WEBVTT

NOTE duration:"00:55:43"

NOTE recognizability:0.829

NOTE language:en-us

NOTE Confidence: 0.744377118888889

00:00:00.000 --> 00:00:04.120 Is a special lecture in our Yale Cancer

NOTE Confidence: 0.744377118888889

00:00:04.120 --> 00:00:08.200 Center Grand Rounds series and it's

NOTE Confidence: 0.744377118888889

00:00:08.200 --> 00:00:10.675 the Blanche Tolman lecture series.

NOTE Confidence: 0.744377118888889

00:00:10.680 --> 00:00:12.674 So this lecture series was established

NOTE Confidence: 0.744377118888889

00:00:12.674 --> 00:00:15.236 in 2012 by Doctor Marvin Sears,

NOTE Confidence: 0.744377118888889

00:00:15.240 --> 00:00:16.350 who I believe will be

NOTE Confidence: 0.9242030325

00:00:16.360 --> 00:00:17.728 attending today as well.

NOTE Confidence: 0.797876849285714

00:00:18.440 --> 00:00:20.432 Dr. Sears was a long time chair and

NOTE Confidence: 0.797876849285714

00:00:20.432 --> 00:00:22.401 founder of of of Thermology and Visual

NOTE Confidence: 0.797876849285714

00:00:22.401 --> 00:00:24.505 Sciences at Yale and the lecture was

NOTE Confidence: 0.797876849285714

00:00:24.505 --> 00:00:26.413 established in honor of his mother,

NOTE Confidence: 0.797876849285714

00:00:26.420 --> 00:00:28.790 Blanche Tallman, who passed away

NOTE Confidence: 0.797876849285714

00:00:28.790 --> 00:00:30.686 from acute myeloid leukemia.

NOTE Confidence: 0.797876849285714

00:00:30.690 --> 00:00:31.634 So to our delight,

NOTE Confidence: 0.797876849285714

00:00:31.634 --> 00:00:33.376 this was the first lecture series at

NOTE Confidence: 0.797876849285714

00:00:33.376 --> 00:00:35.056 year dedicated solely to hematologic

NOTE Confidence: 0.797876849285714

00:00:35.056 --> 00:00:36.766 malignancies and it continues to

NOTE Confidence: 0.797876849285714

00:00:36.766 --> 00:00:38.902 bring to Yale pioneers that have

NOTE Confidence: 0.797876849285714

00:00:38.902 --> 00:00:40.940 made major contributions to our

NOTE Confidence: 0.797876849285714

00:00:40.940 --> 00:00:43.246 understanding of the current trends

NOTE Confidence: 0.797876849285714

00:00:43.246 --> 00:00:44.488 and hematologic malignancies.

NOTE Confidence: 0.797876849285714

00:00:44.490 --> 00:00:47.416 So it is an absolute pleasure to

NOTE Confidence: 0.797876849285714

00:00:47.416 --> 00:00:49.779 introduce the actor Irene Gabriel

NOTE Confidence: 0.797876849285714

00:00:49.779 --> 00:00:52.098 today as our special lecturer.

NOTE Confidence: 0.797876849285714

00:00:52.098 --> 00:00:54.402 So Doctor Gabriel is professor of

NOTE Confidence: 0.797876849285714

00:00:54.402 --> 00:00:56.640 medicine at Harvard Medical School.

NOTE Confidence: 0.797876849285714

00:00:56.640 --> 00:00:59.016 She received her MD from Cairo

NOTE Confidence: 0.797876849285714

00:00:59.016 --> 00:01:01.269 University School of Medicine in Egypt.

NOTE Confidence: 0.797876849285714

00:01:01.270 --> 00:01:02.847 And she then completed her internal

NOTE Confidence: 0.797876849285714

00:01:02.847 --> 00:01:04.832 medicine training at Wayne State

NOTE Confidence: 0.797876849285714

00:01:04.832 --> 00:01:06.420 University and her hematology

NOTE Confidence: 0.797876849285714

00:01:06.478 --> 00:01:08.118 oncology subspecialty training at

NOTE Confidence: 0.797876849285714

00:01:08.118 --> 00:01:10.168 Mayo Clinic College of Medicine.

NOTE Confidence: 0.797876849285714

00:01:10.170 --> 00:01:10.818 In 2005,

NOTE Confidence: 0.797876849285714

00:01:10.818 --> 00:01:12.762 she joined in a Farber Cancer

NOTE Confidence: 0.797876849285714

00:01:12.762 --> 00:01:14.725 Institute in the field of Waldenstrom's

NOTE Confidence: 0.797876849285714

00:01:14.725 --> 00:01:17.150 Macroglobulinemia and a multiple myeloma.

NOTE Confidence: 0.797876849285714

00:01:17.150 --> 00:01:18.086 So doctor Gabrielle,

NOTE Confidence: 0.797876849285714

00:01:18.086 --> 00:01:19.646 as you will all see,

NOTE Confidence: 0.797876849285714

00:01:19.650 --> 00:01:22.158 has risen to become one of the world's

NOTE Confidence: 0.797876849285714

00:01:22.158 --> 00:01:23.690 leaders in the democratic field.

NOTE Confidence: 0.797876849285714

00:01:23.690 --> 00:01:25.466 Not only has she advanced major

NOTE Confidence: 0.797876849285714

00:01:25.466 --> 00:01:27.090 novel treatments to the clinic,

NOTE Confidence: 0.797876849285714

00:01:27.090 --> 00:01:29.589 but she now also focuses on early

NOTE Confidence: 0.797876849285714

00:01:29.589 --> 00:01:31.379 detection and interception to prevent.

NOTE Confidence: 0.797876849285714

00:01:31.380 --> 00:01:34.578 Regression to full blown multiple myeloma.

NOTE Confidence: 0.797876849285714

00:01:34.580 --> 00:01:36.614 Doctor Gabriel has a broad background

NOTE Confidence: 0.797876849285714

00:01:36.614 --> 00:01:38.769 in the biology of multiple myeloma

NOTE Confidence: 0.797876849285714

00:01:38.769 --> 00:01:41.044 and in the bone Marinette so

NOTE Confidence: 0.797876849285714

00:01:41.044 --> 00:01:44.012 important in the focus on M gas

NOTE Confidence: 0.797876849285714

00:01:44.012 --> 00:01:46.590 and smoldering myeloma and again

NOTE Confidence: 0.797876849285714

00:01:46.590 --> 00:01:49.132 preventing disease and her her

NOTE Confidence: 0.797876849285714

00:01:49.132 --> 00:01:50.580 research knowledge expertise allow

NOTE Confidence: 0.797876849285714

00:01:50.580 --> 00:01:52.830 us to define both cell autonomous

NOTE Confidence: 0.797876849285714

00:01:52.830 --> 00:01:54.710 and bone marrow age dependent

NOTE Confidence: 0.797876849285714

00:01:54.710 --> 00:01:56.720 and also genetic and epigenetic

NOTE Confidence: 0.797876849285714

00:01:56.720 --> 00:01:58.180 mechanisms of disease progression.

NOTE Confidence: 0.797876849285714

00:01:58.180 --> 00:02:00.220 And we couldn't be more excited

NOTE Confidence: 0.797876849285714

00:02:00.220 --> 00:02:01.858 to hear your talk today.

NOTE Confidence: 0.797876849285714

00:02:01.860 --> 00:02:04.574 So welcome we wish we were in person but.

NOTE Confidence: 0.797876849285714

00:02:04.574 --> 00:02:05.590 This is still wonderful.

NOTE Confidence: 0.797876849285714

00:02:05.590 --> 00:02:07.094 And at least we didn't have to cancel.

NOTE Confidence: 0.788243106666667

00:02:07.610 --> 00:02:09.248 Yes. Well, thank you so much,

NOTE Confidence: 0.788243106666667

00:02:09.250 --> 00:02:11.070 Stephanie. And as you said,

NOTE Confidence: 0.788243106666667

00:02:11.070 --> 00:02:12.888 it's really a pleasure and honor to be here.

NOTE Confidence: 0.788243106666667

00:02:12.890 --> 00:02:14.570 And I'm sorry that it's not in person,

NOTE Confidence: 0.788243106666667

00:02:14.570 --> 00:02:16.047 but it's New England and we all

NOTE Confidence: 0.788243106666667

00:02:16.047 --> 00:02:17.966 know how to deal with that, I guess.

NOTE Confidence: 0.788243106666667

00:02:17.966 --> 00:02:19.950 So I'll take you through a little bit

NOTE Confidence: 0.788243106666667

00:02:20.011 --> 00:02:21.901 of what we do in the lab and how we

NOTE Confidence: 0.788243106666667

00:02:21.957 --> 00:02:24.970 translated it into the clinic on the

NOTE Confidence: 0.788243106666667

00:02:24.970 --> 00:02:27.370 promise of early detection and interception.

NOTE Confidence: 0.788243106666667

00:02:27.370 --> 00:02:30.250 These are these are my conflicts of interest.

NOTE Confidence: 0.890911035714286

00:02:33.390 --> 00:02:35.819 So I'll just start with a simple

NOTE Confidence: 0.890911035714286

00:02:35.819 --> 00:02:38.289 question that many of us ask ourselves.

NOTE Confidence: 0.890911035714286

00:02:38.290 --> 00:02:39.750 In general, in every Cancer

NOTE Confidence: 0.890911035714286

00:02:39.750 --> 00:02:41.210 Center when you see patients,

NOTE Confidence: 0.890911035714286

00:02:41.210 --> 00:02:42.535 it's because they either had

NOTE Confidence: 0.890911035714286

00:02:42.535 --> 00:02:44.463 symptoms and they want to see their

NOTE Confidence: 0.890911035714286

00:02:44.463 --> 00:02:46.119 primary care doctor or by accident,

NOTE Confidence: 0.890911035714286

00:02:46.120 --> 00:02:47.716 something happened in their blood works.

NOTE Confidence: 0.890911035714286

00:02:47.720 --> 00:02:49.106 They had a little bit of anemia,

NOTE Confidence: 0.890911035714286

00:02:49.110 --> 00:02:51.358 a little bit of a higher white count

NOTE Confidence: 0.890911035714286

00:02:51.358 --> 00:02:53.368 and that led to further workup,

NOTE Confidence: 0.890911035714286

00:02:53.370 --> 00:02:55.519 which led to the diagnosis of cancer

NOTE Confidence: 0.890911035714286

00:02:55.519 --> 00:02:57.730 and then they get referred to you.

NOTE Confidence: 0.890911035714286

00:02:57.730 --> 00:02:59.308 But if you think about it,

NOTE Confidence: 0.890911035714286

00:02:59.310 --> 00:03:00.894 this means that we are waiting

NOTE Confidence: 0.890911035714286

00:03:00.894 --> 00:03:02.470 for things to happen and then.

NOTE Confidence: 0.890911035714286

00:03:02.470 --> 00:03:04.521 We react to cancer and by chance

NOTE Confidence: 0.890911035714286

00:03:04.521 --> 00:03:06.617 some of those made by good luck

NOTE Confidence: 0.890911035714286

00:03:06.617 --> 00:03:08.694 have an early cancer and we can

NOTE Confidence: 0.890911035714286

00:03:08.694 --> 00:03:11.014 diagnose it early and we can cure it.

NOTE Confidence: 0.890911035714286

00:03:11.020 --> 00:03:13.436 But many of them actually have stage three,

NOTE Confidence: 0.890911035714286

00:03:13.440 --> 00:03:14.211 stage four cancer.

NOTE Confidence: 0.890911035714286

00:03:14.211 --> 00:03:16.332 And we do sit down with them and

NOTE Confidence: 0.890911035714286

00:03:16.332 --> 00:03:18.194 say we may give you some treatment,

NOTE Confidence: 0.890911035714286

00:03:18.200 --> 00:03:19.796 but we may not cure the disease.

NOTE Confidence: 0.890911035714286

00:03:19.800 --> 00:03:21.176 And in fact if you think about it,

NOTE Confidence: 0.890911035714286

00:03:21.180 --> 00:03:22.760 pharmaceutical companies as well

NOTE Confidence: 0.890911035714286

00:03:22.760 --> 00:03:25.130 as cancer centers put millions and

NOTE Confidence: 0.890911035714286

00:03:25.196 --> 00:03:27.081 billions of dollars into developing

NOTE Confidence: 0.890911035714286

00:03:27.081 --> 00:03:29.370 therapies that can change to survival

NOTE Confidence: 0.890911035714286

00:03:29.370 --> 00:03:31.722 of metastatic cancer by three or four

NOTE Confidence: 0.890911035714286

00:03:31.722 --> 00:03:33.608 months and we consider that. Success.

NOTE Confidence: 0.890911035714286

00:03:33.608 --> 00:03:36.260 So what can we do to change that?

NOTE Confidence: 0.890911035714286

00:03:36.260 --> 00:03:38.717 How can we become less reactive to

NOTE Confidence: 0.890911035714286

00:03:38.717 --> 00:03:41.677 cancer and be more proactive to cancer,

NOTE Confidence: 0.890911035714286

00:03:41.680 --> 00:03:43.690 trying to find it early before

NOTE Confidence: 0.890911035714286

00:03:43.690 --> 00:03:44.695 it becomes symptomatic,

NOTE Confidence: 0.890911035714286

00:03:44.700 --> 00:03:46.340 trying to define it early.

NOTE Confidence: 0.890911035714286

00:03:46.340 --> 00:03:48.230 And then by doing that you can

NOTE Confidence: 0.890911035714286

00:03:48.230 --> 00:03:50.042 intervene early and make a difference

NOTE Confidence: 0.890911035714286

00:03:50.042 --> 00:03:51.920 in the survival of those patients?

NOTE Confidence: 0.890911035714286

00:03:51.920 --> 00:03:53.810 Now I would probably say that

NOTE Confidence: 0.890911035714286

00:03:53.810 --> 00:03:56.183 myeloma is a great example of that

NOTE Confidence: 0.890911035714286

00:03:56.183 --> 00:03:58.271 as a potential model system for

NOTE Confidence: 0.890911035714286

00:03:58.271 --> 00:04:00.459 early detection and interception.

NOTE Confidence: 0.890911035714286

00:04:00.460 --> 00:04:03.276 We know that myeloma has a well known

NOTE Confidence: 0.890911035714286

00:04:03.276 --> 00:04:05.299 clinically defined precursor condition,

NOTE Confidence: 0.890911035714286

00:04:05.300 --> 00:04:07.136 monoclonal gammopathy of undetermined

NOTE Confidence: 0.890911035714286

00:04:07.136 --> 00:04:09.431 significance and then yet another

NOTE Confidence: 0.890911035714286

00:04:09.431 --> 00:04:11.778 stage of the disease that progresses

NOTE Confidence: 0.890911035714286

00:04:11.778 --> 00:04:13.598 just before the active cancer,

NOTE Confidence: 0.890911035714286

00:04:13.600 --> 00:04:14.740 sort of a stage one,

NOTE Confidence: 0.890911035714286

00:04:14.740 --> 00:04:16.504 stage two breast cancer if you

NOTE Confidence: 0.890911035714286

00:04:16.504 --> 00:04:18.935 want to call it and that's the

NOTE Confidence: 0.890911035714286

00:04:18.935 --> 00:04:20.123 asymptomatic smoldering myeloma

NOTE Confidence: 0.890911035714286

00:04:20.123 --> 00:04:22.609 Now I was lucky enough to be.

NOTE Confidence: 0.890911035714286

00:04:22.610 --> 00:04:24.658 Trained by Bob Kyle at Mayo Clinic who

NOTE Confidence: 0.890911035714286

00:04:24.658 --> 00:04:26.169 actually coined both of those terms,

NOTE Confidence: 0.890911035714286

00:04:26.170 --> 00:04:28.010 monoclonal gammopathy of undetermined

NOTE Confidence: 0.890911035714286

00:04:28.010 --> 00:04:29.850 significance and smoldering myeloma.

NOTE Confidence: 0.890911035714286

00:04:29.850 --> 00:04:31.894 And he had this amazing vision because

NOTE Confidence: 0.890911035714286

00:04:31.894 --> 00:04:33.897 he thought that when he described

NOTE Confidence: 0.890911035714286

00:04:33.897 --> 00:04:35.325 those asymptomatic patients who

NOTE Confidence: 0.890911035714286

00:04:35.325 --> 00:04:37.704 are just walking around with a very

NOTE Confidence: 0.890911035714286

00:04:37.704 --> 00:04:39.269 small tiny monoclonal protein that

NOTE Confidence: 0.890911035714286

00:04:39.269 --> 00:04:40.854 they should actually be watched

NOTE Confidence: 0.890911035714286

00:04:40.854 --> 00:04:42.750 carefully and we they may actually

NOTE Confidence: 0.890911035714286

00:04:42.809 --> 00:04:44.469 progress to develop the disease.

NOTE Confidence: 0.890911035714286

00:04:44.470 --> 00:04:45.289 And in fact,

NOTE Confidence: 0.890911035714286

00:04:45.289 --> 00:04:47.200 him and Jan Waldenstrom had a big

NOTE Confidence: 0.890911035714286

00:04:47.266 --> 00:04:48.882 discussion where Jan Waldenstrom

NOTE Confidence: 0.890911035714286

00:04:48.882 --> 00:04:51.306 wanted to call it benign gammopathy

NOTE Confidence: 0.890911035714286

00:04:51.372 --> 00:04:52.740 because those patients.

NOTE Confidence: 0.890911035714286

00:04:52.740 --> 00:04:54.575 Are completely benign and why

NOTE Confidence: 0.890911035714286

00:04:54.575 --> 00:04:56.043 would we worry them?

NOTE Confidence: 0.890911035714286

00:04:56.050 --> 00:04:58.322 Yet Bob Kyle was so good in thinking

NOTE Confidence: 0.890911035714286

00:04:58.322 --> 00:05:00.816 ahead and thinking that there is a

NOTE Confidence: 0.890911035714286

00:05:00.816 --> 00:05:02.671 potential of cancer development and

NOTE Confidence: 0.890911035714286

00:05:02.738 --> 00:05:04.892 he coined the name of undetermined

NOTE Confidence: 0.890911035714286

00:05:04.892 --> 00:05:06.667 significance to give it that

NOTE Confidence: 0.890911035714286

00:05:06.667 --> 00:05:07.678 sense of urgency,

NOTE Confidence: 0.890911035714286

00:05:07.678 --> 00:05:09.026 of understanding who would

NOTE Confidence: 0.890911035714286

00:05:09.026 --> 00:05:11.005 progress in their lifetime and

NOTE Confidence: 0.890911035714286

00:05:11.005 --> 00:05:12.250 potentially preventing it.

NOTE Confidence: 0.890911035714286

00:05:12.250 --> 00:05:12.926 And indeed,

NOTE Confidence: 0.890911035714286

00:05:12.926 --> 00:05:14.616 even the name smouldering myeloma

NOTE Confidence: 0.890911035714286

00:05:14.616 --> 00:05:16.496 gives you that urgency that it's

NOTE Confidence: 0.890911035714286

00:05:16.496 --> 00:05:18.386 going to be on fire very soon.

NOTE Confidence: 0.946298955

00:05:18.390 --> 00:05:20.226 So let's do something about it.

NOTE Confidence: 0.946298955

00:05:20.230 --> 00:05:22.810 So indeed he had that vision.

NOTE Confidence: 0.946298955

00:05:22.810 --> 00:05:25.148 As we should think of the mechanisms

NOTE Confidence: 0.946298955

00:05:25.148 --> 00:05:27.150 of disease progression in asymptomatic

NOTE Confidence: 0.946298955

00:05:27.150 --> 00:05:29.495 people and potentially intercepting early.

NOTE Confidence: 0.946298955

00:05:29.500 --> 00:05:31.194 Now in the older days we didn't

NOTE Confidence: 0.946298955

00:05:31.194 --> 00:05:33.270 have good drugs, we had melphalan,

NOTE Confidence: 0.946298955

00:05:33.270 --> 00:05:34.620 Prednisone, fat chemotherapy.

NOTE Confidence: 0.946298955

00:05:34.620 --> 00:05:35.715 So maybe intercepting

NOTE Confidence: 0.946298955

00:05:35.715 --> 00:05:37.540 early May not make sense.

NOTE Confidence: 0.946298955

00:05:37.540 --> 00:05:39.521 And indeed the trend or the standard

NOTE Confidence: 0.946298955

00:05:39.521 --> 00:05:41.737 of care was watch and wait until

NOTE Confidence: 0.946298955

00:05:41.737 --> 00:05:43.687 people have symptoms and end organ

NOTE Confidence: 0.946298955

00:05:43.749 --> 00:05:46.066 damage and then we treat them because

NOTE Confidence: 0.946298955

00:05:46.066 --> 00:05:48.104 we have palliative care and myeloma

NOTE Confidence: 0.946298955

00:05:48.104 --> 00:05:50.540 survival is only three to five years,

NOTE Confidence: 0.946298955

00:05:50.540 --> 00:05:52.940 but now we have 30 new drugs approved.

NOTE Confidence: 0.946298955

00:05:52.940 --> 00:05:53.800 For myeloma,

NOTE Confidence: 0.946298955

00:05:53.800 --> 00:05:56.380 we have amazing responses and the

NOTE Confidence: 0.946298955

00:05:56.380 --> 00:05:59.535 question is truly can we change that

NOTE Confidence: 0.946298955

00:05:59.535 --> 00:06:01.311 thinking of disease interception

NOTE Confidence: 0.946298955

00:06:01.311 --> 00:06:03.467 at an earlier time point?

NOTE Confidence: 0.946298955

00:06:03.470 --> 00:06:05.444 Now the other important piece to

NOTE Confidence: 0.946298955

00:06:05.444 --> 00:06:07.845 think about is myeloma is more common

NOTE Confidence: 0.946298955

00:06:07.845 --> 00:06:09.891 in African Americans and people of

NOTE Confidence: 0.946298955

00:06:09.891 --> 00:06:12.148 African descent 2 times or even higher,

NOTE Confidence: 0.946298955

00:06:12.150 --> 00:06:12.958 more common,

NOTE Confidence: 0.946298955

00:06:12.958 --> 00:06:15.382 more common to happen at an

NOTE Confidence: 0.946298955

00:06:15.382 --> 00:06:16.533 earlier younger age.

NOTE Confidence: 0.946298955

00:06:16.533 --> 00:06:17.219 In fact,

NOTE Confidence: 0.946298955

00:06:17.219 --> 00:06:20.128 we know that myeloma is more common because

NOTE Confidence: 0.946298955

00:06:20.128 --> 00:06:22.667 they haven't earlier stage of development,

NOTE Confidence: 0.946298955

00:06:22.667 --> 00:06:24.552 not because usually of an

NOTE Confidence: 0.946298955

00:06:24.552 --> 00:06:26.060 mgus transition to myeloma,

NOTE Confidence: 0.946298955

00:06:26.060 --> 00:06:26.970 not that we know of,

NOTE Confidence: 0.946298955

00:06:26.970 --> 00:06:29.106 but we don't think that there is a

NOTE Confidence: 0.946298955

00:06:29.106 --> 00:06:30.768 faster transition from mgus to myeloma.

NOTE Confidence: 0.946298955

00:06:30.770 --> 00:06:33.070 So really understanding what causes.

NOTE Confidence: 0.946298955

00:06:33.070 --> 00:06:36.101 Early development of MGUS in an African

NOTE Confidence: 0.946298955

00:06:36.101 --> 00:06:39.009 American population at the younger age could.

NOTE Confidence: 0.946298955

00:06:39.010 --> 00:06:40.822 That you help us understand why

NOTE Confidence: 0.946298955

00:06:40.822 --> 00:06:42.030 they've developed Milo memoir,

NOTE Confidence: 0.946298955

00:06:42.030 --> 00:06:43.760 but also intercepting it early

NOTE Confidence: 0.946298955

00:06:43.760 --> 00:06:45.490 because most of those patients,

NOTE Confidence: 0.946298955

00:06:45.490 --> 00:06:46.650 by the time they're diagnosed,

NOTE Confidence: 0.946298955

00:06:46.650 --> 00:06:48.002 they're either misdiagnosed because

NOTE Confidence: 0.946298955

00:06:48.002 --> 00:06:50.030 anemia is very common in African

NOTE Confidence: 0.946298955

00:06:50.081 --> 00:06:51.965 Americans or because of renal failure.

NOTE Confidence: 0.946298955

00:06:51.970 --> 00:06:52.506 And again,

NOTE Confidence: 0.946298955

00:06:52.506 --> 00:06:53.846 renal failure is more common.

NOTE Confidence: 0.946298955

00:06:53.850 --> 00:06:55.410 So they are getting misdiagnosed.

NOTE Confidence: 0.946298955

00:06:55.410 --> 00:06:56.790 They don't have the World Cup.

NOTE Confidence: 0.946298955

00:06:56.790 --> 00:06:58.393 And even when they have the World

NOTE Confidence: 0.946298955

00:06:58.393 --> 00:07:00.110 Cup and the disease assessment,

NOTE Confidence: 0.946298955

00:07:00.110 --> 00:07:02.238 they do not get the access to clinical

NOTE Confidence: 0.946298955

00:07:02.238 --> 00:07:04.159 trials and to car T and to transplant

NOTE Confidence: 0.946298955

00:07:04.159 --> 00:07:06.249 and all of the options that we have,

NOTE Confidence: 0.946298955

00:07:06.250 --> 00:07:08.065 so the survival of myeloma

NOTE Confidence: 0.946298955

00:07:08.065 --> 00:07:09.154 in African Americans.

NOTE Confidence: 0.946298955

00:07:09.160 --> 00:07:11.410 Unfortunately, it's still very poor.

NOTE Confidence: 0.946298955

00:07:11.410 --> 00:07:14.146 Despite all of the amazing advances we have,

NOTE Confidence: 0.946298955

00:07:14.150 --> 00:07:16.320 we still have a huge discrepancy there.

NOTE Confidence: 0.946298955

00:07:16.320 --> 00:07:18.750 So potentially closing that gap would

NOTE Confidence: 0.946298955

00:07:18.750 --> 00:07:21.232 be critical for us to understand

NOTE Confidence: 0.946298955

00:07:21.232 --> 00:07:23.990 how to change the survival of Milo.

NOTE Confidence: 0.946298955

00:07:23.990 --> 00:07:25.430 So with that in mind,

NOTE Confidence: 0.946298955

00:07:25.430 --> 00:07:27.326 our hypothesis really our model is

NOTE Confidence: 0.946298955

00:07:27.326 --> 00:07:29.772 why are we doing it any different

NOTE Confidence: 0.946298955

00:07:29.772 --> 00:07:30.888 than other cancers?

NOTE Confidence: 0.946298955

00:07:30.890 --> 00:07:33.106 If you think of breast cancer for example,

NOTE Confidence: 0.946298955

00:07:33.110 --> 00:07:34.970 you screen early because cancer

NOTE Confidence: 0.946298955

00:07:34.970 --> 00:07:36.086 screening saves lives.

NOTE Confidence: 0.946298955

00:07:36.090 --> 00:07:37.746 And I would tell you that the blood

NOTE Confidence: 0.946298955

00:07:37.746 --> 00:07:39.348 test for a serum protein Electro.

NOTE Confidence: 0.946298955

00:07:39.350 --> 00:07:41.975 Races and monoclonal protein is much easier,

NOTE Confidence: 0.946298955

00:07:41.980 --> 00:07:44.182 more sensitive and more specific and

NOTE Confidence: 0.946298955

00:07:44.182 --> 00:07:46.274 potentially much better for us because

NOTE Confidence: 0.946298955

00:07:46.274 --> 00:07:48.241 I would rather get a blood sample

NOTE Confidence: 0.946298955

00:07:48.241 --> 00:07:50.419 done than mammography or colonoscopy.

NOTE Confidence: 0.946298955

00:07:50.420 --> 00:07:51.880 It's much easier to do.

NOTE Confidence: 0.946298955

00:07:51.880 --> 00:07:53.938 But even though we with that,

NOTE Confidence: 0.946298955

00:07:53.940 --> 00:07:55.638 we don't screen for blood cancers.

NOTE Confidence: 0.946298955

00:07:55.640 --> 00:07:56.850 They're easy to screen but

NOTE Confidence: 0.946298955

00:07:56.850 --> 00:07:58.060 we don't screen for them.

NOTE Confidence: 0.946298955

00:07:58.060 --> 00:08:00.412 And even when we find the monoclonal

NOTE Confidence: 0.946298955

00:08:00.412 --> 00:08:02.218 gammopathy is when I find mgus,

NOTE Confidence: 0.946298955

00:08:02.220 --> 00:08:03.755 and it's very common in

NOTE Confidence: 0.946298955

00:08:03.755 --> 00:08:04.676 the general population,

NOTE Confidence: 0.946298955

00:08:04.680 --> 00:08:07.090 3 to 5% over the age of 50 or even

NOTE Confidence: 0.859871240666667

00:08:07.162 --> 00:08:09.357 when I find smoldering myeloma.

NOTE Confidence: 0.859871240666667

00:08:09.360 --> 00:08:12.177 The standard of care to date is still telling

NOTE Confidence: 0.859871240666667

00:08:12.177 --> 00:08:14.870 them watch and wait until you have anemia,

NOTE Confidence: 0.859871240666667

00:08:14.870 --> 00:08:17.222 renal failure, fractures in your bones or

NOTE Confidence: 0.859871240666667

00:08:17.222 --> 00:08:19.751 lesions in your bones, and high calcium,

NOTE Confidence: 0.859871240666667

00:08:19.751 --> 00:08:21.953 what we call the crab criteria.

NOTE Confidence: 0.859871240666667

00:08:21.960 --> 00:08:24.053 That would be just like telling a

NOTE Confidence: 0.859871240666667

00:08:24.053 --> 00:08:25.785 woman with breast cancer, DCIS,

NOTE Confidence: 0.859871240666667

00:08:25.785 --> 00:08:28.270 or stage one, stage two breast cancer.

NOTE Confidence: 0.859871240666667

00:08:28.270 --> 00:08:30.110 You know what, you're asymptomatic.

NOTE Confidence: 0.859871240666667

00:08:30.110 --> 00:08:32.078 Go watch and wait until you

NOTE Confidence: 0.859871240666667

00:08:32.078 --> 00:08:33.062 have metastases everywhere,

NOTE Confidence: 0.859871240666667

00:08:33.070 --> 00:08:34.250 fractures in your bones,

NOTE Confidence: 0.859871240666667

00:08:34.250 --> 00:08:35.725 and then I'll treat you.

NOTE Confidence: 0.859871240666667

00:08:35.730 --> 00:08:37.786 Now you'll have a lawsuit when that case.

NOTE Confidence: 0.859871240666667

00:08:37.790 --> 00:08:39.477 So why are we not getting lawsuits?

NOTE Confidence: 0.859871240666667

00:08:39.480 --> 00:08:42.680 Myeloma, when we do that exact same idea.

NOTE Confidence: 0.859871240666667

00:08:42.680 --> 00:08:44.848 So really we need to rethink the way

NOTE Confidence: 0.859871240666667

00:08:44.848 --> 00:08:47.288 we think of treatment of myeloma and

NOTE Confidence: 0.859871240666667

00:08:47.288 --> 00:08:49.524 retrain ourselves to think that's not

NOTE Confidence: 0.859871240666667

00:08:49.524 --> 00:08:51.534 actually the right way of thinking.

NOTE Confidence: 0.859871240666667

00:08:51.540 --> 00:08:52.214 Maybe again,

NOTE Confidence: 0.859871240666667

00:08:52.214 --> 00:08:54.236 30-40 years ago when we only

NOTE Confidence: 0.859871240666667

00:08:54.236 --> 00:08:55.840 had melphalan at Prednisone,

NOTE Confidence: 0.859871240666667

00:08:55.840 --> 00:08:57.420 it was a good idea.

NOTE Confidence: 0.859871240666667

00:08:57.420 --> 00:08:59.300 Right now it may not be a good idea to

NOTE Confidence: 0.859871240666667

00:08:59.350 --> 00:09:01.366 watch and wait for those patients or as

NOTE Confidence: 0.859871240666667

00:09:01.366 --> 00:09:03.292 my patients call it, watch and worry.

NOTE Confidence: 0.859871240666667

00:09:03.292 --> 00:09:05.236 So how do we change that?

NOTE Confidence: 0.859871240666667

00:09:05.240 --> 00:09:07.700 We have three different areas or

NOTE Confidence: 0.859871240666667

00:09:07.700 --> 00:09:10.349 pillars of work that we're doing.

NOTE Confidence: 0.859871240666667

00:09:10.350 --> 00:09:12.470 Both in the lab and in the clinic we said,

NOTE Confidence: 0.859871240666667

00:09:12.470 --> 00:09:13.966 well, let's detect early,

NOTE Confidence: 0.859871240666667

00:09:13.966 --> 00:09:15.836 let's screen early because currently

NOTE Confidence: 0.859871240666667

00:09:15.836 --> 00:09:18.278 most patients with mgus and smoldering

NOTE Confidence: 0.859871240666667

00:09:18.278 --> 00:09:20.288 myeloma are found purely incidentally.

NOTE Confidence: 0.859871240666667

00:09:20.290 --> 00:09:22.075 So let's really understand better

NOTE Confidence: 0.859871240666667

00:09:22.075 --> 00:09:23.860 when you screen those patients,

NOTE Confidence: 0.859871240666667

00:09:23.860 --> 00:09:25.724 what is the prevalence but also who will

NOTE Confidence: 0.859871240666667

00:09:25.724 --> 00:09:27.598 progress and who will not in their lifetime.

NOTE Confidence: 0.859871240666667

00:09:27.600 --> 00:09:29.225 The next question is let's

NOTE Confidence: 0.859871240666667

00:09:29.225 --> 00:09:30.525 risk stratify those patients.

NOTE Confidence: 0.859871240666667

00:09:30.530 --> 00:09:32.492 Not every mgus we diagnose will

NOTE Confidence: 0.859871240666667

00:09:32.492 --> 00:09:34.610 go on to progress to myeloma.

NOTE Confidence: 0.859871240666667

00:09:34.610 --> 00:09:36.810 So the question is who in their lifetime

NOTE Confidence: 0.859871240666667

00:09:36.810 --> 00:09:38.169 will progress to myeloma because

NOTE Confidence: 0.859871240666667

00:09:38.169 --> 00:09:40.280 these are the ones you want to treat.

NOTE Confidence: 0.859871240666667

00:09:40.280 --> 00:09:40.838 And the others,

NOTE Confidence: 0.859871240666667

00:09:40.838 --> 00:09:42.140 you want to tell them you're OK,

NOTE Confidence: 0.859871240666667

00:09:42.140 --> 00:09:44.310 you're going to live a normal life

NOTE Confidence: 0.859871240666667

00:09:44.310 --> 00:09:46.028 without having to develop myeloma

NOTE Confidence: 0.859871240666667

00:09:46.028 --> 00:09:48.206 and that differential is critical so

NOTE Confidence: 0.859871240666667

00:09:48.206 --> 00:09:50.789 that you can truly personalize that

NOTE Confidence: 0.859871240666667

00:09:50.789 --> 00:09:52.577 risk stratification for patients.

NOTE Confidence: 0.859871240666667

00:09:52.580 --> 00:09:53.960 And then the third one is,

NOTE Confidence: 0.859871240666667

00:09:53.960 --> 00:09:55.780 unless you know that you can change

NOTE Confidence: 0.859871240666667

00:09:55.780 --> 00:09:57.380 the survival of those patients,

NOTE Confidence: 0.859871240666667

00:09:57.380 --> 00:09:58.920 unless you can really intercept

NOTE Confidence: 0.859871240666667

00:09:58.920 --> 00:10:00.152 and change their survival,

NOTE Confidence: 0.859871240666667

00:10:00.160 --> 00:10:01.516 why are you screening for it?

NOTE Confidence: 0.859871240666667

00:10:01.520 --> 00:10:02.615 Because otherwise you're

NOTE Confidence: 0.859871240666667

00:10:02.615 --> 00:10:04.440 causing anxiety and no change.

NOTE Confidence: 0.859871240666667

00:10:04.440 --> 00:10:06.680 So truly I reverse it usually and say

NOTE Confidence: 0.859871240666667

00:10:06.680 --> 00:10:08.369 interception is more important because

NOTE Confidence: 0.859871240666667

00:10:08.369 --> 00:10:10.517 without interception we should not be.

NOTE Confidence: 0.859871240666667

00:10:10.520 --> 00:10:12.722 Training and we should not be

NOTE Confidence: 0.859871240666667

00:10:12.722 --> 00:10:13.823 stratifying those patients.

NOTE Confidence: 0.859871240666667

00:10:13.830 --> 00:10:15.930 So let's start with early

NOTE Confidence: 0.859871240666667

00:10:15.930 --> 00:10:18.030 detection and why it matters.

NOTE Confidence: 0.859871240666667

00:10:18.030 --> 00:10:20.928 We have seen lots of nationwide studies,

NOTE Confidence: 0.859871240666667

00:10:20.930 --> 00:10:23.108 the first one in Olmsted County

NOTE Confidence: 0.859871240666667

00:10:23.108 --> 00:10:24.896 where we indeed know the prevalence

NOTE Confidence: 0.859871240666667

00:10:24.896 --> 00:10:26.679 of emcas in the general population

NOTE Confidence: 0.859871240666667

00:10:26.679 --> 00:10:28.770 3 to 5% over the age of 50.

NOTE Confidence: 0.859871240666667

00:10:28.770 --> 00:10:30.768 But that was found in mostly

NOTE Confidence: 0.859871240666667

00:10:30.768 --> 00:10:32.522 Caucasian population in the area

NOTE Confidence: 0.859871240666667

00:10:32.522 --> 00:10:34.307 of Olmsted County in Minnesota.

NOTE Confidence: 0.859871240666667

00:10:34.310 --> 00:10:35.426 So the question was,

NOTE Confidence: 0.859871240666667

00:10:35.426 --> 00:10:37.613 can we really detect in a much

NOTE Confidence: 0.859871240666667

00:10:37.613 --> 00:10:39.853 more sensitive way than serum

NOTE Confidence: 0.859871240666667

00:10:39.853 --> 00:10:40.749 protein electrophoresis?

NOTE Confidence: 0.859871240666667

00:10:40.750 --> 00:10:42.244 And in the high risk population

NOTE Confidence: 0.859871240666667

00:10:42.244 --> 00:10:43.840 not in the general population,

NOTE Confidence: 0.859871240666667

00:10:43.840 --> 00:10:45.820 what is the prevalence of monoclonal

NOTE Confidence: 0.859871240666667

00:10:45.820 --> 00:10:48.164 hemoptysis and does a treaty occur in

NOTE Confidence: 0.859871240666667

00:10:48.164 --> 00:10:50.096 a younger age in African Americans?

NOTE Confidence: 0.896335315517241

00:10:50.100 --> 00:10:52.557 So there has been some studies indicating

NOTE Confidence: 0.896335315517241

00:10:52.557 --> 00:10:55.347 that people of African descent as well as

NOTE Confidence: 0.896335315517241

00:10:55.347 --> 00:10:57.787 people with a first degree family member

NOTE Confidence: 0.896335315517241

00:10:57.787 --> 00:11:00.279 are likely two to three times higher,

NOTE Confidence: 0.896335315517241

00:11:00.280 --> 00:11:02.674 have a higher chance of developing myeloma.

NOTE Confidence: 0.896335315517241

00:11:02.680 --> 00:11:04.680 So we wanted to ask why in high

NOTE Confidence: 0.896335315517241

00:11:04.680 --> 00:11:06.521 risk screen population and this was

NOTE Confidence: 0.896335315517241

00:11:06.521 --> 00:11:08.759 started four years ago with the help

NOTE Confidence: 0.896335315517241

00:11:08.759 --> 00:11:10.823 of a stand up to cancer Dream Team.

NOTE Confidence: 0.896335315517241

00:11:10.830 --> 00:11:13.458 Application where we started to say

NOTE Confidence: 0.896335315517241

00:11:13.458 --> 00:11:16.410 let's screen in the US for myeloma

NOTE Confidence: 0.896335315517241

00:11:16.410 --> 00:11:18.418 and we said we will do it nationwide.

NOTE Confidence: 0.896335315517241

00:11:18.420 --> 00:11:19.191 So it's online.

NOTE Confidence: 0.896335315517241

00:11:19.191 --> 00:11:20.476 As you can see here,

NOTE Confidence: 0.896335315517241

00:11:20.480 --> 00:11:22.451 you get a QR code and if you meet

NOTE Confidence: 0.896335315517241

00:11:22.451 --> 00:11:23.980 the eligibility criteria,

NOTE Confidence: 0.896335315517241

00:11:23.980 --> 00:11:25.359 you can sign up wherever you are

NOTE Confidence: 0.896335315517241

00:11:25.359 --> 00:11:26.799 and we send you a kit at home.

NOTE Confidence: 0.896335315517241

00:11:26.800 --> 00:11:28.347 You go to a quest diagnostic and

NOTE Confidence: 0.896335315517241

00:11:28.347 --> 00:11:29.920 you send us the blood sample.

NOTE Confidence: 0.896335315517241

00:11:29.920 --> 00:11:31.320 And the second thing we did is

NOTE Confidence: 0.896335315517241

00:11:31.320 --> 00:11:33.020 we did it by mass spectrometry,

NOTE Confidence: 0.896335315517241

00:11:33.020 --> 00:11:36.098 which is much more sensitive than

NOTE Confidence: 0.896335315517241

00:11:36.098 --> 00:11:37.637 serum protein electrophoresis.

NOTE Confidence: 0.896335315517241

00:11:37.640 --> 00:11:38.980 Now to do that effort,

NOTE Confidence: 0.896335315517241

00:11:38.980 --> 00:11:41.526 we said that we want to screen 30,000

NOTE Confidence: 0.896335315517241

00:11:41.526 --> 00:11:44.256 individuals to potentially get 10%

NOTE Confidence: 0.896335315517241

00:11:44.260 --> 00:11:46.280 screen positive because that's the

NOTE Confidence: 0.896335315517241

00:11:46.280 --> 00:11:48.711 number that from our preliminary data

NOTE Confidence: 0.896335315517241

00:11:48.711 --> 00:11:51.140 indicated we will have a positive number.

NOTE Confidence: 0.896335315517241

00:11:51.140 --> 00:11:53.555 And then we will follow those 3000

NOTE Confidence: 0.896335315517241

00:11:53.555 --> 00:11:55.220 people to understand genomics,

NOTE Confidence: 0.896335315517241

00:11:55.220 --> 00:11:57.900 genetics mechanisms of disease progression,

NOTE Confidence: 0.896335315517241

00:11:57.900 --> 00:12:00.400 immune microenvironment or non immune

NOTE Confidence: 0.896335315517241

00:12:00.400 --> 00:12:02.400 epidemiological causes like obesity,

NOTE Confidence: 0.896335315517241

00:12:02.400 --> 00:12:02.811 inflammation,

NOTE Confidence: 0.896335315517241

00:12:02.811 --> 00:12:04.455 autoimmune diseases and of

NOTE Confidence: 0.896335315517241

00:12:04.455 --> 00:12:06.099 course develop therapeutics and

NOTE Confidence: 0.896335315517241

00:12:06.099 --> 00:12:07.638 imaging modalities for those.

NOTE Confidence: 0.896335315517241

00:12:07.640 --> 00:12:10.330 People now as we started,

NOTE Confidence: 0.896335315517241

00:12:10.330 --> 00:12:12.138 we really had to learn to have boots

NOTE Confidence: 0.896335315517241

00:12:12.138 --> 00:12:14.230 on the ground to really do the effort

NOTE Confidence: 0.896335315517241

00:12:14.230 --> 00:12:16.607 because if you talk to anyone about myeloma,

NOTE Confidence: 0.896335315517241

00:12:16.610 --> 00:12:17.638 even the African American

NOTE Confidence: 0.896335315517241

00:12:17.638 --> 00:12:18.666 population would tell you,

NOTE Confidence: 0.896335315517241

00:12:18.670 --> 00:12:19.822 I didn't even know.

NOTE Confidence: 0.896335315517241

00:12:19.822 --> 00:12:22.070 There is more common in the black

NOTE Confidence: 0.896335315517241

00:12:22.070 --> 00:12:24.020 community than in the white population.

NOTE Confidence: 0.896335315517241

00:12:24.020 --> 00:12:26.378 So we have to do effort to even educate

NOTE Confidence: 0.896335315517241

00:12:26.378 --> 00:12:28.564 what is myeloma to gain the trust

NOTE Confidence: 0.896335315517241

00:12:28.564 --> 00:12:30.272 of the African American population

NOTE Confidence: 0.896335315517241

00:12:30.272 --> 00:12:32.307 and then start screening them.

NOTE Confidence: 0.896335315517241

00:12:32.310 --> 00:12:33.927 And that was a lot of effort

NOTE Confidence: 0.896335315517241

00:12:33.927 --> 00:12:35.488 from a team that we hired,

NOTE Confidence: 0.896335315517241

00:12:35.490 --> 00:12:37.370 just going to church events,

NOTE Confidence: 0.896335315517241

00:12:37.370 --> 00:12:38.441 going to healthcare.

NOTE Confidence: 0.896335315517241

00:12:38.441 --> 00:12:38.798 Events,

NOTE Confidence: 0.896335315517241

00:12:38.798 --> 00:12:40.583 understanding how to work with

NOTE Confidence: 0.896335315517241

00:12:40.583 --> 00:12:42.363 our Congress people like Ayanna

NOTE Confidence: 0.896335315517241

00:12:42.363 --> 00:12:44.403 Presley here and of course COVID

NOTE Confidence: 0.896335315517241

00:12:44.465 --> 00:12:46.641 hit and all our effort got shot down

NOTE Confidence: 0.896335315517241

00:12:46.641 --> 00:12:48.530 because you cannot do that on zoom.

NOTE Confidence: 0.896335315517241

00:12:48.530 --> 00:12:50.321 So it really took us a lot of effort

NOTE Confidence: 0.896335315517241

00:12:50.321 --> 00:12:52.005 to try and restart all of this.

NOTE Confidence: 0.896335315517241

00:12:52.010 --> 00:12:54.082 And indeed we just started to go back

NOTE Confidence: 0.896335315517241

00:12:54.082 --> 00:12:56.100 to health fair events and restarting it

NOTE Confidence: 0.896335315517241

00:12:56.100 --> 00:12:58.370 while while we were in COVID we said,

NOTE Confidence: 0.896335315517241

00:12:58.370 --> 00:13:01.170 well let's look at datasets and samples

NOTE Confidence: 0.896335315517241

00:13:01.170 --> 00:13:04.369 that are already collected in other cohorts.

NOTE Confidence: 0.896335315517241

00:13:04.370 --> 00:13:06.349 And this is when we turned to

NOTE Confidence: 0.896335315517241

00:13:06.350 --> 00:13:07.590 the mass general, Brigham,

NOTE Confidence: 0.896335315517241

00:13:07.590 --> 00:13:08.520 so mass general.

NOTE Confidence: 0.896335315517241

00:13:08.520 --> 00:13:10.722 Brigham is a huge sample collection

NOTE Confidence: 0.896335315517241

00:13:10.722 --> 00:13:13.252 study that's been going on now for the

NOTE Confidence: 0.896335315517241

00:13:13.252 --> 00:13:15.568 last 10 years with samples as well

NOTE Confidence: 0.896335315517241

00:13:15.568 --> 00:13:17.920 as of course clinical data annotation

NOTE Confidence: 0.896335315517241

00:13:17.991 --> 00:13:20.097 from all of the partners healthcare

NOTE Confidence: 0.896335315517241

00:13:20.097 --> 00:13:22.587 system or MGB as we call it now.

NOTE Confidence: 0.896335315517241

00:13:22.590 --> 00:13:25.146 So we collected the same criteria,

NOTE Confidence: 0.896335315517241

00:13:25.150 --> 00:13:27.665 African-American or people of first

NOTE Confidence: 0.896335315517241

00:13:27.665 --> 00:13:30.180 degree family members from 80,000

NOTE Confidence: 0.896335315517241

00:13:30.261 --> 00:13:32.760 samples that we have in MGB and

NOTE Confidence: 0.896335315517241

00:13:32.760 --> 00:13:34.892 total enrolled so far is 12,592

NOTE Confidence: 0.896335315517241

00:13:34.892 --> 00:13:38.144 of those from the US is

NOTE Confidence: 0.85803577875

00:13:38.150 --> 00:13:42.210 6485. We also opened a promised South

NOTE Confidence: 0.85803577875

00:13:42.210 --> 00:13:44.498 Africa one where actually they're

NOTE Confidence: 0.85803577875

00:13:44.498 --> 00:13:47.124 getting almost to 2000 samples now

NOTE Confidence: 0.85803577875

00:13:47.124 --> 00:13:49.060 that they've recruited prospectively.

NOTE Confidence: 0.85803577875

00:13:49.060 --> 00:13:50.880 And we're also going on into opening

NOTE Confidence: 0.85803577875

00:13:50.880 --> 00:13:52.949 it now in Israel because of the

NOTE Confidence: 0.85803577875

00:13:52.949 --> 00:13:54.785 family histories as well as many

NOTE Confidence: 0.85803577875

00:13:54.843 --> 00:13:56.595 other countries that we can do.

NOTE Confidence: 0.85803577875

00:13:56.600 --> 00:13:58.856 And we were screening in my lab almost

NOTE Confidence: 0.85803577875

00:13:58.856 --> 00:14:00.897 1000 samples a week and we can do

NOTE Confidence: 0.85803577875

00:14:00.897 --> 00:14:02.223 even more because mass spectrometry

NOTE Confidence: 0.85803577875

00:14:02.223 --> 00:14:04.428 can get to a higher throughput level

NOTE Confidence: 0.85803577875

00:14:04.428 --> 00:14:06.820 and you can then get detection of

NOTE Confidence: 0.85803577875

00:14:06.820 --> 00:14:09.020 monoclonal proteins as well as light.

NOTE Confidence: 0.85803577875

00:14:09.020 --> 00:14:11.330 Machines in a very quantitative way

NOTE Confidence: 0.85803577875

00:14:11.330 --> 00:14:13.950 compared to serum protein electrophoresis.

NOTE Confidence: 0.85803577875

00:14:13.950 --> 00:14:17.253 In fact, we set up the normals for binding

NOTE Confidence: 0.85803577875

00:14:17.253 --> 00:14:20.887 site and now we are part of their FDA

NOTE Confidence: 0.85803577875

00:14:20.887 --> 00:14:23.490 approval hopefully soon for binding site.

NOTE Confidence: 0.85803577875

00:14:23.490 --> 00:14:25.594 So these are just some of the numbers

NOTE Confidence: 0.85803577875

00:14:25.594 --> 00:14:27.416 showing you from MGB from promised

NOTE Confidence: 0.85803577875

00:14:27.416 --> 00:14:28.966 South Africa and promised us.

NOTE Confidence: 0.85803577875

00:14:28.970 --> 00:14:30.818 But this is the largest number of

NOTE Confidence: 0.85803577875

00:14:30.818 --> 00:14:32.376 African Americans who have been screened

NOTE Confidence: 0.85803577875

00:14:32.376 --> 00:14:34.355 to date as well as people with family

NOTE Confidence: 0.85803577875

00:14:34.355 --> 00:14:36.029 history and it was interesting when

NOTE Confidence: 0.85803577875

00:14:36.029 --> 00:14:38.187 we saw families with 567 members.

NOTE Confidence: 0.85803577875

00:14:38.187 --> 00:14:41.260 We have mgus and myeloma and lymphoma.

NOTE Confidence: 0.85803577875

00:14:41.260 --> 00:14:43.594 Now you start asking questions of

NOTE Confidence: 0.85803577875

00:14:43.594 --> 00:14:45.566 germline events of events that

NOTE Confidence: 0.85803577875

00:14:45.566 --> 00:14:47.624 really can lead to that development

NOTE Confidence: 0.85803577875

00:14:47.624 --> 00:14:49.779 in an early risk population.

NOTE Confidence: 0.85803577875

00:14:49.780 --> 00:14:51.663 So this is the paper that we

NOTE Confidence: 0.85803577875

00:14:51.663 --> 00:14:53.678 published last year just for the 1st

NOTE Confidence: 0.85803577875

00:14:53.678 --> 00:14:55.394 7000 people and now we're actually

NOTE Confidence: 0.85803577875

00:14:55.457 --> 00:14:57.197 going on for the larger cohort.

NOTE Confidence: 0.85803577875

00:14:57.200 --> 00:14:59.066 And as you can see here,

NOTE Confidence: 0.85803577875

00:14:59.070 --> 00:15:01.622 the people with a family history of a

NOTE Confidence: 0.85803577875

00:15:01.622 --> 00:15:05.708 blood cancer were 3866 and people of

NOTE Confidence: 0.85803577875

00:15:05.708 --> 00:15:08.660 African descent or blacks were 2439.

NOTE Confidence: 0.85803577875

00:15:08.660 --> 00:15:10.340 And this is the mass spectrometry

NOTE Confidence: 0.85803577875

00:15:10.340 --> 00:15:12.580 and I call this the Christmas tree.

NOTE Confidence: 0.85803577875

00:15:12.580 --> 00:15:14.700 So mass spectrometry is quantifiable

NOTE Confidence: 0.85803577875

00:15:14.700 --> 00:15:17.511 and you can also reflects it to

NOTE Confidence: 0.85803577875

00:15:17.511 --> 00:15:19.667 LCMS to give you a further detection

NOTE Confidence: 0.85803577875

00:15:19.667 --> 00:15:21.620 of the monoclonal protein.

NOTE Confidence: 0.85803577875

00:15:21.620 --> 00:15:24.308 So all of these were truly monoclonal

NOTE Confidence: 0.85803577875

00:15:24.308 --> 00:15:27.180 proteins that were quantified and verified.

NOTE Confidence: 0.85803577875

00:15:27.180 --> 00:15:29.168 What we found is anything above 1

NOTE Confidence: 0.85803577875

00:15:29.168 --> 00:15:31.045 gram per liter is something that

NOTE Confidence: 0.85803577875

00:15:31.045 --> 00:15:33.285 you can also detect by serum protein

NOTE Confidence: 0.85803577875

00:15:33.346 --> 00:15:35.271 electrophoresis because we did spap

NOTE Confidence: 0.85803577875

00:15:35.271 --> 00:15:37.554 the traditional method in the sum of

NOTE Confidence: 0.85803577875

00:15:37.554 --> 00:15:39.350 the samples or in almost all of the samples.

NOTE Confidence: 0.85803577875

00:15:39.350 --> 00:15:41.961 If we did anything below that at

NOTE Confidence: 0.85803577875

00:15:41.961 --> 00:15:43.670 .2 grams per liter,

NOTE Confidence: 0.85803577875

00:15:43.670 --> 00:15:45.394 you could potentially also

NOTE Confidence: 0.85803577875

00:15:45.394 --> 00:15:46.687 detected by immunofixation,

NOTE Confidence: 0.85803577875

00:15:46.690 --> 00:15:48.862 but of course you have quantification

NOTE Confidence: 0.85803577875

00:15:48.862 --> 00:15:50.310 and much more sensitivity

NOTE Confidence: 0.85803577875

00:15:50.372 --> 00:15:51.808 by the mass spectrometry.

NOTE Confidence: 0.85803577875

00:15:51.810 --> 00:15:54.290 So we kept those terms as they are.

NOTE Confidence: 0.85803577875

00:15:54.290 --> 00:15:55.650 But interestingly and I still

NOTE Confidence: 0.85803577875

00:15:55.650 --> 00:15:57.656 remember it when we got the first

NOTE Confidence: 0.85803577875

00:15:57.656 --> 00:15:59.426 data because we couldn't believe it,

NOTE Confidence: 0.85803577875

00:15:59.430 --> 00:16:01.936 we found another 20% of people with

NOTE Confidence: 0.85803577875

00:16:01.936 --> 00:16:03.421 very small monoclonal gammopathy

NOTE Confidence: 0.85803577875

00:16:03.421 --> 00:16:05.794 that were much lower than the level

NOTE Confidence: 0.85803577875

00:16:05.794 --> 00:16:08.368 that we can detect by immunofixation.

NOTE Confidence: 0.85803577875

00:16:08.370 --> 00:16:09.250 And at first we said,

NOTE Confidence: 0.85803577875

00:16:09.250 --> 00:16:10.820 well these are probably errors,

NOTE Confidence: 0.85803577875

00:16:10.820 --> 00:16:12.264 so we reconfirmed them.

NOTE Confidence: 0.85803577875

00:16:12.264 --> 00:16:15.158 Maybe these are people who have infections,

NOTE Confidence: 0.85803577875

00:16:15.158 --> 00:16:16.966 so we rescreen them.

NOTE Confidence: 0.85803577875

00:16:16.970 --> 00:16:18.858 We kept going on to try and understand

NOTE Confidence: 0.85803577875

00:16:18.858 --> 00:16:20.509 what this is and we finally said,

NOTE Confidence: 0.85803577875

00:16:20.510 --> 00:16:23.114 well no one has they've ever discovered

NOTE Confidence: 0.85803577875

00:16:23.114 --> 00:16:24.840 very small monoclonal proteins.

NOTE Confidence: 0.85803577875

00:16:24.840 --> 00:16:27.225 Let's let the research tell us what it is.

NOTE Confidence: 0.85803577875

00:16:27.230 --> 00:16:28.760 Now we wanted to term this

NOTE Confidence: 0.85803577875

00:16:28.760 --> 00:16:29.780 something separate that mgus

NOTE Confidence: 0.77078895047619

00:16:29.830 --> 00:16:30.718 because we really didn't

NOTE Confidence: 0.77078895047619

00:16:30.718 --> 00:16:32.290 know if this is mgus or not.

NOTE Confidence: 0.77078895047619

00:16:32.290 --> 00:16:33.890 So we called it mgip,

NOTE Confidence: 0.77078895047619

00:16:33.890 --> 00:16:35.792 monoclonal gammopathy of

NOTE Confidence: 0.77078895047619

00:16:35.792 --> 00:16:38.328 indeterminate potential alert ship.

NOTE Confidence: 0.77078895047619

00:16:38.330 --> 00:16:40.358 Don't let him have the praises

NOTE Confidence: 0.77078895047619

00:16:40.358 --> 00:16:41.372 of indeterminate potential.

NOTE Confidence: 0.77078895047619

00:16:41.380 --> 00:16:43.977 And the story goes that David Steensma

NOTE Confidence: 0.77078895047619

00:16:43.977 --> 00:16:47.057 is the one who coined the name chip.

NOTE Confidence: 0.77078895047619

00:16:47.060 --> 00:16:48.356 And I saw him once and he said,

NOTE Confidence: 0.77078895047619

00:16:48.360 --> 00:16:50.800 well I called chip based on M Gus.

NOTE Confidence: 0.77078895047619

00:16:50.800 --> 00:16:52.200 I was trying to imitate

NOTE Confidence: 0.77078895047619

00:16:52.200 --> 00:16:53.600 what doctor Kyle had done.

NOTE Confidence: 0.77078895047619

00:16:53.600 --> 00:16:55.496 So now we called M give based on

NOTE Confidence: 0.77078895047619

00:16:55.496 --> 00:16:57.990 chip and it keeps going round and

NOTE Confidence: 0.77078895047619

00:16:57.990 --> 00:16:59.558 round in hematological malignancies.

NOTE Confidence: 0.77078895047619

00:16:59.560 --> 00:17:01.729 But what is this chip and what is this

NOTE Confidence: 0.77078895047619

00:17:01.729 --> 00:17:04.276 mgus prevalence in this high risk population?

NOTE Confidence: 0.77078895047619

00:17:04.280 --> 00:17:06.114 So you can see here by age

NOTE Confidence: 0.77078895047619

00:17:06.114 --> 00:17:07.780 that mgip is very common,

NOTE Confidence: 0.77078895047619

00:17:07.780 --> 00:17:09.550 almost 20% of the population.

NOTE Confidence: 0.77078895047619

00:17:09.550 --> 00:17:10.522 It increases with age,

NOTE Confidence: 0.77078895047619

00:17:10.522 --> 00:17:13.004 but as you go on with age the M

NOTE Confidence: 0.77078895047619

00:17:13.004 --> 00:17:14.609 Gus proportion of those monoclonal

NOTE Confidence: 0.77078895047619

00:17:14.609 --> 00:17:16.522 gammopathy is increases more and then

NOTE Confidence: 0.77078895047619

00:17:16.522 --> 00:17:18.726 light chain mgus was actually a very

NOTE Confidence: 0.77078895047619

00:17:18.726 --> 00:17:20.606 small number in that population.

NOTE Confidence: 0.77078895047619

00:17:20.610 --> 00:17:24.514 If I just take a standard values 3% of

NOTE Confidence: 0.77078895047619

00:17:24.514 --> 00:17:26.224 the population in general population

NOTE Confidence: 0.77078895047619

00:17:26.224 --> 00:17:28.264 is what doctor Kyle had described

NOTE Confidence: 0.77078895047619

00:17:28.264 --> 00:17:30.490 before and that was based on Spep.

NOTE Confidence: 0.77078895047619

00:17:30.490 --> 00:17:33.255 If you double it because of the

NOTE Confidence: 0.77078895047619

00:17:33.255 --> 00:17:35.104 higher risk population which is

NOTE Confidence: 0.77078895047619

00:17:35.104 --> 00:17:37.455 true 6% in our population are espec

NOTE Confidence: 0.77078895047619

00:17:37.455 --> 00:17:40.178 positive and then if you look by mass.

NOTE Confidence: 0.77078895047619

00:17:40.180 --> 00:17:42.064 That trauma too because it's much

NOTE Confidence: 0.77078895047619

00:17:42.064 --> 00:17:44.017 more sensitive and can get you

NOTE Confidence: 0.77078895047619

00:17:44.017 --> 00:17:46.018 immunofixation than we are 13% and

NOTE Confidence: 0.77078895047619

00:17:46.018 --> 00:17:48.566 that's not even accounting for the mgip.

NOTE Confidence: 0.77078895047619

00:17:48.570 --> 00:17:51.586 So a large proportion of our high risk

NOTE Confidence: 0.77078895047619

00:17:51.586 --> 00:17:54.164 individuals have mgus and we need to

NOTE Confidence: 0.77078895047619

00:17:54.164 --> 00:17:56.190 understand better why they have it,

NOTE Confidence: 0.77078895047619

00:17:56.190 --> 00:17:57.875 but also who would progress

NOTE Confidence: 0.77078895047619

00:17:57.875 --> 00:17:58.886 in their lifetime.

NOTE Confidence: 0.77078895047619

00:17:58.890 --> 00:18:02.048 Now in general all monoclonal gammopathy's

NOTE Confidence: 0.77078895047619

00:18:02.048 --> 00:18:03.888 were associated with worse overall

NOTE Confidence: 0.77078895047619

00:18:03.888 --> 00:18:06.688 survival and it was not because of myeloma,

NOTE Confidence: 0.77078895047619

00:18:06.690 --> 00:18:08.796 it was also because of many

NOTE Confidence: 0.77078895047619

00:18:08.796 --> 00:18:10.200 other all caused mortalities.

NOTE Confidence: 0.77078895047619

00:18:10.200 --> 00:18:11.450 Autoimmune diseases,

NOTE Confidence: 0.77078895047619

00:18:11.450 --> 00:18:12.700 cardiovascular disease,

NOTE Confidence: 0.77078895047619

00:18:12.700 --> 00:18:14.575 many other lymphomas.

NOTE Confidence: 0.77078895047619

00:18:14.580 --> 00:18:16.494 So we started seeing maybe mgus

NOTE Confidence: 0.77078895047619

00:18:16.494 --> 00:18:18.167 and immune dysregulation in those

NOTE Confidence: 0.77078895047619

00:18:18.167 --> 00:18:19.877 patients may have other effects,

NOTE Confidence: 0.77078895047619

00:18:19.880 --> 00:18:21.404 not just myeloma development.

NOTE Confidence: 0.77078895047619

00:18:21.404 --> 00:18:24.187 And thus lead is leading us to

NOTE Confidence: 0.77078895047619

00:18:24.187 --> 00:18:25.899 understand more into correlations

NOTE Confidence: 0.77078895047619

00:18:25.899 --> 00:18:28.039 of mgus and chip mutations,

NOTE Confidence: 0.77078895047619

00:18:28.040 --> 00:18:29.440 both of them cause inflammation,

NOTE Confidence: 0.77078895047619

00:18:29.440 --> 00:18:30.984 potentially increased cardiovascular risk.

NOTE Confidence: 0.77078895047619

00:18:30.984 --> 00:18:33.300 We're trying to understand how that

NOTE Confidence: 0.77078895047619

00:18:33.352 --> 00:18:35.578 regulates the immune system and immune aging,

NOTE Confidence: 0.77078895047619

00:18:35.580 --> 00:18:37.320 how it correlates with autoimmune

NOTE Confidence: 0.77078895047619

00:18:37.320 --> 00:18:39.700 diseases and so many other questions.

NOTE Confidence: 0.77078895047619

00:18:39.700 --> 00:18:41.940 But what we were intrigued by is

NOTE Confidence: 0.77078895047619

00:18:41.940 --> 00:18:44.367 those M Gibbs and why were they

NOTE Confidence: 0.77078895047619

00:18:44.367 --> 00:18:46.455 present in many of those people.

NOTE Confidence: 0.77078895047619

00:18:46.460 --> 00:18:48.637 And most of those M gifts were

NOTE Confidence: 0.77078895047619

00:18:48.637 --> 00:18:51.224 actually IG M Mgip, not IG or IGA.

NOTE Confidence: 0.77078895047619

00:18:51.224 --> 00:18:53.060 So the first thing we said.

NOTE Confidence: 0.77078895047619

00:18:53.060 --> 00:18:55.748 Well, maybe it's an isotype class switch.

NOTE Confidence: 0.77078895047619

00:18:55.750 --> 00:18:57.700 This is the precursor of myeloma

NOTE Confidence: 0.77078895047619

00:18:57.700 --> 00:18:59.689 and it's IGM positive and then

NOTE Confidence: 0.77078895047619

00:18:59.689 --> 00:19:01.880 it's class switches to IgG as it

NOTE Confidence: 0.77078895047619

00:19:01.880 --> 00:19:03.941 progresses and this is the first

NOTE Confidence: 0.77078895047619

00:19:03.941 --> 00:19:05.626 event that requires the mutations.

NOTE Confidence: 0.77078895047619

00:19:05.630 --> 00:19:07.705 The other possibility was maybe

NOTE Confidence: 0.77078895047619

00:19:07.705 --> 00:19:10.234 these are lymphomas and they secrete

NOTE Confidence: 0.77078895047619

00:19:10.234 --> 00:19:12.894 very low levels of IGM that's non

NOTE Confidence: 0.77078895047619

00:19:12.894 --> 00:19:15.223 detectable by spep and in general

NOTE Confidence: 0.77078895047619

00:19:15.223 --> 00:19:17.461 we don't even screen for lymphomas

NOTE Confidence: 0.77078895047619

00:19:17.470 --> 00:19:19.018 by serum protein electrophoresis.

NOTE Confidence: 0.77078895047619

00:19:19.018 --> 00:19:21.340 So we're under we're not detecting

NOTE Confidence: 0.77078895047619

00:19:21.402 --> 00:19:23.334 enough of the cells and low grade.

NOTE Confidence: 0.77078895047619

00:19:23.340 --> 00:19:25.158 Performers and now we have a

NOTE Confidence: 0.77078895047619

00:19:25.158 --> 00:19:26.370 technology that can be

NOTE Confidence: 0.87823653631579

00:19:26.434 --> 00:19:28.604 more sensitive and indeed for us to

NOTE Confidence: 0.87823653631579

00:19:28.604 --> 00:19:31.060 prove that, we took samples from healthy

NOTE Confidence: 0.87823653631579

00:19:31.060 --> 00:19:33.629 donors from two people who have mgus,

NOTE Confidence: 0.87823653631579

00:19:33.630 --> 00:19:35.542 one of them had mgus and mcgiff and

NOTE Confidence: 0.87823653631579

00:19:35.542 --> 00:19:37.569 from 2 participants who had mgip.

NOTE Confidence: 0.87823653631579

00:19:37.570 --> 00:19:41.003 And we did CD19 and CD138 selection of

NOTE Confidence: 0.87823653631579

00:19:41.003 --> 00:19:42.900 the peripheral blood because we don't have

NOTE Confidence: 0.87823653631579

00:19:42.952 --> 00:19:44.686 bone marrow biopsies on those patients.

NOTE Confidence: 0.87823653631579

00:19:44.690 --> 00:19:47.258 And indeed we did first single

NOTE Confidence: 0.87823653631579

00:19:47.258 --> 00:19:48.970 cell sequencing for VDJ,

NOTE Confidence: 0.87823653631579

00:19:48.970 --> 00:19:51.338 so now for the BCR to see if

NOTE Confidence: 0.87823653631579

00:19:51.338 --> 00:19:53.567 they have clonal BCR in those.

NOTE Confidence: 0.87823653631579

00:19:53.570 --> 00:19:55.691 Patients and then of course we did

NOTE Confidence: 0.87823653631579

00:19:55.691 --> 00:19:57.000 gene expression profiling afterwards

NOTE Confidence: 0.87823653631579

00:19:57.000 --> 00:19:59.040 with the single cell RNA sequencing.

NOTE Confidence: 0.87823653631579

00:19:59.040 --> 00:20:00.685 And what was surprising as you can

NOTE Confidence: 0.87823653631579

00:20:00.685 --> 00:20:02.699 see here for this patient for example,

NOTE Confidence: 0.87823653631579

00:20:02.700 --> 00:20:06.060 they had one clone that was all VDJ,

NOTE Confidence: 0.87823653631579

00:20:06.060 --> 00:20:08.156 the same clone and you can see that

NOTE Confidence: 0.87823653631579

00:20:08.156 --> 00:20:10.400 in this patient all of those cells.

NOTE Confidence: 0.87823653631579

00:20:10.400 --> 00:20:12.213 So this is single cell RNA sequencing

NOTE Confidence: 0.87823653631579

00:20:12.213 --> 00:20:12.990 and the blood,

NOTE Confidence: 0.87823653631579

00:20:12.990 --> 00:20:15.139 all of the cells were for one

NOTE Confidence: 0.87823653631579

00:20:15.139 --> 00:20:17.060 clone only in that patient.

NOTE Confidence: 0.87823653631579

00:20:17.060 --> 00:20:19.223 And then this second patient had two

NOTE Confidence: 0.87823653631579

00:20:19.223 --> 00:20:21.166 different clones as you can see one

NOTE Confidence: 0.87823653631579

00:20:21.166 --> 00:20:23.050 of them was very high which is the.

NOTE Confidence: 0.87823653631579

00:20:23.050 --> 00:20:25.080 The red one here and then the

NOTE Confidence: 0.87823653631579

00:20:25.080 --> 00:20:27.218 second one here in the orange one.

NOTE Confidence: 0.87823653631579

00:20:27.220 --> 00:20:29.405 And indeed we reconfirmed that

NOTE Confidence: 0.87823653631579

00:20:29.405 --> 00:20:30.279 those patients,

NOTE Confidence: 0.87823653631579

00:20:30.280 --> 00:20:32.848 one of them was indeed an early CLL

NOTE Confidence: 0.87823653631579

00:20:32.848 --> 00:20:35.083 case because we did flow cytometry

NOTE Confidence: 0.87823653631579

00:20:35.083 --> 00:20:37.369 and because this patient had almost

NOTE Confidence: 0.87823653631579

00:20:37.439 --> 00:20:39.260 60% of the cells are all clonal,

NOTE Confidence: 0.87823653631579

00:20:39.260 --> 00:20:41.150 we were able to do whole genome

NOTE Confidence: 0.87823653631579

00:20:41.150 --> 00:20:42.400 sequencing on that sample.

NOTE Confidence: 0.87823653631579

00:20:42.400 --> 00:20:45.235 And indeed it was an atypical lymphoma,

NOTE Confidence: 0.87823653631579

00:20:45.240 --> 00:20:47.515 likely a post germinal B cell lymphoma.

NOTE Confidence: 0.87823653631579

00:20:47.520 --> 00:20:50.160 So either DLBCL or something like

NOTE Confidence: 0.87823653631579

00:20:50.160 --> 00:20:52.601 a marginal zone which was MIT

NOTE Confidence: 0.87823653631579

00:20:52.601 --> 00:20:54.406 88 positive and it had.

NOTE Confidence: 0.87823653631579

00:20:54.410 --> 00:20:56.944 Copy number alterations as you see here,

NOTE Confidence: 0.87823653631579

00:20:56.950 --> 00:20:57.810 chromosome 3,

NOTE Confidence: 0.87823653631579

00:20:57.810 --> 00:20:59.960 chromosome 18 with a gain

NOTE Confidence: 0.87823653631579

00:20:59.960 --> 00:21:01.250 of those chromosomes.

NOTE Confidence: 0.87823653631579

00:21:01.250 --> 00:21:03.530 So indeed by both DNA,

NOTE Confidence: 0.87823653631579

00:21:03.530 --> 00:21:05.396 by protein level in flow cytometry

NOTE Confidence: 0.87823653631579

00:21:05.396 --> 00:21:07.228 and by RNA sequencing we were

NOTE Confidence: 0.87823653631579

00:21:07.228 --> 00:21:09.090 able to indicate that two of those

NOTE Confidence: 0.87823653631579

00:21:09.090 --> 00:21:10.249 cases were lymphomas.

NOTE Confidence: 0.87823653631579

00:21:10.250 --> 00:21:12.266 Now we're expanding that cohort to

NOTE Confidence: 0.87823653631579

00:21:12.266 --> 00:21:13.981 another 4050 samples with single

NOTE Confidence: 0.87823653631579

00:21:13.981 --> 00:21:15.829 cell RNA sequencing and then it

NOTE Confidence: 0.87823653631579

00:21:15.829 --> 00:21:17.707 will be followed by DNA sequencing

NOTE Confidence: 0.87823653631579

00:21:17.707 --> 00:21:19.786 of course if we find this positive,

NOTE Confidence: 0.87823653631579

00:21:19.790 --> 00:21:22.286 but that opens the door for saying we

NOTE Confidence: 0.87823653631579

00:21:22.286 --> 00:21:24.610 can screen also for other lymphomas.

NOTE Confidence: 0.87823653631579

00:21:24.610 --> 00:21:25.940 And not just for myeloma.

NOTE Confidence: 0.87823653631579

00:21:25.940 --> 00:21:27.949 And the question is what are all

NOTE Confidence: 0.87823653631579

00:21:27.949 --> 00:21:29.600 of those monoclonal gammopathy is

NOTE Confidence: 0.87823653631579

00:21:29.600 --> 00:21:31.415 doing in our general population.

NOTE Confidence: 0.87823653631579

00:21:31.420 --> 00:21:33.296 So to answer some of those questions,

NOTE Confidence: 0.87823653631579

00:21:33.300 --> 00:21:35.778 we're moving on to other bigger cohorts.

NOTE Confidence: 0.87823653631579

00:21:35.780 --> 00:21:38.380 So now we're talking to the UK Biobank,

NOTE Confidence: 0.87823653631579

00:21:38.380 --> 00:21:40.124 they have a half a million samples that

NOTE Confidence: 0.87823653631579

00:21:40.124 --> 00:21:41.678 have been collected over 20 years.

NOTE Confidence: 0.87823653631579

00:21:41.680 --> 00:21:44.038 We're talking to end Haynes and

NOTE Confidence: 0.87823653631579

00:21:44.038 --> 00:21:46.345 trying to get samples from NHANES

NOTE Confidence: 0.87823653631579

00:21:46.345 --> 00:21:49.050 as you can see here 7937 another

NOTE Confidence: 0.87823653631579

00:21:49.050 --> 00:21:51.381 8000 and PLO another 14,000.

NOTE Confidence: 0.87823653631579

00:21:51.381 --> 00:21:53.069 We are also trying to see if we

NOTE Confidence: 0.87823653631579

00:21:53.069 --> 00:21:54.619 can get access to the million.

NOTE Confidence: 0.87823653631579

00:21:54.620 --> 00:21:56.825 Veterans project to all of us and

NOTE Confidence: 0.87823653631579

00:21:56.825 --> 00:21:58.903 many other cohorts that have already

NOTE Confidence: 0.87823653631579

00:21:58.903 --> 00:22:00.688 collected large numbers of samples

NOTE Confidence: 0.87823653631579

00:22:00.688 --> 00:22:03.358 to ask big questions of what is the

NOTE Confidence: 0.87823653631579

00:22:03.358 --> 00:22:05.045 prevalence in high risk population,

NOTE Confidence: 0.87823653631579

00:22:05.045 --> 00:22:07.595 but also what are those early

NOTE Confidence: 0.87823653631579

00:22:07.595 --> 00:22:09.325 monoclonal democracies doing to

NOTE Confidence: 0.87823653631579

00:22:09.325 --> 00:22:10.507 the general population.

NOTE Confidence: 0.87823653631579

00:22:10.510 --> 00:22:12.070 And then of course we have

NOTE Confidence: 0.87823653631579

00:22:12.070 --> 00:22:13.110 collaborations with all link

NOTE Confidence: 0.833448604347826

00:22:13.164 --> 00:22:14.868 to try and look at the protein level

NOTE Confidence: 0.833448604347826

00:22:14.868 --> 00:22:16.530 in those patients with proteomics.

NOTE Confidence: 0.833448604347826

00:22:16.530 --> 00:22:18.048 So the next step I'll take

NOTE Confidence: 0.833448604347826

00:22:18.048 --> 00:22:19.060 you through is understanding

NOTE Confidence: 0.833448604347826

00:22:19.106 --> 00:22:20.670 mechanisms of disease progression.

NOTE Confidence: 0.833448604347826

00:22:20.670 --> 00:22:23.428 If you have mgus or smoldering myeloma,

NOTE Confidence: 0.833448604347826

00:22:23.430 --> 00:22:24.900 you want to know what is.

NOTE Confidence: 0.833448604347826

00:22:24.900 --> 00:22:26.748 My personal risk of going on to

NOTE Confidence: 0.833448604347826

00:22:26.748 --> 00:22:28.043 dissolve myeloma and I don't

NOTE Confidence: 0.833448604347826

00:22:28.043 --> 00:22:29.604 have in the slides here what we

NOTE Confidence: 0.833448604347826

00:22:29.604 --> 00:22:31.210 just published yesterday night,

NOTE Confidence: 0.833448604347826

00:22:31.210 --> 00:22:33.128 it just came out in Lancet hematology,

NOTE Confidence: 0.833448604347826

00:22:33.130 --> 00:22:35.356 a new dynamic model to understand

NOTE Confidence: 0.833448604347826

00:22:35.356 --> 00:22:37.657 risk of progression because we know

NOTE Confidence: 0.833448604347826

00:22:37.657 --> 00:22:39.527 that the current clinical criteria,

NOTE Confidence: 0.833448604347826

00:22:39.530 --> 00:22:41.364 20% plasma cells in your bone marrow,

NOTE Confidence: 0.833448604347826

00:22:41.370 --> 00:22:42.486 2 grams M spike,

NOTE Confidence: 0.833448604347826

00:22:42.486 --> 00:22:44.613 20 light chain ratio for a smoldering

NOTE Confidence: 0.833448604347826

00:22:44.613 --> 00:22:47.336 myeloma are good but not good enough

NOTE Confidence: 0.833448604347826

00:22:47.336 --> 00:22:49.784 because they give you a 50% chance of

NOTE Confidence: 0.833448604347826

00:22:49.784 --> 00:22:51.866 progression in two years and that's

NOTE Confidence: 0.833448604347826

00:22:51.866 --> 00:22:53.550 basically like flipping a coin,

NOTE Confidence: 0.833448604347826

00:22:53.550 --> 00:22:55.382 50% chance of progressing.

NOTE Confidence: 0.833448604347826

00:22:55.382 --> 00:22:57.840 50% said chance of not progressing.

NOTE Confidence: 0.833448604347826

00:22:57.840 --> 00:22:59.375 So we need something better

NOTE Confidence: 0.833448604347826

00:22:59.375 --> 00:23:01.340 than that or to improve on it.

NOTE Confidence: 0.833448604347826

00:23:01.340 --> 00:23:02.858 So we developed a dynamic model

NOTE Confidence: 0.833448604347826

00:23:02.858 --> 00:23:04.898 and now this is a risk calculator.

NOTE Confidence: 0.833448604347826

00:23:04.900 --> 00:23:05.548 Any patient,

NOTE Confidence: 0.833448604347826

00:23:05.548 --> 00:23:07.816 any physician can use the risk calculator

NOTE Confidence: 0.833448604347826

00:23:07.816 --> 00:23:10.095 and have the prediction of five years,

NOTE Confidence: 0.833448604347826

00:23:10.100 --> 00:23:11.524 10 years, 20 years,

NOTE Confidence: 0.833448604347826

00:23:11.524 --> 00:23:13.304 what is my personal risk

NOTE Confidence: 0.833448604347826

00:23:13.304 --> 00:23:15.160 based on clinical markers.

NOTE Confidence: 0.833448604347826

00:23:15.160 --> 00:23:17.220 But clinical markers are

NOTE Confidence: 0.833448604347826

00:23:17.220 --> 00:23:18.556 assessing the tumor burden,

NOTE Confidence: 0.833448604347826

00:23:18.556 --> 00:23:20.560 how many cancer cells you have.

NOTE Confidence: 0.833448604347826

00:23:20.560 --> 00:23:22.856 It doesn't give you the underlying biology,

NOTE Confidence: 0.833448604347826

00:23:22.860 --> 00:23:24.480 how fast are they growing.

NOTE Confidence: 0.833448604347826

00:23:24.480 --> 00:23:25.532 So we need more.

NOTE Confidence: 0.833448604347826

00:23:25.532 --> 00:23:27.110 And that the dynamic model helps

NOTE Confidence: 0.833448604347826

00:23:27.172 --> 00:23:28.720 you because the more data you

NOTE Confidence: 0.833448604347826

00:23:28.720 --> 00:23:30.410 enter in the light chain increase

NOTE Confidence: 0.833448604347826

00:23:30.410 --> 00:23:31.910 or the M spike increase,

NOTE Confidence: 0.833448604347826

00:23:31.910 --> 00:23:33.660 it gives you the dynamics

NOTE Confidence: 0.833448604347826

00:23:33.660 --> 00:23:34.710 of tumor progression.

NOTE Confidence: 0.833448604347826

00:23:34.710 --> 00:23:37.524 But we need something as the genomics

NOTE Confidence: 0.833448604347826

00:23:37.524 --> 00:23:39.890 and immune and other factors.

NOTE Confidence: 0.833448604347826

00:23:39.890 --> 00:23:42.338 So here's one of the first papers we

NOTE Confidence: 0.833448604347826

00:23:42.338 --> 00:23:44.777 published a few years ago where we

NOTE Confidence: 0.833448604347826

00:23:44.777 --> 00:23:46.730 looked at whole exome sequencing in

NOTE Confidence: 0.833448604347826

00:23:46.730 --> 00:23:48.710 250 patients with smoldering myeloma.

NOTE Confidence: 0.833448604347826

00:23:48.710 --> 00:23:50.460 And now we expanded it of course

NOTE Confidence: 0.833448604347826

00:23:50.460 --> 00:23:51.210 so many others.

NOTE Confidence: 0.833448604347826

00:23:51.210 --> 00:23:53.770 And we found that there were three main

NOTE Confidence: 0.833448604347826

00:23:53.770 --> 00:23:55.358 mechanisms of genomic aberrations.

NOTE Confidence: 0.833448604347826

00:23:55.358 --> 00:23:58.186 That leads to progression or that are

NOTE Confidence: 0.833448604347826

00:23:58.186 --> 00:23:59.726 associated strongly with progression

NOTE Confidence: 0.833448604347826

00:23:59.726 --> 00:24:02.399 to myeloma and these were MAP kinase

NOTE Confidence: 0.833448604347826

00:24:02.399 --> 00:24:04.109 mutations like ANRAS and Karas

NOTE Confidence: 0.833448604347826

00:24:04.110 --> 00:24:06.574 ATM and ATR and P53 mutations DNA

NOTE Confidence: 0.833448604347826

00:24:06.574 --> 00:24:09.225 repair pathway and of course make

NOTE Confidence: 0.833448604347826

00:24:09.225 --> 00:24:10.749 alterations or translocations.

NOTE Confidence: 0.833448604347826

00:24:10.750 --> 00:24:13.009 In fact I think that if we have Mike,

NOTE Confidence: 0.833448604347826

00:24:13.010 --> 00:24:15.320 we already have myeloma and potentially

NOTE Confidence: 0.833448604347826

00:24:15.320 --> 00:24:17.742 some of those alterations are all

NOTE Confidence: 0.833448604347826

00:24:17.742 --> 00:24:19.378 secondary mutations and secondary

NOTE Confidence: 0.833448604347826

00:24:19.378 --> 00:24:21.514 alterations that occur when you're

NOTE Confidence: 0.833448604347826

00:24:21.514 --> 00:24:23.266 already going towards myeloma,

NOTE Confidence: 0.833448604347826

00:24:23.270 --> 00:24:24.956 when there is no coming back

NOTE Confidence: 0.833448604347826

00:24:24.956 --> 00:24:25.799 and hopefully these.

NOTE Confidence: 0.833448604347826

00:24:25.800 --> 00:24:28.640 Will become routine in our

NOTE Confidence: 0.833448604347826

00:24:28.640 --> 00:24:30.490 understanding of if someone has

NOTE Confidence: 0.833448604347826

00:24:30.490 --> 00:24:32.730 smoldering myeloma and has one of

NOTE Confidence: 0.833448604347826

00:24:32.730 --> 00:24:35.026 those likely they have very high risk

NOTE Confidence: 0.833448604347826

00:24:35.026 --> 00:24:37.446 of progression and we should consider

NOTE Confidence: 0.833448604347826

00:24:37.446 --> 00:24:39.146 therapeutic interventions in them.

NOTE Confidence: 0.833448604347826

00:24:39.150 --> 00:24:42.206 Now what we found lately is that one,

NOTE Confidence: 0.833448604347826

00:24:42.210 --> 00:24:43.668 many of our patients don't get

NOTE Confidence: 0.833448604347826

00:24:43.668 --> 00:24:44.958 bone marrow biopsies or serial

NOTE Confidence: 0.833448604347826

00:24:44.958 --> 00:24:46.308 bone marrow biopsies and two,

NOTE Confidence: 0.833448604347826

00:24:46.310 --> 00:24:48.182 whole exome sequencing is OK and

NOTE Confidence: 0.833448604347826

00:24:48.182 --> 00:24:50.189 it's not good enough because it

NOTE Confidence: 0.833448604347826

00:24:50.189 --> 00:24:52.265 doesn't give you the primary events,

NOTE Confidence: 0.833448604347826

00:24:52.270 --> 00:24:54.340 the translocations that occur in those

NOTE Confidence: 0.833448604347826

00:24:54.340 --> 00:24:55.980 patients. So this is a paper that.

NOTE Confidence: 0.833448604347826

00:24:55.980 --> 00:24:57.758 Just got published a few weeks ago.

NOTE Confidence: 0.833448604347826

00:24:57.760 --> 00:24:59.998 Work from Ankit and John Batiste

NOTE Confidence: 0.833448604347826

00:24:59.998 --> 00:25:01.490 where we took circulating

NOTE Confidence: 0.753337883333333

00:25:01.558 --> 00:25:03.014 tumor cells, isolated them,

NOTE Confidence: 0.753337883333333

00:25:03.014 --> 00:25:05.750 developed a method of low input DNA and

NOTE Confidence: 0.753337883333333

00:25:05.821 --> 00:25:08.082 were able to do whole genome sequencing

NOTE Confidence: 0.753337883333333

00:25:08.082 --> 00:25:10.526 from as low as 30 to 50 cells that

NOTE Confidence: 0.753337883333333

00:25:10.526 --> 00:25:12.166 you can get in the peripheral blood.

NOTE Confidence: 0.753337883333333

00:25:12.166 --> 00:25:13.558 So you can see in mgus

NOTE Confidence: 0.753337883333333

00:25:13.558 --> 00:25:14.770 and smoldering myeloma.

NOTE Confidence: 0.753337883333333

00:25:14.770 --> 00:25:17.283 Many of them have small numbers of

NOTE Confidence: 0.753337883333333

00:25:17.283 --> 00:25:19.613 circulating tumor cells and when you are

NOTE Confidence: 0.753337883333333

00:25:19.613 --> 00:25:21.770 able to capture them and purify them,

NOTE Confidence: 0.753337883333333

00:25:21.770 --> 00:25:23.414 you can do whole genome sequencing

NOTE Confidence: 0.753337883333333

00:25:23.414 --> 00:25:25.427 and you don't even have to go

NOTE Confidence: 0.753337883333333

00:25:25.427 --> 00:25:26.579 deep sequencing because the.

NOTE Confidence: 0.753337883333333

00:25:26.580 --> 00:25:29.009 Security is so good in those samples.

NOTE Confidence: 0.753337883333333

00:25:29.010 --> 00:25:31.240 So indeed we had head-to-head

NOTE Confidence: 0.753337883333333

00:25:31.240 --> 00:25:33.024 comparison of circulating tumor

NOTE Confidence: 0.753337883333333

00:25:33.024 --> 00:25:35.276 cells versus bone marrow cells so

NOTE Confidence: 0.753337883333333

00:25:35.276 --> 00:25:37.773 that you can show indeed that all

NOTE Confidence: 0.753337883333333

00:25:37.773 --> 00:25:39.849 of the clonal and subclonal events

NOTE Confidence: 0.753337883333333

00:25:39.849 --> 00:25:41.330 can also happen in the blood.

NOTE Confidence: 0.753337883333333

00:25:41.330 --> 00:25:43.109 And you don't need the bone marrow biopsy,

NOTE Confidence: 0.753337883333333

00:25:43.110 --> 00:25:46.086 but also head-to-head comparison to fish,

NOTE Confidence: 0.753337883333333

00:25:46.090 --> 00:25:47.658 which is the standard of care that

NOTE Confidence: 0.753337883333333

00:25:47.658 --> 00:25:49.078 we have right now in myeloma,

NOTE Confidence: 0.753337883333333

00:25:49.080 --> 00:25:51.228 yet another 50 year old technology.

NOTE Confidence: 0.753337883333333

00:25:51.230 --> 00:25:52.490 So indeed, of course,

NOTE Confidence: 0.753337883333333

00:25:52.490 --> 00:25:54.380 no surprise there that whole genome

NOTE Confidence: 0.753337883333333

00:25:54.436 --> 00:25:56.146 sequencing is better than fish,

NOTE Confidence: 0.753337883333333

00:25:56.150 --> 00:25:56.686 indeed it.

NOTE Confidence: 0.753337883333333

00:25:56.686 --> 00:25:58.562 And get you all of the translocations,

NOTE Confidence: 0.753337883333333

00:25:58.570 --> 00:25:59.914 but it can get you much more.

NOTE Confidence: 0.753337883333333

00:25:59.920 --> 00:26:00.919 You get mutations,

NOTE Confidence: 0.753337883333333

00:26:00.919 --> 00:26:02.584 you get copy number alterations,

NOTE Confidence: 0.753337883333333

00:26:02.590 --> 00:26:04.225 you can even get translocations

NOTE Confidence: 0.753337883333333

00:26:04.225 --> 00:26:05.860 you couldn't detect by fish.

NOTE Confidence: 0.753337883333333

00:26:05.860 --> 00:26:07.460 And indeed because you're purifying

NOTE Confidence: 0.753337883333333

00:26:07.460 --> 00:26:09.060 small numbers of cells especially

NOTE Confidence: 0.753337883333333

00:26:09.109 --> 00:26:10.269 in the peripheral bloods,

NOTE Confidence: 0.753337883333333

00:26:10.270 --> 00:26:13.166 you can do that multiple times during the

NOTE Confidence: 0.753337883333333

00:26:13.166 --> 00:26:15.519 serial development of a patients progression.

NOTE Confidence: 0.753337883333333

00:26:15.520 --> 00:26:17.249 So you can ask the question when

NOTE Confidence: 0.753337883333333

00:26:17.249 --> 00:26:18.640 the MIC clone is growing,

NOTE Confidence: 0.753337883333333

00:26:18.640 --> 00:26:20.551 what is going on and when can

NOTE Confidence: 0.753337883333333

00:26:20.551 --> 00:26:21.960 I treat this patient.

NOTE Confidence: 0.753337883333333

00:26:21.960 --> 00:26:24.736 Now I'll move on to single cell and

NOTE Confidence: 0.753337883333333

00:26:24.736 --> 00:26:27.169 I borrowed this slide from Aviva.

NOTE Confidence: 0.753337883333333

00:26:27.170 --> 00:26:28.922 Who basically tries to tell you why do

NOTE Confidence: 0.753337883333333

00:26:28.922 --> 00:26:30.889 we need to go to the single cell level,

NOTE Confidence: 0.753337883333333

00:26:30.890 --> 00:26:32.200 and it's basically when you

NOTE Confidence: 0.753337883333333

00:26:32.200 --> 00:26:32.986 do bulk sequencing,

NOTE Confidence: 0.753337883333333

00:26:32.990 --> 00:26:34.358 whether it's whole genome

NOTE Confidence: 0.753337883333333

00:26:34.358 --> 00:26:36.068 sequencing or bulk RNA sequencing,

NOTE Confidence: 0.753337883333333

00:26:36.070 --> 00:26:37.672 you're sequencing all of the cells

NOTE Confidence: 0.753337883333333

00:26:37.672 --> 00:26:39.210 mushed together like a smoothie.

NOTE Confidence: 0.753337883333333

00:26:39.210 --> 00:26:40.210 Now it tastes good,

NOTE Confidence: 0.753337883333333

00:26:40.210 --> 00:26:42.123 but you can't really tell the differences

NOTE Confidence: 0.753337883333333

00:26:42.123 --> 00:26:44.265 between a strawberry and a Raspberry.

NOTE Confidence: 0.753337883333333

00:26:44.270 --> 00:26:46.574 You can't even tell if it's a good

NOTE Confidence: 0.753337883333333

00:26:46.574 --> 00:26:48.288 Raspberry versus a mutant Raspberry.

NOTE Confidence: 0.753337883333333

00:26:48.290 --> 00:26:50.030 Single cell sequencing gives you that.

NOTE Confidence: 0.753337883333333

00:26:50.030 --> 00:26:51.950 It gives you that ability to

NOTE Confidence: 0.753337883333333

00:26:51.950 --> 00:26:53.630 differentiate them from each other.

NOTE Confidence: 0.753337883333333

00:26:53.630 --> 00:26:55.865 And of course spatial transcriptomics

NOTE Confidence: 0.753337883333333

00:26:55.865 --> 00:26:57.206 or spatial sequencing.

NOTE Confidence: 0.753337883333333

00:26:57.210 --> 00:26:59.170 Is the ultimate goal where you get

NOTE Confidence: 0.753337883333333

00:26:59.170 --> 00:27:01.375 the whole fruit tart and you can

NOTE Confidence: 0.753337883333333

00:27:01.375 --> 00:27:03.000 understand better the localization of

NOTE Confidence: 0.753337883333333

00:27:03.000 --> 00:27:05.298 all of those cells in the environment.

NOTE Confidence: 0.753337883333333

00:27:05.300 --> 00:27:07.197 So what we did is we said,

NOTE Confidence: 0.753337883333333

00:27:07.200 --> 00:27:07.459 well,

NOTE Confidence: 0.753337883333333

00:27:07.459 --> 00:27:09.013 let's look at the tumor cells

NOTE Confidence: 0.753337883333333

00:27:09.013 --> 00:27:10.899 in the bone marrow compartment.

NOTE Confidence: 0.753337883333333

00:27:10.900 --> 00:27:12.396 And this is a study where we did

NOTE Confidence: 0.753337883333333

00:27:12.396 --> 00:27:13.672 it in collaboration with MIT

NOTE Confidence: 0.753337883333333

00:27:13.672 --> 00:27:15.376 and of course with the broad.

NOTE Confidence: 0.753337883333333

00:27:15.380 --> 00:27:17.484 All of our work is with the Broad

NOTE Confidence: 0.753337883333333

00:27:17.484 --> 00:27:19.301 Institute where we said we're lucky

NOTE Confidence: 0.753337883333333

00:27:19.301 --> 00:27:21.143 enough in mgus and smoldering myeloma

NOTE Confidence: 0.753337883333333

00:27:21.197 --> 00:27:23.565 that not all of the plasma cells are

NOTE Confidence: 0.753337883333333

00:27:23.565 --> 00:27:25.027 actually malignant plasma cells we

NOTE Confidence: 0.753337883333333

00:27:25.027 --> 00:27:27.450 have some of them are normal plasma cells.

NOTE Confidence: 0.753337883333333

00:27:27.450 --> 00:27:30.942 So the potential here is instead of

NOTE Confidence: 0.753337883333333

00:27:30.942 --> 00:27:32.846 looking at interpatient variability,

NOTE Confidence: 0.753337883333333

00:27:32.850 --> 00:27:34.370 healthy versus cancer patients,

NOTE Confidence: 0.753337883333333

00:27:34.370 --> 00:27:36.650 we can actually look at the

NOTE Confidence: 0.753337883333333

00:27:36.715 --> 00:27:38.389 intra patient variability,

NOTE Confidence: 0.753337883333333

00:27:38.390 --> 00:27:39.234 healthy cells,

NOTE Confidence: 0.753337883333333

00:27:39.234 --> 00:27:40.922 plasma cells within one

NOTE Confidence: 0.753337883333333

00:27:40.922 --> 00:27:42.610 patient versus malignant plasma

NOTE Confidence: 0.791874297272727

00:27:42.678 --> 00:27:44.354 cells. And now you can ask the

NOTE Confidence: 0.791874297272727

00:27:44.354 --> 00:27:45.853 questions of here are the normal

NOTE Confidence: 0.791874297272727

00:27:45.853 --> 00:27:47.575 plasma cells here are the malignant

NOTE Confidence: 0.791874297272727

00:27:47.575 --> 00:27:49.267 plasma cells from the same patient,

NOTE Confidence: 0.791874297272727

00:27:49.270 --> 00:27:51.433 what are the differences in them and

NOTE Confidence: 0.791874297272727

00:27:51.433 --> 00:27:54.070 can I understand that mechanism of early

NOTE Confidence: 0.791874297272727

00:27:54.070 --> 00:27:55.722 genomic events and transcriptional

NOTE Confidence: 0.791874297272727

00:27:55.722 --> 00:27:57.840 changes that occur with malignant?

NOTE Confidence: 0.791874297272727

00:27:57.840 --> 00:27:58.370 Transformation,

NOTE Confidence: 0.791874297272727

00:27:58.370 --> 00:28:01.550 even within the same neoplastic cells,

NOTE Confidence: 0.791874297272727

00:28:01.550 --> 00:28:03.278 I can find subclusters that are

NOTE Confidence: 0.791874297272727

00:28:03.278 --> 00:28:04.790 very different from each other.

NOTE Confidence: 0.791874297272727

00:28:04.790 --> 00:28:06.610 There is a proliferating cluster.

NOTE Confidence: 0.791874297272727

00:28:06.610 --> 00:28:08.647 There is some that have higher expression

NOTE Confidence: 0.791874297272727

00:28:08.647 --> 00:28:10.885 of certain genes and that can help you

NOTE Confidence: 0.791874297272727

00:28:10.885 --> 00:28:12.650 understand when the patient is treated,

NOTE Confidence: 0.791874297272727

00:28:12.650 --> 00:28:14.720 which subcluster may respond and which

NOTE Confidence: 0.791874297272727

00:28:14.720 --> 00:28:16.809 one may be resistant to therapy.

NOTE Confidence: 0.791874297272727

00:28:16.810 --> 00:28:19.310 Now we moved on to do even more work on that.

NOTE Confidence: 0.791874297272727

00:28:19.310 --> 00:28:21.802 So this was presented in Ash this

NOTE Confidence: 0.791874297272727

00:28:21.802 --> 00:28:24.506 year where we showed 245 samples

NOTE Confidence: 0.791874297272727

00:28:24.506 --> 00:28:26.150 from 234 patients.

NOTE Confidence: 0.791874297272727

00:28:26.150 --> 00:28:28.638 Here we did not only do the jacks.

NOTE Confidence: 0.791874297272727

00:28:28.640 --> 00:28:30.950 The gene expression single cell sequencing,

NOTE Confidence: 0.791874297272727

00:28:30.950 --> 00:28:32.636 but we also did BCR profiling

NOTE Confidence: 0.791874297272727

00:28:32.636 --> 00:28:34.390 on all of those patients.

NOTE Confidence: 0.791874297272727

00:28:34.390 --> 00:28:36.638 So now you can get with the VGA

NOTE Confidence: 0.791874297272727

00:28:36.638 --> 00:28:39.118 or with the BCR sequencing the

NOTE Confidence: 0.791874297272727

00:28:39.118 --> 00:28:40.958 clonality of those patients.

NOTE Confidence: 0.791874297272727

00:28:40.960 --> 00:28:43.319 So this just shows you the potential

NOTE Confidence: 0.791874297272727

00:28:43.319 --> 00:28:45.140 of really understanding the tumor

NOTE Confidence: 0.791874297272727

00:28:45.140 --> 00:28:46.640 compartment in those patients.

NOTE Confidence: 0.791874297272727

00:28:46.640 --> 00:28:48.160 We've done the same thing

NOTE Confidence: 0.791874297272727

00:28:48.160 --> 00:28:49.376 on circulating tumor cells,

NOTE Confidence: 0.791874297272727

00:28:49.380 --> 00:28:51.340 but I'm not showing that data here.

NOTE Confidence: 0.791874297272727

00:28:51.340 --> 00:28:53.833 So of course with a huge number of samples,

NOTE Confidence: 0.791874297272727

00:28:53.840 --> 00:28:56.464 what was very interesting is indeed all of

NOTE Confidence: 0.791874297272727

00:28:56.464 --> 00:28:58.769 the malignant samples cluster separately.

NOTE Confidence: 0.791874297272727

00:28:58.770 --> 00:28:59.766 It was not surprising.

NOTE Confidence: 0.791874297272727

00:28:59.766 --> 00:29:01.641 We saw that before and the normal

NOTE Confidence: 0.791874297272727

00:29:01.641 --> 00:29:03.246 plasma cells clustered together from

NOTE Confidence: 0.791874297272727

00:29:03.246 --> 00:29:05.501 all of the patients and indeed the more

NOTE Confidence: 0.791874297272727

00:29:05.501 --> 00:29:07.336 you look at the number of cells are

NOTE Confidence: 0.791874297272727

00:29:07.336 --> 00:29:08.932 increasing as you go on to myeloma,

NOTE Confidence: 0.791874297272727

00:29:08.940 --> 00:29:11.500 the malignant versus normal compartment.

NOTE Confidence: 0.791874297272727

00:29:11.500 --> 00:29:13.786 But what was interesting is we

NOTE Confidence: 0.791874297272727

00:29:13.786 --> 00:29:14.929 compared head-to-head cytogenetics

NOTE Confidence: 0.791874297272727

00:29:14.929 --> 00:29:17.099 from those patients with fish or when

NOTE Confidence: 0.791874297272727

00:29:17.099 --> 00:29:18.994 we have whole genome sequencing to

NOTE Confidence: 0.791874297272727

00:29:18.994 --> 00:29:21.034 the single cell RNA sequencing data.

NOTE Confidence: 0.791874297272727

00:29:21.040 --> 00:29:23.352 And indeed you can see that the hyper

NOTE Confidence: 0.791874297272727

00:29:23.352 --> 00:29:25.454 deployed cases were confirmed, the 414,

NOTE Confidence: 0.791874297272727

00:29:25.454 --> 00:29:28.132 you can confirm it with FGFR 311,

NOTE Confidence: 0.791874297272727

00:29:28.132 --> 00:29:30.806 fourteen with cycling. 11416 and so on.

NOTE Confidence: 0.791874297272727

00:29:30.806 --> 00:29:32.844 So you can be very accurate in

NOTE Confidence: 0.791874297272727

00:29:32.844 --> 00:29:34.949 understanding who has a specific

NOTE Confidence: 0.791874297272727

00:29:34.949 --> 00:29:35.370 translocation.

NOTE Confidence: 0.791874297272727

00:29:35.370 --> 00:29:39.296 But then we said well 50% of our samples

NOTE Confidence: 0.791874297272727

00:29:39.296 --> 00:29:41.970 did not even have good fish information.

NOTE Confidence: 0.791874297272727

00:29:41.970 --> 00:29:44.682 Either it failed which happens a lot or

NOTE Confidence: 0.791874297272727

00:29:44.682 --> 00:29:47.201 they give us the fish information with

NOTE Confidence: 0.791874297272727

00:29:47.201 --> 00:29:50.010 an igh partner that we cannot detect.

NOTE Confidence: 0.791874297272727

00:29:50.010 --> 00:29:51.650 So we were basically blinded

NOTE Confidence: 0.791874297272727

00:29:51.650 --> 00:29:53.290 to know what is happening.

NOTE Confidence: 0.791874297272727

00:29:53.290 --> 00:29:56.098 So we used our single cell RNA sequencing

NOTE Confidence: 0.791874297272727

00:29:56.098 --> 00:29:58.856 to generate what could potentially be the.

NOTE Confidence: 0.791874297272727

00:29:58.860 --> 00:30:01.170 Cytogenetic information of those patients.

NOTE Confidence: 0.791874297272727

00:30:01.170 --> 00:30:03.510 So you can see here that all of the

NOTE Confidence: 0.791874297272727

00:30:03.510 --> 00:30:05.645 unavailable or we didn't know what they were,

NOTE Confidence: 0.791874297272727

00:30:05.650 --> 00:30:08.716 we were able to reclassify them into

NOTE Confidence: 0.791874297272727

00:30:08.716 --> 00:30:10.030 specific cytogenetic abnormalities.

NOTE Confidence: 0.791874297272727

00:30:10.030 --> 00:30:12.064 And this is the confusion matrix

NOTE Confidence: 0.791874297272727

00:30:12.064 --> 00:30:14.061 showing you that indeed all of

NOTE Confidence: 0.791874297272727

00:30:14.061 --> 00:30:15.801 the unclassified we were able to

NOTE Confidence: 0.791874297272727

00:30:15.801 --> 00:30:18.050 get them into a 4141114 and so on.

NOTE Confidence: 0.791874297272727

00:30:18.050 --> 00:30:19.600 Biggest number was the hyper

NOTE Confidence: 0.791874297272727

00:30:19.600 --> 00:30:20.410 deployed numbers.

NOTE Confidence: 0.791874297272727

00:30:20.410 --> 00:30:22.154 So that can tell you that you can

NOTE Confidence: 0.791874297272727

00:30:22.154 --> 00:30:23.808 use RNA sequencing to basically

NOTE Confidence: 0.791874297272727

00:30:23.808 --> 00:30:25.748 predict what are the cytogenetic

NOTE Confidence: 0.791874297272727

00:30:25.748 --> 00:30:27.748 abnormalities at the single cell level.

NOTE Confidence: 0.791874297272727

00:30:27.750 --> 00:30:29.280 So now you can really say.

NOTE Confidence: 0.791874297272727

00:30:29.280 --> 00:30:31.790 Subclusters of those patients and

NOTE Confidence: 0.791874297272727

00:30:31.790 --> 00:30:34.300 subclonal abnormalities and we took

NOTE Confidence: 0.843883088695652

00:30:34.375 --> 00:30:37.175 it even more because we have potentially

NOTE Confidence: 0.843883088695652

00:30:37.175 --> 00:30:39.978 the ability to identify rare events.

NOTE Confidence: 0.843883088695652

00:30:39.980 --> 00:30:42.488 You can now find 814 translocation

NOTE Confidence: 0.843883088695652

00:30:42.488 --> 00:30:44.160 extremely rare in myeloma.

NOTE Confidence: 0.843883088695652

00:30:44.160 --> 00:30:45.910 We miss it in many patients and

NOTE Confidence: 0.843883088695652

00:30:45.910 --> 00:30:47.946 now we can find it with this math

NOTE Confidence: 0.843883088695652

00:30:47.946 --> 00:30:50.307 A and you can even look at their

NOTE Confidence: 0.843883088695652

00:30:50.307 --> 00:30:51.739 expression of certain genes.

NOTE Confidence: 0.843883088695652

00:30:51.740 --> 00:30:53.150 So for example they express

NOTE Confidence: 0.843883088695652

00:30:53.150 --> 00:30:54.278 high levels of Mike,

NOTE Confidence: 0.843883088695652

00:30:54.280 --> 00:30:56.850 they don't express other levels

NOTE Confidence: 0.843883088695652

00:30:56.850 --> 00:30:59.790 of other genes for example in 14.

NOTE Confidence: 0.843883088695652

00:30:59.790 --> 00:31:02.340 16 or in 1420 translocations.

NOTE Confidence: 0.843883088695652

00:31:02.340 --> 00:31:04.932 So now you can really go into the genetics

NOTE Confidence: 0.843883088695652

00:31:04.932 --> 00:31:06.983 and the transcriptional changes that

NOTE Confidence: 0.843883088695652

00:31:06.983 --> 00:31:09.533 are occurring in those rare events.

NOTE Confidence: 0.843883088695652

00:31:09.540 --> 00:31:11.404 So when you go back to also looking

NOTE Confidence: 0.843883088695652

00:31:11.404 --> 00:31:13.074 at the normal versus malignant

NOTE Confidence: 0.843883088695652

00:31:13.074 --> 00:31:14.598 cells in those patients,

NOTE Confidence: 0.843883088695652

00:31:14.600 --> 00:31:16.744 you can also ask questions that are very

NOTE Confidence: 0.843883088695652

00:31:16.744 --> 00:31:18.976 specific to the phenotype of those patients.

NOTE Confidence: 0.843883088695652

00:31:18.980 --> 00:31:19.910 So for example,

NOTE Confidence: 0.843883088695652

00:31:19.910 --> 00:31:22.647 we always think that CD 56 is highly

NOTE Confidence: 0.843883088695652

00:31:22.647 --> 00:31:25.117 expressed on malignant plasma cells.

NOTE Confidence: 0.843883088695652

00:31:25.120 --> 00:31:27.502 That's not actually true for the

NOTE Confidence: 0.843883088695652

00:31:27.502 --> 00:31:29.944 small numbers of 1416 and 14.

NOTE Confidence: 0.843883088695652

00:31:29.944 --> 00:31:30.766 20 cells,

NOTE Confidence: 0.843883088695652

00:31:30.770 --> 00:31:32.486 they are negative for CD 56

NOTE Confidence: 0.843883088695652

00:31:32.486 --> 00:31:33.910 and you can go on.

NOTE Confidence: 0.843883088695652

00:31:33.910 --> 00:31:36.250 So now you can really say if I'm going

NOTE Confidence: 0.843883088695652

00:31:36.250 --> 00:31:38.989 to develop a therapeutic target not BCMA,

NOTE Confidence: 0.843883088695652

00:31:38.990 --> 00:31:39.614 but others,

NOTE Confidence: 0.843883088695652

00:31:39.614 --> 00:31:41.486 I want to understand whether it's

NOTE Confidence: 0.843883088695652

00:31:41.486 --> 00:31:43.433 highly expressed on those cells with

NOTE Confidence: 0.843883088695652

00:31:43.433 --> 00:31:44.701 certain genetic abnormalities and

NOTE Confidence: 0.843883088695652

00:31:44.701 --> 00:31:46.777 those are the patients that I will not

NOTE Confidence: 0.843883088695652

00:31:46.777 --> 00:31:48.890 or I will include in my clinical trial.

NOTE Confidence: 0.843883088695652

00:31:48.890 --> 00:31:51.729 Now moving on to the gene expression data,

NOTE Confidence: 0.843883088695652

00:31:51.730 --> 00:31:54.586 you can see here these are the

NOTE Confidence: 0.843883088695652

00:31:54.586 --> 00:31:56.780 top highly expressed or the top.

NOTE Confidence: 0.843883088695652

00:31:56.780 --> 00:31:58.031 Significantly downregulated genes

NOTE Confidence: 0.843883088695652

00:31:58.031 --> 00:32:00.533 across the spectrum from mgus to

NOTE Confidence: 0.843883088695652

00:32:00.533 --> 00:32:02.039 smoldering myeloma to myeloma.

NOTE Confidence: 0.843883088695652

00:32:02.040 --> 00:32:03.370 And because again we have

NOTE Confidence: 0.843883088695652

00:32:03.370 --> 00:32:04.434 huge numbers of cells,

NOTE Confidence: 0.843883088695652

00:32:04.440 --> 00:32:05.574 you have more,

NOTE Confidence: 0.843883088695652

00:32:05.574 --> 00:32:08.220 you have a better ability to detect

NOTE Confidence: 0.843883088695652

00:32:08.299 --> 00:32:10.074 genes that really are modulated

NOTE Confidence: 0.843883088695652

00:32:10.074 --> 00:32:12.989 as you go on to progress like.

NOTE Confidence: 0.843883088695652

00:32:12.990 --> 00:32:14.838 T3 which is a leukemia growth factor

NOTE Confidence: 0.843883088695652

00:32:14.838 --> 00:32:16.682 as well or transcriptional factor as

NOTE Confidence: 0.843883088695652

00:32:16.682 --> 00:32:18.999 well as many other genes that get

NOTE Confidence: 0.843883088695652

00:32:19.062 --> 00:32:20.946 down regulated as you progress but

NOTE Confidence: 0.843883088695652

00:32:20.946 --> 00:32:23.280 also you can identify new targets

NOTE Confidence: 0.843883088695652

00:32:23.280 --> 00:32:25.420 potentially for developing therapeutics

NOTE Confidence: 0.843883088695652

00:32:25.420 --> 00:32:28.688 or new by specifics or new cartes.

NOTE Confidence: 0.843883088695652

00:32:28.690 --> 00:32:31.588 And then we developed a signature

NOTE Confidence: 0.843883088695652

00:32:31.590 --> 00:32:33.739 that was developed not from the normal

NOTE Confidence: 0.843883088695652

00:32:33.739 --> 00:32:35.653 plasma cells but from the malignant

NOTE Confidence: 0.843883088695652

00:32:35.653 --> 00:32:37.525 plasma cells and it was increasing

NOTE Confidence: 0.843883088695652

00:32:37.525 --> 00:32:39.628 as you go on from mgus to myeloma.

NOTE Confidence: 0.843883088695652

00:32:39.630 --> 00:32:42.332 And that signature by NMF by non

NOTE Confidence: 0.843883088695652

00:32:42.332 --> 00:32:44.562 matrix factorization was able to also

NOTE Confidence: 0.843883088695652

00:32:44.562 --> 00:32:46.886 detect when we applied it to compass

NOTE Confidence: 0.843883088695652

00:32:46.959 --> 00:32:49.465 data which is the overt myeloma data,

NOTE Confidence: 0.843883088695652

00:32:49.470 --> 00:32:51.480 it showed us a progression free

NOTE Confidence: 0.843883088695652

00:32:51.480 --> 00:32:52.820 survival and overall survival

NOTE Confidence: 0.843883088695652

00:32:52.882 --> 00:32:54.826 difference and it could be predictive

NOTE Confidence: 0.843883088695652

00:32:54.826 --> 00:32:57.010 of prognostic risk in those patients.

NOTE Confidence: 0.843883088695652

00:32:57.010 --> 00:32:58.590 So if you put that.

NOTE Confidence: 0.843883088695652

00:32:58.590 --> 00:33:00.984 In those patients as well as

NOTE Confidence: 0.843883088695652

00:33:00.984 --> 00:33:03.070 looking at the proliferation index,

NOTE Confidence: 0.843883088695652

00:33:03.070 --> 00:33:04.445 you can actually stratify the

NOTE Confidence: 0.843883088695652

00:33:04.445 --> 00:33:05.545 patients as low risk,

NOTE Confidence: 0.843883088695652

00:33:05.550 --> 00:33:07.446 intermediate and high risk even in

NOTE Confidence: 0.843883088695652

00:33:07.446 --> 00:33:09.649 the compass data in those patients.

NOTE Confidence: 0.843883088695652

00:33:09.650 --> 00:33:11.477 We then applied it to the gene

NOTE Confidence: 0.843883088695652

00:33:11.477 --> 00:33:13.208 expression data to all gene expression

NOTE Confidence: 0.843883088695652

00:33:13.208 --> 00:33:15.294 data from mgus to myeloma and indeed

NOTE Confidence: 0.843883088695652

00:33:15.352 --> 00:33:17.110 show that this can be predictive.

NOTE Confidence: 0.843883088695652

00:33:17.110 --> 00:33:19.378 So again not only genomics like

NOTE Confidence: 0.843883088695652

00:33:19.378 --> 00:33:21.370 DNA data that we have.

NOTE Confidence: 0.843883088695652

00:33:21.370 --> 00:33:23.225 Like map kinase mutations and so on

NOTE Confidence: 0.843883088695652

00:33:23.225 --> 00:33:25.129 can be predictive of who will progress.

NOTE Confidence: 0.843883088695652

00:33:25.130 --> 00:33:26.770 Now at the RNA level,

NOTE Confidence: 0.856670312105263

00:33:26.770 --> 00:33:28.378 we also have a gene expression

NOTE Confidence: 0.856670312105263

00:33:28.378 --> 00:33:30.103 profile that can be predictive of

NOTE Confidence: 0.856670312105263

00:33:30.103 --> 00:33:32.189 who would progress and who will not.

NOTE Confidence: 0.856670312105263

00:33:32.190 --> 00:33:34.570 So moving on to the immune system,

NOTE Confidence: 0.856670312105263

00:33:34.570 --> 00:33:37.030 here I'm showing you that the

NOTE Confidence: 0.856670312105263

00:33:37.030 --> 00:33:39.610 tumor system is an ecosystem.

NOTE Confidence: 0.856670312105263

00:33:39.610 --> 00:33:41.410 You cannot look only at the cancer cells,

NOTE Confidence: 0.856670312105263

00:33:41.410 --> 00:33:43.453 you need to look at the cancer and immune

NOTE Confidence: 0.856670312105263

00:33:43.453 --> 00:33:45.623 cells and of course not immune cells to

NOTE Confidence: 0.856670312105263

00:33:45.623 --> 00:33:47.409 understand better what causes progression.

NOTE Confidence: 0.856670312105263

00:33:47.410 --> 00:33:49.360 So the first thing we did a few years ago

NOTE Confidence: 0.856670312105263

00:33:49.411 --> 00:33:51.266 is again we did single cell sequencing.

NOTE Confidence: 0.856670312105263

00:33:51.270 --> 00:33:53.454 Of the immune cells in the bone marrow

NOTE Confidence: 0.856670312105263

00:33:53.454 --> 00:33:55.319 from MGUS smoldering to myeloma.

NOTE Confidence: 0.856670312105263

00:33:55.320 --> 00:33:57.231 And indeed what was surprising is we

NOTE Confidence: 0.856670312105263

00:33:57.231 --> 00:33:58.771 found that there were compositional

NOTE Confidence: 0.856670312105263

00:33:58.771 --> 00:34:01.095 changes that happened as early as mgus.

NOTE Confidence: 0.856670312105263

00:34:01.100 --> 00:34:02.780 It looked almost like myeloma.

NOTE Confidence: 0.856670312105263

00:34:02.780 --> 00:34:04.621 And we were shocked because we usually

NOTE Confidence: 0.856670312105263

00:34:04.621 --> 00:34:06.440 think that mgus is a benign disease.

NOTE Confidence: 0.856670312105263

00:34:06.440 --> 00:34:07.178 You're walking around,

NOTE Confidence: 0.856670312105263

00:34:07.178 --> 00:34:09.500 you have a very small chance of progression.

NOTE Confidence: 0.856670312105263

00:34:09.500 --> 00:34:11.390 Why would your immune system be so

NOTE Confidence: 0.856670312105263

00:34:11.390 --> 00:34:13.280 altered that it looks like myeloma?

NOTE Confidence: 0.856670312105263

00:34:13.280 --> 00:34:15.198 So we found T regs are increased,

NOTE Confidence: 0.856670312105263

00:34:15.200 --> 00:34:16.628 16 monocytes are increased,

NOTE Confidence: 0.856670312105263

00:34:16.628 --> 00:34:18.056 NK cells are altered,

NOTE Confidence: 0.856670312105263

00:34:18.060 --> 00:34:20.478 and then later on you have

NOTE Confidence: 0.856670312105263

00:34:20.478 --> 00:34:21.687 further functional changes.

NOTE Confidence: 0.856670312105263

00:34:21.690 --> 00:34:25.050 You have loss of the memory cytotoxic

NOTE Confidence: 0.856670312105263

00:34:25.050 --> 00:34:28.330 CD8 cells and then you start having less

NOTE Confidence: 0.856670312105263

00:34:28.406 --> 00:34:31.024 granzyme K which are the earlier stem

NOTE Confidence: 0.856670312105263

00:34:31.024 --> 00:34:34.307 cells and more granzyme B in those patients.

NOTE Confidence: 0.856670312105263

00:34:34.310 --> 00:34:35.480 And this is just showing you

NOTE Confidence: 0.856670312105263

00:34:35.480 --> 00:34:36.260 some of those changes.

NOTE Confidence: 0.856670312105263

00:34:36.260 --> 00:34:38.801 You can see here those memory excitotoxic

NOTE Confidence: 0.856670312105263

00:34:38.801 --> 00:34:40.918 cells almost completely depleted in

NOTE Confidence: 0.856670312105263

00:34:40.918 --> 00:34:42.666 patients with smoldering myeloma,

NOTE Confidence: 0.856670312105263

00:34:42.670 --> 00:34:43.730 sorry, with overt myeloma.

NOTE Confidence: 0.856670312105263

00:34:43.730 --> 00:34:46.018 So we went on to ask a couple

NOTE Confidence: 0.856670312105263

00:34:46.018 --> 00:34:46.966 of other questions.

NOTE Confidence: 0.856670312105263

00:34:46.970 --> 00:34:47.568 One is,

NOTE Confidence: 0.856670312105263

00:34:47.568 --> 00:34:49.661 are those changes altered if I treat

NOTE Confidence: 0.856670312105263

00:34:49.661 --> 00:34:50.950 someone with smoldering myeloma

NOTE Confidence: 0.856670312105263

00:34:50.950 --> 00:34:53.560 and can we expand that in also the

NOTE Confidence: 0.856670312105263

00:34:53.560 --> 00:34:55.430 peripheral blood of those patients?

NOTE Confidence: 0.856670312105263

00:34:55.430 --> 00:34:57.590 So this is work by Romanos,

NOTE Confidence: 0.856670312105263

00:34:57.590 --> 00:34:59.870 just got published a couple of weeks ago,

NOTE Confidence: 0.856670312105263

00:34:59.870 --> 00:35:03.020 again also in cancer cell where we took

NOTE Confidence: 0.856670312105263

00:35:03.020 --> 00:35:05.330 samples from patients on a clinical trial.

NOTE Confidence: 0.856670312105263

00:35:05.330 --> 00:35:07.420 With Elotuzumab limited dexamethasone 51

NOTE Confidence: 0.856670312105263

00:35:07.420 --> 00:35:10.308 patients who were treated on high risk

NOTE Confidence: 0.856670312105263

00:35:10.308 --> 00:35:12.522 smoldering trial and we took samples

NOTE Confidence: 0.856670312105263

00:35:12.522 --> 00:35:14.776 baseline cycle nine and end of therapy.

NOTE Confidence: 0.856670312105263

00:35:14.780 --> 00:35:16.376 And what we found is we

NOTE Confidence: 0.856670312105263

00:35:16.376 --> 00:35:17.960 found a couple of things.

NOTE Confidence: 0.856670312105263

00:35:17.960 --> 00:35:19.228 First is of course,

NOTE Confidence: 0.856670312105263

00:35:19.228 --> 00:35:21.130 the compositional changes were very similar

NOTE Confidence: 0.856670312105263

00:35:21.185 --> 00:35:23.193 to what you expected in our other study,

NOTE Confidence: 0.856670312105263

00:35:23.200 --> 00:35:26.260 but now it's a much bigger #190 samples.

NOTE Confidence: 0.856670312105263

00:35:26.260 --> 00:35:28.735 So indeed more T regs,

NOTE Confidence: 0.856670312105263

00:35:28.740 --> 00:35:32.560 more CD4 TNS and so on.

NOTE Confidence: 0.856670312105263

00:35:32.560 --> 00:35:34.042 But what we found that was

NOTE Confidence: 0.856670312105263

00:35:34.042 --> 00:35:35.579 interesting is a couple of things.

NOTE Confidence: 0.856670312105263

00:35:35.580 --> 00:35:35.878 One,

NOTE Confidence: 0.856670312105263

00:35:35.878 --> 00:35:37.666 because we had single cell TCR

NOTE Confidence: 0.856670312105263

00:35:37.666 --> 00:35:39.639 sequencing on all of those patients,

NOTE Confidence: 0.856670312105263

00:35:39.640 --> 00:35:41.794 we found that you actually have

NOTE Confidence: 0.856670312105263

00:35:41.794 --> 00:35:43.650 a significant change in the

NOTE Confidence: 0.856670312105263

00:35:43.650 --> 00:35:45.726 diversity of the T cells even

NOTE Confidence: 0.856670312105263

00:35:45.726 --> 00:35:47.360 in early smoldering myeloma.

NOTE Confidence: 0.856670312105263

00:35:47.360 --> 00:35:49.624 So this is just showing you when I

NOTE Confidence: 0.856670312105263

00:35:49.624 --> 00:35:51.998 resample the TCR in all of those patients,

NOTE Confidence: 0.856670312105263

00:35:52.000 --> 00:35:54.672 always we had a smaller diversity in the

NOTE Confidence: 0.856670312105263

00:35:54.672 --> 00:35:56.698 healthy compared to smoldering myeloma.

NOTE Confidence: 0.856670312105263

00:35:56.700 --> 00:35:58.632 So it shrinks significantly and you

NOTE Confidence: 0.856670312105263

00:35:58.632 --> 00:36:00.687 would think that it shrinks because

NOTE Confidence: 0.856670312105263

00:36:00.687 --> 00:36:02.793 you have one clone that expands.

NOTE Confidence: 0.856670312105263

00:36:02.800 --> 00:36:05.770 So the diversity is smaller and indeed.

NOTE Confidence: 0.856670312105263

00:36:05.770 --> 00:36:07.310 It is clonal expansion,

NOTE Confidence: 0.856670312105263

00:36:07.310 --> 00:36:08.426 but it's not just one clone,

NOTE Confidence: 0.856670312105263

00:36:08.430 --> 00:36:09.954 it's multiple clones and

NOTE Confidence: 0.856670312105263

00:36:09.954 --> 00:36:12.240 some of them are very small

NOTE Confidence: 0.85436714

00:36:12.317 --> 00:36:15.029 clones that expand in those patients.

NOTE Confidence: 0.85436714

00:36:15.030 --> 00:36:17.070 Now, interestingly, that expansion

NOTE Confidence: 0.85436714

00:36:17.070 --> 00:36:19.932 was merely in granzyme BC8T cells.

NOTE Confidence: 0.85436714

00:36:19.932 --> 00:36:21.987 As well as T regs,

NOTE Confidence: 0.85436714

00:36:21.990 --> 00:36:23.575 and you can see it here, uh,

NOTE Confidence: 0.85436714

00:36:23.575 --> 00:36:26.060 nicely that those clonal T cell expansions

NOTE Confidence: 0.85436714

00:36:26.060 --> 00:36:29.009 were in the CD 8 terms in those patients.

NOTE Confidence: 0.85436714

00:36:29.010 --> 00:36:31.522 So that tells you the immune system is

NOTE Confidence: 0.85436714

00:36:31.522 --> 00:36:33.929 trying to react to the cancer cells,

NOTE Confidence: 0.85436714

00:36:33.930 --> 00:36:35.454 but it's exhaustive and it cannot

NOTE Confidence: 0.85436714

00:36:35.454 --> 00:36:37.674 do a very good job in responding to

NOTE Confidence: 0.85436714

00:36:37.674 --> 00:36:39.390 those cancer cells and that could

NOTE Confidence: 0.85436714

00:36:39.448 --> 00:36:41.393 potentially be useful for therapeutic

NOTE Confidence: 0.85436714

00:36:41.393 --> 00:36:42.949 interventions in the future,

NOTE Confidence: 0.85436714

00:36:42.950 --> 00:36:46.326 especially with TCR therapeutics as we go on.

NOTE Confidence: 0.85436714

00:36:46.330 --> 00:36:48.530 Now, the other question we said is can

NOTE Confidence: 0.85436714

00:36:48.530 --> 00:36:51.170 we use the immune system as a biomarker?

NOTE Confidence: 0.85436714

00:36:51.170 --> 00:36:52.064 Of disease progression,

NOTE Confidence: 0.85436714

00:36:52.064 --> 00:36:53.852 can I use an immune signature

NOTE Confidence: 0.85436714

00:36:53.852 --> 00:36:55.575 that tells me this patient will

NOTE Confidence: 0.85436714

00:36:55.575 --> 00:36:56.940 respond to therapy or not?

NOTE Confidence: 0.85436714

00:36:56.940 --> 00:36:58.725 And after therapy did they

NOTE Confidence: 0.85436714

00:36:58.725 --> 00:37:00.153 normalize their immune system.

NOTE Confidence: 0.85436714

00:37:00.160 --> 00:37:02.104 So indeed we found the signature

NOTE Confidence: 0.85436714

00:37:02.104 --> 00:37:04.067 that is predictive of response which

NOTE Confidence: 0.85436714

00:37:04.067 --> 00:37:06.467 is if you are reactive to the tumor

NOTE Confidence: 0.85436714

00:37:06.533 --> 00:37:08.717 cells then you have a better chance

NOTE Confidence: 0.85436714

00:37:08.717 --> 00:37:11.031 of responding to therapy and a

NOTE Confidence: 0.85436714

00:37:11.031 --> 00:37:12.859 long-term progression free survival.

NOTE Confidence: 0.85436714

00:37:12.860 --> 00:37:15.282 And post therapy if you normalize your

NOTE Confidence: 0.85436714

00:37:15.282 --> 00:37:17.726 immune system indeed you have a much

NOTE Confidence: 0.85436714

00:37:17.726 --> 00:37:19.401 better progression free survival and

NOTE Confidence: 0.85436714

00:37:19.401 --> 00:37:21.906 that tells us that indeed those patients.

NOTE Confidence: 0.85436714

00:37:21.910 --> 00:37:24.034 Can have that normalization of the

NOTE Confidence: 0.85436714

00:37:24.034 --> 00:37:26.050 immune system along with MRD and

NOTE Confidence: 0.85436714

00:37:26.050 --> 00:37:27.670 we're hoping to apply that for

NOTE Confidence: 0.85436714

00:37:27.670 --> 00:37:29.770 all of the future studies so that

NOTE Confidence: 0.85436714

00:37:29.770 --> 00:37:31.586 you don't only look for Mart,

NOTE Confidence: 0.85436714

00:37:31.586 --> 00:37:34.114 you also look for pin in those patients

NOTE Confidence: 0.85436714

00:37:34.114 --> 00:37:36.458 both therapy and your normalization.

NOTE Confidence: 0.85436714

00:37:36.460 --> 00:37:38.556 And this is just showing you some of

NOTE Confidence: 0.85436714

00:37:38.556 --> 00:37:40.607 those factors specifically for grand time,

NOTE Confidence: 0.85436714

00:37:40.610 --> 00:37:40.935 OK,

NOTE Confidence: 0.85436714

00:37:40.935 --> 00:37:43.210 as you go on to that normalization

NOTE Confidence: 0.85436714

00:37:43.210 --> 00:37:44.560 in those patients,

NOTE Confidence: 0.85436714

00:37:44.560 --> 00:37:46.675 now we moved on into the blood and said,

NOTE Confidence: 0.85436714

00:37:46.680 --> 00:37:48.528 can we use the blood instead of the

NOTE Confidence: 0.85436714

00:37:48.528 --> 00:37:50.220 bone marrow again in those patients.

NOTE Confidence: 0.85436714

00:37:50.220 --> 00:37:52.439 So indeed here is just showing you

NOTE Confidence: 0.85436714

00:37:52.439 --> 00:37:54.466 the volcano plot of those patients

NOTE Confidence: 0.85436714

00:37:54.466 --> 00:37:56.818 and indeed you have the same changes

NOTE Confidence: 0.85436714

00:37:56.883 --> 00:37:59.286 in the blood as you have in the bone

NOTE Confidence: 0.85436714

00:37:59.286 --> 00:38:01.468 marrow of those patients and the same

NOTE Confidence: 0.85436714

00:38:01.468 --> 00:38:04.000 thing also happens for the T cell receptor.

NOTE Confidence: 0.85436714

00:38:04.000 --> 00:38:05.917 So this is just showing you the T cell

NOTE Confidence: 0.85436714

00:38:05.917 --> 00:38:07.287 diversity and the peripheral blood.

NOTE Confidence: 0.85436714

00:38:07.290 --> 00:38:09.036 And it mimicked exactly what happens

NOTE Confidence: 0.85436714

00:38:09.036 --> 00:38:11.210 in the bone marrow of those patients.

NOTE Confidence: 0.85436714

00:38:11.210 --> 00:38:12.071 Not only that,

NOTE Confidence: 0.85436714

00:38:12.071 --> 00:38:14.080 if I just do another confusion plot

NOTE Confidence: 0.85436714

00:38:14.147 --> 00:38:16.240 and say give me randomly anyone who

NOTE Confidence: 0.85436714

00:38:16.240 --> 00:38:18.235 has a peripheral blood sample and I

NOTE Confidence: 0.85436714

00:38:18.235 --> 00:38:20.609 will tell you if they have mgus or not.

NOTE Confidence: 0.85436714

00:38:20.609 --> 00:38:22.520 It was very predictive in the blood

NOTE Confidence: 0.85436714

00:38:22.581 --> 00:38:24.492 by the immune cell signature that I

NOTE Confidence: 0.85436714

00:38:24.492 --> 00:38:26.507 can tell you this one is healthy,

NOTE Confidence: 0.85436714

00:38:26.510 --> 00:38:27.558 this one is mgus.

NOTE Confidence: 0.85436714

00:38:27.558 --> 00:38:29.635 Now that opened the door for us to

NOTE Confidence: 0.85436714

00:38:29.635 --> 00:38:31.411 say can we use it also for cancer

NOTE Confidence: 0.85436714

00:38:31.472 --> 00:38:32.669 screening in general.

NOTE Confidence: 0.85436714

00:38:32.670 --> 00:38:34.554 And this is something that we're

NOTE Confidence: 0.85436714

00:38:34.554 --> 00:38:36.090 trying to develop right now.

NOTE Confidence: 0.85436714

00:38:36.090 --> 00:38:37.330 So with that we have.

NOTE Confidence: 0.85436714

00:38:37.330 --> 00:38:38.144 Big data,

NOTE Confidence: 0.85436714

00:38:38.144 --> 00:38:38.958 big questions,

NOTE Confidence: 0.85436714

00:38:38.958 --> 00:38:42.035 which means that we have 317 new samples

NOTE Confidence: 0.85436714

00:38:42.035 --> 00:38:44.105 that we sequenced bone marrow and

NOTE Confidence: 0.85436714

00:38:44.105 --> 00:38:46.321 peripheral blood to really ask those

NOTE Confidence: 0.85436714

00:38:46.321 --> 00:38:48.131 bigger questions of immune regulation

NOTE Confidence: 0.85436714

00:38:48.196 --> 00:38:49.976 in mgus and smoldering myeloma.

NOTE Confidence: 0.85436714

00:38:49.980 --> 00:38:51.870 And now you can have more

NOTE Confidence: 0.85436714

00:38:51.870 --> 00:38:53.130 expression data that really

NOTE Confidence: 0.857445490526316

00:38:53.193 --> 00:38:54.909 defines the progression signatures

NOTE Confidence: 0.857445490526316

00:38:54.909 --> 00:38:57.054 because you have more samples,

NOTE Confidence: 0.857445490526316

00:38:57.060 --> 00:38:59.082 you can differentiate what causes progression

NOTE Confidence: 0.857445490526316

00:38:59.082 --> 00:39:01.020 from mgus to smoldering to myeloma,

NOTE Confidence: 0.857445490526316

00:39:01.020 --> 00:39:04.317 not causes what is associated with it.

NOTE Confidence: 0.857445490526316

00:39:04.320 --> 00:39:05.755 Hopefully causative would be all

NOTE Confidence: 0.857445490526316

00:39:05.755 --> 00:39:07.380 of the functional studies that we.

NOTE Confidence: 0.857445490526316

00:39:07.380 --> 00:39:09.783 Can do in vivo and in vitro to say

NOTE Confidence: 0.857445490526316

00:39:09.783 --> 00:39:11.965 what is really causing progression

NOTE Confidence: 0.857445490526316

00:39:11.965 --> 00:39:14.274 in those patients and then of

NOTE Confidence: 0.857445490526316

00:39:14.274 --> 00:39:16.122 course at the gene expression level.

NOTE Confidence: 0.857445490526316

00:39:16.130 --> 00:39:18.010 So at the compositional changes,

NOTE Confidence: 0.857445490526316

00:39:18.010 --> 00:39:20.377 most of the things happen at mgus and then

NOTE Confidence: 0.857445490526316

00:39:20.377 --> 00:39:22.706 they stay constant or increased slightly.

NOTE Confidence: 0.857445490526316

00:39:22.710 --> 00:39:24.897 But at the signatures of the genes you have

NOTE Confidence: 0.857445490526316

00:39:24.897 --> 00:39:27.468 a huge difference in interference signaling.

NOTE Confidence: 0.857445490526316

00:39:27.470 --> 00:39:29.612 You see that sudden change of granzyme

NOTE Confidence: 0.857445490526316

00:39:29.612 --> 00:39:31.701 B increasing and you have more of

NOTE Confidence: 0.857445490526316

00:39:31.701 --> 00:39:33.369 those granzyme BCZ its cells that

NOTE Confidence: 0.857445490526316

00:39:33.430 --> 00:39:35.341 are more senescent as you can see

NOTE Confidence: 0.857445490526316

00:39:35.341 --> 00:39:37.594 here with their expression of KR.

NOTE Confidence: 0.857445490526316

00:39:37.594 --> 00:39:39.506 One and less cytolytic.

NOTE Confidence: 0.857445490526316

00:39:39.510 --> 00:39:41.706 So they're not capable of really

NOTE Confidence: 0.857445490526316

00:39:41.706 --> 00:39:43.576 responding to the cancer cells

NOTE Confidence: 0.857445490526316

00:39:43.576 --> 00:39:45.956 and this is just showing you how

NOTE Confidence: 0.857445490526316

00:39:45.956 --> 00:39:48.217 altered immune system goes on from

NOTE Confidence: 0.857445490526316

00:39:48.217 --> 00:39:50.107 progression from mgus to myeloma.

NOTE Confidence: 0.857445490526316

00:39:50.110 --> 00:39:51.262 And then again because

NOTE Confidence: 0.857445490526316

00:39:51.262 --> 00:39:52.702 we have so many samples,

NOTE Confidence: 0.857445490526316

00:39:52.710 --> 00:39:54.118 especially low risk smoldering,

NOTE Confidence: 0.857445490526316

00:39:54.118 --> 00:39:56.548 which we think is likely more like

NOTE Confidence: 0.857445490526316

00:39:56.548 --> 00:39:58.361 an mgus and some of those mgus

NOTE Confidence: 0.857445490526316

00:39:58.361 --> 00:40:00.328 look more like smoldering myeloma.

NOTE Confidence: 0.857445490526316

00:40:00.330 --> 00:40:02.022 So the clinical factors of what

NOTE Confidence: 0.857445490526316

00:40:02.022 --> 00:40:04.465 we call mgus and what we call

NOTE Confidence: 0.857445490526316

00:40:04.465 --> 00:40:06.550 smoldering myeloma may actually be

NOTE Confidence: 0.857445490526316

00:40:06.550 --> 00:40:08.040 biologically completely different.

NOTE Confidence: 0.857445490526316

00:40:08.040 --> 00:40:09.590 And they are intermixed with

NOTE Confidence: 0.857445490526316

00:40:09.590 --> 00:40:10.830 mgus and smoldering myeloma.

NOTE Confidence: 0.857445490526316

00:40:10.830 --> 00:40:14.380 We have biological relevance from each other.

NOTE Confidence: 0.857445490526316

00:40:14.380 --> 00:40:16.473 So you can see here huge diversity

NOTE Confidence: 0.857445490526316

00:40:16.473 --> 00:40:18.353 changes that occur in some of the

NOTE Confidence: 0.857445490526316

00:40:18.353 --> 00:40:20.251 MGA samples as well as the smoldering

NOTE Confidence: 0.857445490526316

00:40:20.251 --> 00:40:22.506 myeloma samples in those populations.

NOTE Confidence: 0.857445490526316

00:40:22.510 --> 00:40:23.566 And then finally,

NOTE Confidence: 0.857445490526316

00:40:23.566 --> 00:40:25.678 we're starting to look at the

NOTE Confidence: 0.857445490526316

00:40:25.678 --> 00:40:27.120 spatial transcriptomics.

NOTE Confidence: 0.857445490526316

00:40:27.120 --> 00:40:28.744 But until then we started to look

NOTE Confidence: 0.857445490526316

00:40:28.744 --> 00:40:30.376 at the cells that basically are

NOTE Confidence: 0.857445490526316

00:40:30.376 --> 00:40:31.556 adhered to each other.

NOTE Confidence: 0.857445490526316

00:40:31.560 --> 00:40:33.800 What is close to a myeloma cell when

NOTE Confidence: 0.857445490526316

00:40:33.800 --> 00:40:35.821 we pull it in a CD130 is selection,

NOTE Confidence: 0.857445490526316

00:40:35.821 --> 00:40:38.040 and indeed we found many of the.

NOTE Confidence: 0.857445490526316

00:40:38.040 --> 00:40:43.367 B cells, granzyme key positive cells and.

NOTE Confidence: 0.857445490526316

00:40:43.370 --> 00:40:44.819 Megakaryocytes were highly,

NOTE Confidence: 0.857445490526316

00:40:44.819 --> 00:40:45.302 uh,

NOTE Confidence: 0.857445490526316

00:40:45.302 --> 00:40:46.268 you know,

NOTE Confidence: 0.857445490526316

00:40:46.270 --> 00:40:48.232 uh attached to the tumor cells

NOTE Confidence: 0.857445490526316

00:40:48.232 --> 00:40:50.654 indicating that there is a lot of

NOTE Confidence: 0.857445490526316

00:40:50.654 --> 00:40:52.050 interaction between those cells.

NOTE Confidence: 0.857445490526316

00:40:52.050 --> 00:40:53.947 So in the last few minutes I'll

NOTE Confidence: 0.857445490526316

00:40:53.947 --> 00:40:55.168 talk about clinical interception

NOTE Confidence: 0.857445490526316

00:40:55.168 --> 00:40:57.244 and we have done many clinical

NOTE Confidence: 0.857445490526316

00:40:57.244 --> 00:40:58.660 trials throughout the years,

NOTE Confidence: 0.857445490526316

00:40:58.660 --> 00:41:00.522 but now we're thinking of it more

NOTE Confidence: 0.857445490526316

00:41:00.522 --> 00:41:02.108 of that specific interception being

NOTE Confidence: 0.857445490526316

00:41:02.108 --> 00:41:03.943 precise in our interception what

NOTE Confidence: 0.857445490526316

00:41:03.943 --> 00:41:05.790 we call precision interception.

NOTE Confidence: 0.857445490526316

00:41:05.790 --> 00:41:07.624 So in the older days we have

NOTE Confidence: 0.857445490526316

00:41:07.624 --> 00:41:10.153 shown there is a proof of concept

NOTE Confidence: 0.857445490526316

00:41:10.153 --> 00:41:11.833 that indeed observation versus

NOTE Confidence: 0.857445490526316

00:41:11.833 --> 00:41:13.350 treatment treatment is better.

NOTE Confidence: 0.857445490526316

00:41:13.350 --> 00:41:14.995 In progression free survival and

NOTE Confidence: 0.857445490526316

00:41:14.995 --> 00:41:17.085 in one case overall survival with

NOTE Confidence: 0.857445490526316

00:41:17.085 --> 00:41:18.637 the Lenalidomide index studies.

NOTE Confidence: 0.857445490526316

00:41:18.640 --> 00:41:20.575 But these were early events

NOTE Confidence: 0.857445490526316

00:41:20.575 --> 00:41:21.736 or early attempts.

NOTE Confidence: 0.857445490526316

00:41:21.740 --> 00:41:24.236 Let's do something better than that.

NOTE Confidence: 0.857445490526316

00:41:24.240 --> 00:41:26.315 So our efforts are divided

NOTE Confidence: 0.857445490526316

00:41:26.315 --> 00:41:27.560 into early prevention,

NOTE Confidence: 0.857445490526316

00:41:27.560 --> 00:41:29.015 metformin, intermittent fasting,

NOTE Confidence: 0.857445490526316

00:41:29.015 --> 00:41:31.440 things that really prevent progression.

NOTE Confidence: 0.857445490526316

00:41:31.440 --> 00:41:33.240 Then we have targeted approaches,

NOTE Confidence: 0.857445490526316

00:41:33.240 --> 00:41:35.208 MAP kinase mutations,

NOTE Confidence: 0.857445490526316

00:41:35.208 --> 00:41:37.770 1114 with venetoclax, we're looking

NOTE Confidence: 0.857445490526316

00:41:37.770 --> 00:41:39.540 at synthetically salty in one queue,

NOTE Confidence: 0.857445490526316

00:41:39.540 --> 00:41:41.220 abnormalities and so on.

NOTE Confidence: 0.857445490526316

00:41:41.220 --> 00:41:42.900 Then we have Immunotherapeutics,

NOTE Confidence: 0.857445490526316

00:41:42.900 --> 00:41:43.312 vaccines,

NOTE Confidence: 0.857445490526316

00:41:43.312 --> 00:41:45.784 T cell therapy with carton by

NOTE Confidence: 0.857445490526316

00:41:45.784 --> 00:41:47.320 specifics and so on,

NOTE Confidence: 0.857445490526316

00:41:47.320 --> 00:41:48.528 and then novel combinations.

NOTE Confidence: 0.857445490526316

00:41:48.528 --> 00:41:50.840 And we're doing now 4 drug regimen.

NOTE Confidence: 0.792223144166667

00:41:50.840 --> 00:41:52.640 There are RVD, which is basically

NOTE Confidence: 0.792223144166667

00:41:52.640 --> 00:41:54.510 the standard of care of myeloma.

NOTE Confidence: 0.792223144166667

00:41:54.510 --> 00:41:56.472 Bringing it on into an earlier

NOTE Confidence: 0.792223144166667

00:41:56.472 --> 00:41:58.870 setting with the idea that can we

NOTE Confidence: 0.792223144166667

00:41:58.870 --> 00:42:00.910 cure the patients at the earlier

NOTE Confidence: 0.792223144166667

00:42:00.910 --> 00:42:02.979 precursor stages and at least can we

NOTE Confidence: 0.792223144166667

00:42:02.979 --> 00:42:05.041 make sure that we do never develop

NOTE Confidence: 0.792223144166667

00:42:05.041 --> 00:42:06.943 end organ damage in those patients.

NOTE Confidence: 0.792223144166667

00:42:06.950 --> 00:42:08.378 So I'll just give you a couple

NOTE Confidence: 0.792223144166667

00:42:08.378 --> 00:42:09.629 of examples of those trials.

NOTE Confidence: 0.792223144166667

00:42:09.630 --> 00:42:11.946 This one is ongoing right now,

NOTE Confidence: 0.792223144166667

00:42:11.950 --> 00:42:13.534 immunol prism and this is the

NOTE Confidence: 0.792223144166667

00:42:13.534 --> 00:42:15.550 first time we treat patients with

NOTE Confidence: 0.792223144166667

00:42:15.550 --> 00:42:17.350 immunotherapy in smoldering myeloma.

NOTE Confidence: 0.792223144166667

00:42:17.350 --> 00:42:19.594 So we chose these inclusion criteria

NOTE Confidence: 0.792223144166667

00:42:19.594 --> 00:42:21.494 for high risk smoldering myeloma

NOTE Confidence: 0.792223144166667

00:42:21.494 --> 00:42:22.842 and we're randomizing patients

NOTE Confidence: 0.792223144166667

00:42:22.842 --> 00:42:25.270 2 to one to tech listenable.

NOTE Confidence: 0.792223144166667

00:42:25.270 --> 00:42:28.020 Bcma CD3 antibody by specific

NOTE Confidence: 0.792223144166667

00:42:28.020 --> 00:42:29.670 antibody or landex,

NOTE Confidence: 0.792223144166667

00:42:29.670 --> 00:42:32.162 our first six patients were only to

NOTE Confidence: 0.792223144166667

00:42:32.162 --> 00:42:34.139 Christmas because the FDA mandated that

NOTE Confidence: 0.792223144166667

00:42:34.139 --> 00:42:37.110 we go very slowly and we do lose reduction.

NOTE Confidence: 0.792223144166667

00:42:37.110 --> 00:42:38.740 And then now we're actually

NOTE Confidence: 0.792223144166667

00:42:38.740 --> 00:42:40.736 randomizing patients and we're up to

NOTE Confidence: 0.792223144166667

00:42:40.736 --> 00:42:42.261 18 patients currently either treated

NOTE Confidence: 0.792223144166667

00:42:42.261 --> 00:42:44.502 or going to treat soon with the

NOTE Confidence: 0.792223144166667

00:42:44.502 --> 00:42:46.107 primary endpoint of response rate.

NOTE Confidence: 0.792223144166667

00:42:46.110 --> 00:42:47.940 And I can tell you preliminary,

NOTE Confidence: 0.792223144166667

00:42:47.940 --> 00:42:50.280 we are not seeing the same rate of CRS.

NOTE Confidence: 0.792223144166667

00:42:50.280 --> 00:42:51.911 We are not seeing the same rate

NOTE Confidence: 0.792223144166667

00:42:51.911 --> 00:42:53.548 of infections you see in other

NOTE Confidence: 0.792223144166667

00:42:53.548 --> 00:42:55.023 patients and we're seeing impressive

NOTE Confidence: 0.792223144166667

00:42:55.023 --> 00:42:56.379 responses in those patients.

NOTE Confidence: 0.792223144166667

00:42:56.380 --> 00:42:57.962 And then of course the other option

NOTE Confidence: 0.792223144166667

00:42:57.962 --> 00:43:00.141 is can I use the one and done cartee

NOTE Confidence: 0.792223144166667

00:43:00.141 --> 00:43:01.708 therapy as early as possible when

NOTE Confidence: 0.792223144166667

00:43:01.708 --> 00:43:03.612 you have less tumor burden and when

NOTE Confidence: 0.792223144166667

00:43:03.612 --> 00:43:05.535 you have better T cell response

NOTE Confidence: 0.792223144166667

00:43:05.535 --> 00:43:07.580 and potentially will this be a

NOTE Confidence: 0.792223144166667

00:43:07.580 --> 00:43:09.245 curative intent in our patients.

NOTE Confidence: 0.792223144166667

00:43:09.250 --> 00:43:11.670 So we're hoping to open soon the first

NOTE Confidence: 0.792223144166667

00:43:11.670 --> 00:43:14.454 car T therapy in early precursor settings

NOTE Confidence: 0.792223144166667

00:43:14.454 --> 00:43:16.730 in high risk smoldering myeloma.

NOTE Confidence: 0.792223144166667

00:43:16.730 --> 00:43:18.137 And I can tell you when I

NOTE Confidence: 0.792223144166667

00:43:18.137 --> 00:43:19.190 submitted it to the FDA,

NOTE Confidence: 0.792223144166667

00:43:19.190 --> 00:43:20.880 the first thing I got

NOTE Confidence: 0.792223144166667

00:43:20.880 --> 00:43:22.232 back was absolutely not,

NOTE Confidence: 0.792223144166667

00:43:22.240 --> 00:43:24.624 you're not doing this and we were able

NOTE Confidence: 0.792223144166667

00:43:24.624 --> 00:43:26.897 to convince the FDA to give us the Ind.

NOTE Confidence: 0.792223144166667

00:43:26.900 --> 00:43:29.660 And we're hoping soon to open that trial.

NOTE Confidence: 0.792223144166667

00:43:29.660 --> 00:43:30.494 So with that,

NOTE Confidence: 0.792223144166667

00:43:30.494 --> 00:43:32.440 I hope I convince you that early

NOTE Confidence: 0.792223144166667

00:43:32.504 --> 00:43:34.589 detection and early interception in

NOTE Confidence: 0.792223144166667

00:43:34.589 --> 00:43:36.674 one disease like myeloma matters.

NOTE Confidence: 0.792223144166667

00:43:36.680 --> 00:43:38.384 And hopefully this can be applied

NOTE Confidence: 0.792223144166667

00:43:38.384 --> 00:43:40.374 to many other diseases and we can

NOTE Confidence: 0.792223144166667

00:43:40.374 --> 00:43:41.964 change the survival of our patients.

NOTE Confidence: 0.792223144166667

00:43:41.970 --> 00:43:44.418 And I want to thank of course amazing people,

NOTE Confidence: 0.792223144166667

00:43:44.420 --> 00:43:46.980 the lab, the clinical teams.

NOTE Confidence: 0.792223144166667

00:43:46.980 --> 00:43:48.505 And our collaborators from really

NOTE Confidence: 0.792223144166667

00:43:48.505 --> 00:43:49.725 all over the world,

NOTE Confidence: 0.792223144166667

00:43:49.730 --> 00:43:51.284 but all of course our funders

NOTE Confidence: 0.792223144166667

00:43:51.284 --> 00:43:53.140 stand up to cancer, MRI, FLS,

NOTE Confidence: 0.792223144166667

00:43:53.140 --> 00:43:53.550 NIH,

NOTE Confidence: 0.792223144166667

00:43:53.550 --> 00:43:55.190 our collaboration with gadgets

NOTE Confidence: 0.792223144166667

00:43:55.190 --> 00:43:57.209 who just basically does everything

NOTE Confidence: 0.792223144166667

00:43:57.209 --> 00:43:59.363 with us at the Broad Institute

NOTE Confidence: 0.792223144166667

00:43:59.363 --> 00:44:01.238 and above all our patients.

NOTE Confidence: 0.792223144166667

00:44:01.240 --> 00:44:01.790 Thank you.

NOTE Confidence: 0.85799748

00:44:05.450 --> 00:44:07.690 I mean, absolutely spectacular,

NOTE Confidence: 0.85799748

00:44:07.690 --> 00:44:09.160 incredibly, incredibly exciting.

NOTE Confidence: 0.85799748

00:44:09.160 --> 00:44:11.435 So we have doctor nefarious

NOTE Confidence: 0.85799748

00:44:11.435 --> 00:44:14.670 here as our panelist too.

NOTE Confidence: 0.85799748

00:44:14.670 --> 00:44:20.070 And maybe I have a quick question.

NOTE Confidence: 0.85799748

00:44:20.070 --> 00:44:22.570 Do you see correlations between,

NOTE Confidence: 0.85799748

00:44:22.570 --> 00:44:25.030 you know, the mutational spectrum and

NOTE Confidence: 0.85799748

00:44:25.030 --> 00:44:29.270 then the immune environment? Yeah.

NOTE Confidence: 0.594678492

00:44:29.710 --> 00:44:32.030 How do they happen? Yeah, we

NOTE Confidence: 0.946640661666667

00:44:32.040 --> 00:44:34.776 haven't even started putting it together.

NOTE Confidence: 0.946640661666667

00:44:34.780 --> 00:44:37.844 I mean it's it's an so if any

NOTE Confidence: 0.946640661666667

00:44:37.844 --> 00:44:39.070 bioinformaticians you have,

NOTE Confidence: 0.946640661666667

00:44:39.070 --> 00:44:40.194 please come because we

NOTE Confidence: 0.946640661666667

00:44:40.194 --> 00:44:41.599 have enough data for many,

NOTE Confidence: 0.946640661666667

00:44:41.600 --> 00:44:43.616 many years to analyze the data.

NOTE Confidence: 0.946640661666667

00:44:43.620 --> 00:44:46.113 But yes, now that we have that many samples,

NOTE Confidence: 0.946640661666667

00:44:46.120 --> 00:44:47.884 you can start asking the question

NOTE Confidence: 0.946640661666667

00:44:47.884 --> 00:44:50.499 in an 1114 or in a certain mutation,

NOTE Confidence: 0.946640661666667

00:44:50.500 --> 00:44:52.156 what are the immune, that's regulations.

NOTE Confidence: 0.946640661666667

00:44:52.160 --> 00:44:54.029 The older samples were very small numbers

NOTE Confidence: 0.946640661666667

00:44:54.029 --> 00:44:56.100 and of course if you start subdividing,

NOTE Confidence: 0.946640661666667

00:44:56.100 --> 00:44:58.718 if P53 haven't foreseen, you don't have.

NOTE Confidence: 0.946640661666667

00:44:58.720 --> 00:44:59.450 Of data.

NOTE Confidence: 0.946640661666667

00:44:59.450 --> 00:45:02.005 But now as we're enlarging the cohorts,

NOTE Confidence: 0.946640661666667

00:45:02.010 --> 00:45:04.110 we will start to see that correlation.

NOTE Confidence: 0.11864579

00:45:09.990 --> 00:45:11.240 Now you wanna ask a question,

NOTE Confidence: 0.767392458

00:45:11.250 --> 00:45:12.674 I think there there is a question in

NOTE Confidence: 0.767392458

00:45:12.674 --> 00:45:14.539 the chat, but Irene congratulations

NOTE Confidence: 0.767392458

00:45:14.539 --> 00:45:17.054 on your really tremendous success

NOTE Confidence: 0.767392458

00:45:17.054 --> 00:45:19.889 and in terms of promise study,

NOTE Confidence: 0.767392458

00:45:19.890 --> 00:45:23.026 I think that's really a successful enrollment

NOTE Confidence: 0.767392458

00:45:23.026 --> 00:45:25.968 and of extensive data generated there.

NOTE Confidence: 0.767392458

00:45:25.970 --> 00:45:28.510 In terms of potential future

NOTE Confidence: 0.767392458

00:45:28.510 --> 00:45:29.526 clinical applications,

NOTE Confidence: 0.767392458

00:45:29.530 --> 00:45:31.595 I mean terms like number needed to

NOTE Confidence: 0.767392458

00:45:31.595 --> 00:45:33.608 screen are used for breast cancer,

NOTE Confidence: 0.767392458

00:45:33.610 --> 00:45:35.630 80 or 100 seems acceptable.

NOTE Confidence: 0.767392458

00:45:35.630 --> 00:45:37.328 What's your sense of number of

NOTE Confidence: 0.767392458

00:45:37.328 --> 00:45:38.805 needed to screen potentially for

NOTE Confidence: 0.767392458

00:45:38.805 --> 00:45:40.245 high risk patients with myeloma?

NOTE Confidence: 0.767392458

00:45:40.250 --> 00:45:43.076 Or perhaps those with family history.

NOTE Confidence: 0.767392458

00:45:43.080 --> 00:45:43.690 Yeah,

NOTE Confidence: 0.907051688333333

00:45:43.700 --> 00:45:45.344 great question. And this is indeed

NOTE Confidence: 0.907051688333333

00:45:45.344 --> 00:45:46.921 exactly the question of how can

NOTE Confidence: 0.907051688333333

00:45:46.921 --> 00:45:48.199 we make it standard of care,

NOTE Confidence: 0.907051688333333

00:45:48.200 --> 00:45:49.604 what is needed for us to

NOTE Confidence: 0.907051688333333

00:45:49.604 --> 00:45:51.140 switch to an early detection.

NOTE Confidence: 0.907051688333333

00:45:51.140 --> 00:45:53.443 I think unlike breast cancer and other

NOTE Confidence: 0.907051688333333

00:45:53.443 --> 00:45:55.733 solid tumors where you know that if you

NOTE Confidence: 0.907051688333333

00:45:55.733 --> 00:45:58.018 cut it and the patient survived in mgus,

NOTE Confidence: 0.907051688333333

00:45:58.020 --> 00:46:00.477 if you find it, what is the,

NOTE Confidence: 0.907051688333333

00:46:00.480 --> 00:46:01.912 what's the relevance, right,

NOTE Confidence: 0.907051688333333

00:46:01.912 --> 00:46:03.344 because we know sensitivity

NOTE Confidence: 0.907051688333333

00:46:03.344 --> 00:46:04.758 and specificity is very good.

NOTE Confidence: 0.907051688333333

00:46:04.760 --> 00:46:06.656 So that's not the problem that we have.

NOTE Confidence: 0.907051688333333

00:46:06.660 --> 00:46:09.180 So I think what we have thought

NOTE Confidence: 0.907051688333333

00:46:09.180 --> 00:46:10.260 of is actually.

NOTE Confidence: 0.907051688333333

00:46:10.260 --> 00:46:12.510 That showed that indeed interception

NOTE Confidence: 0.907051688333333

00:46:12.510 --> 00:46:14.310 matters because then early

NOTE Confidence: 0.907051688333333

00:46:14.310 --> 00:46:16.143 detection would matter and 13%

NOTE Confidence: 0.907051688333333

00:46:16.143 --> 00:46:17.808 prevalence is a huge number.

NOTE Confidence: 0.907051688333333

00:46:17.810 --> 00:46:18.951 I mean these are not numbers you

NOTE Confidence: 0.907051688333333

00:46:18.951 --> 00:46:20.209 see in any other cancer right,

NOTE Confidence: 0.907051688333333

00:46:20.210 --> 00:46:21.988 breast or lung and all of those.

NOTE Confidence: 0.907051688333333

00:46:21.990 --> 00:46:24.580 So a high risk population being African

NOTE Confidence: 0.907051688333333

00:46:24.580 --> 00:46:27.101 American or of African descent or

NOTE Confidence: 0.907051688333333

00:46:27.101 --> 00:46:28.967 black or first degree family members

NOTE Confidence: 0.907051688333333

00:46:28.967 --> 00:46:31.110 should be such a low hanging fruit.

NOTE Confidence: 0.907051688333333

00:46:31.110 --> 00:46:33.644 Like you don't need to justify numbers

NOTE Confidence: 0.907051688333333

00:46:33.644 --> 00:46:35.926 needed to treat with the 13% prevalence.

NOTE Confidence: 0.907051688333333

00:46:35.926 --> 00:46:38.770 And that's just mgus if you add the M

NOTE Confidence: 0.907051688333333

00:46:38.836 --> 00:46:40.896 *** which could be the taxing lymphomas.

NOTE Confidence: 0.907051688333333

00:46:40.900 --> 00:46:42.622 Now we have a huge number of

NOTE Confidence: 0.907051688333333

00:46:42.622 --> 00:46:44.084 people walking around with early

NOTE Confidence: 0.907051688333333

00:46:44.084 --> 00:46:45.089 lymphomas and myelomas.

NOTE Confidence: 0.8786183

00:46:46.520 --> 00:46:49.550 And if I, if I may just ask one more in terms

NOTE Confidence: 0.885824233125

00:46:49.625 --> 00:46:51.215 of I think you put you,

NOTE Confidence: 0.885824233125

00:46:51.220 --> 00:46:53.173 you had some of this in the slides in

NOTE Confidence: 0.885824233125

00:46:53.173 --> 00:46:55.452 terms of you know fasting or metformin

NOTE Confidence: 0.885824233125

00:46:55.452 --> 00:46:56.788 or other metabolic interventions.

NOTE Confidence: 0.885824233125

00:46:56.790 --> 00:46:58.720 What's your potential vision on

NOTE Confidence: 0.885824233125

00:46:58.720 --> 00:47:00.650 preventive intervention for those who

NOTE Confidence: 0.885824233125

00:47:00.710 --> 00:47:02.670 you capture as mgus or early stage?

NOTE Confidence: 0.885824233125

00:47:02.670 --> 00:47:03.966 What's your current counseling

NOTE Confidence: 0.885824233125

00:47:03.966 --> 00:47:05.450 that you provide? Yeah,

NOTE Confidence: 0.885631910555556

00:47:05.460 --> 00:47:07.134 so you know the interceptions are

NOTE Confidence: 0.885631910555556

00:47:07.134 --> 00:47:08.867 easy because I can give something

NOTE Confidence: 0.885631910555556

00:47:08.867 --> 00:47:10.553 and I can see the response.

NOTE Confidence: 0.885631910555556

00:47:10.560 --> 00:47:12.877 But then so many patients have this

NOTE Confidence: 0.885631910555556

00:47:12.877 --> 00:47:15.043 earlier factors and there's a lot

NOTE Confidence: 0.885631910555556

00:47:15.043 --> 00:47:16.888 of questions of obesity microbiome.

NOTE Confidence: 0.885631910555556

00:47:16.890 --> 00:47:18.820 Metabolic pathways, so we're starting

NOTE Confidence: 0.885631910555556

00:47:18.820 --> 00:47:20.750 to do now microbiome studies.

NOTE Confidence: 0.885631910555556

00:47:20.750 --> 00:47:22.418 We're starting to do metabolic changes

NOTE Confidence: 0.885631910555556

00:47:22.418 --> 00:47:24.480 and immune and again they come together,

NOTE Confidence: 0.885631910555556

00:47:24.480 --> 00:47:25.575 right, the microbiome,

NOTE Confidence: 0.885631910555556

00:47:25.575 --> 00:47:27.400 the metabolomics and the immune

NOTE Confidence: 0.885631910555556

00:47:27.400 --> 00:47:29.208 dysregulation to lead to progression.

NOTE Confidence: 0.885631910555556

00:47:29.210 --> 00:47:31.730 So a lot of that effort we're starting

NOTE Confidence: 0.885631910555556

00:47:31.730 --> 00:47:34.034 to work on because that can also

NOTE Confidence: 0.885631910555556

00:47:34.034 --> 00:47:35.498 be therapeutically intervened with

NOTE Confidence: 0.885631910555556

00:47:35.498 --> 00:47:37.373 whether you have microbiome therapy

NOTE Confidence: 0.885631910555556

00:47:37.373 --> 00:47:39.188 or of course other mechanisms.

NOTE Confidence: 0.885631910555556

00:47:39.190 --> 00:47:41.386 And then Catherine Mayernik and Betsy

NOTE Confidence: 0.885631910555556

00:47:41.386 --> 00:47:43.663 O'Donnell are amazing and trying to

NOTE Confidence: 0.885631910555556

00:47:43.663 --> 00:47:45.925 develop other studies like that metformin,

NOTE Confidence: 0.885631910555556

00:47:45.930 --> 00:47:46.700 intermittent fasting.

NOTE Confidence: 0.885631910555556

00:47:46.700 --> 00:47:49.010 Exercise and fitness things that can

NOTE Confidence: 0.885631910555556

00:47:49.010 --> 00:47:51.399 really help modulate the lifestyle of

NOTE Confidence: 0.885631910555556

00:47:51.399 --> 00:47:52.959 patients for modifications basically

NOTE Confidence: 0.885631910555556

00:47:52.959 --> 00:47:55.178 that can help prevent progression.

NOTE Confidence: 0.651024306

00:47:56.630 --> 00:47:58.020 Yeah, I think your former

NOTE Confidence: 0.635570715

00:47:58.030 --> 00:47:59.428 answer may have to Natalia may

NOTE Confidence: 0.721241593846154

00:47:59.440 --> 00:48:02.312 have answered the question in the chat um

NOTE Confidence: 0.721241593846154

00:48:02.312 --> 00:48:05.510 by um Manju Prasad who's asking is risk

NOTE Confidence: 0.721241593846154

00:48:05.510 --> 00:48:07.490 stratification for mgas being offered

NOTE Confidence: 0.721241593846154

00:48:07.490 --> 00:48:10.020 to patients in the clinical setting.

NOTE Confidence: 0.76735268525

00:48:10.410 --> 00:48:12.456 Yeah. So actually our publication that

NOTE Confidence: 0.76735268525

00:48:12.456 --> 00:48:14.369 just came out yesterday and Nancy

NOTE Confidence: 0.76735268525

00:48:14.370 --> 00:48:17.214 mythology was specifically to ask that

NOTE Confidence: 0.76735268525

00:48:17.214 --> 00:48:19.308 question because many of our patients

NOTE Confidence: 0.76735268525

00:48:19.310 --> 00:48:20.521 don't have a bone marrow biopsy.

NOTE Confidence: 0.76735268525

00:48:20.521 --> 00:48:21.907 So you think they have mgus,

NOTE Confidence: 0.76735268525

00:48:21.910 --> 00:48:23.703 they actually have smoldering myeloma and

NOTE Confidence: 0.76735268525

00:48:23.703 --> 00:48:26.770 then you don't even know and as I said the.

NOTE Confidence: 0.76735268525

00:48:26.770 --> 00:48:28.512 Clinical annotation of what is mgus

NOTE Confidence: 0.76735268525

00:48:28.512 --> 00:48:30.548 and what smoldering myeloma is so

NOTE Confidence: 0.822001147142857

00:48:30.560 --> 00:48:32.765 hard because the bone marrow is patchy.

NOTE Confidence: 0.822001147142857

00:48:32.770 --> 00:48:35.220 So I can have a 10% plasma cells

NOTE Confidence: 0.822001147142857

00:48:35.220 --> 00:48:37.820 but I'm really mgus or I'm not

NOTE Confidence: 0.822001147142857

00:48:37.820 --> 00:48:40.170 really small ring myeloma. So the

NOTE Confidence: 0.7761632

00:48:40.220 --> 00:48:41.568 Pangea model was actually

NOTE Confidence: 0.812718934545455

00:48:42.420 --> 00:48:44.190 6700 participants where we annotated

NOTE Confidence: 0.812718934545455

00:48:44.190 --> 00:48:46.686 all of their clinical data and we

NOTE Confidence: 0.812718934545455

00:48:46.686 --> 00:48:48.346 developed the clinical model of

NOTE Confidence: 0.812718934545455

00:48:48.346 --> 00:48:50.299 progression based on dynamic numbers.

NOTE Confidence: 0.812718934545455

00:48:50.300 --> 00:48:51.716 If they're M spike is increasing,

NOTE Confidence: 0.812718934545455

00:48:51.720 --> 00:48:53.658 if their light chains chain is

NOTE Confidence: 0.812718934545455

00:48:53.658 --> 00:48:55.480 increasing hemoglobin it would freezing,

NOTE Confidence: 0.812718934545455

00:48:55.480 --> 00:48:56.479 creatinine is increasing.

NOTE Confidence: 0.812718934545455

00:48:56.479 --> 00:48:58.477 Remember all of those are blood

NOTE Confidence: 0.812718934545455

00:48:58.477 --> 00:49:00.427 things and then we added bone marrow,

NOTE Confidence: 0.812718934545455

00:49:00.430 --> 00:49:02.347 uh, as well as age and we did the

NOTE Confidence: 0.812718934545455

00:49:02.347 --> 00:49:04.074 model with or without bone marrow

NOTE Confidence: 0.812718934545455

00:49:04.074 --> 00:49:05.818 biopsy to help you really say

NOTE Confidence: 0.812718934545455

00:49:05.818 --> 00:49:07.449 if I had a bone marrow biopsy,

NOTE Confidence: 0.812718934545455

00:49:07.450 --> 00:49:08.002 here's the risk,

NOTE Confidence: 0.812718934545455

00:49:08.002 --> 00:49:09.490 if I don't have the bone marrow box,

NOTE Confidence: 0.812718934545455

00:49:09.490 --> 00:49:10.348 here's the risk.

NOTE Confidence: 0.812718934545455

00:49:10.348 --> 00:49:13.205 But it was a model for all small ring model.

NOTE Confidence: 0.812718934545455

00:49:13.205 --> 00:49:14.630 So I would use it.

NOTE Confidence: 0.812718934545455

00:49:14.630 --> 00:49:16.550 It's available online there is calculated.

NOTE Confidence: 0.812718934545455

00:49:16.550 --> 00:49:18.170 So look up angia and hopefully

NOTE Confidence: 0.812718934545455

00:49:18.170 --> 00:49:19.590 you'll be able to find.

NOTE Confidence: 0.13883433

00:49:21.880 --> 00:49:25.640 Other conflicts? And considering the

NOTE Confidence: 0.13883433

00:49:25.640 --> 00:49:27.880 fact that so many of these younger

NOTE Confidence: 0.13883433

00:49:27.945 --> 00:49:30.045 patients who are diagnosed with full

NOTE Confidence: 0.13883433

00:49:30.045 --> 00:49:32.158 blown myeloma in their 30s or 40s,

NOTE Confidence: 0.13883433

00:49:32.160 --> 00:49:34.648 you'd have to conceive that there are likely

NOTE Confidence: 0.13883433

00:49:34.648 --> 00:49:37.217 have had endust from their teenage years.

NOTE Confidence: 0.13883433

00:49:37.220 --> 00:49:40.541 So I wonder if you have any germ line

NOTE Confidence: 0.13883433

00:49:40.541 --> 00:49:43.510 genomic data within the within the

NOTE Confidence: 0.13883433

00:49:43.510 --> 00:49:45.821 promise cohort or elsewhere? Yeah.

NOTE Confidence: 0.13883433

00:49:45.821 --> 00:49:48.530 So we are trying to sequence right now all

NOTE Confidence: 0.13883433

00:49:48.598 --> 00:49:51.300 of the samples which won't even sequencing.

NOTE Confidence: 0.13883433

00:49:51.300 --> 00:49:54.867 Uh, the MGB cohort already had their

NOTE Confidence: 0.13883433

00:49:54.867 --> 00:49:57.069 smooth arrays or now they're actually

NOTE Confidence: 0.13883433

00:49:57.069 --> 00:49:59.147 redoing whole thing security in the

NOTE Confidence: 0.13883433

00:49:59.147 --> 00:50:01.268 same samples and then of course many

NOTE Confidence: 0.13883433

00:50:01.333 --> 00:50:03.259 of those other folks had already.

NOTE Confidence: 0.13883433

00:50:03.260 --> 00:50:05.018 So you're right, we're trying to

NOTE Confidence: 0.13883433

00:50:05.018 --> 00:50:08.590 actually do that all of this data.

NOTE Confidence: 0.13883433

00:50:08.590 --> 00:50:12.608 OK, I think they're having some static

NOTE Confidence: 0.13883433

00:50:12.610 --> 00:50:14.800 from me or from somewhere else.

NOTE Confidence: 0.497013415

00:50:16.170 --> 00:50:19.412 Nope, it's. OK, it may have been

NOTE Confidence: 0.497013415

00:50:19.412 --> 00:50:21.428 your computer, but let me umm,

NOTE Confidence: 0.497013415

00:50:21.430 --> 00:50:22.310 so there this Mendez

NOTE Confidence: 0.8933679625

00:50:22.320 --> 00:50:24.824 is asking a question in the question answer.

NOTE Confidence: 0.8933679625

00:50:24.830 --> 00:50:26.386 So how do you think of

NOTE Confidence: 0.8933679625

00:50:26.386 --> 00:50:27.998 mgip compared to lymphoid,

NOTE Confidence: 0.8933679625

00:50:28.000 --> 00:50:30.758 clonal hematopoiesis and is in GIMP

NOTE Confidence: 0.8933679625

00:50:30.758 --> 00:50:32.844 and the absence of lymphoma CL and

NOTE Confidence: 0.8933679625

00:50:32.844 --> 00:50:34.399 manifestation of lymphoid cloning,

NOTE Confidence: 0.8933679625

00:50:34.400 --> 00:50:38.040 hematopoiesis and then any information

NOTE Confidence: 0.8933679625

00:50:38.040 --> 00:50:40.952 on overlapping somatic mutations.

NOTE Confidence: 0.8933679625

00:50:40.960 --> 00:50:42.528 So great question. So we work very

NOTE Confidence: 0.738766877647059

00:50:42.540 --> 00:50:44.340 closely with Ben Ebert and Lachelle

NOTE Confidence: 0.738766877647059

00:50:44.340 --> 00:50:46.365 weeks and others to understand really

NOTE Confidence: 0.738766877647059

00:50:46.365 --> 00:50:48.275 the interlink between Chip and.

NOTE Confidence: 0.738766877647059

00:50:48.280 --> 00:50:50.786 Mgus and we are, as we speak,

NOTE Confidence: 0.738766877647059

00:50:50.790 --> 00:50:54.998 trying to sequence all our samples for that.

NOTE Confidence: 0.738766877647059

00:50:55.000 --> 00:50:56.533 It's hard to know whether there is

NOTE Confidence: 0.738766877647059

00:50:56.533 --> 00:50:58.200 an overlap of the mutations or not.

NOTE Confidence: 0.738766877647059

00:50:58.200 --> 00:51:00.495 I think we need to 1st see how many of them

NOTE Confidence: 0.738766877647059

00:51:00.495 --> 00:51:02.754 do have chip and then we try to understand.

NOTE Confidence: 0.738766877647059

00:51:02.760 --> 00:51:04.712 We worked with Dan Lando where we took

NOTE Confidence: 0.738766877647059

00:51:04.712 --> 00:51:06.885 some of our chip samples from myeloma and

NOTE Confidence: 0.738766877647059

00:51:06.885 --> 00:51:09.139 we did the single cell sequencing data,

NOTE Confidence: 0.738766877647059

00:51:09.140 --> 00:51:11.149 but most of the chip mutations were

NOTE Confidence: 0.738766877647059

00:51:11.149 --> 00:51:13.064 in the myeloid lineage and not

NOTE Confidence: 0.738766877647059

00:51:13.064 --> 00:51:14.380 in the lymphoid lineage.

NOTE Confidence: 0.738766877647059

00:51:14.380 --> 00:51:15.715 But that brings up the

NOTE Confidence: 0.738766877647059

00:51:15.715 --> 00:51:16.516 lymphoid chip question.

NOTE Confidence: 0.738766877647059

00:51:16.520 --> 00:51:17.996 And again until we have more

NOTE Confidence: 0.738766877647059

00:51:17.996 --> 00:51:19.593 data we don't know the answer

NOTE Confidence: 0.738766877647059

00:51:19.593 --> 00:51:20.978 but it's a great question.

NOTE Confidence: 0.790463533333333

00:51:22.210 --> 00:51:24.389 We have another question from American

NOTE Confidence: 0.790463533333333

00:51:24.390 --> 00:51:26.860 Idol and I think this highlights

NOTE Confidence: 0.839159103333333

00:51:26.870 --> 00:51:28.718 how important is it is that we

NOTE Confidence: 0.839159103333333

00:51:28.718 --> 00:51:29.987 think mechanism and disease

NOTE Confidence: 0.839159103333333

00:51:29.987 --> 00:51:32.060 agnostic and across specialties.

NOTE Confidence: 0.839159103333333

00:51:32.060 --> 00:51:33.988 So Amir is of course loving you talk.

NOTE Confidence: 0.752938765714286

00:51:34.000 --> 00:51:36.926 And then right we have similar similar

NOTE Confidence: 0.752938765714286

00:51:36.930 --> 00:51:42.205 issues in chips because MB spectrum in terms

NOTE Confidence: 0.752938765714286

00:51:42.205 --> 00:51:44.413 of difficulties of response assessment.

NOTE Confidence: 0.752938765714286

00:51:44.413 --> 00:51:47.317 And So what do you think the primary

NOTE Confidence: 0.752938765714286

00:51:47.317 --> 00:51:50.420 endpoint of early phase trial for high risk

NOTE Confidence: 0.752938765714286

00:51:50.420 --> 00:51:52.284 smoldering myeloma should be the great?

NOTE Confidence: 0.752938765714286

00:51:52.284 --> 00:51:53.594 Question, because if we wait

NOTE Confidence: 0.752938765714286

00:51:53.594 --> 00:51:54.860 for progression to myeloma,

NOTE Confidence: 0.752938765714286

00:51:54.860 --> 00:51:56.712 especially if you treat them in the

NOTE Confidence: 0.752938765714286

00:51:56.712 --> 00:51:58.060 observation arm with Rev depth,

NOTE Confidence: 0.752938765714286

00:51:58.060 --> 00:52:00.970 you're wait for another 1520 years.

NOTE Confidence: 0.752938765714286

00:52:00.970 --> 00:52:03.085 So we do have a meeting with the FDA,

NOTE Confidence: 0.752938765714286

00:52:03.090 --> 00:52:05.941 which actually is in Madrid to ask those

NOTE Confidence: 0.752938765714286

00:52:05.941 --> 00:52:07.326 questions. What are the endpoints?

NOTE Confidence: 0.752938765714286

00:52:07.330 --> 00:52:08.980 Can we get accelerated endpoints?

NOTE Confidence: 0.752938765714286

00:52:08.980 --> 00:52:12.050 Can we look at response, can we look at RT?

NOTE Confidence: 0.752938765714286

00:52:12.050 --> 00:52:14.802 Can we consider pure as a sustained MRD

NOTE Confidence: 0.752938765714286

00:52:14.802 --> 00:52:16.970 negative disease for four to five years?

NOTE Confidence: 0.752938765714286

00:52:16.970 --> 00:52:18.728 These are all great questions that

NOTE Confidence: 0.752938765714286

00:52:18.728 --> 00:52:21.104 we need answers to be able to design

NOTE Confidence: 0.752938765714286

00:52:21.104 --> 00:52:22.167 for this property. Yes.

NOTE Confidence: 0.752938765714286

00:52:22.167 --> 00:52:23.823 Let me maybe go back then to the

NOTE Confidence: 0.860350535

00:52:23.840 --> 00:52:25.500 interplay between the immune

NOTE Confidence: 0.860350535

00:52:25.500 --> 00:52:27.160 system and your clone.

NOTE Confidence: 0.860350535

00:52:27.160 --> 00:52:29.456 So do you expect that if you

NOTE Confidence: 0.860350535

00:52:29.456 --> 00:52:30.819 get rid of the malignant clone,

NOTE Confidence: 0.860350535

00:52:30.819 --> 00:52:33.093 however small, that it would have

NOTE Confidence: 0.860350535

00:52:33.093 --> 00:52:35.600 an effect on the immune system?

NOTE Confidence: 0.85161698

00:52:36.340 --> 00:52:37.180 Oh, I don't know.

NOTE Confidence: 0.85161698

00:52:37.180 --> 00:52:38.020 That's a great question.

NOTE Confidence: 0.85161698

00:52:38.020 --> 00:52:39.140 Will it normalize, right?

NOTE Confidence: 0.85161698

00:52:39.140 --> 00:52:40.756 I mean, if you look at the therapy

NOTE Confidence: 0.85161698

00:52:40.756 --> 00:52:41.979 we gave to those patients and

NOTE Confidence: 0.85161698

00:52:41.979 --> 00:52:43.174 when they were MRD negative,

NOTE Confidence: 0.85161698

00:52:43.180 --> 00:52:45.380 they normalized their immune system.

NOTE Confidence: 0.85161698

00:52:45.380 --> 00:52:46.720 But the other question is

NOTE Confidence: 0.85161698

00:52:46.720 --> 00:52:47.792 which one started first?

NOTE Confidence: 0.85161698

00:52:47.800 --> 00:52:48.920 Is it the chicken and the egg?

NOTE Confidence: 0.85161698

00:52:48.920 --> 00:52:50.384 And was it already an immune

NOTE Confidence: 0.85161698

00:52:50.384 --> 00:52:51.999 dysregulation that led to those clones?

NOTE Confidence: 0.85161698

00:52:52.000 --> 00:52:52.350 Growing.

NOTE Confidence: 0.85161698

00:52:52.350 --> 00:52:54.450 And is that already there even

NOTE Confidence: 0.85161698

00:52:54.450 --> 00:52:57.263 when you get rid of the MRI of the

NOTE Confidence: 0.85161698

00:52:57.263 --> 00:52:59.276 clone that years and years later

NOTE Confidence: 0.85161698

00:52:59.276 --> 00:53:01.296 yet another mutation will occur

NOTE Confidence: 0.85161698

00:53:01.296 --> 00:53:03.596 because the soil is fertile, right?

NOTE Confidence: 0.85161698

00:53:03.596 --> 00:53:05.044 So I don't know.

NOTE Confidence: 0.85161698

00:53:05.050 --> 00:53:06.568 And I'd love to get samples,

NOTE Confidence: 0.85161698

00:53:06.570 --> 00:53:07.382 for example,

NOTE Confidence: 0.85161698

00:53:07.382 --> 00:53:09.006 from patients before they

NOTE Confidence: 0.85161698

00:53:09.006 --> 00:53:11.439 develop mgus so that we know

NOTE Confidence: 0.85161698

00:53:11.439 --> 00:53:12.907 which one happens first.

NOTE Confidence: 0.85161698

00:53:12.910 --> 00:53:14.548 But these are all great questions

NOTE Confidence: 0.85161698

00:53:14.548 --> 00:53:16.324 that we would love to collaborate

NOTE Confidence: 0.85161698

00:53:16.324 --> 00:53:18.530 with people and answer them together.

NOTE Confidence: 0.727924032857143

00:53:21.890 --> 00:53:23.640 Awesome. We have a little more Natalia.

NOTE Confidence: 0.831996064

00:53:24.130 --> 00:53:26.930 Any questions from your team?

NOTE Confidence: 0.831996064

00:53:26.930 --> 00:53:29.461 Yeah, I mean, I think, uh, perhaps, uh,

NOTE Confidence: 0.831996064

00:53:29.461 --> 00:53:32.800 to answer amers question and perhaps a,

NOTE Confidence: 0.831996064

00:53:32.800 --> 00:53:36.136 an immune endpoint should be a

NOTE Confidence: 0.831996064

00:53:36.136 --> 00:53:37.804 potential secondary endpoint,

NOTE Confidence: 0.831996064

00:53:37.810 --> 00:53:40.502 how to normalize that

NOTE Confidence: 0.831996064

00:53:40.502 --> 00:53:41.848 immunosuppressive environment,

NOTE Confidence: 0.831996064

00:53:41.850 --> 00:53:44.260 you know what potential interventional

NOTE Confidence: 0.831996064

00:53:44.260 --> 00:53:46.188 strategies like whether it's

NOTE Confidence: 0.831996064

00:53:46.188 --> 00:53:47.970 nutritional or microbiome or

NOTE Confidence: 0.831996064

00:53:47.970 --> 00:53:50.030 metabolomic strategies that could be,

NOTE Confidence: 0.831996064

00:53:50.030 --> 00:53:52.207 I don't think we pay enough attention

NOTE Confidence: 0.831996064

00:53:52.207 --> 00:53:53.804 to weight loss interventions

NOTE Confidence: 0.831996064

00:53:53.804 --> 00:53:55.516 or exercise interventions in

NOTE Confidence: 0.831996064

00:53:55.516 --> 00:53:57.330 myeloma and there's so much.

NOTE Confidence: 0.831996064

00:53:57.330 --> 00:53:59.202 Data you made parallels Irene with

NOTE Confidence: 0.831996064

00:53:59.202 --> 00:54:01.216 breast cancer and there's so much

NOTE Confidence: 0.831996064

00:54:01.216 --> 00:54:02.636 commonality between the diseases,

NOTE Confidence: 0.831996064

00:54:02.640 --> 00:54:04.204 the role of inflammation,

NOTE Confidence: 0.831996064

00:54:04.204 --> 00:54:05.377 the obesity etcetera.

NOTE Confidence: 0.831996064

00:54:05.380 --> 00:54:07.500 So I I don't think we pay enough

NOTE Confidence: 0.831996064

00:54:07.500 --> 00:54:09.254 attention to those kind of

NOTE Confidence: 0.831996064

00:54:09.254 --> 00:54:10.806 interventions in myeloma prevention

NOTE Confidence: 0.831996064

00:54:10.806 --> 00:54:12.894 and even relapse prevention once

NOTE Confidence: 0.831996064

00:54:12.894 --> 00:54:15.039 you have successfully treated them.

NOTE Confidence: 0.831996064

00:54:15.040 --> 00:54:16.528 Your thoughts on that?

NOTE Confidence: 0.861487791

00:54:17.700 --> 00:54:19.723 Absolutely. And I think you and Betsy

NOTE Confidence: 0.861487791

00:54:19.723 --> 00:54:21.214 O'Donnell would really, you know,

NOTE Confidence: 0.861487791

00:54:21.214 --> 00:54:23.086 talk for hours because we're even

NOTE Confidence: 0.861487791

00:54:23.086 --> 00:54:24.798 thinking should we use some of

NOTE Confidence: 0.861487791

00:54:24.798 --> 00:54:26.110 those new obesity drugs, right?

NOTE Confidence: 0.861487791

00:54:26.110 --> 00:54:28.470 Like, there are so many things that we

NOTE Confidence: 0.861487791

00:54:28.470 --> 00:54:30.477 can do to prevent progression and some

NOTE Confidence: 0.861487791

00:54:30.477 --> 00:54:32.970 of them may be in our hands right now.

NOTE Confidence: 0.708418995

00:54:35.420 --> 00:54:36.200 Yeah, excellent.

NOTE Confidence: 0.78088813625

00:54:38.470 --> 00:54:41.025 So we're getting close to to running

NOTE Confidence: 0.78088813625

00:54:41.025 --> 00:54:44.020 clock and I don't see additional

NOTE Confidence: 0.580323506

00:54:44.630 --> 00:54:48.590 questions. Um, well, I'm Erin,

NOTE Confidence: 0.580323506

00:54:48.590 --> 00:54:51.156 thank you so much for this really

NOTE Confidence: 0.580323506

00:54:51.156 --> 00:54:53.204 spectacular grand rounds and

NOTE Confidence: 0.580323506

00:54:53.204 --> 00:54:55.320 congratulations on these amazing

NOTE Confidence: 0.580323506

00:54:55.320 --> 00:54:58.094 advances that are clearly, you know,

NOTE Confidence: 0.580323506

00:54:58.094 --> 00:55:00.356 advancing prevention which is so amazing

NOTE Confidence: 0.580323506

00:55:00.356 --> 00:55:03.022 for many patients and then treatment.

NOTE Confidence: 0.580323506

00:55:03.022 --> 00:55:05.462 So thank you. Thank you for sticking

NOTE Confidence: 0.580323506

00:55:05.462 --> 00:55:08.398 through you know with the zoom only option.

NOTE Confidence: 0.580323506

00:55:08.400 --> 00:55:10.395 And we look forward to you know,

NOTE Confidence: 0.580323506

00:55:10.400 --> 00:55:11.780 getting together in person

NOTE Confidence: 0.580323506

00:55:11.780 --> 00:55:13.160 and collaborating for sure.

NOTE Confidence: 0.888757123636364

00:55:13.590 --> 00:55:15.140 Absolutely. Thank you again and

NOTE Confidence: 0.888757123636364

00:55:15.140 --> 00:55:16.930 definitely look forward to seeing you.

NOTE Confidence: 0.888757123636364

00:55:16.930 --> 00:55:18.946 Not in person, but this was a

NOTE Confidence: 0.888757123636364

00:55:18.946 --> 00:55:21.020 good alternative. Fantastic

NOTE Confidence: 0.74254241

00:55:21.030 --> 00:55:22.656 talk, Harry. Thank you so much.

NOTE Confidence: 0.82808761

00:55:22.810 --> 00:55:23.920 Thank you, everyone.