53.791 --> 00:31:55.513 week for clinical trials meeting and I

NOTE Confidence: 0.5511806

00:31:55.552 --> 00:31:57.050 think at that meeting we're going to

NOTE Confidence: 0.5511806

00:31:57.050 --> 00:31:58.724 discuss this trial because as a paradigm

NOTE Confidence: 0.5511806

00:31:58.724 --> 00:32:00.460 what should the right end point be,

NOTE Confidence: 0.5511806

00:32:00.460 --> 00:32:02.420 you know in in patients

NOTE Confidence: 0.5511806

00:32:02.420 --> 00:32:03.544 in the accident setting.

NOTE Confidence: 0.5511806

00:32:03.544 --> 00:32:05.230 But I think we've shown that

NOTE Confidence: 0.5511806

00:32:05.291 --> 00:32:07.090 disease free survival works. OK.

NOTE Confidence: 0.5511806

00:32:07.090 --> 00:32:09.260 And here's a little plug for Katie.

NOTE Confidence: 0.5511806

00:32:09.260 --> 00:32:11.340 I don't have time to talk about this,

NOTE Confidence: 0.5511806

00:32:11.340 --> 00:32:13.300 but Katie and and Sarah and Mark,

NOTE Confidence: 0.5511806

00:32:13.300 --> 00:32:14.436 what an amazing team,

NOTE Confidence: 0.5511806

00:32:14.436 --> 00:32:15.856 Mark's a little younger there.

NOTE Confidence: 0.5511806

00:32:15.860 --> 00:32:18.176 So here, here, here's the group,

NOTE Confidence: 0.5511806

00:32:18.180 --> 00:32:18.450 I'm,

NOTE Confidence: 0.5511806

00:32:18.450 --> 00:32:20.340 I'm a little older so here here's

NOTE Confidence: 0.5511806

00:32:20.340 --> 00:32:22.148 here's the group that that that's

NOTE Confidence: 0.5511806

00:32:22.148 --> 00:32:23.966 been meeting and you know Mark's

NOTE Confidence: 0.5511806

00:32:24.024 --> 00:32:25.860 now the Chief of Pharmacology and

NOTE Confidence: 0.5511806

00:32:25.860 --> 00:32:27.322 super duper team obtaining samples.

NOTE Confidence: 0.5511806

00:32:27.322 --> 00:32:29.219 You can see we have Anna and

NOTE Confidence: 0.5511806

00:32:29.219 --> 00:32:30.920 Heather and the entire team are

NOTE Confidence: 0.5511806

00:32:30.920 --> 00:32:32.300 getting samples from the clinic.

NOTE Confidence: 0.5511806

00:32:32.300 --> 00:32:33.536 We're banking the samples,

NOTE Confidence: 0.5511806

00:32:33.536 --> 00:32:35.081 we're looking at these samples

NOTE Confidence: 0.5511806

00:32:35.081 --> 00:32:36.726 that's how science is going to be

NOTE Confidence: 0.5511806

00:32:36.726 --> 00:32:37.900 made and understanding resistance.

NOTE Confidence: 0.5511806

00:32:37.900 --> 00:32:40.810 And then we also have a project three of

NOTE Confidence: 0.5511806

00:32:40.810 --> 00:32:42.658 the spore looking at brain metastases.

NOTE Confidence: 0.5511806

00:32:42.660 --> 00:32:43.944 I'm just putting a little plug

NOTE Confidence: 0.5511806

00:32:43.944 --> 00:32:45.220 in for that that project.

NOTE Confidence: 0.5511806

00:32:45.220 --> 00:32:47.278 No time to talk about it today.

NOTE Confidence: 0.5511806

00:32:47.280 --> 00:32:48.400 And then we oh, this is important.

NOTE Confidence: 0.5511806

00:32:48.400 --> 00:32:49.960 We have an alliance with AstraZeneca.

NOTE Confidence: 0.5511806

00:32:49.960 --> 00:32:51.418 This has been critical for the

NOTE Confidence: 0.5511806

00:32:51.418 --> 00:32:52.658 sport because by developing industry

NOTE Confidence: 0.5511806

00:32:52.658 --> 00:32:54.212 alliances and this is one of the

NOTE Confidence: 0.5511806

00:32:54.212 --> 00:32:55.747 things I've been working on with the

NOTE Confidence: 0.5511806

00:32:55.747 --> 00:32:57.136 Dean's office in the last year and

NOTE Confidence: 0.5511806

00:32:57.136 --> 00:32:58.312 a half and I'm really enjoying it,

NOTE Confidence: 0.5511806

00:32:58.320 --> 00:33:00.078 working very closely with MENA Wang,

NOTE Confidence: 0.5511806

00:33:00.080 --> 00:33:01.280 who's pictured down here.

NOTE Confidence: 0.5511806

00:33:01.280 --> 00:33:03.600 And here's Kathy Lynch from Yale Ventures.

NOTE Confidence: 0.5511806

00:33:03.600 --> 00:33:04.192 There's Pat.

NOTE Confidence: 0.5511806

00:33:04.192 --> 00:33:05.080 We, we, we,

NOTE Confidence: 0.5511806

00:33:05.080 --> 00:33:07.880 we started this together about 5-7 years ago.

NOTE Confidence: 0.5511806

00:33:07.880 --> 00:33:11.960 Here we are in Cambridge 2017 and

NOTE Confidence: 0.5511806

00:33:11.960 --> 00:33:14.302 2022 we all look the same and and

NOTE Confidence: 0.5511806

00:33:14.302 --> 00:33:16.568 you can see that this this is just

NOTE Confidence: 0.5511806

00:33:16.568 --> 00:33:17.844 an amazing collaboration because

NOTE Confidence: 0.5511806

00:33:17.844 --> 00:33:19.560 that's how we're we're really making

NOTE Confidence: 0.5511806

00:33:19.560 --> 00:33:21.780 difference and I I got to move on but

NOTE Confidence: 0.5511806

00:33:21.780 --> 00:33:23.469 this this is the timeline of that

NOTE Confidence: 0.5511806

00:33:23.469 --> 00:33:25.317 alliance and here's the most recent

NOTE Confidence: 0.5511806

00:33:25.317 --> 00:33:27.219 visit actually Dean Brown was with us.

NOTE Confidence: 0.5511806

00:33:27.220 --> 00:33:28.950 We we're really we're getting

NOTE Confidence: 0.5511806

00:33:28.950 --> 00:33:30.900 funds but we're getting drugs

NOTE Confidence: 0.5511806

00:33:30.900 --> 00:33:33.140 and compounds test compounds.

NOTE Confidence: 0.5511806

00:33:33.140 --> 00:33:34.176 Marcus I see in the front row.

NOTE Confidence: 0.5511806

00:33:34.180 --> 00:33:35.454 I know he's very excited about this.

NOTE Confidence: 0.5511806

00:33:35.460 --> 00:33:36.881 It really is the way we're bringing

NOTE Confidence: 0.5511806

00:33:36.881 --> 00:33:38.262 this in and we're expanding this

NOTE Confidence: 0.5511806

00:33:38.262 --> 00:33:39.702 now to head and neck cancers.

NOTE Confidence: 0.5511806

00:33:39.710 --> 00:33:41.432 We're heading to breast cancer and

NOTE Confidence: 0.5511806

00:33:41.432 --> 00:33:43.189 other other cancers in the future.

NOTE Confidence: 0.5511806

00:33:43.190 --> 00:33:44.758 So this is going to be something

NOTE Confidence: 0.5511806

00:33:44.758 --> 00:33:45.710 that's with AstraZeneca and

NOTE Confidence: 0.5511806

00:33:45.710 --> 00:33:46.670 other companies that will,

NOTE Confidence: 0.71490145

00:33:46.670 --> 00:33:48.870 I think be very important.

NOTE Confidence: 0.71490145

00:33:48.870 --> 00:33:50.270 So just in the last 20 minutes,

NOTE Confidence: 0.71490145

00:33:50.270 --> 00:33:53.550 a little bit about immunotherapy.

NOTE Confidence: 0.71490145

00:33:53.550 --> 00:33:56.000 That's also an amazing new paradigm in

NOTE Confidence: 0.71490145

00:33:56.000 --> 00:33:58.015 lung cancer targeting immunotherapy and

NOTE Confidence: 0.71490145

00:33:58.015 --> 00:34:00.265 of course the checkpoint inhibitors.

NOTE Confidence: 0.71490145

00:34:00.270 --> 00:34:01.150 You know, the first trials

NOTE Confidence: 0.71490145

00:34:01.150 --> 00:34:02.030 were done here at Yale.

NOTE Confidence: 0.71490145

00:34:02.030 --> 00:34:03.626 I don't know if everyone realizes that.

NOTE Confidence: 0.71490145

00:34:03.630 --> 00:34:05.583 And of course, we have Lee Ping Chen here.

NOTE Confidence: 0.71490145

00:34:05.590 --> 00:34:07.528 There's a very nice article about

NOTE Confidence: 0.71490145

00:34:07.528 --> 00:34:09.311 him in fierce Biotech yesterday

NOTE Confidence: 0.71490145

00:34:09.311 --> 00:34:11.885 talking about his contribution to the

NOTE Confidence: 0.71490145

00:34:11.885 --> 00:34:13.759 development and discovery of PDL 1.

NOTE Confidence: 0.71490145

00:34:13.760 --> 00:34:15.272 So this is the probably the

NOTE Confidence: 0.71490145

00:34:15.272 --> 00:34:16.680 first responder in lung cancer.

NOTE Confidence: 0.71490145

00:34:16.680 --> 00:34:17.600 I don't know if Scott.

NOTE Confidence: 0.71490145

00:34:17.600 --> 00:34:18.945 Scott's probably in clinic now

NOTE Confidence: 0.71490145

00:34:18.945 --> 00:34:20.832 because that's why he sees so many

NOTE Confidence: 0.71490145

00:34:20.832 --> 00:34:22.314 patients and helps so many people.

NOTE Confidence: 0.71490145

00:34:22.320 --> 00:34:24.558 So this is a patient Maureen

NOTE Confidence: 0.71490145

00:34:24.560 --> 00:34:26.234 who came to Yale Squamous lung

NOTE Confidence: 0.71490145

00:34:26.234 --> 00:34:28.002 cancer wasn't a candidate for any

NOTE Confidence: 0.71490145

00:34:28.002 --> 00:34:29.198 of those targeted therapies,

NOTE Confidence: 0.71490145

00:34:29.200 --> 00:34:31.080 3 times refractory lung cancer.

NOTE Confidence: 0.71490145

00:34:31.080 --> 00:34:32.420 And June 2010 she went

NOTE Confidence: 0.71490145

00:34:32.420 --> 00:34:34.080 on the trial of MDX one,

NOTE Confidence: 0.71490145

00:34:34.080 --> 00:34:36.568 one O 6 that Mario was running with

NOTE Confidence: 0.71490145

00:34:36.568 --> 00:34:38.895 Scott and Harriet and you can see these

NOTE Confidence: 0.71490145

00:34:38.895 --> 00:34:40.788 large tumors in her lung and her liver.

NOTE Confidence: 0.71490145

00:34:40.790 --> 00:34:42.130 Within months they responded.

NOTE Confidence: 0.71490145

00:34:42.130 --> 00:34:44.483 The trial was for two years of

NOTE Confidence: 0.71490145

00:34:44.483 --> 00:34:46.145 what we now know as novolumab.

NOTE Confidence: 0.71490145

00:34:46.150 --> 00:34:47.470 Here she is a year 8,

NOTE Confidence: 0.71490145

00:34:47.470 --> 00:34:49.108 but her X-rays look this way.

NOTE Confidence: 0.71490145

00:34:49.110 --> 00:34:50.090 Now she comes back.

NOTE Confidence: 0.71490145

00:34:50.090 --> 00:34:50.825 We've seen her.

NOTE Confidence: 0.71490145

00:34:50.830 --> 00:34:52.244 I'm sure Tara's seen her at some

NOTE Confidence: 0.71490145

00:34:52.244 --> 00:34:53.190 of the survivor events.

NOTE Confidence: 0.71490145

00:34:53.190 --> 00:34:55.134 This is the promise of a phase one

NOTE Confidence: 0.71490145

00:34:55.134 --> 00:34:56.869 trial of new drug development.

NOTE Confidence: 0.71490145

00:34:56.870 --> 00:34:59.586 The problem is this is only 15%

NOTE Confidence: 0.71490145

00:34:59.590 --> 00:35:00.646 but for This is why everyone

NOTE Confidence: 0.71490145

00:35:00.646 --> 00:35:01.830 wants to work in this field.

NOTE Confidence: 0.71490145

00:35:01.830 --> 00:35:03.310 We see a light at the end of the tunnel.

NOTE Confidence: 0.71490145

00:35:03.310 --> 00:35:04.750 It's just a very long tunnel,

NOTE Confidence: 0.71490145

00:35:04.750 --> 00:35:06.416 but we know that 15% of patients

NOTE Confidence: 0.71490145

00:35:06.416 --> 00:35:07.748 are going to benefit.

NOTE Confidence: 0.71490145

00:35:07.750 --> 00:35:11.060 And then Scott and he he ran

NOTE Confidence: 0.71490145

00:35:11.060 --> 00:35:12.560 this trial OO 3:00 and basically

NOTE Confidence: 0.71490145

00:35:12.560 --> 00:35:14.086 this is an actuarial survival

NOTE Confidence: 0.71490145

00:35:14.086 --> 00:35:15.910 curve because it's now with more

NOTE Confidence: 0.71490145

00:35:15.963 --> 00:35:17.505 than five years of follow up.

NOTE Confidence: 0.71490145

00:35:17.510 --> 00:35:20.288 He published this in JCO in 2018 at

NOTE Confidence: 0.71490145

00:35:20.288 --> 00:35:22.871 five years in the refractory setting on

NOTE Confidence: 0.71490145

00:35:22.871 --> 00:35:25.790 the volnab 16% of patients are alive.

NOTE Confidence: 0.71490145

00:35:25.790 --> 00:35:27.430 And when I use this slide to teach

NOTE Confidence: 0.71490145

00:35:27.430 --> 00:35:29.070 in my clinical trials course,

NOTE Confidence: 0.71490145

00:35:29.070 --> 00:35:31.238 I talk about the tail of the curve

NOTE Confidence: 0.71490145

00:35:31.238 --> 00:35:32.841 because this is a non proportional hazards.

NOTE Confidence: 0.71490145

00:35:32.841 --> 00:35:34.312 You have two slopes, 1 here,

NOTE Confidence: 0.71490145

00:35:34.312 --> 00:35:34.754 one here.

NOTE Confidence: 0.71490145

00:35:34.754 --> 00:35:36.564 We know that there's a tail problem is

NOTE Confidence: 0.71490145

00:35:36.564 --> 00:35:38.590 how do we get more people off the tail.

NOTE Confidence: 0.71490145

00:35:38.590 --> 00:35:40.310 These patients have primary resistance.

NOTE Confidence: 0.71490145

00:35:40.310 --> 00:35:41.750 There are other things going on.

NOTE Confidence: 0.71490145

00:35:41.750 --> 00:35:43.030 Maybe it's another checkpoint,

NOTE Confidence: 0.71490145

00:35:43.030 --> 00:35:44.950 maybe it's a regulatory T cell.

NOTE Confidence: 0.71490145

00:35:44.950 --> 00:35:46.114 This is why we shouldn't just

NOTE Confidence: 0.71490145

00:35:46.114 --> 00:35:47.152 study the next PD1 inhibitor

NOTE Confidence: 0.71490145

00:35:47.152 --> 00:35:48.466 or the next PDL 1 inhibitor.

NOTE Confidence: 0.71490145

00:35:48.470 --> 00:35:49.814 We need to think about what's going

NOTE Confidence: 0.71490145

00:35:49.814 --> 00:35:51.164 on in the micro environment and

NOTE Confidence: 0.71490145

00:35:51.164 --> 00:35:52.865 I'll show you how we're doing that.

NOTE Confidence: 0.71490145

00:35:52.870 --> 00:35:55.300 So just quickly keynote one, Paul.

NOTE Confidence: 0.71490145

00:35:55.300 --> 00:36:00.110 ADA ran this trial here at Yale a decade ago.

NOTE Confidence: 0.71490145

00:36:00.110 --> 00:36:01.470 It was Melanoma lung cancer,

NOTE Confidence: 0.71490145

00:36:01.470 --> 00:36:02.566 small cell lung cancer.

NOTE Confidence: 0.71490145

00:36:02.566 --> 00:36:04.098 This was with Keytruda with

NOTE Confidence: 0.71490145

00:36:04.098 --> 00:36:06.222 tembrelizumab that led to a trial

NOTE Confidence: 0.71490145

00:36:06.222 --> 00:36:08.448 that I LED called KEYNOTE 10,

NOTE Confidence: 0.71490145

00:36:08.450 --> 00:36:10.648 which established PDL 1 as a biomarker.

NOTE Confidence: 0.71490145

00:36:10.650 --> 00:36:11.890 If you have high levels of PDL one,

NOTE Confidence: 0.2752451

00:36:11.890 --> 00:36:14.758 you do better than if you have lower levels.

NOTE Confidence: 0.2752451

00:36:14.758 --> 00:36:16.528 That led to using the,

NOTE Confidence: 0.2752451

00:36:16.530 --> 00:36:18.948 the pembrolizumab in the frontline setting

NOTE Confidence: 0.2752451

00:36:18.948 --> 00:36:21.968 and then that led to accurate therapy.

NOTE Confidence: 0.2752451

00:36:21.970 --> 00:36:23.842 Sarah Goldberg and and and Harriet

NOTE Confidence: 0.2752451

00:36:23.842 --> 00:36:25.090 working with Veronica Shang,

NOTE Confidence: 0.2752451

00:36:25.090 --> 00:36:26.250 they did the first study,

NOTE Confidence: 0.2752451

00:36:26.250 --> 00:36:28.138 the very first study and this is when

NOTE Confidence: 0.2752451

00:36:28.138 --> 00:36:29.848 we're saying we we can get this study.

NOTE Confidence: 0.2752451

00:36:29.850 --> 00:36:31.530 We got this still plan on in three

NOTE Confidence: 0.2752451

00:36:31.530 --> 00:36:32.898 months and we're getting back to that.

NOTE Confidence: 0.2752451

00:36:32.900 --> 00:36:34.736 They did a study where investigator

NOTE Confidence: 0.2752451

00:36:34.736 --> 00:36:36.355 initiated study where they took

NOTE Confidence: 0.2752451

00:36:36.355 --> 00:36:37.699 pembrolizumab because we're already

NOTE Confidence: 0.2752451

00:36:37.699 --> 00:36:40.160 working with Merck and they did it in

NOTE Confidence: 0.2752451

00:36:40.160 --> 00:36:41.854 and we're still getting data from this.

NOTE Confidence: 0.2752451

00:36:41.860 --> 00:36:43.660 And we took patients with small brain meds,

NOTE Confidence: 0.2752451

00:36:43.660 --> 00:36:45.636 they had to be less than two centimeters

NOTE Confidence: 0.2752451

00:36:45.636 --> 00:36:48.054 and we treated those patients with, with,

NOTE Confidence: 0.2752451

00:36:48.054 --> 00:36:50.418 with the drug without any radiation.

NOTE Confidence: 0.2752451

00:36:50.420 --> 00:36:51.980 If someone's going to live for 2-3 years,

NOTE Confidence: 0.2752451

00:36:51.980 --> 00:36:53.912 the the one year survival with pembrolizumab

NOTE Confidence: 0.2752451

00:36:53.912 --> 00:36:55.972 and a high PDL one patient is 35%.

NOTE Confidence: 0.2752451

00:36:55.972 --> 00:36:57.876 So if you're going to be alive,

NOTE Confidence: 0.2752451

00:36:57.880 --> 00:36:59.595 actually the five year survival is 35%,

NOTE Confidence: 0.2752451

00:36:59.600 --> 00:36:59.856 excuse me.

NOTE Confidence: 0.2752451

00:36:59.856 --> 00:37:01.240 So if you're going to be alive in five years,

NOTE Confidence: 0.2752451

00:37:01.240 --> 00:37:03.112 you'd rather be alive without any

NOTE Confidence: 0.2752451

00:37:03.112 --> 00:37:04.360 cognitive impairment from radiation.

NOTE Confidence: 0.2752451

00:37:04.360 --> 00:37:05.935 So this was really established in this

NOTE Confidence: 0.2752451

00:37:05.935 --> 00:37:07.458 trial that was both a collaboration

NOTE Confidence: 0.2752451

00:37:07.458 --> 00:37:09.060 between Melanoma and the lung cancer

NOTE Confidence: 0.2752451

00:37:09.060 --> 00:37:10.806 group and you can see here's extra

NOTE Confidence: 0.2752451

00:37:10.806 --> 00:37:12.045 cerebral response and brain response

NOTE Confidence: 0.2752451

00:37:12.045 --> 00:37:14.040 and you can see they're about equal.

NOTE Confidence: 0.2752451

00:37:14.040 --> 00:37:15.720 And Harriet, it won't tell you this,

NOTE Confidence: 0.2752451

00:37:15.720 --> 00:37:16.644 but I'll tell you this and it

NOTE Confidence: 0.2752451

00:37:16.644 --> 00:37:17.400 wasn't the New York Times.

NOTE Confidence: 0.2752451

00:37:17.400 --> 00:37:19.530 So I'm not reaching any, any confidentiality.

NOTE Confidence: 0.2752451

00:37:19.530 --> 00:37:22.315 But when a 99 year old ex president had

NOTE Confidence: 0.2752451

00:37:22.315 --> 00:37:24.635 Melanoma in the brain about eight years ago,

NOTE Confidence: 0.2752451

00:37:24.640 --> 00:37:26.110 they called us at Yale.

NOTE Confidence: 0.2752451

00:37:26.110 --> 00:37:28.112 And while Curran asked what are you

NOTE Confidence: 0.2752451

00:37:28.112 --> 00:37:29.790 doing with pembrolizumab in that setting?

NOTE Confidence: 0.2752451

00:37:29.790 --> 00:37:30.714 And you can,

NOTE Confidence: 0.2752451

00:37:30.714 --> 00:37:32.870 you can put the pieces together yourself.

NOTE Confidence: 0.2752451

00:37:32.870 --> 00:37:34.310 So what about precision medicine?

NOTE Confidence: 0.2752451

00:37:34.310 --> 00:37:36.390 How can that help?

NOTE Confidence: 0.2752451

00:37:36.390 --> 00:37:36.910 Well,

NOTE Confidence: 0.2752451

00:37:36.910 --> 00:37:37.494 David RIM,

NOTE Confidence: 0.2752451

00:37:37.494 --> 00:37:39.538 I was asked to be the discussion

NOTE Confidence: 0.2752451

00:37:39.538 --> 00:37:41.630 at ASCO about six years ago for

NOTE Confidence: 0.2752451

00:37:41.630 --> 00:37:42.830 the early studies on the Volumab.

NOTE Confidence: 0.2752451

00:37:42.830 --> 00:37:44.702 So I went to my my good friend David,

NOTE Confidence: 0.2752451

00:37:44.710 --> 00:37:46.348 who by the way used to work on breast

NOTE Confidence: 0.2752451

00:37:46.348 --> 00:37:47.736 cancer and he moved over to lung

NOTE Confidence: 0.2752451

00:37:47.736 --> 00:37:49.214 cancer and now Eric's getting him back

NOTE Confidence: 0.2752451

00:37:49.214 --> 00:37:50.747 and I'm a little worried about that.

NOTE Confidence: 0.2752451

00:37:50.750 --> 00:37:52.110 But but but it's OK.

NOTE Confidence: 0.2752451

00:37:52.110 --> 00:37:53.630 He works on the head and export too.

NOTE Confidence: 0.2752451

00:37:53.630 --> 00:37:55.800 The very the pathologists are

NOTE Confidence: 0.2752451

00:37:55.800 --> 00:37:56.668 your pathologists,

NOTE Confidence: 0.2752451

00:37:56.670 --> 00:37:58.590 your your your statisticians,

NOTE Confidence: 0.2752451

00:37:58.590 --> 00:38:00.030 critical core members.

NOTE Confidence: 0.2752451

00:38:00.030 --> 00:38:00.830 For any of these grants,

NOTE Confidence: 0.2752451

00:38:00.830 --> 00:38:02.195 you've got to have a good course

NOTE Confidence: 0.2752451

00:38:02.195 --> 00:38:03.560 and that we always get exceptional

NOTE Confidence: 0.2752451

00:38:03.560 --> 00:38:05.024 thanks to David and Kurt and

NOTE Confidence: 0.2752451

00:38:05.024 --> 00:38:06.467 now Sonia's working with them.

NOTE Confidence: 0.2752451

00:38:06.470 --> 00:38:07.970 So you can see, I said, David,

NOTE Confidence: 0.2752451

00:38:07.970 --> 00:38:10.070 why is this PDL one marker so,

NOTE Confidence: 0.2752451

00:38:10.070 --> 00:38:11.753 so bad And Li Ping was with us and

NOTE Confidence: 0.2752451

00:38:11.753 --> 00:38:13.670 Li Ping said of course it's not bad.

NOTE Confidence: 0.2752451

00:38:13.670 --> 00:38:14.720 I discovered it.

NOTE Confidence: 0.2752451

00:38:14.720 --> 00:38:16.120 It's actually very good,

NOTE Confidence: 0.2752451

00:38:16.120 --> 00:38:17.835 but you just don't measure it properly.

NOTE Confidence: 0.2752451

00:38:17.840 --> 00:38:19.720 And then David made this slide for me

NOTE Confidence: 0.2752451

00:38:19.720 --> 00:38:21.280 that everyone's now used and and I

NOTE Confidence: 0.2752451

00:38:21.280 --> 00:38:22.918 make sure the credit was there David.

NOTE Confidence: 0.2752451

00:38:22.920 --> 00:38:25.074 So everyone uses this and and

NOTE Confidence: 0.2752451

00:38:25.074 --> 00:38:26.510 David has done very

NOTE Confidence: 0.734546

00:38:26.587 --> 00:38:28.280 well at meetings and and and

NOTE Confidence: 0.734546

00:38:28.280 --> 00:38:29.680 being involved in the panels.

NOTE Confidence: 0.734546

00:38:29.680 --> 00:38:31.360 Here's one piece of lung cancer,

NOTE Confidence: 0.734546

00:38:31.360 --> 00:38:33.509 one tissue piece and two different areas.

NOTE Confidence: 0.734546

00:38:33.510 --> 00:38:35.750 One area is stone cold negative for PDL,

NOTE Confidence: 0.734546

00:38:35.750 --> 00:38:37.766 one for two different antibodies and one

NOTE Confidence: 0.734546

00:38:37.766 --> 00:38:39.817 area is positive with two different results,

NOTE Confidence: 0.734546

00:38:39.817 --> 00:38:41.179 you know slightly different and it

NOTE Confidence: 0.734546

00:38:41.179 --> 00:38:42.469 it matters where you measure it.

NOTE Confidence: 0.734546

00:38:42.470 --> 00:38:43.710 The the green is cytokeratin,

NOTE Confidence: 0.734546

00:38:43.710 --> 00:38:45.630 so that's tumor. The the blue,

NOTE Confidence: 0.734546

00:38:45.630 --> 00:38:47.462 the Dappy is the nuclei and that and

NOTE Confidence: 0.734546

00:38:47.462 --> 00:38:49.387 you can see the the red is PDL one.

NOTE Confidence: 0.734546

00:38:49.390 --> 00:38:50.762 It could be either in the tumor

NOTE Confidence: 0.734546

00:38:50.762 --> 00:38:51.350 or the stroma.

NOTE Confidence: 0.734546

00:38:51.350 --> 00:38:52.970 So it's the variability of

NOTE Confidence: 0.734546

00:38:52.970 --> 00:38:54.590 measurement and the sensitivity asset.

NOTE Confidence: 0.734546

00:38:54.590 --> 00:38:56.711 But you gotta have PDL ONE for

NOTE Confidence: 0.734546

00:38:56.711 --> 00:38:59.069 PD1 and PDL 1 blockers to work.

NOTE Confidence: 0.734546

00:38:59.070 --> 00:39:01.110 And we have, we're so fortunate.

NOTE Confidence: 0.734546

00:39:01.110 --> 00:39:03.684 So Katie deserved 2 awards last

NOTE Confidence: 0.734546

00:39:03.684 --> 00:39:06.980 week because she and Scott set up

NOTE Confidence: 0.734546

00:39:06.980 --> 00:39:09.460 this amazing repeat biopsy program.

NOTE Confidence: 0.734546

00:39:09.460 --> 00:39:11.004 That's why we got to make sure the

NOTE Confidence: 0.734546

00:39:11.004 --> 00:39:12.418 freezers are backed up in our office.

NOTE Confidence: 0.734546

00:39:12.420 --> 00:39:14.036 And we also have to make sure we

NOTE Confidence: 0.734546

00:39:14.036 --> 00:39:15.440 have more liquid nitrogen because

NOTE Confidence: 0.734546

00:39:15.440 --> 00:39:17.010 these samples are so valuable

NOTE Confidence: 0.734546

00:39:17.010 --> 00:39:18.458 because for the last decade,

NOTE Confidence: 0.734546

00:39:18.460 --> 00:39:20.056 the lung group has been collecting

NOTE Confidence: 0.734546

00:39:20.056 --> 00:39:21.899 samples when someone comes in and they

NOTE Confidence: 0.734546

00:39:21.899 --> 00:39:23.119 have recurrent disease and they've

NOTE Confidence: 0.734546

00:39:23.119 --> 00:39:24.656 putting a little plug in for the.

NOTE Confidence: 0.734546

00:39:24.660 --> 00:39:26.325 When someone comes in and

NOTE Confidence: 0.734546

00:39:26.325 --> 00:39:27.657 they have recurrent disease,

NOTE Confidence: 0.734546

00:39:27.660 --> 00:39:29.390 we actually get consent to

NOTE Confidence: 0.734546

00:39:29.390 --> 00:39:30.774 get their old biopsy.

NOTE Confidence: 0.734546

00:39:30.780 --> 00:39:31.900 And then when we get the new biopsy,

NOTE Confidence: 0.734546

00:39:31.900 --> 00:39:33.817 the biopsy's done with the help of the team.

NOTE Confidence: 0.734546

00:39:33.820 --> 00:39:35.160 And there's Anna and Heather

NOTE Confidence: 0.734546

00:39:35.160 --> 00:39:36.500 works with her sometimes goopang,

NOTE Confidence: 0.734546

00:39:36.500 --> 00:39:37.652 I don't know if he's here

NOTE Confidence: 0.734546

00:39:37.652 --> 00:39:38.420 or maybe he's online.

NOTE Confidence: 0.734546

00:39:38.420 --> 00:39:40.544 The team gets a fresh biopsy and and we

NOTE Confidence: 0.734546

00:39:40.544 --> 00:39:42.655 get fresh tissue and we get paraffin,

NOTE Confidence: 0.734546

00:39:42.660 --> 00:39:44.140 we make transgenic, we make,

NOTE Confidence: 0.734546

00:39:44.140 --> 00:39:47.376 we make PDX mice, This is, this is.

NOTE Confidence: 0.734546

00:39:47.376 --> 00:39:49.044 And zenta or pathologist is usually

NOTE Confidence: 0.734546

00:39:49.044 --> 00:39:51.175 there to make sure we get good tissue.

NOTE Confidence: 0.734546

00:39:51.180 --> 00:39:52.636 This is the key,

NOTE Confidence: 0.734546

00:39:52.636 --> 00:39:54.456 having samples from refractory patients.

NOTE Confidence: 0.734546

00:39:54.460 --> 00:39:55.740 We started this with TKIS,

NOTE Confidence: 0.734546

00:39:55.740 --> 00:39:57.860 but then we did this with IO agents.

NOTE Confidence: 0.734546

00:39:57.860 --> 00:39:59.476 We went and have the spore 10 years

NOTE Confidence: 0.734546

00:39:59.476 --> 00:40:01.330 ago if we didn't have this data set.

NOTE Confidence: 0.734546

00:40:01.330 --> 00:40:03.276 And we've used this both with our

NOTE Confidence: 0.734546

00:40:03.276 --> 00:40:04.970 own samples and with industry.

NOTE Confidence: 0.734546

00:40:04.970 --> 00:40:06.720 This is a very nice trial that

NOTE Confidence: 0.734546

00:40:06.720 --> 00:40:08.818 Scott and I and others did with

NOTE Confidence: 0.734546

00:40:08.818 --> 00:40:11.236 the drug known as MDX 1107.

NOTE Confidence: 0.734546

00:40:11.236 --> 00:40:13.502 Now it's known as pembro as a tezalizumab.

NOTE Confidence: 0.734546

00:40:13.502 --> 00:40:15.820 So this was a phase one trial which we

NOTE Confidence: 0.734546

00:40:15.820 --> 00:40:17.898 led here at Yale and it actually was

NOTE Confidence: 0.734546

00:40:17.898 --> 00:40:19.928 published in Nature almost a decade ago.

NOTE Confidence: 0.734546

00:40:19.930 --> 00:40:20.902 But in this trial,

NOTE Confidence: 0.734546

00:40:20.902 --> 00:40:22.360 we had patients with lung cancer

NOTE Confidence: 0.734546

00:40:22.416 --> 00:40:24.089 who responded to a PDL 1 inhibitor.

NOTE Confidence: 0.734546

00:40:24.090 --> 00:40:25.910 But because we could get those fresh

NOTE Confidence: 0.734546

00:40:25.910 --> 00:40:27.988 biopsies, we had pre and post biopsies.

NOTE Confidence: 0.734546

00:40:27.990 --> 00:40:29.604 So here's a prebiopsy on this

NOTE Confidence: 0.734546

00:40:29.604 --> 00:40:31.137 responding patient and you can see

NOTE Confidence: 0.734546

00:40:31.137 --> 00:40:32.753 you know CD 8 positive T cells and

NOTE Confidence: 0.734546

00:40:32.802 --> 00:40:34.386 then post you can see a lot more.

NOTE Confidence: 0.734546

00:40:34.390 --> 00:40:35.846 This is what you call the adaptive

NOTE Confidence: 0.734546

00:40:35.846 --> 00:40:36.262 immune response.

NOTE Confidence: 0.734546

00:40:36.270 --> 00:40:36.824 This is,

NOTE Confidence: 0.734546

00:40:36.824 --> 00:40:38.763 this is the blocking the PD1 PDL

NOTE Confidence: 0.734546

00:40:38.763 --> 00:40:40.464 one up regulation of interferon

NOTE Confidence: 0.734546

00:40:40.464 --> 00:40:42.841 T cells coming to the tumor and

NOTE Confidence: 0.734546

00:40:42.841 --> 00:40:44.226 then using an RNA chip.

NOTE Confidence: 0.6175327

00:40:44.230 --> 00:40:45.366 And why did this?

NOTE Confidence: 0.6175327

00:40:45.366 --> 00:40:47.070 Why did we get this trial?

NOTE Confidence: 0.6175327

00:40:47.070 --> 00:40:48.750 Ira Melman, good old Ira Melman

NOTE Confidence: 0.6175327

00:40:48.750 --> 00:40:50.375 had moved to Genentech and I

NOTE Confidence: 0.6175327

00:40:50.375 --> 00:40:51.950 went out and had dinner with him.

NOTE Confidence: 0.6175327

00:40:51.950 --> 00:40:54.190 I I had remembered IRA from cell

NOTE Confidence: 0.6175327

00:40:54.190 --> 00:40:55.668 biology that was when I was at

NOTE Confidence: 0.6175327

00:40:55.668 --> 00:40:56.653 Rockefeller done but but still

NOTE Confidence: 0.6175327

00:40:56.653 --> 00:40:57.997 I knew Ira and Ira helped us to

NOTE Confidence: 0.6175327

00:40:57.997 --> 00:40:59.420 get this trial and and with IRA's

NOTE Confidence: 0.6175327

00:40:59.420 --> 00:41:00.911 group did this work for us the

NOTE Confidence: 0.6175327

00:41:00.911 --> 00:41:02.827 RNA shift and you can see pre and

NOTE Confidence: 0.6175327

00:41:02.827 --> 00:41:04.668 post green is pre yellow is post.

NOTE Confidence: 0.6175327

00:41:04.670 --> 00:41:06.133 You can see this is an example

NOTE Confidence: 0.6175327

00:41:06.133 --> 00:41:07.293 of what's happening when the

NOTE Confidence: 0.6175327

00:41:07.293 --> 00:41:08.269 immune response is active.

NOTE Confidence: 0.6175327

00:41:08.270 --> 00:41:10.391 So we we understand what the active

NOTE Confidence: 0.6175327

00:41:10.391 --> 00:41:12.317 immune response is how is how do we

NOTE Confidence: 0.6175327

00:41:12.317 --> 00:41:14.230 get this to go on in every patient

NOTE Confidence: 0.6175327

00:41:14.230 --> 00:41:15.658 20% of patients responded in that

NOTE Confidence: 0.6175327

00:41:15.658 --> 00:41:17.396 trial but the other 80% did not

NOTE Confidence: 0.6175327

00:41:17.396 --> 00:41:19.517 and those patients that did not we

NOTE Confidence: 0.6175327

00:41:19.517 --> 00:41:21.202 described in this paper the immune

NOTE Confidence: 0.6175327

00:41:21.202 --> 00:41:23.188 desert you know CD 8 before and

NOTE Confidence: 0.6175327

00:41:23.188 --> 00:41:25.024 after the tumor just laughs at,

NOTE Confidence: 0.6175327

00:41:25.030 --> 00:41:26.738 at the PDL 1 inhibitor nothing happens

NOTE Confidence: 0.6175327

00:41:26.738 --> 00:41:28.663 or you can have a non functional

NOTE Confidence: 0.6175327

00:41:28.663 --> 00:41:30.367 immune response where you have some

NOTE Confidence: 0.6175327

00:41:30.423 --> 00:41:32.263 CD8 cells and maybe a few more posts.

NOTE Confidence: 0.6175327

00:41:32.270 --> 00:41:33.712 But if you look at that immune

NOTE Confidence: 0.6175327

00:41:33.712 --> 00:41:35.054 shift completely flat and then this

NOTE Confidence: 0.6175327

00:41:35.054 --> 00:41:36.184 is actually something we're seeing

NOTE Confidence: 0.6175327

00:41:36.184 --> 00:41:37.701 more and more of and I don't have

NOTE Confidence: 0.6175327

00:41:37.701 --> 00:41:39.282 time to talk about it today but our

NOTE Confidence: 0.6175327

00:41:39.282 --> 00:41:40.931 next trial on the sport is going

NOTE Confidence: 0.6175327

00:41:40.931 --> 00:41:42.709 to target this that that the cells

NOTE Confidence: 0.6175327

00:41:42.709 --> 00:41:44.375 that get inhibited that can't get

NOTE Confidence: 0.6175327

00:41:44.375 --> 00:41:46.339 to the tumor because you get this

NOTE Confidence: 0.6175327

00:41:46.339 --> 00:41:48.193 line of interference and we call

NOTE Confidence: 0.6175327

00:41:48.193 --> 00:41:50.550 this the the immune excluded cells.

NOTE Confidence: 0.6175327

00:41:50.550 --> 00:41:52.200 So more to come on this,

NOTE Confidence: 0.6175327

00:41:52.200 --> 00:41:56.040 I'm going to skip this for the sake of time.

NOTE Confidence: 0.6175327

00:41:56.040 --> 00:41:57.120 We just have to do a little editing.

NOTE Confidence: 0.27132082

00:42:01.880 --> 00:42:04.760 So I I will just say that now all

NOTE Confidence: 0.27132082

00:42:04.760 --> 00:42:07.637 these agents are moving up up front.

NOTE Confidence: 0.27132082

00:42:07.640 --> 00:42:09.607 We're we're now in the process of

NOTE Confidence: 0.27132082

00:42:09.607 --> 00:42:11.296 taking immune therapies that are being

NOTE Confidence: 0.27132082

00:42:11.296 --> 00:42:12.874 used in the neo accurate setting.

NOTE Confidence: 0.27132082

00:42:12.880 --> 00:42:14.826 And it's actually a very fertile time

NOTE Confidence: 0.27132082

00:42:14.826 --> 00:42:16.918 because when we sit at the tumor board,

NOTE Confidence: 0.27132082

00:42:16.920 --> 00:42:18.873 we have to decide are we going to do

NOTE Confidence: 0.27132082

00:42:18.873 --> 00:42:20.263 surgery and accurate therapy like

NOTE Confidence: 0.27132082

00:42:20.263 --> 00:42:21.949 I showed you for TKI inhibitor.

NOTE Confidence: 0.27132082

00:42:21.950 --> 00:42:24.113 So we're going to use the neoactivant

NOTE Confidence: 0.27132082

00:42:24.113 --> 00:42:26.389 therapy 1st and we're seeing about 15%

NOTE Confidence: 0.27132082

00:42:26.390 --> 00:42:30.950 half CR rate and a 30 to 40% minor CR

NOTE Confidence: 0.27132082

00:42:30.950 --> 00:42:34.460 rate PR minor major PR rate, excuse me,

NOTE Confidence: 0.27132082

00:42:34.460 --> 00:42:36.350 when we use these agents upfront.

NOTE Confidence: 0.27132082

00:42:36.350 --> 00:42:38.702 So that's going to be the next stage

NOTE Confidence: 0.27132082

00:42:38.702 --> 00:42:40.196 neoactivant trials and I just want

NOTE Confidence: 0.27132082

00:42:40.196 --> 00:42:41.910 to make a plug for tumor boards.

NOTE Confidence: 0.27132082

00:42:41.910 --> 00:42:43.296 This is sort of what our tumor

NOTE Confidence: 0.27132082

00:42:43.296 --> 00:42:44.230 boards look like lately.

NOTE Confidence: 0.27132082

00:42:44.230 --> 00:42:45.733 So I I would just like to as long

NOTE Confidence: 0.27132082

00:42:45.733 --> 00:42:47.321 as I have the podium today encourage

NOTE Confidence: 0.27132082

00:42:47.321 --> 00:42:49.378 people to go to tumor board and start

NOTE Confidence: 0.27132082

00:42:49.378 --> 00:42:50.748 having our tumor boards hybrid.

NOTE Confidence: 0.27132082

00:42:50.750 --> 00:42:52.486 We can't have them all in person

NOTE Confidence: 0.27132082

00:42:52.486 --> 00:42:53.590 because we're 15 sites.

NOTE Confidence: 0.27132082

00:42:53.590 --> 00:42:55.125 But the tumor board discussions

NOTE Confidence: 0.27132082

00:42:55.125 --> 00:42:57.230 are going to be really critical.

NOTE Confidence: 0.27132082

00:42:57.230 --> 00:42:59.127 These are drugs that were approved from

NOTE Confidence: 0.27132082

00:42:59.127 --> 00:43:00.910 Yale LED studies very proud of that.

NOTE Confidence: 0.27132082

00:43:00.910 --> 00:43:02.730 All these drugs had some of their

NOTE Confidence: 0.27132082

00:43:02.730 --> 00:43:04.372 first studies here at Yale in the

NOTE Confidence: 0.27132082

00:43:04.372 --> 00:43:05.989 lung program and we have many more

NOTE Confidence: 0.27132082

00:43:05.989 --> 00:43:07.828 to come and we're seeing that in

NOTE Confidence: 0.27132082

00:43:07.828 --> 00:43:09.973 all of our programs and that's our

NOTE Confidence: 0.27132082

00:43:09.973 --> 00:43:11.385 experimental Therapeutics or DT.

NOTE Confidence: 0.27132082

00:43:11.390 --> 00:43:12.910 We can do the science on these studies.

NOTE Confidence: 0.27132082

00:43:12.910 --> 00:43:15.182 But the reason I skipped is I'm much

NOTE Confidence: 0.27132082

00:43:15.182 --> 00:43:17.390 more interested to tell you about the future.

NOTE Confidence: 0.27132082

00:43:17.390 --> 00:43:19.231 So we're we now have to target

NOTE Confidence: 0.27132082

00:43:19.231 --> 00:43:20.803 immunotherapy but I showed you at

NOTE Confidence: 0.27132082

00:43:20.803 --> 00:43:22.497 the beginning of my talk was how

NOTE Confidence: 0.27132082

00:43:22.553 --> 00:43:23.869 we used targeted therapy.

NOTE Confidence: 0.27132082

00:43:23.870 --> 00:43:26.024 We understood the target brought it

NOTE Confidence: 0.27132082

00:43:26.024 --> 00:43:29.126 earlier to have the greatest advantage and

NOTE Confidence: 0.27132082

00:43:29.126 --> 00:43:33.010 I told you about the the biobank we have.

NOTE Confidence: 0.27132082

00:43:33.010 --> 00:43:35.210 Well let me show you how it has paid off.

NOTE Confidence: 0.27132082

00:43:35.210 --> 00:43:36.995 So here we had patients who had

NOTE Confidence: 0.27132082

00:43:36.995 --> 00:43:38.387 immune therapy and they responded

NOTE Confidence: 0.27132082

00:43:38.387 --> 00:43:40.389 and then they had more immune therapy

NOTE Confidence: 0.27132082

00:43:40.389 --> 00:43:41.848 and they became resistant.

NOTE Confidence: 0.27132082

00:43:41.850 --> 00:43:43.890 So thanks to that poor protocol that we've

NOTE Confidence: 0.27132082

00:43:43.890 --> 00:43:45.768 had running for I guess what what Katie,

NOTE Confidence: 0.27132082

00:43:45.770 --> 00:43:46.850 12 years or or more,

NOTE Confidence: 0.27132082

00:43:46.850 --> 00:43:47.244 right.

NOTE Confidence: 0.27132082

00:43:47.244 --> 00:43:49.608 And we now have tumor tissue,

NOTE Confidence: 0.27132082

00:43:49.610 --> 00:43:52.140 germline DNA pretreatment and that

NOTE Confidence: 0.27132082

00:43:52.140 --> 00:43:54.442 resistance and working with Rick

NOTE Confidence: 0.27132082

00:43:54.442 --> 00:43:56.366 Lifton a number of years back before

NOTE Confidence: 0.27132082

00:43:56.366 --> 00:43:57.849 he left and and his lab,

NOTE Confidence: 0.27132082

00:43:57.850 --> 00:44:01.084 we we we sequenced all those tumors.

NOTE Confidence: 0.27132082

00:44:01.090 --> 00:44:02.722 And very interestingly you can see

NOTE Confidence: 0.27132082

00:44:02.722 --> 00:44:04.860 here the 14 tumors and you can see

NOTE Confidence: 0.27132082

00:44:04.860 --> 00:44:06.450 the first response shown here in

NOTE Confidence: 0.27132082

00:44:06.450 --> 00:44:08.130 the green and the resistance shown

NOTE Confidence: 0.27132082

00:44:08.130 --> 00:44:09.568 in the yellow triangle.

NOTE Confidence: 0.27132082

00:44:09.570 --> 00:44:11.298 So we had pre and post samples on

NOTE Confidence: 0.27132082

00:44:11.298 --> 00:44:12.739 patients who responded and then

NOTE Confidence: 0.27132082

00:44:12.739 --> 00:44:14.329 became resistant to immune therapy.

NOTE Confidence: 0.27132082

00:44:14.330 --> 00:44:15.882 And you can see it was from a

NOTE Confidence: 0.27132082

00:44:15.882 --> 00:44:17.089 hodgepodge of different trials,

NOTE Confidence: 0.27132082

00:44:17.090 --> 00:44:19.334 some with anti PDL 1, some with anti PD.

NOTE Confidence: 0.27132082

00:44:19.334 --> 00:44:21.166 One the drugs are different but quite

NOTE Confidence: 0.27132082

00:44:21.166 --> 00:44:23.035 frankly for this type of analysis I

NOTE Confidence: 0.27132082

00:44:23.035 --> 00:44:25.125 don't think it makes much of a difference.

NOTE Confidence: 0.27132082

00:44:25.130 --> 00:44:26.768 Well, two stories emerge from this.

NOTE Confidence: 0.75460684

00:44:26.770 --> 00:44:28.186 They've both been published

NOTE Confidence: 0.75460684

00:44:28.186 --> 00:44:29.248 several years back,

NOTE Confidence: 0.75460684

00:44:29.250 --> 00:44:30.930 one that that Katie and Scott LED

NOTE Confidence: 0.75460684

00:44:30.930 --> 00:44:32.450 where we actually had one patient.

NOTE Confidence: 0.75460684

00:44:32.450 --> 00:44:34.448 This patient was on Tremolomab and

NOTE Confidence: 0.75460684

00:44:34.448 --> 00:44:36.573 Debiolomab had a tumor that responded

NOTE Confidence: 0.75460684

00:44:36.573 --> 00:44:38.408 and then it became resistant.

NOTE Confidence: 0.75460684

00:44:38.410 --> 00:44:39.625 And actually by looking at

NOTE Confidence: 0.75460684

00:44:39.625 --> 00:44:41.130 the the biopsies pre and post,

NOTE Confidence: 0.75460684

00:44:41.130 --> 00:44:44.213 we didn't see much different in PDL one.

NOTE Confidence: 0.75460684

00:44:44.213 --> 00:44:47.330 But what we did see is this is

NOTE Confidence: 0.75460684

00:44:47.330 --> 00:44:49.410 loss of beta 2 microglobulin.

NOTE Confidence: 0.75460684

00:44:49.410 --> 00:44:51.209 So if you look at copy number,

NOTE Confidence: 0.75460684

00:44:51.210 --> 00:44:53.688 there was already lost a pre immunotherapy.

NOTE Confidence: 0.75460684

00:44:53.690 --> 00:44:55.196 The patient had already lost one

NOTE Confidence: 0.75460684

00:44:55.196 --> 00:44:57.010 copy of Beta 2 microglobulin.

NOTE Confidence: 0.75460684

00:44:57.010 --> 00:44:58.690 And then when the patient became resistant,

NOTE Confidence: 0.75460684

00:44:58.690 --> 00:45:01.084 they lost both copies of Beta 2

NOTE Confidence: 0.75460684

00:45:01.084 --> 00:45:02.860 blackroglobulin and Beta 2 microglobulin of

NOTE Confidence: 0.75460684

00:45:02.860 --> 00:45:04.869 course is an essential component of MHC one.

NOTE Confidence: 0.75460684

00:45:04.870 --> 00:45:07.030 So these tumors lost the ability

NOTE Confidence: 0.75460684

00:45:07.030 --> 00:45:09.790 to present neo anakin to T cells.

NOTE Confidence: 0.75460684

00:45:09.790 --> 00:45:11.218 So we are actually seeing that about

NOTE Confidence: 0.75460684

00:45:11.218 --> 00:45:12.706 five to 10% of the time in lung cancer.

NOTE Confidence: 0.75460684

00:45:12.710 --> 00:45:15.070 So these patients are going

NOTE Confidence: 0.75460684

00:45:15.070 --> 00:45:16.270 to need more of this.

NOTE Confidence: 0.75460684

00:45:16.270 --> 00:45:17.790 This immune approach won't work.

NOTE Confidence: 0.75460684

00:45:17.790 --> 00:45:19.708 We need to use other other ways.

NOTE Confidence: 0.75460684

00:45:19.710 --> 00:45:21.066 Maybe the innate immune system's going

NOTE Confidence: 0.75460684

00:45:21.066 --> 00:45:22.925 to be the way we target these tumors

NOTE Confidence: 0.75460684

00:45:22.925 --> 00:45:24.550 and K cells or something like that.

NOTE Confidence: 0.75460684

00:45:24.550 --> 00:45:26.575 And then what what Kurt and and David did

NOTE Confidence: 0.75460684

00:45:26.575 --> 00:45:28.898 is this is quantitative amino fluorescence.

NOTE Confidence: 0.75460684

00:45:28.900 --> 00:45:30.148 We took a whole bunch of

NOTE Confidence: 0.75460684

00:45:30.148 --> 00:45:30.772 samples of responders,

NOTE Confidence: 0.75460684

00:45:30.780 --> 00:45:31.340 non responders.

NOTE Confidence: 0.75460684

00:45:31.340 --> 00:45:33.020 These are samples that Scott had

NOTE Confidence: 0.75460684

00:45:33.020 --> 00:45:34.467 collected over the years and we

NOTE Confidence: 0.75460684

00:45:34.467 --> 00:45:35.721 looked at those samples and we

NOTE Confidence: 0.75460684

00:45:35.770 --> 00:45:38.110 stained for CD3 and and when double

NOTE Confidence: 0.75460684

00:45:38.110 --> 00:45:40.340 labeling and we looked at CD3.

NOTE Confidence: 0.75460684

00:45:40.340 --> 00:45:41.897 So we looked for tumors that were low CD3,

NOTE Confidence: 0.75460684

00:45:41.900 --> 00:45:43.164 so low T cells.

NOTE Confidence: 0.75460684

00:45:43.164 --> 00:45:45.699 We looked at tumors that were low CD3,

NOTE Confidence: 0.75460684

00:45:45.700 --> 00:45:47.986 high CD3 and low grand Simon Ki 67 and

NOTE Confidence: 0.75460684

00:45:47.986 --> 00:45:50.343 the idea there were these are tumors

NOTE Confidence: 0.75460684

00:45:50.343 --> 00:45:52.800 that were not activated in their T cells.

NOTE Confidence: 0.75460684

00:45:52.800 --> 00:45:54.571 And then we looked at some tumors

NOTE Confidence: 0.75460684

00:45:54.571 --> 00:45:56.610 that were high CD3 and high Granzyme

NOTE Confidence: 0.75460684

00:45:56.610 --> 00:45:59.409 and KS 67 and that Granzyme and KS 67

NOTE Confidence: 0.75460684

00:45:59.409 --> 00:46:01.959 are the are the white and the green.

NOTE Confidence: 0.75460684

00:46:01.960 --> 00:46:04.120 And I would have predicted that

NOTE Confidence: 0.75460684

00:46:04.120 --> 00:46:06.133 this is the group Group C here

NOTE Confidence: 0.75460684

00:46:06.133 --> 00:46:07.279 that would have done the best.

NOTE Confidence: 0.75460684

00:46:07.280 --> 00:46:09.560 But interestingly the group that did

NOTE Confidence: 0.75460684

00:46:09.560 --> 00:46:11.985 best was you can see here's here's

NOTE Confidence: 0.75460684

00:46:11.985 --> 00:46:14.519 the the type 2 group shown here,

NOTE Confidence: 0.75460684

00:46:14.520 --> 00:46:17.778 high CD3 and low granzyme and low KS 67.

NOTE Confidence: 0.75460684

00:46:17.780 --> 00:46:19.444 So why is the group that has many

NOTE Confidence: 0.75460684

00:46:19.444 --> 00:46:21.238 T cells but has the non activated

NOTE Confidence: 0.75460684

00:46:21.238 --> 00:46:22.298 T cells doing better?

NOTE Confidence: 0.75460684

00:46:22.300 --> 00:46:24.208 And that was something we really

NOTE Confidence: 0.75460684

00:46:24.208 --> 00:46:25.764 couldn't explain until recently when

NOTE Confidence: 0.75460684

00:46:25.764 --> 00:46:27.620 Li Ping Chen and and Kurt and others.

NOTE Confidence: 0.75460684

00:46:27.620 --> 00:46:30.511 Miguel Sanam Ahmed who was in Li

NOTE Confidence: 0.75460684

00:46:30.511 --> 00:46:32.700 Ping's lab did a study and actually

NOTE Confidence: 0.75460684

00:46:32.700 --> 00:46:34.060 using citep analysis showed that

NOTE Confidence: 0.75460684

00:46:34.116 --> 00:46:35.551 many of those T cells that are

NOTE Confidence: 0.75460684

00:46:35.551 --> 00:46:36.939 in the tumor are burned out,

NOTE Confidence: 0.75460684

00:46:36.940 --> 00:46:38.128 they're they're not active.

NOTE Confidence: 0.75460684

00:46:38.128 --> 00:46:39.613 And it probably explains why

NOTE Confidence: 0.75460684

00:46:39.613 --> 00:46:40.835 chemotherapy works with immunotherapy

NOTE Confidence: 0.75460684

00:46:40.835 --> 00:46:42.300 because chemotherapy kills the T

NOTE Confidence: 0.75460684

00:46:42.300 --> 00:46:44.115 cells that are in the tumor micro

NOTE Confidence: 0.75460684

00:46:44.115 --> 00:46:45.300 environment making room for more

NOTE Confidence: 0.75460684

00:46:45.300 --> 00:46:47.100 active and newer T cells to come in.

NOTE Confidence: 0.75460684

00:46:47.100 --> 00:46:48.864 This is a work in progress and we need

NOTE Confidence: 0.75460684

00:46:48.864 --> 00:46:50.578 fresh tumor samples to study this more.

NOTE Confidence: 0.75460684

00:46:50.580 --> 00:46:51.834 But the idea is that it's

NOTE Confidence: 0.75460684

00:46:51.834 --> 00:46:52.670 the quality of the

NOTE Confidence: 0.7446454

00:46:52.722 --> 00:46:54.339 T cells of the tumor that matters,

NOTE Confidence: 0.7446454

00:46:54.340 --> 00:46:56.140 not just whether the T

NOTE Confidence: 0.7446454

00:46:56.140 --> 00:46:57.940 cells are there or not.

NOTE Confidence: 0.7446454

00:46:57.940 --> 00:46:58.860 In the last few minutes,

NOTE Confidence: 0.7446454

00:46:58.860 --> 00:47:00.420 I just want to tell you about one

NOTE Confidence: 0.7446454

00:47:00.420 --> 00:47:01.697 more story and that's how how,

NOTE Confidence: 0.7446454

00:47:01.700 --> 00:47:04.094 how we, how we, how we look at resistance.

NOTE Confidence: 0.7446454

00:47:04.100 --> 00:47:06.212 So what we're thinking here in

NOTE Confidence: 0.7446454

00:47:06.212 --> 00:47:08.578 our group is when we looked at

NOTE Confidence: 0.7446454

00:47:08.580 --> 00:47:10.500 250 cases of of lung cancer,

NOTE Confidence: 0.7446454

00:47:10.500 --> 00:47:13.996 you can see that about 70% of these

NOTE Confidence: 0.7446454

00:47:13.996 --> 00:47:16.949 tumors were high PDL one and high kill.

NOTE Confidence: 0.7446454

00:47:16.950 --> 00:47:18.381 So they have a lot of PDL one and

NOTE Confidence: 0.7446454

00:47:18.381 --> 00:47:19.867 a lot of T cells in the tumor.

NOTE Confidence: 0.7446454

00:47:19.870 --> 00:47:21.676 These are probably the tumors that

NOTE Confidence: 0.7446454

00:47:21.676 --> 00:47:23.670 responded quite well to immunotherapy.

NOTE Confidence: 0.7446454

00:47:23.670 --> 00:47:25.542 But here's another 26% of tumors

NOTE Confidence: 0.7446454

00:47:25.542 --> 00:47:26.790 that have high tail.

NOTE Confidence: 0.7446454

00:47:26.790 --> 00:47:29.310 There's a lot of blue but no PDL 1,

NOTE Confidence: 0.7446454

00:47:29.310 --> 00:47:30.550 so probably suggest there's

NOTE Confidence: 0.7446454

00:47:30.550 --> 00:47:31.790 another checkpoint in play.

NOTE Confidence: 0.7446454

00:47:31.790 --> 00:47:34.345 And then very interestingly 45 or twenty

NOTE Confidence: 0.6714045

00:47:36.710 --> 00:47:38.468 7057% of lung cancers are cold.

NOTE Confidence: 0.6714045

00:47:38.470 --> 00:47:40.115 So it's really these type 1 tumors

NOTE Confidence: 0.6714045

00:47:40.115 --> 00:47:41.428 I've already talked to you about.

NOTE Confidence: 0.6714045

00:47:41.430 --> 00:47:42.230 These are the type 2.

NOTE Confidence: 0.6714045

00:47:42.230 --> 00:47:43.034 I'm sorry, these,

NOTE Confidence: 0.6714045

00:47:43.034 --> 00:47:44.910 these are the tumors that probably respond,

NOTE Confidence: 0.6714045

00:47:44.910 --> 00:47:46.840 have a durable responder, Maureen.

NOTE Confidence: 0.6714045

00:47:46.840 --> 00:47:47.720 They either require resistance

NOTE Confidence: 0.6714045

00:47:47.720 --> 00:47:49.371 like I just showed you or they're

NOTE Confidence: 0.6714045

00:47:49.371 --> 00:47:50.523 probably resistant for mechanisms

NOTE Confidence: 0.6714045

00:47:50.523 --> 00:47:51.675 we don't yet understand.

NOTE Confidence: 0.6714045

00:47:51.680 --> 00:47:53.402 But it's the other other tumor types

NOTE Confidence: 0.6714045

00:47:53.402 --> 00:47:54.914 that we've been targeting in the

NOTE Confidence: 0.6714045

00:47:54.914 --> 00:47:56.601 spore and type three of the tumors

NOTE Confidence: 0.6714045

00:47:56.655 --> 00:47:58.354 that must have some other checkpoint.

NOTE Confidence: 0.6714045

00:47:58.354 --> 00:48:01.438 So Li Ping and you know,

NOTE Confidence: 0.6714045

00:48:01.440 --> 00:48:03.029 I became involved with this 'cause I

NOTE Confidence: 0.6714045

00:48:03.029 --> 00:48:04.640 did a sabbatical in this lab in 2015

NOTE Confidence: 0.6714045

00:48:04.640 --> 00:48:06.600 and they were working on this project.

NOTE Confidence: 0.6714045

00:48:06.600 --> 00:48:07.872 I said can we bring this

NOTE Confidence: 0.6714045

00:48:07.872 --> 00:48:08.720 project into the spore?

NOTE Confidence: 0.6714045

00:48:08.720 --> 00:48:09.470 And and he,

NOTE Confidence: 0.6714045

00:48:09.470 --> 00:48:11.220 he said sure he was developing it

NOTE Confidence: 0.6714045

00:48:11.278 --> 00:48:13.093 with a company called Nexcure and

NOTE Confidence: 0.6714045

00:48:13.093 --> 00:48:14.514 this is a drug known as cyclic

NOTE Confidence: 0.6714045

00:48:14.514 --> 00:48:16.167 15 and I'm running low on time,

NOTE Confidence: 0.6714045

00:48:16.170 --> 00:48:18.807 but basically this is a homolog to PDL one

NOTE Confidence: 0.6714045

00:48:18.810 --> 00:48:21.730 and in in tumors that are interferon high,

NOTE Confidence: 0.6714045

00:48:21.730 --> 00:48:23.248 you know that activates PDL one,

NOTE Confidence: 0.6714045

00:48:23.250 --> 00:48:25.364 but it actually down regulates cyclic 15.

NOTE Confidence: 0.6714045

00:48:25.370 --> 00:48:27.128 So it makes sense that this,

NOTE Confidence: 0.6714045

00:48:27.130 --> 00:48:27.848 this marker,

NOTE Confidence: 0.6714045

00:48:27.848 --> 00:48:28.207 this,

NOTE Confidence: 0.6714045

00:48:28.207 --> 00:48:30.361 this protein might be more important

NOTE Confidence: 0.6714045

00:48:30.361 --> 00:48:32.767 in tumors that are PDL one negative

NOTE Confidence: 0.6714045

00:48:32.770 --> 00:48:34.410 and actually that's been shown.

NOTE Confidence: 0.6714045

00:48:34.410 --> 00:48:36.072 So here's cyclic 15 and here's

NOTE Confidence: 0.6714045

00:48:36.072 --> 00:48:38.039 PDL one and you can see in

NOTE Confidence: 0.6714045

00:48:38.039 --> 00:48:40.142 tumors that that have cyclic 15,

NOTE Confidence: 0.6714045

00:48:40.142 --> 00:48:42.500 it's a suppressor of T cells.

NOTE Confidence: 0.6714045

00:48:42.500 --> 00:48:44.383 So the idea was could this be

NOTE Confidence: 0.6714045

00:48:44.383 --> 00:48:45.958 an alternate target we can use

NOTE Confidence: 0.6714045

00:48:45.958 --> 00:48:47.374 in these tumors that are low

NOTE Confidence: 0.6714045

00:48:47.374 --> 00:48:49.098 PDL one and the answer is yes,

NOTE Confidence: 0.6714045

00:48:49.100 --> 00:48:50.540 we were involved in the phase one trial,

NOTE Confidence: 0.6714045

00:48:50.540 --> 00:48:52.376 Pat Larusso was API on that.

NOTE Confidence: 0.6714045

00:48:52.380 --> 00:48:53.778 We did that with a company,

NOTE Confidence: 0.6714045

00:48:53.780 --> 00:48:55.180 There's a company sponsored trial.

NOTE Confidence: 0.6714045

00:48:55.180 --> 00:48:56.708 Often times you have to do the first

NOTE Confidence: 0.6714045

00:48:56.708 --> 00:48:58.072 trial with a company and then your

NOTE Confidence: 0.6714045

00:48:58.072 --> 00:48:59.380 next trial can be your own Ind.

NOTE Confidence: 0.6714045

00:48:59.380 --> 00:49:00.892 So the first trial was a company

NOTE Confidence: 0.6714045

00:49:00.892 --> 00:49:02.291 sponsored trial and you can see

NOTE Confidence: 0.6714045

00:49:02.291 --> 00:49:03.471 here's patients two patients with

NOTE Confidence: 0.6714045

00:49:03.471 --> 00:49:04.698 lung cancer who had response,

NOTE Confidence: 0.6714045

00:49:04.700 --> 00:49:06.060 one with a complete response,

NOTE Confidence: 0.6714045

00:49:06.060 --> 00:49:08.660 one with a partial response.

NOTE Confidence: 0.6714045

00:49:08.660 --> 00:49:09.896 That response and lung cancer wasn't

NOTE Confidence: 0.6714045

00:49:09.896 --> 00:49:11.640 here at Yale but this was a patient

NOTE Confidence: 0.6714045

00:49:11.640 --> 00:49:12.730 who had already had immunotherapy

NOTE Confidence: 0.6714045

00:49:12.730 --> 00:49:14.277 and failed and you can see they're

NOTE Confidence: 0.6714045

00:49:14.277 --> 00:49:15.711 responding to the CIGLIC 15.

NOTE Confidence: 0.6714045

00:49:15.711 --> 00:49:19.568 But the phase one team we Katie Kirk

NOTE Confidence: 0.6714045

00:49:19.568 --> 00:49:21.280 was here we got a nice picture at

NOTE Confidence: 0.6714045

00:49:21.331 --> 00:49:23.043 least she she did the picture not me

NOTE Confidence: 0.6714045

00:49:23.043 --> 00:49:24.967 she had her own photographer with and

NOTE Confidence: 0.6714045

00:49:24.967 --> 00:49:27.300 and then this is what I want to show you.

NOTE Confidence: 0.6714045

00:49:27.300 --> 00:49:28.710 Scott Gettinger has these data I

NOTE Confidence: 0.6714045

00:49:28.710 --> 00:49:29.960 presented on his behalf because

NOTE Confidence: 0.6714045

00:49:29.960 --> 00:49:31.255 he couldn't make the meeting.

NOTE Confidence: 0.6714045

00:49:31.260 --> 00:49:32.540 But this is Scott's work.

NOTE Confidence: 0.6714045

00:49:32.540 --> 00:49:34.922 Scott has LED a trial of NC 318,

NOTE Confidence: 0.6714045

00:49:34.922 --> 00:49:36.577 which is the antibody against

NOTE Confidence: 0.6714045

00:49:36.577 --> 00:49:38.332 ciglic 15 and this is totally

NOTE Confidence: 0.6714045

00:49:38.332 --> 00:49:38.878 investigator initiated.

NOTE Confidence: 0.6714045

00:49:38.880 --> 00:49:40.808 Yale holds the I and D We've put

NOTE Confidence: 0.6714045

00:49:40.808 --> 00:49:42.680 almost 40 patients on this trial.

NOTE Confidence: 0.6714045

00:49:42.680 --> 00:49:44.480 We have two arms of the drug alone,

NOTE Confidence: 0.6714045

00:49:44.480 --> 00:49:45.190 different schedules.

NOTE Confidence: 0.6714045

00:49:45.190 --> 00:49:47.675 Then we combine the drug with pembrolizumab,

NOTE Confidence: 0.6714045

00:49:47.680 --> 00:49:48.772 the PD1 inhibitor.

NOTE Confidence: 0.6714045

00:49:48.772 --> 00:49:52.019 We also have an arm of IO naive patients.

NOTE Confidence: 0.6714045

00:49:52.019 --> 00:49:53.078 We're just starting,

NOTE Confidence: 0.66993445

00:49:53.080 --> 00:49:55.120 so we've been studying this here at Yale.

NOTE Confidence: 0.66993445

00:49:55.120 --> 00:49:56.485 We've been getting biopsies pre and post

NOTE Confidence: 0.66993445

00:49:56.485 --> 00:49:58.239 and again I don't have a lot of time left,

NOTE Confidence: 0.66993445

00:49:58.240 --> 00:50:00.264 but I'll just get cut to the chase.

NOTE Confidence: 0.66993445

00:50:00.270 --> 00:50:01.700 The biomarker that David's been

NOTE Confidence: 0.66993445

00:50:01.700 --> 00:50:03.550 developing has been helpful to to date.

NOTE Confidence: 0.66993445

00:50:03.550 --> 00:50:04.690 We as always happens,

NOTE Confidence: 0.66993445

00:50:04.690 --> 00:50:06.400 we don't get biomarker on the

NOTE Confidence: 0.66993445

00:50:06.462 --> 00:50:08.070 patients that have the best response.

NOTE Confidence: 0.66993445

00:50:08.070 --> 00:50:09.380 We actually just had another

NOTE Confidence: 0.66993445

00:50:09.380 --> 00:50:09.904 response yesterday.

NOTE Confidence: 0.66993445

00:50:09.910 --> 00:50:10.576 So stay tuned.

NOTE Confidence: 0.66993445

00:50:10.576 --> 00:50:12.435 But what we have done is we've looked

NOTE Confidence: 0.66993445

00:50:12.435 --> 00:50:14.164 at patients and we've looked at a

NOTE Confidence: 0.66993445

00:50:14.164 --> 00:50:15.706 number of patients have benefited

NOTE Confidence: 0.66993445

00:50:15.706 --> 00:50:17.692 some of them that are getting

NOTE Confidence: 0.66993445

00:50:17.692 --> 00:50:19.278 pembrolizumab plus cyclip 15 and

NOTE Confidence: 0.66993445

00:50:19.278 --> 00:50:21.150 some of them cyclip 15 alone.

NOTE Confidence: 0.66993445

00:50:21.150 --> 00:50:23.110 And you can see we're seeing PRS,

NOTE Confidence: 0.66993445

00:50:23.110 --> 00:50:24.671 I'll tell you as someone who works

NOTE Confidence: 0.66993445

00:50:24.671 --> 00:50:26.758 in this field of lung cancer to see

NOTE Confidence: 0.66993445

00:50:26.758 --> 00:50:28.128 an immuno refractory patient respond,

NOTE Confidence: 0.66993445

00:50:28.130 --> 00:50:30.242 you can count on one hand how often

NOTE Confidence: 0.66993445

00:50:30.242 --> 00:50:32.490 that happens with some of these new agents.

NOTE Confidence: 0.66993445

00:50:32.490 --> 00:50:33.810 So we're very excited about this.

NOTE Confidence: 0.66993445

00:50:33.810 --> 00:50:35.320 We're trying to understand the

NOTE Confidence: 0.66993445

00:50:35.320 --> 00:50:35.924 molecular mechanisms,

NOTE Confidence: 0.66993445

00:50:35.930 --> 00:50:38.219 but we've had four responders now to

NOTE Confidence: 0.66993445

00:50:38.219 --> 00:50:40.648 the combo and one to a single agent

NOTE Confidence: 0.66993445

00:50:40.650 --> 00:50:42.568 and actually pictures are worth 1000 words.

NOTE Confidence: 0.66993445

00:50:42.570 --> 00:50:44.635 So here's that patient who had got

NOTE Confidence: 0.66993445

00:50:44.635 --> 00:50:46.838 the single agent liver lesion that's

NOTE Confidence: 0.66993445

00:50:46.838 --> 00:50:48.685 responded and here are three examples

NOTE Confidence: 0.66993445

00:50:48.685 --> 00:50:51.096 of patients who are responding to the combo.

NOTE Confidence: 0.66993445

00:50:51.100 --> 00:50:52.788 So we are we are seeing activity here

NOTE Confidence: 0.66993445

00:50:52.788 --> 00:50:54.362 and we're in the process of working

NOTE Confidence: 0.66993445

00:50:54.362 --> 00:50:55.989 with next Cure and with other other

NOTE Confidence: 0.66993445

00:50:55.989 --> 00:50:58.560 groups to decide what our next trial will be.

NOTE Confidence: 0.66993445

00:50:58.560 --> 00:51:00.020 So I'm going to skip this.

NOTE Confidence: 0.66993445

00:51:00.020 --> 00:51:01.497 I'm, I'm running, I was very ambitious.

NOTE Confidence: 0.66993445

00:51:01.500 --> 00:51:04.416 I haven't given our live talk in many years,

NOTE Confidence: 0.66993445

00:51:04.420 --> 00:51:04.657 OK.

NOTE Confidence: 0.66993445

00:51:04.657 --> 00:51:06.553 But what I do want to tell you

NOTE Confidence: 0.66993445

00:51:06.553 --> 00:51:08.216 about is just get to the end.

NOTE Confidence: 0.66993445

00:51:08.220 --> 00:51:11.379 So what I've tried to show you today is

NOTE Confidence: 0.66993445

00:51:11.380 --> 00:51:13.456 we're making progress in this disease.

NOTE Confidence: 0.66993445

00:51:13.460 --> 00:51:14.508 It's really phenomenal progress.

NOTE Confidence: 0.66993445

00:51:14.508 --> 00:51:16.080 It doesn't always seem like that

NOTE Confidence: 0.66993445

00:51:16.129 --> 00:51:17.099 if you're on the inside,

NOTE Confidence: 0.66993445

00:51:17.100 --> 00:51:18.748 but you know if you look back at

NOTE Confidence: 0.66993445

00:51:18.748 --> 00:51:20.459 it from a 2030 year perspective,

NOTE Confidence: 0.66993445

00:51:20.460 --> 00:51:22.413 we we we now have patients with lung cancer.

NOTE Confidence: 0.66993445

00:51:22.420 --> 00:51:24.030 Ironically the patients who are

NOTE Confidence: 0.66993445

00:51:24.030 --> 00:51:26.062 smokers who have many more mutations

NOTE Confidence: 0.66993445

00:51:26.062 --> 00:51:28.589 probably have the chance of cure with

NOTE Confidence: 0.66993445

00:51:28.589 --> 00:51:30.635 immunotherapy and as we move that

NOTE Confidence: 0.66993445

00:51:30.635 --> 00:51:32.531 immunotherapy earlier maybe even more so.

NOTE Confidence: 0.66993445

00:51:32.540 --> 00:51:34.270 But the targeted therapy produces

NOTE Confidence: 0.66993445

00:51:34.270 --> 00:51:36.000 amazing benefit and quality of

NOTE Confidence: 0.66993445

00:51:36.057 --> 00:51:37.873 life and if we use it earlier I

NOTE Confidence: 0.66993445

00:51:37.873 --> 00:51:39.679 believe we could probably cure some

NOTE Confidence: 0.66993445

00:51:39.679 --> 00:51:40.975 patients there as well.

NOTE Confidence: 0.66993445

00:51:40.980 --> 00:51:42.906 The theme I think of of Yale as a

NOTE Confidence: 0.66993445

00:51:42.906 --> 00:51:44.875 whole and certainly of the lung group

NOTE Confidence: 0.66993445

00:51:44.880 --> 00:51:46.320 is that we used to call these Darts.

NOTE Confidence: 0.66993445

00:51:46.320 --> 00:51:49.460 I haven't made the change the slide,

NOTE Confidence: 0.66993445

00:51:49.460 --> 00:51:51.260 but our clinical trials team uses

NOTE Confidence: 0.66993445

00:51:51.260 --> 00:51:53.502 the institutional science and our

NOTE Confidence: 0.66993445

00:51:53.502 --> 00:51:54.986 industry collaborations to develop

NOTE Confidence: 0.66993445

00:51:54.986 --> 00:51:57.215 trials that lead to advances grants

NOTE Confidence: 0.66993445

00:51:57.215 --> 00:51:59.261 and we're feeding on that cycle

NOTE Confidence: 0.66993445

00:51:59.261 --> 00:52:01.494 and we're building a team that's

NOTE Confidence: 0.66993445

00:52:01.494 --> 00:52:03.354 focusing on lung cancer advances.

NOTE Confidence: 0.66993445

00:52:03.360 --> 00:52:06.720 We have many other you know targets.

NOTE Confidence: 0.66993445

00:52:06.720 --> 00:52:08.960 We're working with Aaron Rings,

NOTE Confidence: 0.66993445

00:52:08.960 --> 00:52:10.676 Teen BP and the Melanoma group

NOTE Confidence: 0.66993445

00:52:10.676 --> 00:52:12.350 and the lung group as well.

NOTE Confidence: 0.66993445

00:52:12.350 --> 00:52:15.150 CD 93 is a target for vascular permeability.

NOTE Confidence: 0.66993445

00:52:15.150 --> 00:52:16.575 We're starting to work with

NOTE Confidence: 0.66993445

00:52:16.575 --> 00:52:18.000 here at Yale with Lee

NOTE Confidence: 0.43922126

00:52:18.061 --> 00:52:19.746 Ping and other other targets.

NOTE Confidence: 0.43922126

00:52:19.750 --> 00:52:21.310 And I didn't know Don was going to be here,

NOTE Confidence: 0.43922126

00:52:21.310 --> 00:52:22.890 but you know we're certainly

NOTE Confidence: 0.43922126

00:52:22.890 --> 00:52:24.830 interested in the flip as well.

NOTE Confidence: 0.43922126

00:52:24.830 --> 00:52:25.616 We're doing trials.

NOTE Confidence: 0.43922126

00:52:25.616 --> 00:52:27.760 This is an example of a biomarker adaptive

NOTE Confidence: 0.43922126

00:52:27.760 --> 00:52:29.396 trial we did with with with Merck.

NOTE Confidence: 0.43922126

00:52:29.396 --> 00:52:30.608 But I'd rather tell you about

NOTE Confidence: 0.43922126

00:52:30.608 --> 00:52:31.783 the trial that we're developing

NOTE Confidence: 0.43922126

00:52:31.783 --> 00:52:33.434 in the last minute called the I

NOTE Confidence: 0.43922126

00:52:33.434 --> 00:52:34.549 Bulldog trial and Maina's here.

NOTE Confidence: 0.43922126

00:52:34.550 --> 00:52:35.774 So Maina's been coordinating

NOTE Confidence: 0.43922126

00:52:35.774 --> 00:52:37.298 with us doing a great job.

NOTE Confidence: 0.43922126

00:52:37.298 --> 00:52:39.030 How are we going to do another

NOTE Confidence: 0.43922126

00:52:39.030 --> 00:52:40.595 battle trial here at Yale?

NOTE Confidence: 0.43922126

00:52:40.600 --> 00:52:42.608 What I would suggest is we have to

NOTE Confidence: 0.43922126

00:52:42.608 --> 00:52:44.376 pull together and and do a trial

NOTE Confidence: 0.43922126

00:52:44.376 --> 00:52:46.187 where we now take advantage of the

NOTE Confidence: 0.43922126

00:52:46.187 --> 00:52:47.837 pathology that I've shown you today

NOTE Confidence: 0.43922126

00:52:47.840 --> 00:52:49.952 of the science here at Yale and of

NOTE Confidence: 0.43922126

00:52:49.952 --> 00:52:52.090 our ability to do clinical trials and

NOTE Confidence: 0.43922126

00:52:52.090 --> 00:52:54.160 lead that next generation of studies.

NOTE Confidence: 0.43922126

00:52:54.160 --> 00:52:57.152 And we are now looking for new ideas.

NOTE Confidence: 0.43922126

00:52:57.152 --> 00:52:57.704 Here's,

NOTE Confidence: 0.43922126

00:52:57.704 --> 00:53:00.074 here's our current idea that we've

NOTE Confidence: 0.43922126

00:53:00.074 --> 00:53:01.264 been shopping around and we've

NOTE Confidence: 0.43922126

00:53:01.264 --> 00:53:02.608 had meetings with three different

NOTE Confidence: 0.43922126

00:53:02.608 --> 00:53:04.376 pharma groups in the last month

NOTE Confidence: 0.43922126

00:53:04.376 --> 00:53:05.316 and they're all interested.

NOTE Confidence: 0.43922126

00:53:05.316 --> 00:53:07.159 So we'll have to see who works with us.

NOTE Confidence: 0.43922126

00:53:07.160 --> 00:53:08.804 We, we're really excited about this

NOTE Confidence: 0.43922126

00:53:08.804 --> 00:53:11.228 and we're going to do real time tumor blood,

NOTE Confidence: 0.43922126

00:53:11.230 --> 00:53:12.402 real time immune profiling.

NOTE Confidence: 0.43922126

00:53:12.402 --> 00:53:13.867 We can do that here.

NOTE Confidence: 0.43922126

00:53:13.870 --> 00:53:16.102 We can do it in a clear appropriate way.

NOTE Confidence: 0.43922126

00:53:16.110 --> 00:53:17.766 And then we're going to initially

NOTE Confidence: 0.43922126

00:53:17.766 --> 00:53:19.390 equally randomized patients to treatments.

NOTE Confidence: 0.43922126

00:53:19.390 --> 00:53:21.056 But then once we learn about how

NOTE Confidence: 0.43922126

00:53:21.056 --> 00:53:22.190 these biomarkers pretend response,

NOTE Confidence: 0.43922126

00:53:22.190 --> 00:53:23.905 we're going to do a biomarker enrichment,

NOTE Confidence: 0.43922126

00:53:23.910 --> 00:53:25.850 adaptive randomization and Steve

NOTE Confidence: 0.43922126

00:53:25.850 --> 00:53:29.470 Miles very excited to do that with us.

NOTE Confidence: 0.43922126

00:53:29.470 --> 00:53:31.269 Here's the team that's working on that,

NOTE Confidence: 0.43922126

00:53:31.270 --> 00:53:32.642 just the core team,

NOTE Confidence: 0.43922126

00:53:32.642 --> 00:53:34.357 but we'll be getting everyone

NOTE Confidence: 0.43922126

00:53:34.357 --> 00:53:35.349 involved very soon.

NOTE Confidence: 0.43922126

00:53:35.350 --> 00:53:36.822 So as I conclude,

NOTE Confidence: 0.43922126

00:53:36.822 --> 00:53:39.030 can we cure metastatic lung cancer?

NOTE Confidence: 0.43922126

00:53:39.030 --> 00:53:41.712 Yes, I couldn't have said that 10 years ago,

NOTE Confidence: 0.43922126

00:53:41.720 --> 00:53:43.680 but only in some cases.

NOTE Confidence: 0.43922126

00:53:43.680 --> 00:53:45.744 We have 12 plus year survivors

NOTE Confidence: 0.43922126

00:53:45.744 --> 00:53:47.680 from our very first trials.

NOTE Confidence: 0.43922126

00:53:47.680 --> 00:53:48.840 Treatment was well tolerated

NOTE Confidence: 0.43922126

00:53:48.840 --> 00:53:50.000 and retreatment was possible.

NOTE Confidence: 0.43922126

00:53:50.000 --> 00:53:50.600 I didn't show you that,

NOTE Confidence: 0.43922126

00:53:50.600 --> 00:53:52.000 but sometimes you can retreat,

NOTE Confidence: 0.43922126

00:53:52.000 --> 00:53:53.272 but we don't even know what

NOTE Confidence: 0.43922126

00:53:53.272 --> 00:53:54.400 the markers are for that.

NOTE Confidence: 0.43922126

00:53:54.400 --> 00:53:55.513 But the problem is we don't have

NOTE Confidence: 0.43922126

00:53:55.513 --> 00:53:56.919 any way of knowing this in advance.

NOTE Confidence: 0.43922126

00:53:56.920 --> 00:53:59.237 We've got to do more biomarker work.

NOTE Confidence: 0.43922126

00:53:59.240 --> 00:54:01.277 So do we need to personalize immunotherapy?

NOTE Confidence: 0.43922126

00:54:01.280 --> 00:54:01.873 Absolutely.

NOTE Confidence: 0.43922126

00:54:01.873 --> 00:54:04.838 We spent 20 years personalizing

NOTE Confidence: 0.43922126

00:54:04.840 --> 00:54:05.496 targeted therapy.

NOTE Confidence: 0.43922126

00:54:05.496 --> 00:54:08.120 You'll you'll hear about that next June 10th,

NOTE Confidence: 0.43922126

00:54:08.120 --> 00:54:09.890 but we're still not there yet.

NOTE Confidence: 0.43922126

00:54:09.890 --> 00:54:11.846 We need biomarkers and better combos.

NOTE Confidence: 0.43922126

00:54:11.850 --> 00:54:13.610 We need innovative trial designs.

NOTE Confidence: 0.43922126

00:54:13.610 --> 00:54:15.766 But the future for this is now,

NOTE Confidence: 0.43922126

00:54:15.770 --> 00:54:17.030 so last slides,

NOTE Confidence: 0.43922126

00:54:17.030 --> 00:54:19.130 we need to personalize immunotherapy,

NOTE Confidence: 0.43922126

00:54:19.130 --> 00:54:20.510 identify biomarkers and

NOTE Confidence: 0.43922126

00:54:20.510 --> 00:54:21.890 improve combination therapy,

NOTE Confidence: 0.43922126

00:54:21.890 --> 00:54:23.542 identify new targets and

NOTE Confidence: 0.43922126

00:54:23.542 --> 00:54:24.368 rational combinations,

NOTE Confidence: 0.43922126

00:54:24.370 --> 00:54:25.870 establish novel endpoints,

NOTE Confidence: 0.43922126

00:54:25.870 --> 00:54:27.370 innovative trial designs.

NOTE Confidence: 0.43922126

00:54:27.370 --> 00:54:28.530 We can do that here,

NOTE Confidence: 0.43922126

00:54:28.530 --> 00:54:30.190 address mechanisms of resistance

NOTE Confidence: 0.43922126

00:54:30.190 --> 00:54:31.850 and bring disease early.

NOTE Confidence: 0.43922126

00:54:31.850 --> 00:54:34.685 It's sort of reads like the CCSG.

NOTE Confidence: 0.43922126

00:54:34.690 --> 00:54:35.458 We can do it,

NOTE Confidence: 0.43922126

00:54:35.458 --> 00:54:36.926 but I'm just my charge on this

NOTE Confidence: 0.43922126

00:54:36.926 --> 00:54:38.528 first ground round to the Friday.

NOTE Confidence: 0.43922126

00:54:38.530 --> 00:54:41.050 To the fellows, the scientists here,

NOTE Confidence: 0.43922126

00:54:41.050 --> 00:54:42.034 the translational scientists,

NOTE Confidence: 0.43922126

00:54:42.034 --> 00:54:42.362 everyone.

NOTE Confidence: 0.43922126

00:54:42.362 --> 00:54:44.002 We're we're a continuum from

NOTE Confidence: 0.43922126

00:54:44.002 --> 00:54:45.652 the clinic and the lab working

NOTE Confidence: 0.43922126

00:54:45.652 --> 00:54:46.927 together to help the patient.

NOTE Confidence: 0.43922126

00:54:46.930 --> 00:54:48.850 We need to develop drugs in real time,

NOTE Confidence: 0.34805804

00:54:48.850 --> 00:54:50.130 and it's only going to be with science.

NOTE Confidence: 0.34805804

00:54:50.130 --> 00:54:51.467 Ben Lewis here, He gave an amazing

NOTE Confidence: 0.34805804

00:54:51.467 --> 00:54:52.888 talk the other day on a trial

NOTE Confidence: 0.34805804

00:54:52.888 --> 00:54:53.888 that we're doing with ipilumab,

NOTE Confidence: 0.34805804

00:54:53.890 --> 00:54:54.520 nivolumab biomarkers.

NOTE Confidence: 0.34805804

00:54:54.520 --> 00:54:56.410 That's going to be the future.

NOTE Confidence: 0.34805804

00:54:56.410 --> 00:54:59.330 But then to translate those into new studies,

NOTE Confidence: 0.34805804

00:54:59.330 --> 00:55:00.688 So I'll just end with a picture.

NOTE Confidence: 0.34805804

00:55:00.690 --> 00:55:01.730 So this is Ben's talk.

NOTE Confidence: 0.34805804

00:55:01.730 --> 00:55:03.270 The other day we had 50 people

NOTE Confidence: 0.34805804

00:55:03.270 --> 00:55:04.570 at a translational lung meeting.

NOTE Confidence: 0.34805804

00:55:04.570 --> 00:55:07.307 Katie and Sarah have been organizing this.

NOTE Confidence: 0.34805804

00:55:07.310 --> 00:55:08.630 This is how we're going to make progress.

NOTE Confidence: 0.34805804

00:55:08.630 --> 00:55:10.190 We have to meet on a regular basis,

NOTE Confidence: 0.34805804

00:55:10.190 --> 00:55:11.318 go over our science,

NOTE Confidence: 0.34805804

00:55:11.318 --> 00:55:13.350 do as many Iits as we can.

NOTE Confidence: 0.34805804

00:55:13.350 --> 00:55:15.190 This trial actually was a trial of ipilumab,

NOTE Confidence: 0.34805804

00:55:15.190 --> 00:55:16.840 nivolumab that we went to meet

NOTE Confidence: 0.34805804

00:55:16.840 --> 00:55:18.240 with Bristol-Myers at the Yale

NOTE Confidence: 0.34805804

00:55:18.240 --> 00:55:19.470 Club about six years ago.

NOTE Confidence: 0.34805804

00:55:19.470 --> 00:55:20.253 Several of us,

NOTE Confidence: 0.34805804

00:55:20.253 --> 00:55:22.509 and we're not running it under our own ID,

NOTE Confidence: 0.34805804

00:55:22.510 --> 00:55:23.950 but we're getting the samples.

NOTE Confidence: 0.34805804

00:55:23.950 --> 00:55:25.070 We just got to get the samples

NOTE Confidence: 0.34805804

00:55:25.070 --> 00:55:26.228 here and get the science here.

NOTE Confidence: 0.34805804

00:55:26.230 --> 00:55:27.910 So we can make the next step.

NOTE Confidence: 0.34805804

00:55:27.910 --> 00:55:29.482 So with that I'll just end

NOTE Confidence: 0.34805804

00:55:29.482 --> 00:55:30.880 by saying save the date.

NOTE Confidence: 0.34805804

00:55:30.880 --> 00:55:32.609 Katie and I and and the whole

NOTE Confidence: 0.34805804

00:55:32.609 --> 00:55:34.263 committee are are gonna hold the

NOTE Confidence: 0.34805804

00:55:34.263 --> 00:55:35.683 interest for meeting here next

NOTE Confidence: 0.34805804

00:55:35.683 --> 00:55:37.576 June and we're gonna be celebrating

NOTE Confidence: 0.34805804

00:55:37.576 --> 00:55:39.156 20 years of EGFR mutations.

NOTE Confidence: 0.34805804

00:55:39.160 --> 00:55:41.011 The guest list is is everyone's

NOTE Confidence: 0.34805804

00:55:41.011 --> 00:55:42.277 saying yes and we're gonna we're

NOTE Confidence: 0.34805804

00:55:42.277 --> 00:55:43.239 the hotels will be full.

NOTE Confidence: 0.34805804

00:55:43.240 --> 00:55:43.980 So with that off,

NOTE Confidence: 0.34805804

00:55:43.980 --> 00:55:44.720 thank you very much.

NOTE Confidence: 0.45548692

00:55:51.820 --> 00:55:53.115 It's it's the hour. But I'm happy

NOTE Confidence: 0.45548692

00:55:53.115 --> 00:55:54.353 to take one or two questions

NOTE Confidence: 0.45548692

00:55:54.353 --> 00:55:55.619 I I'm supposed to look online

NOTE Confidence: 0.45548692

00:55:59.900 --> 00:56:00.660 a lot of people online.

NOTE Confidence: 0.45548692

00:56:00.660 --> 00:56:01.460 Oh, here's a question.

NOTE Confidence: 0.26020557

00:56:09.740 --> 00:56:10.964 Can you comment on giving the

NOTE Confidence: 0.26020557

00:56:10.964 --> 00:56:12.242 therapy of the new, Yeah, so,

NOTE Confidence: 0.26020557

00:56:12.242 --> 00:56:13.628 so new immunotherapy and the accurate

NOTE Confidence: 0.26020557

00:56:13.628 --> 00:56:15.138 setting does seem to have some benefit.

NOTE Confidence: 0.26020557

00:56:15.140 --> 00:56:17.660 The, the results are a bit mixed with

NOTE Confidence: 0.26020557

00:56:17.660 --> 00:56:19.624 the tezalizumab in a trial known as

NOTE Confidence: 0.26020557

00:56:19.624 --> 00:56:21.642 Keno 10 in the accurate setting in

NOTE Confidence: 0.26020557

00:56:21.642 --> 00:56:23.738 patients that were PDL one more than 1%,

NOTE Confidence: 0.26020557

00:56:23.740 --> 00:56:25.980 the hazard ratio is about point 6.7.

NOTE Confidence: 0.26020557

00:56:25.980 --> 00:56:28.586 So there is, there is a benefit but when

NOTE Confidence: 0.26020557

00:56:28.586 --> 00:56:30.050 if you look at those patients who were

NOTE Confidence: 0.26020557

00:56:30.097 --> 00:56:31.700 PDL one negative in their initial sample,

NOTE Confidence: 0.26020557

00:56:31.700 --> 00:56:33.440 there was no benefit at all.

NOTE Confidence: 0.26020557

00:56:33.440 --> 00:56:35.280 Hembalizumab interestingly in a

NOTE Confidence: 0.26020557

00:56:35.280 --> 00:56:37.580 very similar trial didn't didn't

NOTE Confidence: 0.26020557

00:56:37.580 --> 00:56:39.220 see any biomarker prevalence but

NOTE Confidence: 0.26020557

00:56:39.220 --> 00:56:41.320 they did see a benefit as well.

NOTE Confidence: 0.26020557

00:56:41.320 --> 00:56:43.252 My sense is that neoadjuvant is

NOTE Confidence: 0.26020557

00:56:43.252 --> 00:56:45.027 probably better because when you and

NOTE Confidence: 0.26020557

00:56:45.027 --> 00:56:46.896 and it comes from Melanoma I see

NOTE Confidence: 0.26020557

00:56:46.896 --> 00:56:48.690 Marcus shaking his head yes in in

NOTE Confidence: 0.26020557

00:56:48.690 --> 00:56:50.397 Melanoma and in lung cancer you you

NOTE Confidence: 0.26020557

00:56:50.397 --> 00:56:52.197 have a tumor and you have the lymph

NOTE Confidence: 0.26020557

00:56:52.200 --> 00:56:53.838 nodes that are involved as well.

NOTE Confidence: 0.26020557

00:56:53.840 --> 00:56:55.471 So if you use your your immunotherapy

NOTE Confidence: 0.26020557

00:56:55.471 --> 00:56:56.789 in the Neoactivate setting you've got

NOTE Confidence: 0.26020557

00:56:56.789 --> 00:56:58.445 the tumor in situ in in its micro

NOTE Confidence: 0.26020557

00:56:58.445 --> 00:56:59.795 environment with its lymph nodes.

NOTE Confidence: 0.26020557

00:56:59.800 --> 00:57:01.920 So you really get the entire T cell

NOTE Confidence: 0.26020557

00:57:01.920 --> 00:57:03.800 micro environment I think you know affected.

NOTE Confidence: 0.26020557

00:57:03.800 --> 00:57:04.752 So it's it's better.

NOTE Confidence: 0.26020557

00:57:04.752 --> 00:57:06.180 The problem is we're only going

NOTE Confidence: 0.26020557

00:57:06.233 --> 00:57:07.809 to be able to do neo activate on

NOTE Confidence: 0.26020557

00:57:07.809 --> 00:57:09.079 a selected group of patients.

NOTE Confidence: 0.26020557

00:57:09.080 --> 00:57:11.272 What we're seeing now is I'm sorry I

NOTE Confidence: 0.26020557

00:57:11.272 --> 00:57:12.560 didn't have time to show those data,

NOTE Confidence: 0.26020557

00:57:12.560 --> 00:57:14.248 but you know it works but you have

NOTE Confidence: 0.26020557

00:57:14.248 --> 00:57:15.671 to pick carefully because you're

NOTE Confidence: 0.26020557

00:57:15.671 --> 00:57:17.567 not going to really take someone

NOTE Confidence: 0.26020557

00:57:17.567 --> 00:57:19.422 who's not a candidate for surgery

NOTE Confidence: 0.26020557

00:57:19.422 --> 00:57:20.902 and bring them towards surgery.

NOTE Confidence: 0.26020557

00:57:20.910 --> 00:57:22.464 So we have to be somewhat selective.

NOTE Confidence: 0.26020557

00:57:22.470 --> 00:57:24.270 But at tumor board we'll look at a case,

NOTE Confidence: 0.26020557

00:57:24.270 --> 00:57:26.160 we'll say this patient looks like

NOTE Confidence: 0.26020557

00:57:26.160 --> 00:57:27.420 they're surgically resectable they

NOTE Confidence: 0.26020557

00:57:27.472 --> 00:57:29.440 they can take the three months to get

NOTE Confidence: 0.26020557

00:57:29.440 --> 00:57:31.054 the neoadjuvant therapy and and we're

NOTE Confidence: 0.26020557

00:57:31.054 --> 00:57:32.668 treating those patients in that way.

NOTE Confidence: 0.26020557

00:57:32.670 --> 00:57:35.562 Some of them might not be in that situation

NOTE Confidence: 0.26020557

00:57:35.562 --> 00:57:38.234 And and chemo radiation David you know is,

NOTE Confidence: 0.26020557

00:57:38.234 --> 00:57:39.574 is very is with immunotherapy

NOTE Confidence: 0.26020557

00:57:39.574 --> 00:57:41.030 is also very beneficial.

NOTE Confidence: 0.26020557

00:57:41.030 --> 00:57:43.310 So we have multiple options.

NOTE Confidence: 0.26020557

00:57:43.310 --> 00:57:44.906 I'll leave you with this word.

NOTE Confidence: 0.26020557

00:57:44.910 --> 00:57:46.046 Everyone should get immunotherapy

NOTE Confidence: 0.26020557

00:57:46.046 --> 00:57:47.750 in some way if they can.

NOTE Confidence: 0.26020557

00:57:47.750 --> 00:57:48.060 They,

NOTE Confidence: 0.26020557

00:57:48.060 --> 00:57:49.920 the patients that don't get immunotherapy

NOTE Confidence: 0.26020557

00:57:49.920 --> 00:57:52.187 would be ones who have autoimmunity or

NOTE Confidence: 0.26020557

00:57:52.187 --> 00:57:53.787 some reason that they're intolerant

NOTE Confidence: 0.26020557

00:57:53.787 --> 00:57:55.713 or certainly those with molecular

NOTE Confidence: 0.26020557

00:57:55.713 --> 00:57:57.540 drivers because in those cases we know

NOTE Confidence: 0.26020557

00:57:57.540 --> 00:57:59.059 immunotherapy doesn't seem to work as well.

NOTE Confidence: 0.26020557

00:57:59.060 --> 00:58:00.620 But I'd say if there's any

NOTE Confidence: 0.26020557

00:58:00.620 --> 00:58:01.660 hint of metastatic disease,

NOTE Confidence: 0.26020557

00:58:01.660 --> 00:58:03.716 I try to find ways that I can

NOTE Confidence: 0.26020557

00:58:03.716 --> 00:58:04.980 give immunotherapy to a patient.

NOTE Confidence: 0.26020557

00:58:04.980 --> 00:58:05.180 Yes,

NOTE Confidence: 0.26020557

00:58:05.180 --> 00:58:05.380 because

NOTE Confidence: 0.28358683

00:58:07.860 --> 00:58:07.940 you

NOTE Confidence: 0.28358683

00:58:10.220 --> 00:58:12.597 give her her expression so much more comment.

NOTE Confidence: 0.28358683

00:58:12.597 --> 00:58:16.770 Any thoughts on have we target that or why

NOTE Confidence: 0.28358683

00:58:16.770 --> 00:58:18.914 doesn't EGFR inhibition work for those?

NOTE Confidence: 0.28358683

00:58:18.914 --> 00:58:19.766 Yeah, we we've tried that.

NOTE Confidence: 0.28358683

00:58:19.766 --> 00:58:21.330 In fact that was the mark as we worked

NOTE Confidence: 0.28358683

00:58:21.330 --> 00:58:22.749 at an MD Anderson and actually we worked

NOTE Confidence: 0.28358683

00:58:22.749 --> 00:58:24.285 with Jose Bazaga on that many years ago.

NOTE Confidence: 0.28358683

00:58:24.290 --> 00:58:26.174 We thought it would be EGFR

NOTE Confidence: 0.28358683

00:58:26.174 --> 00:58:27.610 expression and and that is helpful.

NOTE Confidence: 0.28358683

00:58:27.610 --> 00:58:28.786 You know, if you're using an

NOTE Confidence: 0.28358683

00:58:28.786 --> 00:58:30.106 antibody that could be, you know,

NOTE Confidence: 0.28358683

00:58:30.106 --> 00:58:31.446 if you're using satuximab in,

NOTE Confidence: 0.28358683

00:58:31.450 --> 00:58:32.245 in certain tumors.

NOTE Confidence: 0.28358683

00:58:32.245 --> 00:58:34.311 But but it really isn't, it's it's not,

NOTE Confidence: 0.28358683

00:58:34.311 --> 00:58:35.546 it's not the absolute level

NOTE Confidence: 0.28358683

00:58:35.546 --> 00:58:37.128 of EGFR but it's the quality,

NOTE Confidence: 0.28358683

00:58:37.130 --> 00:58:38.918 it's it's whether it's being driven

NOTE Confidence: 0.28358683

00:58:38.918 --> 00:58:40.812 by those mutations and you know the

NOTE Confidence: 0.28358683

00:58:40.812 --> 00:58:42.934 TKI is you know where the you know if

NOTE Confidence: 0.28358683

00:58:42.934 --> 00:58:44.906 you've got that addicted tumor that then

NOTE Confidence: 0.28358683

00:58:44.906 --> 00:58:47.210 the TKI is will have that amazing effect.

NOTE Confidence: 0.28358683

00:58:47.210 --> 00:58:48.624 But you know the expression can be

NOTE Confidence: 0.28358683

00:58:48.624 --> 00:58:49.889 helpful maybe for AD CS right now,

NOTE Confidence: 0.28358683

00:58:49.890 --> 00:58:51.500 now now there's a whole new now

NOTE Confidence: 0.28358683

00:58:51.500 --> 00:58:53.623 that now that we're sort of at a

NOTE Confidence: 0.28358683

00:58:53.623 --> 00:58:55.003 standstill with a new immunotherapy

NOTE Confidence: 0.28358683

00:58:55.056 --> 00:58:56.691 resistant drugs and with new

NOTE Confidence: 0.28358683

00:58:56.691 --> 00:58:58.326 targeted drugs for EGFR resistance.

NOTE Confidence: 0.28358683

00:58:58.330 --> 00:59:00.164 We're using the address now with with,

NOTE Confidence: 0.28358683

00:59:00.170 --> 00:59:03.086 with with with with with payloads.

NOTE Confidence: 0.28358683

00:59:03.090 --> 00:59:04.650 So that might be an an area done since early

NOTE Confidence: 0.340776916666667

00:59:07.810 --> 00:59:10.082 detection, this subject key

NOTE Confidence: 0.340776916666667

00:59:10.082 --> 00:59:12.300 piece puzzle, what are your

NOTE Confidence: 0.340776916666667

00:59:12.300 --> 00:59:13.700 thoughts on possible innovation?

NOTE Confidence: 0.34262696

00:59:15.780 --> 00:59:18.223 Well certainly you know there's the the

NOTE Confidence: 0.34262696

00:59:18.223 --> 00:59:20.733 easy one which is screening which now

NOTE Confidence: 0.34262696

00:59:20.733 --> 00:59:22.597 with helical CTS and low dose CTS it

NOTE Confidence: 0.34262696

00:59:22.597 --> 00:59:24.468 does pick lung cancers up earlier and

NOTE Confidence: 0.34262696

00:59:24.468 --> 00:59:26.459 it's been shown to improve survival.

NOTE Confidence: 0.34262696

00:59:26.460 --> 00:59:29.140 You know in the US only about 7% of patients

NOTE Confidence: 0.34262696

00:59:29.140 --> 00:59:31.340 eligible for screening get screened.

NOTE Confidence: 0.34262696

00:59:31.340 --> 00:59:32.992 You know the criteria were a bit

NOTE Confidence: 0.34262696

00:59:32.992 --> 00:59:34.257 strict they've they've been reused a

NOTE Confidence: 0.34262696

00:59:34.257 --> 00:59:35.997 bit but you know it has to have been

NOTE Confidence: 0.34262696

00:59:35.997 --> 00:59:37.473 someone who's had a smoking history.

NOTE Confidence: 0.34262696

00:59:37.480 --> 00:59:38.356 So of course it it it,

NOTE Confidence: 0.34262696

00:59:38.360 --> 00:59:40.103 it doesn't take into account any of

NOTE Confidence: 0.34262696

00:59:40.103 --> 00:59:41.868 these patients who are the never smokers

NOTE Confidence: 0.34262696

00:59:41.868 --> 00:59:44.120 or the light smokers which are the ones

NOTE Confidence: 0.34262696

00:59:44.120 --> 00:59:45.720 that have these different mutations.

NOTE Confidence: 0.34262696

00:59:45.720 --> 00:59:48.060 Certainly you know looking in in

NOTE Confidence: 0.34262696

00:59:48.060 --> 00:59:50.696 the DNA and and and and CTDNAI think

NOTE Confidence: 0.34262696

00:59:50.696 --> 00:59:52.360 that's going to be the way to go.

NOTE Confidence: 0.34262696

00:59:52.360 --> 00:59:55.000 We're already using that for minimal

NOTE Confidence: 0.34262696

00:59:55.000 --> 00:59:57.080 residual disease both to determine

NOTE Confidence: 0.34262696

00:59:57.080 --> 00:59:59.250 whether or not patients need more therapy

NOTE Confidence: 0.34262696

00:59:59.250 --> 01:00:01.033 and and now of course we can look at

NOTE Confidence: 0.34262696

01:00:01.033 --> 01:00:02.475 the quality of of what we're finding,

NOTE Confidence: 0.34262696

01:00:02.480 --> 01:00:04.237 you know what are the new mutations,

NOTE Confidence: 0.34262696

01:00:04.240 --> 01:00:05.364 those techniques are getting

NOTE Confidence: 0.34262696

01:00:05.364 --> 01:00:06.488 more and more sensitive.

NOTE Confidence: 0.34262696

01:00:06.490 --> 01:00:08.205 I'll tell you in the enduro trial

NOTE Confidence: 0.34262696

01:00:08.210 --> 01:00:10.800 we only picked up you know post

NOTE Confidence: 0.34262696

01:00:10.800 --> 01:00:13.090 resection a sample 1020% of the time.

NOTE Confidence: 0.34262696

01:00:13.090 --> 01:00:15.526 So. So even though many of them,

NOTE Confidence: 0.34262696

01:00:15.530 --> 01:00:16.660 many more of them probably

NOTE Confidence: 0.34262696

01:00:16.660 --> 01:00:17.564 did have residual disease,

NOTE Confidence: 0.34262696

01:00:17.570 --> 01:00:19.285 but it's getting more and more sensitive.

NOTE Confidence: 0.34262696

01:00:19.290 --> 01:00:20.448 Now you asked about you know,

NOTE Confidence: 0.34262696

01:00:20.450 --> 01:00:22.250 screening someone with a history

NOTE Confidence: 0.34262696

01:00:22.250 --> 01:00:24.426 or family history or will we

NOTE Confidence: 0.34262696

01:00:24.426 --> 01:00:26.286 start looking for for tumor DNA,

NOTE Confidence: 0.34262696

01:00:26.290 --> 01:00:27.930 think we need a lot more work to do that.

NOTE Confidence: 0.34262696

01:00:27.930 --> 01:00:29.154 But you know the techniques are

NOTE Confidence: 0.34262696

01:00:29.154 --> 01:00:30.410 getting so much more sensitive.

NOTE Confidence: 0.34262696

01:00:30.410 --> 01:00:31.454 Certainly if you know that someone

NOTE Confidence: 0.34262696

01:00:31.454 --> 01:00:32.968 has a tumor or if they have Melanoma,

NOTE Confidence: 0.34262696

01:00:32.970 --> 01:00:34.050 you know what the antigens are.

NOTE Confidence: 0.34262696

01:00:34.050 --> 01:00:36.106 So you know what what panel to look

NOTE Confidence: 0.34262696

01:00:36.106 --> 01:00:38.140 for and lung cancer which has so

NOTE Confidence: 0.34262696

01:00:38.140 --> 01:00:40.068 many different you know types of

NOTE Confidence: 0.34262696

01:00:40.068 --> 01:00:41.126 mutations there is what Charlie

NOTE Confidence: 0.34262696

01:00:41.126 --> 01:00:42.598 Swanton is doing now and I would I

NOTE Confidence: 0.34262696

01:00:42.598 --> 01:00:43.844 would put my money on his approach.

NOTE Confidence: 0.34262696

01:00:43.850 --> 01:00:45.586 You know there would be spoke models

NOTE Confidence: 0.34262696

01:00:45.586 --> 01:00:47.260 where you actually can sequence a tumor

NOTE Confidence: 0.34262696

01:00:47.260 --> 01:00:48.908 get a panel of mutations and that

NOTE Confidence: 0.34262696

01:00:48.908 --> 01:00:50.570 makes your your sensitivity much more,

NOTE Confidence: 0.34262696

01:00:50.570 --> 01:00:51.130 much better

NOTE Confidence: 0.5640116

01:00:54.490 --> 01:00:56.074 absolutely. And you know that's something

NOTE Confidence: 0.5640116

01:00:56.074 --> 01:00:57.726 we've talked about and maybe I know

NOTE Confidence: 0.5640116

01:00:57.726 --> 01:00:59.271 David and I have talked about it in

NOTE Confidence: 0.5640116

01:00:59.271 --> 01:01:00.887 both David's you know we don't we don't

NOTE Confidence: 0.5640116

01:01:00.887 --> 01:01:02.490 really have a liquid approach here.

NOTE Confidence: 0.5640116

01:01:02.490 --> 01:01:04.370 So we need to think about how we're going to

NOTE Confidence: 0.5640116

01:01:04.422 --> 01:01:06.310 maybe that's the way to jump jump forward.

NOTE Confidence: 0.5640116

01:01:06.310 --> 01:01:08.050 You need AI, you need pre

NOTE Confidence: 0.5640116

01:01:08.050 --> 01:01:08.610 competitive collaboration,

NOTE Confidence: 0.5640116

01:01:08.610 --> 01:01:10.970 you need big data sets.

NOTE Confidence: 0.5640116

01:01:10.970 --> 01:01:12.783 There's a meeting in two weeks at

NOTE Confidence: 0.5640116

01:01:12.783 --> 01:01:14.190 the National Academy of Medicine

NOTE Confidence: 0.5640116

01:01:14.190 --> 01:01:15.342 on public private partnerships

NOTE Confidence: 0.5640116

01:01:15.342 --> 01:01:16.930 and you know data sharing.

NOTE Confidence: 0.5640116

01:01:16.930 --> 01:01:17.861 We're going to have the editors of

NOTE Confidence: 0.5640116

01:01:17.861 --> 01:01:18.849 some of the big journals there.

NOTE Confidence: 0.5640116

01:01:18.850 --> 01:01:20.560 We're going to have people from

NOTE Confidence: 0.5640116

01:01:20.560 --> 01:01:22.530 UK Welcome Trust from the NCI.

NOTE Confidence: 0.5640116

01:01:22.530 --> 01:01:23.950 That's, that's what we need

NOTE Confidence: 0.5640116

01:01:23.950 --> 01:01:25.370 to take these big approaches,

NOTE Confidence: 0.5640116

01:01:25.370 --> 01:01:27.540 large sample sets that's love to talk

NOTE Confidence: 0.5640116

01:01:27.540 --> 01:01:30.179 to you more about that get your ideas.

NOTE Confidence: 0.5640116

01:01:30.180 --> 01:01:31.740 I think we better stop because it's late.

NOTE Confidence: 0.5640116

01:01:31.740 --> 01:01:32.734 I'm starting to go a little over.

NOTE Confidence: 0.5640116

01:01:32.740 --> 01:01:33.496 But thank you all for coming.

NOTE Confidence: 0.5640116

01:01:33.500 --> 01:01:35.030 It's it's it's exhilarating to see

NOTE Confidence: 0.5640116

01:01:35.030 --> 01:01:37.020 people in the talk to a live audience.

NOTE Confidence: 0.5640116

01:01:37.020 --> 01:01:37.980 So. So thank you.