

WEBVTT

NOTE duration: "01:28:50.773"

NOTE Confidence: 0.9944308

00:00:00.080 --> 00:00:01.599 Program tonight brought to you

NOTE Confidence: 0.9944308

00:00:01.599 --> 00:00:02.420 by a multidisciplinary

NOTE Confidence: 0.91684854

00:00:03.120 --> 00:00:04.080 group to hear from the

NOTE Confidence: 0.91684854

00:00:04.080 --> 00:00:06.740 Smilow Cancer Center encompassing expertise

NOTE Confidence: 0.8906599

00:00:07.040 --> 00:00:08.740 in all of cutaneous

NOTE Confidence: 0.9996069

00:00:09.039 --> 00:00:09.539 oncology.

NOTE Confidence: 0.96585226

00:00:11.200 --> 00:00:12.480 We're gonna start off the

NOTE Confidence: 0.96585226

00:00:12.480 --> 00:00:13.620 session, which really

NOTE Confidence: 0.99885607

00:00:14.025 --> 00:00:14.525 focuses

NOTE Confidence: 0.9527156

00:00:14.825 --> 00:00:16.925 on gene expression and cutaneous

NOTE Confidence: 0.9445303

00:00:17.704 --> 00:00:19.545 malignancies as we've noticed a

NOTE Confidence: 0.9445303

00:00:19.545 --> 00:00:20.985 real uptake in the use

NOTE Confidence: 0.9445303

00:00:20.985 --> 00:00:22.425 of this. And there's been

NOTE Confidence: 0.9445303

00:00:22.425 --> 00:00:24.505 some really great recent data,

NOTE Confidence: 0.9445303

00:00:24.505 --> 00:00:25.544 a flood of it actually  
NOTE Confidence: 0.9445303

00:00:25.544 --> 00:00:27.724 recently from randomized controlled trials,  
NOTE Confidence: 0.96921134

00:00:28.039 --> 00:00:29.160 as well as some opening  
NOTE Confidence: 0.96921134

00:00:29.160 --> 00:00:30.679 of some clinical trials around  
NOTE Confidence: 0.96921134

00:00:30.679 --> 00:00:31.339 the country.  
NOTE Confidence: 0.9715029

00:00:31.800 --> 00:00:32.680 So we're going to begin  
NOTE Confidence: 0.9715029

00:00:32.680 --> 00:00:34.059 our discussion today,  
NOTE Confidence: 0.7393066

00:00:34.920 --> 00:00:36.219 with doctor Swoozie.  
NOTE Confidence: 0.9936173

00:00:36.680 --> 00:00:37.399 If you'd like to get  
NOTE Confidence: 0.9936173

00:00:37.399 --> 00:00:38.540 us started, please.  
NOTE Confidence: 0.9732878

00:00:41.175 --> 00:00:41.675 Sure.  
NOTE Confidence: 0.9966758

00:00:42.375 --> 00:00:43.995 Just give me one sec.  
NOTE Confidence: 0.99394125

00:00:45.734 --> 00:00:46.954 So hi, everyone.  
NOTE Confidence: 0.9961433

00:00:48.055 --> 00:00:49.894 Oh, did it stop? Hold  
NOTE Confidence: 0.9961433

00:00:49.894 --> 00:00:51.995 on. My screen share stopped.  
NOTE Confidence: 0.9961433

00:00:52.055 --> 00:00:53.754 Let me try again here.

NOTE Confidence: 0.99961823  
00:00:58.490 --> 00:00:59.390 Here we go.  
NOTE Confidence: 0.9575806  
00:01:00.010 --> 00:01:01.530 Hi. I'm Katie Swozzi. I'm  
NOTE Confidence: 0.9575806  
00:01:01.530 --> 00:01:03.390 a Mohsurgent here at Yale,  
NOTE Confidence: 0.9575806  
00:01:03.610 --> 00:01:04.730 and I'm gonna be starting  
NOTE Confidence: 0.9575806  
00:01:04.730 --> 00:01:06.250 us off tonight by discussing  
NOTE Confidence: 0.9575806  
00:01:06.250 --> 00:01:08.090 the role of nomograms and  
NOTE Confidence: 0.9575806  
00:01:08.090 --> 00:01:08.590 introducing,  
NOTE Confidence: 0.9942758  
00:01:09.845 --> 00:01:11.284 the idea about gene expression  
NOTE Confidence: 0.9942758  
00:01:11.284 --> 00:01:13.045 profiling in cutaneous squamous cell  
NOTE Confidence: 0.9942758  
00:01:13.045 --> 00:01:13.545 carcinoma  
NOTE Confidence: 0.9882242  
00:01:14.165 --> 00:01:15.604 with a focus on how  
NOTE Confidence: 0.9882242  
00:01:15.604 --> 00:01:17.444 these tools can help refine  
NOTE Confidence: 0.9882242  
00:01:17.444 --> 00:01:19.284 risk assessment and clinical decision  
NOTE Confidence: 0.9882242  
00:01:19.284 --> 00:01:19.784 making.  
NOTE Confidence: 0.98806936  
00:01:20.405 --> 00:01:22.665 I'll review briefly traditional staging,  
NOTE Confidence: 0.98009276

00:01:23.045 --> 00:01:25.340 introduce nomogram based prediction,  
NOTE Confidence: 0.9875415

00:01:25.799 --> 00:01:28.040 particularly the risk calculator, and  
NOTE Confidence: 0.9875415

00:01:28.040 --> 00:01:29.479 discuss how molecular tools like  
NOTE Confidence: 0.9875415

00:01:29.479 --> 00:01:31.580 GEP may further refine risk.  
NOTE Confidence: 0.934552

00:01:32.119 --> 00:01:33.959 So although most cutaneous squamous  
NOTE Confidence: 0.934552

00:01:33.959 --> 00:01:35.819 cell carcinoma have excellent prognosis,  
NOTE Confidence: 0.934552

00:01:36.119 --> 00:01:38.040 a subset behaves aggressively and  
NOTE Confidence: 0.934552

00:01:38.040 --> 00:01:39.560 the consequences of missing high  
NOTE Confidence: 0.934552

00:01:39.560 --> 00:01:40.575 risk disease are significant.  
NOTE Confidence: 0.9327811

00:01:41.615 --> 00:01:43.295 Rates of unfavorable outcomes are  
NOTE Confidence: 0.9327811

00:01:43.295 --> 00:01:44.414 about three to five percent  
NOTE Confidence: 0.9327811

00:01:44.414 --> 00:01:46.174 for local recurrence, two to  
NOTE Confidence: 0.9327811

00:01:46.174 --> 00:01:47.534 five percent for nodal mets,  
NOTE Confidence: 0.9327811

00:01:47.534 --> 00:01:48.655 and one point five to  
NOTE Confidence: 0.9327811

00:01:48.655 --> 00:01:49.854 three point five percent for  
NOTE Confidence: 0.9327811

00:01:49.854 --> 00:01:52.094 disease specific death. And despite

NOTE Confidence: 0.9327811

00:01:52.094 --> 00:01:53.935 these relatively small percentages, the

NOTE Confidence: 0.9327811

00:01:53.935 --> 00:01:54.435 absolute

NOTE Confidence: 0.9697068

00:01:54.850 --> 00:01:56.370 mortality from cutaneous squamous cell

NOTE Confidence: 0.9697068

00:01:56.370 --> 00:01:57.510 carcinoma is substantial,

NOTE Confidence: 0.9785247

00:01:58.610 --> 00:02:00.070 meeting at least meeting,

NOTE Confidence: 0.9525283

00:02:00.450 --> 00:02:01.970 but, and by most models

NOTE Confidence: 0.9525283

00:02:01.970 --> 00:02:03.510 exceeding that of melanoma.

NOTE Confidence: 0.9574942

00:02:04.370 --> 00:02:05.570 So I did talk about

NOTE Confidence: 0.9574942

00:02:05.570 --> 00:02:06.770 staging in the last one

NOTE Confidence: 0.9574942

00:02:06.770 --> 00:02:07.570 of these sessions, but I

NOTE Confidence: 0.9574942

00:02:07.570 --> 00:02:09.090 did wanna briefly bring it

NOTE Confidence: 0.9574942

00:02:09.090 --> 00:02:10.305 up here. So first here,

NOTE Confidence: 0.9574942

00:02:10.305 --> 00:02:12.185 I'm showing AJCC eight.

NOTE Confidence: 0.9858774

00:02:13.044 --> 00:02:15.465 Staging and, the eighth edition

NOTE Confidence: 0.9858774

00:02:15.685 --> 00:02:17.525 for head and neck cutaneous

NOTE Confidence: 0.9858774

00:02:17.525 --> 00:02:18.505 squamous cell carcinoma  
NOTE Confidence: 0.992482

00:02:19.044 --> 00:02:20.985 attempted to improve risk stratification  
NOTE Confidence: 0.997005

00:02:21.285 --> 00:02:23.385 by expanding the t three  
NOTE Confidence: 0.997005

00:02:23.445 --> 00:02:25.860 group to include deep invasion,  
NOTE Confidence: 0.97777414

00:02:26.560 --> 00:02:28.880 perineural invasion, and minor bone  
NOTE Confidence: 0.97777414

00:02:28.880 --> 00:02:29.380 erosion.  
NOTE Confidence: 0.9804423

00:02:30.240 --> 00:02:31.200 And one of the major  
NOTE Confidence: 0.9804423

00:02:31.200 --> 00:02:33.460 improvements compared with AJCC seven  
NOTE Confidence: 0.9804423

00:02:33.520 --> 00:02:34.800 was that core outcomes are  
NOTE Confidence: 0.9804423

00:02:34.800 --> 00:02:36.480 now concentrated in t three  
NOTE Confidence: 0.9804423

00:02:36.480 --> 00:02:37.700 and t four tumors  
NOTE Confidence: 0.96357363

00:02:38.025 --> 00:02:39.565 rather than across a heterogeneous,  
NOTE Confidence: 0.99786055

00:02:40.345 --> 00:02:41.245 T2 group.  
NOTE Confidence: 0.9520416

00:02:41.625 --> 00:02:43.325 However, even with AJCC8,  
NOTE Confidence: 0.86387366

00:02:43.705 --> 00:02:44.764 there remains substantial  
NOTE Confidence: 0.8772955

00:02:45.065 --> 00:02:46.365 variability in outcomes.

NOTE Confidence: 0.93757427

00:02:46.985 --> 00:02:48.185 So the Brigham and Women's

NOTE Confidence: 0.93757427

00:02:48.185 --> 00:02:50.105 Staging System was developed to

NOTE Confidence: 0.93757427

00:02:50.105 --> 00:02:51.325 address this heterogeneity.

NOTE Confidence: 0.9947221

00:02:52.330 --> 00:02:53.069 This model,

NOTE Confidence: 0.9749539

00:02:53.690 --> 00:02:55.470 identifies four major risk factors,

NOTE Confidence: 0.9749539

00:02:55.530 --> 00:02:56.030 diameter,

NOTE Confidence: 0.98207414

00:02:56.489 --> 00:02:58.889 depth, beyond fat, perineural invasion

NOTE Confidence: 0.98207414

00:02:58.889 --> 00:02:59.690 of greater than point one

NOTE Confidence: 0.98207414

00:02:59.690 --> 00:03:01.870 millimeters, and poorly differentiated histology.

NOTE Confidence: 0.9741505

00:03:03.290 --> 00:03:04.669 And tumors are then classified

NOTE Confidence: 0.9741505

00:03:04.730 --> 00:03:05.690 by their number of risk

NOTE Confidence: 0.9741505

00:03:05.690 --> 00:03:07.544 factors into t one, t

NOTE Confidence: 0.9741505

00:03:07.544 --> 00:03:08.584 two a, t two b,

NOTE Confidence: 0.9741505

00:03:08.584 --> 00:03:09.484 and t three.

NOTE Confidence: 0.9471105

00:03:09.944 --> 00:03:11.385 And Brigham and Women's Staging

NOTE Confidence: 0.9471105

00:03:11.385 --> 00:03:13.165 shows better risk stratification  
NOTE Confidence: 0.964483

00:03:13.784 --> 00:03:15.305 at, t two, t three,  
NOTE Confidence: 0.964483

00:03:15.305 --> 00:03:16.344 and here you can see  
NOTE Confidence: 0.964483

00:03:16.344 --> 00:03:18.105 that t two b tumors  
NOTE Confidence: 0.964483

00:03:18.105 --> 00:03:19.305 have about a twenty percent  
NOTE Confidence: 0.964483

00:03:19.305 --> 00:03:20.584 risk of local recurrence and  
NOTE Confidence: 0.964483

00:03:20.584 --> 00:03:21.325 nodal metastasis  
NOTE Confidence: 0.9273379

00:03:21.625 --> 00:03:22.844 with t two a,  
NOTE Confidence: 0.94820297

00:03:23.430 --> 00:03:24.650 ten percent or below.  
NOTE Confidence: 0.9641098

00:03:25.270 --> 00:03:26.150 And you can see there's,  
NOTE Confidence: 0.9641098

00:03:26.550 --> 00:03:27.450 less stratification,  
NOTE Confidence: 0.87085444

00:03:28.069 --> 00:03:28.810 in AGCC  
NOTE Confidence: 0.94474065

00:03:29.110 --> 00:03:31.050 eight, between t three,  
NOTE Confidence: 0.99444586

00:03:32.230 --> 00:03:33.129 and t two.  
NOTE Confidence: 0.9879744

00:03:33.430 --> 00:03:35.110 And so this improved risk  
NOTE Confidence: 0.9879744

00:03:35.110 --> 00:03:37.530 stratification, but staging remains categorical



NOTE Confidence: 0.9879744  
00:03:37.750 --> 00:03:38.890 rather than individualized.  
NOTE Confidence: 0.9917042  
00:03:39.725 --> 00:03:40.465 So NCCN  
NOTE Confidence: 0.9807783  
00:03:40.765 --> 00:03:42.845 guidelines build further on staging  
NOTE Confidence: 0.9807783  
00:03:42.845 --> 00:03:43.985 incorporating additional  
NOTE Confidence: 0.97177076  
00:03:44.365 --> 00:03:45.965 high risk features and patient  
NOTE Confidence: 0.97177076  
00:03:45.965 --> 00:03:47.805 specific features such as, you  
NOTE Confidence: 0.97177076  
00:03:47.805 --> 00:03:49.165 know, is the tumor primary  
NOTE Confidence: 0.97177076  
00:03:49.165 --> 00:03:50.865 recurrent? Is the patient immunosuppressed?  
NOTE Confidence: 0.99525183  
00:03:51.530 --> 00:03:53.230 Is the location on previously  
NOTE Confidence: 0.9793744  
00:03:53.770 --> 00:03:55.849 irradiated skin? What is the  
NOTE Confidence: 0.9793744  
00:03:55.849 --> 00:03:57.310 growth rate of the tumor?  
NOTE Confidence: 0.97329545  
00:03:58.010 --> 00:03:59.790 And also incorporates different,  
NOTE Confidence: 0.9113143  
00:04:00.330 --> 00:04:01.550 histologic subtypes.  
NOTE Confidence: 0.9912645  
00:04:02.810 --> 00:04:05.050 And NCCN classification is useful,  
NOTE Confidence: 0.9912645  
00:04:05.050 --> 00:04:06.435 but it still groups patients  
NOTE Confidence: 0.9912645

00:04:06.435 --> 00:04:07.795 into low, high risk, and  
NOTE Confidence: 0.9912645

00:04:07.795 --> 00:04:09.395 very high risk rather than  
NOTE Confidence: 0.9912645

00:04:09.395 --> 00:04:11.175 generating individual probabilities.  
NOTE Confidence: 0.97806466

00:04:13.075 --> 00:04:13.895 So nomograms,  
NOTE Confidence: 0.99841464

00:04:14.915 --> 00:04:16.115 this is where nomograms are  
NOTE Confidence: 0.99841464

00:04:16.115 --> 00:04:17.895 particularly helpful. So a nomogram  
NOTE Confidence: 0.99841464

00:04:17.955 --> 00:04:19.875 is a statistical model that  
NOTE Confidence: 0.99841464

00:04:19.875 --> 00:04:22.270 integrates multiple variables to generate  
NOTE Confidence: 0.99841464

00:04:22.270 --> 00:04:23.009 an individualized  
NOTE Confidence: 0.84606457

00:04:23.310 --> 00:04:24.690 probability of prosthesis  
NOTE Confidence: 0.957441

00:04:25.389 --> 00:04:26.050 or death.  
NOTE Confidence: 0.9848068

00:04:26.350 --> 00:04:28.289 And unlike staging systems, nomograms  
NOTE Confidence: 0.9848068

00:04:28.350 --> 00:04:30.669 produce continuous risk estimates rather  
NOTE Confidence: 0.9848068

00:04:30.669 --> 00:04:31.410 than categories.  
NOTE Confidence: 0.9706755

00:04:31.789 --> 00:04:33.150 And this is especially useful  
NOTE Confidence: 0.9706755

00:04:33.150 --> 00:04:35.065 in gray zones. For example,

NOTE Confidence: 0.9706755

00:04:35.125 --> 00:04:36.645 tumors that fall between Brigham

NOTE Confidence: 0.9706755

00:04:36.645 --> 00:04:38.005 and Women staging t two

NOTE Confidence: 0.9706755

00:04:38.005 --> 00:04:39.044 a and t two b,

NOTE Confidence: 0.9706755

00:04:39.044 --> 00:04:40.485 which we commonly refer to

NOTE Confidence: 0.9706755

00:04:40.485 --> 00:04:41.945 as t two a plus.

NOTE Confidence: 0.9764063

00:04:43.685 --> 00:04:45.625 Nomograms can also be, presented

NOTE Confidence: 0.9764063

00:04:45.764 --> 00:04:46.264 graphically

NOTE Confidence: 0.9973563

00:04:46.645 --> 00:04:48.104 or embedded in calculators,

NOTE Confidence: 0.9993594

00:04:48.645 --> 00:04:49.945 making them very clinically

NOTE Confidence: 0.98543584

00:04:50.970 --> 00:04:51.790 practical. So,

NOTE Confidence: 0.8885025

00:04:52.410 --> 00:04:53.950 I briefly mentioned this nomogram,

NOTE Confidence: 0.9645405

00:04:54.810 --> 00:04:56.890 for cutaneous SCC that predicts

NOTE Confidence: 0.9645405

00:04:56.890 --> 00:04:58.490 the risk of recurrence after

NOTE Confidence: 0.9645405

00:04:58.490 --> 00:05:00.330 MOSE, which was published in

NOTE Confidence: 0.9645405

00:05:00.330 --> 00:05:02.010 twenty twenty two, combining clinical

NOTE Confidence: 0.9645405

00:05:02.010 --> 00:05:03.390 factors with two biomarkers,  
NOTE Confidence: 0.9804055

00:05:03.964 --> 00:05:05.005 and here showing the type  
NOTE Confidence: 0.9804055

00:05:05.005 --> 00:05:06.605 of graphical representation of the  
NOTE Confidence: 0.9804055

00:05:06.605 --> 00:05:07.805 nomogram. But the one I  
NOTE Confidence: 0.9804055

00:05:07.805 --> 00:05:09.005 wanted to focus on is  
NOTE Confidence: 0.9804055

00:05:09.005 --> 00:05:11.165 the, risk calculator, which was  
NOTE Confidence: 0.9804055

00:05:11.165 --> 00:05:12.145 developed by,  
NOTE Confidence: 0.8725278

00:05:12.765 --> 00:05:13.964 number of doctor Krishnan and  
NOTE Confidence: 0.8725278

00:05:13.964 --> 00:05:15.325 I's colleagues in the Mose  
NOTE Confidence: 0.8725278

00:05:15.325 --> 00:05:16.205 College. And,  
NOTE Confidence: 0.9967947

00:05:17.449 --> 00:05:19.790 it's a clinically practical nomogram  
NOTE Confidence: 0.9581234

00:05:20.410 --> 00:05:22.270 used to predict metastatic risk,  
NOTE Confidence: 0.9581234

00:05:22.330 --> 00:05:23.770 and it's also available in  
NOTE Confidence: 0.9581234

00:05:23.770 --> 00:05:25.210 an app form that's very,  
NOTE Confidence: 0.9581234

00:05:25.610 --> 00:05:26.430 user friendly.  
NOTE Confidence: 0.9825738

00:05:26.810 --> 00:05:27.930 So I wanted to show

NOTE Confidence: 0.9825738  
00:05:27.930 --> 00:05:29.529 you the risk calculator using  
NOTE Confidence: 0.9825738  
00:05:29.529 --> 00:05:30.810 a case I recently saw  
NOTE Confidence: 0.9825738  
00:05:30.810 --> 00:05:31.955 in clinic. So here's a  
NOTE Confidence: 0.9825738  
00:05:31.955 --> 00:05:33.154 patient who presented for a  
NOTE Confidence: 0.9825738  
00:05:33.154 --> 00:05:34.595 treatment of a cutaneous squamous  
NOTE Confidence: 0.9825738  
00:05:34.595 --> 00:05:35.254 cell carcinoma,  
NOTE Confidence: 0.9729235  
00:05:35.555 --> 00:05:37.095 the right preauricular region.  
NOTE Confidence: 0.9391347  
00:05:37.955 --> 00:05:39.574 And here was her PRIMOs,  
NOTE Confidence: 0.96749276  
00:05:40.675 --> 00:05:42.435 lesion and here's her post  
NOTE Confidence: 0.96749276  
00:05:42.435 --> 00:05:44.194 MOS defect. And so when  
NOTE Confidence: 0.96749276  
00:05:44.194 --> 00:05:45.395 you look at staging for  
NOTE Confidence: 0.96749276  
00:05:45.395 --> 00:05:46.835 her, her PRIMO size was  
NOTE Confidence: 0.96749276  
00:05:46.835 --> 00:05:48.650 one point five centimeters. She  
NOTE Confidence: 0.96749276  
00:05:48.650 --> 00:05:50.650 had very widespread perineural invasion,  
NOTE Confidence: 0.96749276  
00:05:50.650 --> 00:05:51.610 but it was all small  
NOTE Confidence: 0.96749276

00:05:51.610 --> 00:05:52.110 caliber,  
NOTE Confidence: 0.9573444

00:05:52.410 --> 00:05:53.449 and she did have poorly  
NOTE Confidence: 0.9573444

00:05:53.449 --> 00:05:55.790 differentiated histology. So, by staging,  
NOTE Confidence: 0.9573444

00:05:55.850 --> 00:05:57.150 she's either AJCCA  
NOTE Confidence: 0.96517915

00:05:57.529 --> 00:05:58.830 T1 or T2A,  
NOTE Confidence: 0.9618012

00:05:59.290 --> 00:06:00.250 but you just know this  
NOTE Confidence: 0.9618012

00:06:00.250 --> 00:06:01.529 patient is not going to  
NOTE Confidence: 0.9618012

00:06:01.529 --> 00:06:02.510 do well. And,  
NOTE Confidence: 0.99360335

00:06:02.835 --> 00:06:04.375 that that staging is underrepresenting  
NOTE Confidence: 0.99360335

00:06:04.675 --> 00:06:06.055 the biology of her disease.  
NOTE Confidence: 0.9795102

00:06:06.435 --> 00:06:07.555 So let's put her in  
NOTE Confidence: 0.9795102

00:06:07.555 --> 00:06:09.154 the risk calculator. So here,  
NOTE Confidence: 0.9795102

00:06:09.154 --> 00:06:10.115 if we add,  
NOTE Confidence: 0.9775658

00:06:10.755 --> 00:06:11.575 her criteria,  
NOTE Confidence: 0.9092451

00:06:12.835 --> 00:06:13.955 here, you see she's gonna  
NOTE Confidence: 0.9092451

00:06:13.955 --> 00:06:15.095 get credit for a perineural

NOTE Confidence: 0.9092451  
00:06:15.154 --> 00:06:16.980 invasion for the depth of  
NOTE Confidence: 0.9092451  
00:06:16.980 --> 00:06:17.480 invasion.  
NOTE Confidence: 0.8841126  
00:06:18.180 --> 00:06:18.500 And,  
NOTE Confidence: 0.9503506  
00:06:19.060 --> 00:06:20.420 we look at her risk  
NOTE Confidence: 0.9503506  
00:06:20.420 --> 00:06:22.339 calculator, it's gonna reflect a  
NOTE Confidence: 0.9503506  
00:06:22.339 --> 00:06:23.960 lot higher than her staging,  
NOTE Confidence: 0.8322955  
00:06:25.460 --> 00:06:26.520 her risk of neurotoxicity  
NOTE Confidence: 0.9473152  
00:06:27.140 --> 00:06:29.675 being, over thirteen percent and,  
NOTE Confidence: 0.9260937  
00:06:30.375 --> 00:06:31.735 recurrence after mood was about  
NOTE Confidence: 0.9260937  
00:06:31.735 --> 00:06:33.014 twenty percent. So this patient  
NOTE Confidence: 0.9260937  
00:06:33.014 --> 00:06:34.235 will go to our multidisciplinary  
NOTE Confidence: 0.98661906  
00:06:34.694 --> 00:06:36.694 tumor board for consideration of  
NOTE Confidence: 0.98661906  
00:06:36.694 --> 00:06:37.194 adjuvant,  
NOTE Confidence: 0.9789959  
00:06:37.815 --> 00:06:39.335 therapy where her staging may  
NOTE Confidence: 0.9789959  
00:06:39.335 --> 00:06:41.034 not have triggered that alone.  
NOTE Confidence: 0.9981924

00:06:42.060 --> 00:06:43.500 So I'm briefly just gonna  
NOTE Confidence: 0.9981924

00:06:43.500 --> 00:06:44.060 talk about,  
NOTE Confidence: 0.95426625

00:06:44.460 --> 00:06:45.740 GP because doctor Roach is  
NOTE Confidence: 0.95426625

00:06:45.740 --> 00:06:47.279 gonna build on this. But,  
NOTE Confidence: 0.97401714

00:06:47.659 --> 00:06:49.180 for cutaneous SCC, we have  
NOTE Confidence: 0.97401714

00:06:49.180 --> 00:06:50.479 a forty gene expression,  
NOTE Confidence: 0.99826115

00:06:50.860 --> 00:06:52.879 profile test that's clinically available.  
NOTE Confidence: 0.9236546

00:06:54.060 --> 00:06:55.900 This was generated from primary  
NOTE Confidence: 0.9236546

00:06:55.900 --> 00:06:58.215 cutaneous bimicile carcinomas with known  
NOTE Confidence: 0.9236546

00:06:58.215 --> 00:06:59.915 outcomes, so retrospectives,  
NOTE Confidence: 0.9798005

00:07:00.935 --> 00:07:01.675 we developed,  
NOTE Confidence: 0.99051964

00:07:02.855 --> 00:07:04.475 and has not been prospectively,  
NOTE Confidence: 0.908134

00:07:06.055 --> 00:07:08.055 validated yet, but identifies three  
NOTE Confidence: 0.908134

00:07:08.055 --> 00:07:10.295 classes, class one, two a,  
NOTE Confidence: 0.908134

00:07:10.295 --> 00:07:11.530 and two b, the different  
NOTE Confidence: 0.908134

00:07:11.530 --> 00:07:13.150 likelihoods of developing metastasis,



NOTE Confidence: 0.9958903

00:07:14.010 --> 00:07:14.990 at three years.

NOTE Confidence: 0.9461675

00:07:15.450 --> 00:07:16.490 Oh, sorry, this slide looks

NOTE Confidence: 0.9461675

00:07:16.490 --> 00:07:16.990 weird.

NOTE Confidence: 0.9555574

00:07:17.610 --> 00:07:19.290 So, the three classes, Class

NOTE Confidence: 0.9555574

00:07:19.290 --> 00:07:20.590 I is the low biological

NOTE Confidence: 0.9555574

00:07:20.730 --> 00:07:21.770 risk and is about half

NOTE Confidence: 0.9555574

00:07:21.770 --> 00:07:22.750 the study population,

NOTE Confidence: 0.94150627

00:07:23.395 --> 00:07:24.835 Class two a is moderate

NOTE Confidence: 0.94150627

00:07:24.835 --> 00:07:26.435 biologic risk, and, when you

NOTE Confidence: 0.94150627

00:07:26.435 --> 00:07:27.735 look at the hazard ratio

NOTE Confidence: 0.94150627

00:07:27.955 --> 00:07:29.235 here, it's similar to the

NOTE Confidence: 0.94150627

00:07:29.235 --> 00:07:31.794 strongest traditional clinical pathologic factors

NOTE Confidence: 0.94150627

00:07:31.794 --> 00:07:33.814 like perineural invasion, for example.

NOTE Confidence: 0.97994375

00:07:34.115 --> 00:07:35.155 And class two b is

NOTE Confidence: 0.97994375

00:07:35.155 --> 00:07:36.194 very high risk with a

NOTE Confidence: 0.97994375

00:07:36.194 --> 00:07:37.560 greater than fifty percent risk  
NOTE Confidence: 0.97994375

00:07:37.639 --> 00:07:39.080 of metastasis, and you could  
NOTE Confidence: 0.97994375

00:07:39.080 --> 00:07:40.060 see that here.  
NOTE Confidence: 0.72330844

00:07:41.960 --> 00:07:42.460 So,  
NOTE Confidence: 0.9763164

00:07:43.080 --> 00:07:43.960 about a third of the  
NOTE Confidence: 0.9763164

00:07:43.960 --> 00:07:45.560 cases will end up, t  
NOTE Confidence: 0.9763164

00:07:45.560 --> 00:07:46.620 two a. And so,  
NOTE Confidence: 0.9682206

00:07:47.000 --> 00:07:48.200 well, doctor Roche is gonna  
NOTE Confidence: 0.9682206

00:07:48.200 --> 00:07:49.400 talk more about what we  
NOTE Confidence: 0.9682206

00:07:49.400 --> 00:07:51.240 do, with those tumors, and  
NOTE Confidence: 0.9682206

00:07:51.240 --> 00:07:52.620 this is where, you know,  
NOTE Confidence: 0.94754255

00:07:53.675 --> 00:07:55.694 correlation with staging is also,  
NOTE Confidence: 0.98972434

00:07:56.794 --> 00:07:58.555 important. And so, you know,  
NOTE Confidence: 0.98972434

00:07:58.555 --> 00:07:59.914 what are the takeaways here?  
NOTE Confidence: 0.98972434

00:08:00.235 --> 00:08:01.675 Cutaneous squamous cell carcinoma is  
NOTE Confidence: 0.98972434

00:08:01.675 --> 00:08:02.335 a heterogeneous

NOTE Confidence: 0.8549165  
00:08:04.395 --> 00:08:06.095 group, and, accurate  
NOTE Confidence: 0.9990314  
00:08:06.450 --> 00:08:08.150 risk stratification is critical.  
NOTE Confidence: 0.9688016  
00:08:08.610 --> 00:08:10.610 Nomograms such as risk provide  
NOTE Confidence: 0.9688016  
00:08:10.610 --> 00:08:12.710 individual risk prediction and particularly  
NOTE Confidence: 0.9688016  
00:08:12.770 --> 00:08:13.970 helpful in these gray zone  
NOTE Confidence: 0.9688016  
00:08:13.970 --> 00:08:16.550 cases, and gene expression profiling  
NOTE Confidence: 0.85443926  
00:08:17.090 --> 00:08:19.250 adds biologic risk information that  
NOTE Confidence: 0.85443926  
00:08:19.250 --> 00:08:19.615 may further refine management. And  
NOTE Confidence: 0.85443926  
00:08:19.615 --> 00:08:19.672 to further speak about that,  
NOTE Confidence: 0.85443926  
00:08:19.684 --> 00:08:20.230 I'm gonna turn it over  
NOTE Confidence: 0.56268066  
00:08:20.690 --> 00:08:20.715 to  
NOTE Confidence: 0.9825039  
00:08:29.275 --> 00:08:30.335 Thank you, Katie.  
NOTE Confidence: 0.8931605  
00:08:30.635 --> 00:08:32.154 Alright. Let's pull mine out  
NOTE Confidence: 0.8931605  
00:08:32.154 --> 00:08:32.654 here.  
NOTE Confidence: 0.89928687  
00:08:34.170 --> 00:08:36.350 Share. Presenter mode. Okay.  
NOTE Confidence: 0.9524986

00:08:37.210 --> 00:08:39.290 Alright. So I'm Ansley Roach.  
NOTE Confidence: 0.9524986

00:08:39.290 --> 00:08:40.010 I'm a head and neck  
NOTE Confidence: 0.9524986

00:08:40.010 --> 00:08:40.910 surgeon here.  
NOTE Confidence: 0.99012977

00:08:42.250 --> 00:08:43.710 I'm gonna be just speaking  
NOTE Confidence: 0.99012977

00:08:43.770 --> 00:08:44.910 specifically about,  
NOTE Confidence: 0.96269315

00:08:45.610 --> 00:08:48.115 this forty GEP panel and,  
NOTE Confidence: 0.96269315

00:08:48.514 --> 00:08:49.795 also as it pertains to  
NOTE Confidence: 0.96269315

00:08:49.795 --> 00:08:50.694 the head and neck.  
NOTE Confidence: 0.97384167

00:08:51.074 --> 00:08:51.954 But talking a little bit  
NOTE Confidence: 0.97384167

00:08:51.954 --> 00:08:53.154 about its development, because I  
NOTE Confidence: 0.97384167

00:08:53.154 --> 00:08:54.274 think it's important to just  
NOTE Confidence: 0.97384167

00:08:54.274 --> 00:08:56.054 get an understanding of what  
NOTE Confidence: 0.9188383

00:08:56.595 --> 00:08:57.795 of what this, how this  
NOTE Confidence: 0.9188383

00:08:57.795 --> 00:08:59.714 was validated. So just to  
NOTE Confidence: 0.9188383

00:08:59.714 --> 00:09:00.834 recap some of the things  
NOTE Confidence: 0.9188383

00:09:00.834 --> 00:09:02.214 that Doctor. Swozi mentioned,

NOTE Confidence: 0.96751225

00:09:03.330 --> 00:09:04.929 the high risk features that

NOTE Confidence: 0.96751225

00:09:04.929 --> 00:09:06.309 we see in these patients

NOTE Confidence: 0.96751225

00:09:06.450 --> 00:09:07.970 can vary or can be,

NOTE Confidence: 0.96751225

00:09:08.290 --> 00:09:10.150 attributed to the tumor characteristics

NOTE Confidence: 0.96751225

00:09:10.210 --> 00:09:11.570 themselves. And I've listed them

NOTE Confidence: 0.96751225

00:09:11.570 --> 00:09:13.410 here. Essentially, anything greater than

NOTE Confidence: 0.96751225

00:09:13.410 --> 00:09:15.170 two centimeters depth of invasion

NOTE Confidence: 0.96751225

00:09:15.170 --> 00:09:16.850 beyond the subcutaneous fat or

NOTE Confidence: 0.96751225

00:09:16.850 --> 00:09:17.670 six millimeters.

NOTE Confidence: 0.89027077

00:09:18.084 --> 00:09:19.765 Higher risk areas, so specifically

NOTE Confidence: 0.89027077

00:09:19.765 --> 00:09:21.205 the head and neck, hands,

NOTE Confidence: 0.89027077

00:09:21.205 --> 00:09:22.725 feet, the pre tibial region,

NOTE Confidence: 0.89027077

00:09:22.725 --> 00:09:23.845 and the anal genital re

NOTE Confidence: 0.89027077

00:09:23.925 --> 00:09:25.065 reach, areas,

NOTE Confidence: 0.9565836

00:09:26.005 --> 00:09:27.925 poorly defined borders. Reshare your

NOTE Confidence: 0.9565836

00:09:27.925 --> 00:09:29.205 screen? I think it's not  
NOTE Confidence: 0.9565836

00:09:29.205 --> 00:09:30.265 showing up. Sorry.  
NOTE Confidence: 0.9995314

00:09:30.644 --> 00:09:32.245 That's okay. Thank you. Sorry.  
NOTE Confidence: 0.9995314

00:09:32.245 --> 00:09:33.144 Let's see.  
NOTE Confidence: 0.9973364

00:09:34.679 --> 00:09:35.179 Okay.  
NOTE Confidence: 0.9975297

00:09:36.600 --> 00:09:38.220 Share. Sorry about that.  
NOTE Confidence: 0.97664255

00:09:39.880 --> 00:09:41.240 What about this? Is that  
NOTE Confidence: 0.97664255

00:09:41.240 --> 00:09:42.440 good? Okay. Is it in  
NOTE Confidence: 0.97664255

00:09:42.440 --> 00:09:43.880 presenter mode? Or No. So  
NOTE Confidence: 0.97664255

00:09:43.880 --> 00:09:44.760 if you go up and  
NOTE Confidence: 0.97664255

00:09:44.760 --> 00:09:45.640 you could put it in  
NOTE Confidence: 0.97664255

00:09:45.640 --> 00:09:46.540 presenter mode.  
NOTE Confidence: 0.84116185

00:09:47.634 --> 00:09:48.714 Do I do that through  
NOTE Confidence: 0.84116185

00:09:49.074 --> 00:09:49.894 right there.  
NOTE Confidence: 0.9411648

00:09:51.714 --> 00:09:52.995 If you hit slideshow and  
NOTE Confidence: 0.9411648

00:09:52.995 --> 00:09:53.634 then say,

NOTE Confidence: 0.76799935  
00:09:56.514 --> 00:09:56.755 view  
NOTE Confidence: 0.81473243  
00:09:57.634 --> 00:09:59.654 I'm not saying Exit animation.  
NOTE Confidence: 0.99907994  
00:10:02.990 --> 00:10:04.050 What about this?  
NOTE Confidence: 0.9247667  
00:10:04.990 --> 00:10:06.110 No. It just doesn't know.  
NOTE Confidence: 0.9247667  
00:10:06.270 --> 00:10:07.709 Stopped. Okay. Sorry. So I'm  
NOTE Confidence: 0.9247667  
00:10:07.709 --> 00:10:08.910 just gonna do it old  
NOTE Confidence: 0.9247667  
00:10:08.910 --> 00:10:09.410 school.  
NOTE Confidence: 0.9044393  
00:10:11.390 --> 00:10:12.830 Yes. That? Okay. I'm not  
NOTE Confidence: 0.9044393  
00:10:13.230 --> 00:10:14.350 okay. Great. Thank you. Sorry  
NOTE Confidence: 0.9044393  
00:10:14.350 --> 00:10:15.089 about that.  
NOTE Confidence: 0.8789857  
00:10:16.404 --> 00:10:17.785 And then, also  
NOTE Confidence: 0.89384085  
00:10:18.324 --> 00:10:19.545 indications of,  
NOTE Confidence: 0.8834867  
00:10:20.165 --> 00:10:22.485 perineural invasion such as pain  
NOTE Confidence: 0.8834867  
00:10:22.485 --> 00:10:24.884 or paresthesias or, paresis or  
NOTE Confidence: 0.8834867  
00:10:24.884 --> 00:10:25.384 paralysis,  
NOTE Confidence: 0.97085077

00:10:27.045 --> 00:10:27.545 histopathologic  
NOTE Confidence: 0.85007495

00:10:28.084 --> 00:10:29.785 features, so just different histopathologic  
NOTE Confidence: 0.9561045

00:10:30.245 --> 00:10:31.939 subtypes of squamous cell carcinoma,  
NOTE Confidence: 0.9561045

00:10:32.160 --> 00:10:33.699 certainly the PNI and LVI  
NOTE Confidence: 0.9561045

00:10:33.759 --> 00:10:35.360 that Doctor. Swozi mentioned, and  
NOTE Confidence: 0.9561045

00:10:35.360 --> 00:10:37.040 then patient factors. These all  
NOTE Confidence: 0.9561045

00:10:37.040 --> 00:10:38.660 place patients at high risk,  
NOTE Confidence: 0.97252584

00:10:39.360 --> 00:10:41.519 for metastasis, local recurrence of  
NOTE Confidence: 0.97252584

00:10:41.519 --> 00:10:42.579 squamous cell carcinoma.  
NOTE Confidence: 0.9320314

00:10:44.575 --> 00:10:46.495 As in other disease states  
NOTE Confidence: 0.9320314

00:10:46.495 --> 00:10:47.795 such as breast cancer,  
NOTE Confidence: 0.9618928

00:10:48.975 --> 00:10:50.035 there have been,  
NOTE Confidence: 0.8436408

00:10:50.575 --> 00:10:51.715 a a burgeoning  
NOTE Confidence: 0.9750838

00:10:52.095 --> 00:10:54.595 field of gene expression profiling,  
NOTE Confidence: 0.95208865

00:10:55.790 --> 00:10:57.389 in which a essentially, a  
NOTE Confidence: 0.95208865

00:10:57.389 --> 00:10:59.490 proprietary algorithm is used,



NOTE Confidence: 0.9981895  
00:10:59.870 --> 00:11:02.029 to predict metastatic risk or  
NOTE Confidence: 0.9981895  
00:11:02.029 --> 00:11:02.929 risk of recurrence.  
NOTE Confidence: 0.9673218  
00:11:03.630 --> 00:11:04.829 In this there's one that's  
NOTE Confidence: 0.9673218  
00:11:04.829 --> 00:11:06.429 commercially available for squamous cell  
NOTE Confidence: 0.9673218  
00:11:06.429 --> 00:11:07.949 carcinoma. It's a forty gene  
NOTE Confidence: 0.9673218  
00:11:07.949 --> 00:11:08.449 panel.  
NOTE Confidence: 0.95700395  
00:11:09.165 --> 00:11:10.684 They use two gene expression  
NOTE Confidence: 0.95700395  
00:11:10.684 --> 00:11:12.524 signatures. There are thirty four,  
NOTE Confidence: 0.95700395  
00:11:12.845 --> 00:11:14.605 discriminant genes. They're all listed  
NOTE Confidence: 0.95700395  
00:11:14.605 --> 00:11:15.725 here. It's kind of a  
NOTE Confidence: 0.95700395  
00:11:15.725 --> 00:11:17.245 a variety of different sorts  
NOTE Confidence: 0.95700395  
00:11:17.245 --> 00:11:18.705 of genes they're looking for,  
NOTE Confidence: 0.9484004  
00:11:19.165 --> 00:11:19.665 MMPs,  
NOTE Confidence: 0.9798319  
00:11:20.205 --> 00:11:23.005 metabolic related proteins, transcription factors,  
NOTE Confidence: 0.9798319  
00:11:23.005 --> 00:11:24.625 and then some control genes.  
NOTE Confidence: 0.9798319

00:11:24.900 --> 00:11:26.500 And these this testing can  
NOTE Confidence: 0.9798319

00:11:26.500 --> 00:11:28.280 be done on archived FFPE  
NOTE Confidence: 0.9798319

00:11:28.420 --> 00:11:29.380 samples, so it does not  
NOTE Confidence: 0.9798319

00:11:29.380 --> 00:11:30.580 have to be on fresh  
NOTE Confidence: 0.9798319

00:11:30.580 --> 00:11:31.080 tumor.  
NOTE Confidence: 0.99084115

00:11:32.740 --> 00:11:34.760 The this test was,  
NOTE Confidence: 0.85585946

00:11:35.300 --> 00:11:37.059 developed and as doctor Swozi  
NOTE Confidence: 0.85585946

00:11:37.059 --> 00:11:38.840 said, in a retrospective fashion  
NOTE Confidence: 0.96431947

00:11:39.345 --> 00:11:39.845 where,  
NOTE Confidence: 0.9980084

00:11:41.345 --> 00:11:43.204 long term outcomes were available  
NOTE Confidence: 0.9980084

00:11:43.425 --> 00:11:45.024 and evaluated as part of  
NOTE Confidence: 0.9980084

00:11:45.024 --> 00:11:46.245 the validation cohort.  
NOTE Confidence: 0.9325591

00:11:47.264 --> 00:11:48.885 It was a multi institutional  
NOTE Confidence: 0.9325591

00:11:49.105 --> 00:11:50.625 study across con across the  
NOTE Confidence: 0.9325591

00:11:50.625 --> 00:11:51.105 country,  
NOTE Confidence: 0.97632456

00:11:52.260 --> 00:11:54.420 pulling, three twenty one patients

NOTE Confidence: 0.97632456

00:11:54.420 --> 00:11:55.860 for the validation cohort. It

NOTE Confidence: 0.97632456

00:11:55.860 --> 00:11:56.820 was powered to detect a

NOTE Confidence: 0.97632456

00:11:56.820 --> 00:11:58.260 hazard ratio of three year

NOTE Confidence: 0.97632456

00:11:58.260 --> 00:11:58.760 metastasis

NOTE Confidence: 0.99546385

00:11:59.620 --> 00:12:00.760 of two point one.

NOTE Confidence: 0.9779443

00:12:01.300 --> 00:12:03.300 It, included patients that were

NOTE Confidence: 0.9779443

00:12:03.300 --> 00:12:04.179 at least had at least

NOTE Confidence: 0.9779443

00:12:04.179 --> 00:12:05.300 one high risk feature, so

NOTE Confidence: 0.9779443

00:12:05.300 --> 00:12:05.960 at least

NOTE Confidence: 0.93580985

00:12:06.340 --> 00:12:06.840 BWH

NOTE Confidence: 0.9309373

00:12:07.625 --> 00:12:08.605 one, and then

NOTE Confidence: 0.96110344

00:12:09.304 --> 00:12:10.585 a slightly higher risk of

NOTE Confidence: 0.96110344

00:12:10.585 --> 00:12:12.505 metastasis rate for these patients,

NOTE Confidence: 0.96110344

00:12:12.505 --> 00:12:14.105 or rate of metastasis, sixteen

NOTE Confidence: 0.96110344

00:12:14.105 --> 00:12:15.785 point two percent, versus the

NOTE Confidence: 0.96110344

00:12:15.785 --> 00:12:17.545 general population, which ranges anywhere

NOTE Confidence: 0.96110344

00:12:17.545 --> 00:12:18.845 from two to five percent.

NOTE Confidence: 0.91062444

00:12:20.570 --> 00:12:22.009 Similar to the,

NOTE Confidence: 0.9454555

00:12:22.490 --> 00:12:24.190 survival curves that doctor Swozzi

NOTE Confidence: 0.9454555

00:12:24.250 --> 00:12:25.690 shared, you can see here

NOTE Confidence: 0.9454555

00:12:25.690 --> 00:12:26.190 that,

NOTE Confidence: 0.96112216

00:12:26.809 --> 00:12:27.309 the

NOTE Confidence: 0.8512462

00:12:27.690 --> 00:12:29.630 three year metastasis free survival,

NOTE Confidence: 0.9044973

00:12:30.649 --> 00:12:33.285 is separated out, stratified by

NOTE Confidence: 0.9044973

00:12:33.285 --> 00:12:34.885 these classes with class one

NOTE Confidence: 0.9044973

00:12:34.885 --> 00:12:36.345 a, again, the low biological

NOTE Confidence: 0.9044973

00:12:36.645 --> 00:12:37.145 risk,

NOTE Confidence: 0.9436411

00:12:37.845 --> 00:12:39.225 with a three year metastasis

NOTE Confidence: 0.9436411

00:12:39.365 --> 00:12:41.045 free survival about ninety one

NOTE Confidence: 0.9436411

00:12:41.045 --> 00:12:42.645 percent. Two a would be

NOTE Confidence: 0.9436411

00:12:42.645 --> 00:12:43.304 the moderate,

NOTE Confidence: 0.9536316

00:12:44.005 --> 00:12:45.690 moderate risk. That's about eighty

NOTE Confidence: 0.9397685

00:12:46.090 --> 00:12:47.450 percent through your survival. And

NOTE Confidence: 0.9397685

00:12:47.450 --> 00:12:48.890 2b, as we would expect

NOTE Confidence: 0.9397685

00:12:48.890 --> 00:12:50.670 with the highest risk, biological

NOTE Confidence: 0.9397685

00:12:50.730 --> 00:12:51.230 behavior,

NOTE Confidence: 0.8866689

00:12:52.010 --> 00:12:54.170 through your metastasis free survival

NOTE Confidence: 0.8866689

00:12:54.170 --> 00:12:55.470 about forty four percent.

NOTE Confidence: 0.9664243

00:12:58.135 --> 00:12:59.035 Hazard ratio,

NOTE Confidence: 0.9401262

00:12:59.415 --> 00:13:00.934 it was powered to demonstrate

NOTE Confidence: 0.9401262

00:13:00.934 --> 00:13:02.235 this and hazard ratio,

NOTE Confidence: 0.8047269

00:13:03.415 --> 00:13:04.635 for three year metastasis,

NOTE Confidence: 0.9536851

00:13:05.255 --> 00:13:07.015 for 2a was two point

NOTE Confidence: 0.9536851

00:13:07.015 --> 00:13:07.975 four four, and then it

NOTE Confidence: 0.9536851

00:13:07.975 --> 00:13:10.154 increases tenfold. So three year

NOTE Confidence: 0.96220964

00:13:10.679 --> 00:13:12.280 risk of metastasis for 2B

NOTE Confidence: 0.96220964

00:13:12.280 --> 00:13:13.420 tumors is tenfold,  
NOTE Confidence: 0.9740366

00:13:13.880 --> 00:13:14.380 greater,  
NOTE Confidence: 0.92493904

00:13:15.960 --> 00:13:17.400 than class I. And then  
NOTE Confidence: 0.92493904

00:13:17.400 --> 00:13:19.400 the disease specific survival disease  
NOTE Confidence: 0.92493904

00:13:19.400 --> 00:13:21.260 specific death also is significantly  
NOTE Confidence: 0.92493904

00:13:21.480 --> 00:13:22.860 increased, for both,  
NOTE Confidence: 0.97974217

00:13:23.559 --> 00:13:25.100 2A and 2B tumors.  
NOTE Confidence: 0.9962405

00:13:26.345 --> 00:13:27.384 I think it's important to  
NOTE Confidence: 0.9962405

00:13:27.384 --> 00:13:28.345 just look at how this  
NOTE Confidence: 0.9962405

00:13:28.345 --> 00:13:29.324 tool was developed.  
NOTE Confidence: 0.9651591

00:13:29.944 --> 00:13:30.665 It was,  
NOTE Confidence: 0.8050045

00:13:31.944 --> 00:13:32.504 it was,  
NOTE Confidence: 0.9798876

00:13:33.144 --> 00:13:33.884 deep learning,  
NOTE Confidence: 0.9646565

00:13:34.504 --> 00:13:37.004 on training data that was,  
NOTE Confidence: 0.92279714

00:13:37.464 --> 00:13:39.384 one hundred and twenty two  
NOTE Confidence: 0.92279714

00:13:39.384 --> 00:13:39.884 patients.

NOTE Confidence: 0.9757824

00:13:40.429 --> 00:13:41.550 I think it's important to

NOTE Confidence: 0.9757824

00:13:41.550 --> 00:13:42.509 note that as you can

NOTE Confidence: 0.9757824

00:13:42.509 --> 00:13:43.250 see here,

NOTE Confidence: 0.99022025

00:13:44.750 --> 00:13:46.829 the AJCC class t three

NOTE Confidence: 0.99022025

00:13:46.829 --> 00:13:48.190 and t four tumors are

NOTE Confidence: 0.99022025

00:13:48.190 --> 00:13:49.089 quite underrepresented,

NOTE Confidence: 0.97351336

00:13:49.470 --> 00:13:51.069 specifically t four. There's one

NOTE Confidence: 0.97351336

00:13:51.069 --> 00:13:52.269 patient with a t four

NOTE Confidence: 0.97351336

00:13:52.269 --> 00:13:52.769 tumor.

NOTE Confidence: 0.97200227

00:13:53.125 --> 00:13:54.005 And I think the the

NOTE Confidence: 0.97200227

00:13:54.005 --> 00:13:55.285 same can be said for

NOTE Confidence: 0.97200227

00:13:55.285 --> 00:13:57.285 BWH staging, so a pretty

NOTE Confidence: 0.97200227

00:13:57.285 --> 00:13:58.885 small sample size for t

NOTE Confidence: 0.97200227

00:13:58.885 --> 00:14:00.165 two b and t three

NOTE Confidence: 0.97200227

00:14:00.165 --> 00:14:00.665 tumors.

NOTE Confidence: 0.9973977

00:14:01.525 --> 00:14:03.625 When they, trained their,  
NOTE Confidence: 0.9929523

00:14:04.325 --> 00:14:05.065 their model,  
NOTE Confidence: 0.91340566

00:14:05.525 --> 00:14:06.725 and then compared it or  
NOTE Confidence: 0.91340566

00:14:06.725 --> 00:14:08.345 then validated against  
NOTE Confidence: 0.951758

00:14:09.179 --> 00:14:10.860 additional cohort of three twenty  
NOTE Confidence: 0.951758

00:14:10.860 --> 00:14:11.520 one patients,  
NOTE Confidence: 0.89907444

00:14:12.140 --> 00:14:12.620 their,  
NOTE Confidence: 0.95029753

00:14:13.100 --> 00:14:14.540 numbers of T3 and T4  
NOTE Confidence: 0.95029753

00:14:14.540 --> 00:14:16.220 tumors were slightly increased, but  
NOTE Confidence: 0.95029753

00:14:16.220 --> 00:14:17.580 still quite small. So just  
NOTE Confidence: 0.95029753

00:14:17.580 --> 00:14:19.420 seven seven patients with T4  
NOTE Confidence: 0.95029753

00:14:19.420 --> 00:14:21.580 tumors by AJCC eight and  
NOTE Confidence: 0.95029753

00:14:21.580 --> 00:14:23.100 seven with T3 tumors by  
NOTE Confidence: 0.95029753

00:14:23.100 --> 00:14:23.600 BWH.  
NOTE Confidence: 0.96187234

00:14:24.735 --> 00:14:25.235 The,  
NOTE Confidence: 0.96656257

00:14:25.695 --> 00:14:26.575 at the end of their



NOTE Confidence: 0.96656257

00:14:26.575 --> 00:14:28.015 kind of validation study, they

NOTE Confidence: 0.96656257

00:14:28.015 --> 00:14:29.214 found that about half of

NOTE Confidence: 0.96656257

00:14:29.214 --> 00:14:30.654 their patients had this class

NOTE Confidence: 0.96656257

00:14:30.654 --> 00:14:32.415 one low biologic risk. Class

NOTE Confidence: 0.96656257

00:14:32.415 --> 00:14:33.855 2a was just under half

NOTE Confidence: 0.96656257

00:14:33.855 --> 00:14:35.535 with a very small proportion

NOTE Confidence: 0.96656257

00:14:35.535 --> 00:14:36.975 being class 2b, that very

NOTE Confidence: 0.96656257

00:14:36.975 --> 00:14:37.714 high risk.

NOTE Confidence: 0.9874233

00:14:38.710 --> 00:14:39.830 I think it's also interesting

NOTE Confidence: 0.9874233

00:14:39.830 --> 00:14:40.870 to look at some of

NOTE Confidence: 0.9874233

00:14:40.870 --> 00:14:41.350 their,

NOTE Confidence: 0.99028844

00:14:41.830 --> 00:14:43.610 some of their regression data.

NOTE Confidence: 0.9831892

00:14:44.710 --> 00:14:46.650 Their data failed to show,

NOTE Confidence: 0.96974534

00:14:47.270 --> 00:14:48.090 an increased,

NOTE Confidence: 0.9613032

00:14:48.950 --> 00:14:50.150 or a hazard ratio for

NOTE Confidence: 0.9613032

00:14:50.150 --> 00:14:51.830 three year metastasis for T4  
NOTE Confidence: 0.9613032

00:14:51.830 --> 00:14:52.330 tumors.  
NOTE Confidence: 0.9777708

00:14:52.904 --> 00:14:53.945 You would think that by  
NOTE Confidence: 0.9777708

00:14:53.945 --> 00:14:56.264 AJCC criteria T4 tumors, you  
NOTE Confidence: 0.9777708

00:14:56.264 --> 00:14:57.625 would see an increased risk  
NOTE Confidence: 0.9777708

00:14:57.625 --> 00:14:58.904 of three year metastasis. It  
NOTE Confidence: 0.9777708

00:14:58.904 --> 00:15:00.264 just makes sense. These are  
NOTE Confidence: 0.9777708

00:15:00.264 --> 00:15:02.105 advanced stage tumors, but their  
NOTE Confidence: 0.9777708

00:15:02.105 --> 00:15:03.565 data is not showing this.  
NOTE Confidence: 0.9463884

00:15:03.945 --> 00:15:04.904 And the same is true  
NOTE Confidence: 0.9463884

00:15:04.904 --> 00:15:05.644 for the BWH  
NOTE Confidence: 0.96230435

00:15:06.040 --> 00:15:07.400 staging. Their t three tumors,  
NOTE Confidence: 0.96230435

00:15:07.400 --> 00:15:08.760 there's not an increase or  
NOTE Confidence: 0.96230435

00:15:08.760 --> 00:15:10.280 there there's no increased kind  
NOTE Confidence: 0.96230435

00:15:10.280 --> 00:15:11.880 of hazard of, three year  
NOTE Confidence: 0.96230435

00:15:11.880 --> 00:15:12.380 metastasis.

NOTE Confidence: 0.94285846  
00:15:13.480 --> 00:15:14.920 When they kind of change  
NOTE Confidence: 0.94285846  
00:15:14.920 --> 00:15:15.800 the data a little bit  
NOTE Confidence: 0.94285846  
00:15:15.800 --> 00:15:17.000 and combine some of these,  
NOTE Confidence: 0.9593998  
00:15:17.720 --> 00:15:20.195 the the staging, they combined  
NOTE Confidence: 0.9593998  
00:15:20.255 --> 00:15:21.215 t one and t two  
NOTE Confidence: 0.9593998  
00:15:21.215 --> 00:15:22.415 and then combined t three,  
NOTE Confidence: 0.9593998  
00:15:22.415 --> 00:15:23.775 t four, and then they  
NOTE Confidence: 0.9593998  
00:15:23.775 --> 00:15:24.895 did find a,  
NOTE Confidence: 0.98572904  
00:15:25.775 --> 00:15:27.615 an increased hazard of three  
NOTE Confidence: 0.98572904  
00:15:27.615 --> 00:15:28.435 year metastasis  
NOTE Confidence: 0.9945339  
00:15:28.815 --> 00:15:29.315 of  
NOTE Confidence: 0.8284087  
00:15:29.695 --> 00:15:30.195 two,  
NOTE Confidence: 0.8794593  
00:15:31.379 --> 00:15:31.860 with,  
NOTE Confidence: 0.9247074  
00:15:32.259 --> 00:15:33.699 class 2b having a near  
NOTE Confidence: 0.9247074  
00:15:33.699 --> 00:15:34.199 tenfold,  
NOTE Confidence: 0.9894474

00:15:35.139 --> 00:15:36.420 increased risk of three year  
NOTE Confidence: 0.9894474

00:15:36.420 --> 00:15:36.920 metastasis.  
NOTE Confidence: 0.96216786

00:15:37.860 --> 00:15:39.060 But important to note that  
NOTE Confidence: 0.96216786

00:15:39.060 --> 00:15:40.600 advanced stage tumors are underrepresented  
NOTE Confidence: 0.96216786

00:15:40.819 --> 00:15:42.180 in this validation study. So  
NOTE Confidence: 0.96216786

00:15:42.180 --> 00:15:43.379 what raises the question of,  
NOTE Confidence: 0.96216786

00:15:43.379 --> 00:15:44.894 is this a useful tool  
NOTE Confidence: 0.96216786

00:15:44.894 --> 00:15:46.675 for these advanced stage tumors,  
NOTE Confidence: 0.9325207

00:15:47.535 --> 00:15:49.795 T3, T4 by AJCC criteria.  
NOTE Confidence: 0.99685955

00:15:50.894 --> 00:15:52.574 Efforts to look at all  
NOTE Confidence: 0.99685955

00:15:52.574 --> 00:15:53.634 the available literature,  
NOTE Confidence: 0.9561953

00:15:54.095 --> 00:15:55.295 have been made of meta  
NOTE Confidence: 0.9561953

00:15:55.295 --> 00:15:57.375 analysis and systematic review, looked  
NOTE Confidence: 0.9561953

00:15:57.375 --> 00:15:58.274 at all available,  
NOTE Confidence: 0.92856747

00:15:59.700 --> 00:16:00.900 research at the time. This  
NOTE Confidence: 0.92856747

00:16:00.900 --> 00:16:01.780 was a twenty twenty three

NOTE Confidence: 0.92856747

00:16:01.780 --> 00:16:04.020 meta analysis, and they were

NOTE Confidence: 0.92856747

00:16:04.020 --> 00:16:06.100 after they, looked through all

NOTE Confidence: 0.92856747

00:16:06.100 --> 00:16:08.340 available studies, they, found three

NOTE Confidence: 0.92856747

00:16:08.340 --> 00:16:09.700 studies that reached that met

NOTE Confidence: 0.92856747

00:16:09.700 --> 00:16:11.780 inclusion criteria representing just over

NOTE Confidence: 0.92856747

00:16:11.780 --> 00:16:12.705 a thousand patients.

NOTE Confidence: 0.98218846

00:16:13.265 --> 00:16:14.625 They did find similar three

NOTE Confidence: 0.98218846

00:16:14.625 --> 00:16:16.945 year metastasis free survival across

NOTE Confidence: 0.98218846

00:16:16.945 --> 00:16:18.245 classes, where

NOTE Confidence: 0.9031069

00:16:18.625 --> 00:16:19.825 similar to the data I

NOTE Confidence: 0.9031069

00:16:19.825 --> 00:16:21.265 presented earlier and what Doctor.

NOTE Confidence: 0.9031069

00:16:21.265 --> 00:16:22.325 Swozzi presented,

NOTE Confidence: 0.9121022

00:16:22.705 --> 00:16:24.945 class I anywhere from ninety

NOTE Confidence: 0.9121022

00:16:24.945 --> 00:16:25.825 one percent to ninety three

NOTE Confidence: 0.9121022

00:16:25.825 --> 00:16:27.825 percent, three year metastasis free

NOTE Confidence: 0.9121022

00:16:27.825 --> 00:16:28.325 survival.  
NOTE Confidence: 0.97046936

00:16:28.680 --> 00:16:29.800 Two a is slightly worse  
NOTE Confidence: 0.97046936

00:16:29.800 --> 00:16:31.000 at seventy six to eighty  
NOTE Confidence: 0.97046936

00:16:31.000 --> 00:16:32.300 percent. And two b,  
NOTE Confidence: 0.9763922

00:16:32.920 --> 00:16:34.120 the worst of the of  
NOTE Confidence: 0.9763922

00:16:34.120 --> 00:16:35.320 the three with forty three  
NOTE Confidence: 0.9763922

00:16:35.320 --> 00:16:36.540 to forty seven percent  
NOTE Confidence: 0.9423562

00:16:37.000 --> 00:16:38.940 three year metastasis free survival.  
NOTE Confidence: 0.9803099

00:16:40.520 --> 00:16:42.700 Looking at positive predictive value  
NOTE Confidence: 0.9803099

00:16:42.920 --> 00:16:44.140 of the forty GEP,  
NOTE Confidence: 0.95419776

00:16:44.895 --> 00:16:46.435 is actually a fairly,  
NOTE Confidence: 0.982347

00:16:47.135 --> 00:16:49.375 substantial positive predictive value, about  
NOTE Confidence: 0.982347

00:16:49.375 --> 00:16:50.435 fifty five percent,  
NOTE Confidence: 0.861111

00:16:50.895 --> 00:16:52.115 for class 2b  
NOTE Confidence: 0.9383763

00:16:52.575 --> 00:16:54.175 when compared to class one  
NOTE Confidence: 0.9383763

00:16:54.175 --> 00:16:55.315 and class 2a.

NOTE Confidence: 0.99859047

00:16:55.935 --> 00:16:57.215 And when you compare that

NOTE Confidence: 0.99859047

00:16:57.215 --> 00:16:58.575 to the positive predictive value

NOTE Confidence: 0.99859047

00:16:58.575 --> 00:16:59.395 of AJCC

NOTE Confidence: 0.95673966

00:17:00.140 --> 00:17:00.960 and BWH,

NOTE Confidence: 0.99256295

00:17:02.060 --> 00:17:04.060 the forty gene panel is

NOTE Confidence: 0.99256295

00:17:04.060 --> 00:17:05.740 higher. So the positive predictive

NOTE Confidence: 0.99256295

00:17:05.740 --> 00:17:07.580 value for AJCC was just

NOTE Confidence: 0.99256295

00:17:07.580 --> 00:17:08.540 about a third, thirty three

NOTE Confidence: 0.99256295

00:17:08.540 --> 00:17:10.300 percent, and for the Brigham

NOTE Confidence: 0.99256295

00:17:10.300 --> 00:17:11.820 and Women's, thirty six percent.

NOTE Confidence: 0.99256295

00:17:11.820 --> 00:17:12.320 So

NOTE Confidence: 0.98022485

00:17:12.675 --> 00:17:14.595 the positive predictive value for

NOTE Confidence: 0.98022485

00:17:14.595 --> 00:17:16.855 the forty gene, expression profiling

NOTE Confidence: 0.98022485

00:17:16.915 --> 00:17:19.575 test is does outperform AJCC

NOTE Confidence: 0.98022485

00:17:19.875 --> 00:17:20.615 and BWH.

NOTE Confidence: 0.9988534

00:17:22.195 --> 00:17:23.555 To look specifically at head  
NOTE Confidence: 0.9988534

00:17:23.555 --> 00:17:24.035 and neck,  
NOTE Confidence: 0.9822498

00:17:24.835 --> 00:17:26.275 a subset of the original  
NOTE Confidence: 0.9822498

00:17:26.275 --> 00:17:28.135 validation cohort was analyzed.  
NOTE Confidence: 0.704504

00:17:28.740 --> 00:17:29.800 Similar researchers,  
NOTE Confidence: 0.9593079

00:17:30.260 --> 00:17:31.300 on this study as well,  
NOTE Confidence: 0.9593079

00:17:31.300 --> 00:17:32.580 but looking specifically at the  
NOTE Confidence: 0.9593079

00:17:32.580 --> 00:17:33.400 head and neck.  
NOTE Confidence: 0.90761346

00:17:34.100 --> 00:17:36.100 Similar Kaplan Meier curves for  
NOTE Confidence: 0.90761346

00:17:36.100 --> 00:17:37.540 these with class I three  
NOTE Confidence: 0.90761346

00:17:37.540 --> 00:17:39.380 year metastasis free survival ninety  
NOTE Confidence: 0.90761346

00:17:39.380 --> 00:17:40.260 two percent. You can see  
NOTE Confidence: 0.90761346

00:17:40.260 --> 00:17:41.619 the numbers here, seventy six  
NOTE Confidence: 0.90761346

00:17:41.619 --> 00:17:43.140 for class IIa, forty four  
NOTE Confidence: 0.90761346

00:17:43.140 --> 00:17:44.165 for class two b. So  
NOTE Confidence: 0.90761346

00:17:44.165 --> 00:17:45.225 very similar to,



NOTE Confidence: 0.9758136  
00:17:46.085 --> 00:17:46.965 looking at,  
NOTE Confidence: 0.99706155  
00:17:47.365 --> 00:17:48.885 squamous cell carcinomas of the  
NOTE Confidence: 0.99706155  
00:17:48.885 --> 00:17:50.325 entire body, when you look  
NOTE Confidence: 0.99706155  
00:17:50.325 --> 00:17:51.045 at this for head and  
NOTE Confidence: 0.99706155  
00:17:51.045 --> 00:17:51.705 neck cancers.  
NOTE Confidence: 0.99322355  
00:17:54.244 --> 00:17:56.345 The sites represented here,  
NOTE Confidence: 0.9834457  
00:17:57.045 --> 00:17:59.190 where lip and scalp actually  
NOTE Confidence: 0.9834457  
00:17:59.190 --> 00:18:00.230 had the highest rates of  
NOTE Confidence: 0.9834457  
00:18:00.230 --> 00:18:00.730 metastasis.  
NOTE Confidence: 0.99956095  
00:18:01.270 --> 00:18:02.650 The most common locations  
NOTE Confidence: 0.96107227  
00:18:03.109 --> 00:18:05.510 were the, ears, cheeks, and  
NOTE Confidence: 0.96107227  
00:18:05.510 --> 00:18:06.010 scalp.  
NOTE Confidence: 0.97279257  
00:18:06.869 --> 00:18:08.309 But when they looked at  
NOTE Confidence: 0.97279257  
00:18:08.309 --> 00:18:10.070 metastasis rate by location on  
NOTE Confidence: 0.97279257  
00:18:10.070 --> 00:18:11.030 the head and neck, there  
NOTE Confidence: 0.97279257

00:18:11.109 --> 00:18:12.630 they found no difference, in  
NOTE Confidence: 0.97279257

00:18:12.630 --> 00:18:14.375 metastatic events and,  
NOTE Confidence: 0.998733

00:18:15.014 --> 00:18:16.054 location of the head and  
NOTE Confidence: 0.998733

00:18:16.054 --> 00:18:16.554 neck.  
NOTE Confidence: 0.9677092

00:18:17.815 --> 00:18:18.695 And then here you can  
NOTE Confidence: 0.9677092

00:18:18.695 --> 00:18:20.054 see here again depicted the  
NOTE Confidence: 0.9677092

00:18:20.215 --> 00:18:21.575 this is it's very similar  
NOTE Confidence: 0.9677092

00:18:21.575 --> 00:18:23.095 to what, what I presented  
NOTE Confidence: 0.9677092

00:18:23.095 --> 00:18:24.615 with the validation study. This  
NOTE Confidence: 0.9677092

00:18:24.695 --> 00:18:26.375 when you extrapolate out or,  
NOTE Confidence: 0.9514263

00:18:26.980 --> 00:18:28.019 analyze the head and neck  
NOTE Confidence: 0.9514263

00:18:28.019 --> 00:18:29.139 patients, the say it's a  
NOTE Confidence: 0.9514263

00:18:29.139 --> 00:18:30.580 similar positive predictive value of  
NOTE Confidence: 0.9514263

00:18:30.580 --> 00:18:31.960 about fifty five percent,  
NOTE Confidence: 0.9092332

00:18:32.899 --> 00:18:34.500 higher than the positive predictive  
NOTE Confidence: 0.9092332

00:18:34.500 --> 00:18:35.460 value. And that's for the

NOTE Confidence: 0.9092332

00:18:35.460 --> 00:18:36.600 for the for the gene,

NOTE Confidence: 0.9846444

00:18:37.139 --> 00:18:39.375 gene expression profiling test, fifty

NOTE Confidence: 0.9846444

00:18:39.375 --> 00:18:41.395 five percent positive predictive value

NOTE Confidence: 0.95382184

00:18:41.935 --> 00:18:43.455 compared to just thirty seven

NOTE Confidence: 0.95382184

00:18:43.455 --> 00:18:44.515 percent for AJCC

NOTE Confidence: 0.9536325

00:18:44.815 --> 00:18:46.494 eighth edition for advanced stage

NOTE Confidence: 0.9536325

00:18:46.494 --> 00:18:47.875 tumors and the BWH,

NOTE Confidence: 0.9857461

00:18:48.655 --> 00:18:50.095 advanced stage tumors. So, again,

NOTE Confidence: 0.9857461

00:18:50.095 --> 00:18:51.775 it outperforms those two for

NOTE Confidence: 0.9857461

00:18:51.775 --> 00:18:53.155 the positive predictive value.

NOTE Confidence: 0.93366146

00:18:55.270 --> 00:18:57.109 So like the AJCC eighth

NOTE Confidence: 0.93366146

00:18:57.109 --> 00:18:58.730 edition and Brigham women's

NOTE Confidence: 0.9529064

00:18:59.030 --> 00:19:00.869 staging system, the forty gene,

NOTE Confidence: 0.9529064

00:19:01.270 --> 00:19:03.990 expression profile testing does class

NOTE Confidence: 0.9529064

00:19:04.150 --> 00:19:05.590 or it classified lower rates

NOTE Confidence: 0.9529064

00:19:05.590 --> 00:19:06.790 of tumor as high risk  
NOTE Confidence: 0.9529064

00:19:06.790 --> 00:19:08.090 compared to the NCCN.  
NOTE Confidence: 0.90139794

00:19:08.595 --> 00:19:10.034 As doctor Suozzi showed,  
NOTE Confidence: 0.9999223

00:19:10.434 --> 00:19:10.934 NCCN  
NOTE Confidence: 0.98940605

00:19:11.794 --> 00:19:13.475 breaks patients down by low,  
NOTE Confidence: 0.98940605

00:19:13.475 --> 00:19:14.775 high, and very high.  
NOTE Confidence: 0.99574214

00:19:15.155 --> 00:19:16.855 And just by definition,  
NOTE Confidence: 0.9343643

00:19:18.195 --> 00:19:19.554 head and neck is high  
NOTE Confidence: 0.9343643

00:19:19.554 --> 00:19:20.054 risk.  
NOTE Confidence: 0.9962307

00:19:20.434 --> 00:19:22.560 And so this test actually  
NOTE Confidence: 0.96162295

00:19:22.860 --> 00:19:23.920 kind of downstages,  
NOTE Confidence: 0.97987705

00:19:24.940 --> 00:19:25.440 downgrades,  
NOTE Confidence: 0.99694973

00:19:26.460 --> 00:19:27.500 patients of the head and  
NOTE Confidence: 0.99694973

00:19:27.500 --> 00:19:28.000 neck,  
NOTE Confidence: 0.98116565

00:19:28.300 --> 00:19:29.280 whereas the NCCN,  
NOTE Confidence: 0.9997581

00:19:29.900 --> 00:19:31.040 would not do that.

NOTE Confidence: 0.94827366  
00:19:31.420 --> 00:19:32.460 And then when they compared  
NOTE Confidence: 0.94827366  
00:19:32.460 --> 00:19:33.820 these the head and neck  
NOTE Confidence: 0.94827366  
00:19:33.820 --> 00:19:34.320 sites,  
NOTE Confidence: 0.98275197  
00:19:35.804 --> 00:19:36.244 to,  
NOTE Confidence: 0.9855919  
00:19:36.684 --> 00:19:38.284 cancers of all sites of  
NOTE Confidence: 0.9855919  
00:19:38.284 --> 00:19:39.484 the body, they found that  
NOTE Confidence: 0.9855919  
00:19:39.484 --> 00:19:40.845 a higher percentage of cases  
NOTE Confidence: 0.9855919  
00:19:40.845 --> 00:19:42.205 were at moderate risk, so  
NOTE Confidence: 0.9855919  
00:19:42.205 --> 00:19:42.865 at 2a,  
NOTE Confidence: 0.9802769  
00:19:43.325 --> 00:19:44.605 and that a lower percent  
NOTE Confidence: 0.9802769  
00:19:44.605 --> 00:19:46.524 was at, the low risk  
NOTE Confidence: 0.9802769  
00:19:46.524 --> 00:19:47.904 of of class one,  
NOTE Confidence: 0.93142265  
00:19:48.640 --> 00:19:49.760 implying a sort of shift  
NOTE Confidence: 0.93142265  
00:19:49.760 --> 00:19:50.800 to higher risk for head  
NOTE Confidence: 0.93142265  
00:19:50.800 --> 00:19:52.580 and neck region, which we  
NOTE Confidence: 0.90685403

00:19:52.960 --> 00:19:54.100 know that to be true.  
NOTE Confidence: 0.9726946

00:19:54.880 --> 00:19:56.340 So I'm just gonna demonstrate  
NOTE Confidence: 0.9726946

00:19:56.560 --> 00:19:57.520 kind of the impact that  
NOTE Confidence: 0.9726946

00:19:57.520 --> 00:19:59.040 this could have in some  
NOTE Confidence: 0.9726946

00:19:59.040 --> 00:20:00.640 clinical scenarios. So these are  
NOTE Confidence: 0.9726946

00:20:00.640 --> 00:20:01.680 case studies that,  
NOTE Confidence: 0.98204076

00:20:03.325 --> 00:20:04.685 two cases from a case  
NOTE Confidence: 0.98204076

00:20:04.685 --> 00:20:06.285 series published in two thousand  
NOTE Confidence: 0.98204076

00:20:06.285 --> 00:20:08.125 and two, two very similar  
NOTE Confidence: 0.98204076

00:20:08.125 --> 00:20:09.805 patients from just kind of  
NOTE Confidence: 0.98204076

00:20:09.805 --> 00:20:10.465 their history.  
NOTE Confidence: 0.9881218

00:20:11.005 --> 00:20:11.805 So the first is a  
NOTE Confidence: 0.9881218

00:20:11.805 --> 00:20:13.105 sixty five year old male  
NOTE Confidence: 0.9881218

00:20:13.325 --> 00:20:14.625 with a double transplant,  
NOTE Confidence: 0.932345

00:20:15.405 --> 00:20:17.085 with, who developed this sort  
NOTE Confidence: 0.932345

00:20:17.085 --> 00:20:18.220 of small one point three

NOTE Confidence: 0.932345  
00:20:18.220 --> 00:20:20.159 centimeter papule on the temple.  
NOTE Confidence: 0.93700796  
00:20:20.460 --> 00:20:21.980 By AJCC, it's a stage  
NOTE Confidence: 0.93700796  
00:20:21.980 --> 00:20:23.419 one. BWH, it was a  
NOTE Confidence: 0.93700796  
00:20:23.419 --> 00:20:24.480 stage two a.  
NOTE Confidence: 0.94243693  
00:20:25.580 --> 00:20:27.919 He underwent Moe's, surgery,  
NOTE Confidence: 0.9975921  
00:20:28.380 --> 00:20:29.359 several stages.  
NOTE Confidence: 0.9014686  
00:20:30.380 --> 00:20:32.355 There was a an initial,  
NOTE Confidence: 0.99343896  
00:20:32.734 --> 00:20:34.255 initially, all margins were determined  
NOTE Confidence: 0.99343896  
00:20:34.255 --> 00:20:35.135 to be negative, but a  
NOTE Confidence: 0.99343896  
00:20:35.135 --> 00:20:36.895 subsequent analysis showed a small  
NOTE Confidence: 0.99343896  
00:20:36.895 --> 00:20:38.034 focus of,  
NOTE Confidence: 0.99621266  
00:20:38.734 --> 00:20:39.934 of cancer remaining in the  
NOTE Confidence: 0.99621266  
00:20:39.934 --> 00:20:42.115 tumor bed. Patient was notified,  
NOTE Confidence: 0.97195804  
00:20:42.975 --> 00:20:44.975 discussed additional treatment with radiation  
NOTE Confidence: 0.97195804  
00:20:44.975 --> 00:20:46.434 oncology. He declined.  
NOTE Confidence: 0.9780204

00:20:47.160 --> 00:20:47.600 And,  
NOTE Confidence: 0.9767912

00:20:48.040 --> 00:20:49.100 at the time of follow-up,  
NOTE Confidence: 0.9767912

00:20:49.320 --> 00:20:49.800 he,  
NOTE Confidence: 0.99988157

00:20:50.359 --> 00:20:51.580 was without disease.  
NOTE Confidence: 0.9887611

00:20:52.359 --> 00:20:53.720 They tested his tumor, and  
NOTE Confidence: 0.9887611

00:20:53.720 --> 00:20:55.020 it was a class one,  
NOTE Confidence: 0.97834986

00:20:55.720 --> 00:20:57.100 for the forty GEP.  
NOTE Confidence: 0.98664576

00:20:58.600 --> 00:20:59.880 A very similar patient, a  
NOTE Confidence: 0.98664576

00:20:59.880 --> 00:21:00.920 sixty nine year old male,  
NOTE Confidence: 0.98664576

00:21:00.920 --> 00:21:02.845 also liver transplant, several month  
NOTE Confidence: 0.98664576

00:21:02.845 --> 00:21:04.684 history of a similar size  
NOTE Confidence: 0.98664576

00:21:04.684 --> 00:21:06.225 lesion in a similar location.  
NOTE Confidence: 0.9725725

00:21:06.924 --> 00:21:07.984 This one's exophytic,  
NOTE Confidence: 0.9419397

00:21:08.525 --> 00:21:10.205 in its appearance, but similar  
NOTE Confidence: 0.9419397

00:21:10.205 --> 00:21:12.285 staging, AJCC eighth edition one  
NOTE Confidence: 0.9419397

00:21:12.285 --> 00:21:13.265 and then the BWH



NOTE Confidence: 0.99606925  
00:21:13.580 --> 00:21:14.480 t two a.  
NOTE Confidence: 0.99092853  
00:21:14.940 --> 00:21:16.320 So this patient underwent,  
NOTE Confidence: 0.9130427  
00:21:16.780 --> 00:21:19.200 Mohs micrographic surgery, two stages,  
NOTE Confidence: 0.86542386  
00:21:19.740 --> 00:21:20.960 margins were clear,  
NOTE Confidence: 0.9990164  
00:21:21.820 --> 00:21:24.060 very short interval recurrence at  
NOTE Confidence: 0.9990164  
00:21:24.060 --> 00:21:25.040 about four months.  
NOTE Confidence: 0.8795328  
00:21:26.955 --> 00:21:29.935 He consulted with, radiation oncology.  
NOTE Confidence: 0.8795328  
00:21:30.075 --> 00:21:30.815 He received  
NOTE Confidence: 0.87654144  
00:21:31.435 --> 00:21:32.795 he received radiation to the  
NOTE Confidence: 0.87654144  
00:21:32.795 --> 00:21:33.295 temple.  
NOTE Confidence: 0.9823289  
00:21:34.155 --> 00:21:35.855 He developed cervical lymphadenopathy,  
NOTE Confidence: 0.75472707  
00:21:37.275 --> 00:21:37.775 and,  
NOTE Confidence: 0.9752605  
00:21:39.220 --> 00:21:41.060 which was positive for squamous  
NOTE Confidence: 0.9752605  
00:21:41.060 --> 00:21:42.280 cell carcinoma metastasis.  
NOTE Confidence: 0.9812263  
00:21:43.620 --> 00:21:45.220 He, rather than having surgery,  
NOTE Confidence: 0.9812263

00:21:45.220 --> 00:21:46.500 he underwent radiation to the  
NOTE Confidence: 0.9812263  
00:21:46.500 --> 00:21:47.000 neck.  
NOTE Confidence: 0.947323  
00:21:47.380 --> 00:21:48.360 He then developed,  
NOTE Confidence: 0.91038465  
00:21:49.380 --> 00:21:50.600 mediastinal metastasis,  
NOTE Confidence: 0.9597456  
00:21:51.715 --> 00:21:53.955 ultimately was started on it  
NOTE Confidence: 0.9597456  
00:21:53.955 --> 00:21:55.715 was given targeted radiation to  
NOTE Confidence: 0.9597456  
00:21:55.715 --> 00:21:56.294 the lung,  
NOTE Confidence: 0.9681398  
00:21:56.835 --> 00:21:58.595 was trialed on some systemic  
NOTE Confidence: 0.9681398  
00:21:58.595 --> 00:21:59.955 therapy, but he progressed through  
NOTE Confidence: 0.9681398  
00:21:59.955 --> 00:22:00.455 disease,  
NOTE Confidence: 0.9644808  
00:22:01.234 --> 00:22:02.135 and then ultimately,  
NOTE Confidence: 0.96253633  
00:22:02.674 --> 00:22:03.975 succumbed to his disease.  
NOTE Confidence: 0.98435867  
00:22:04.940 --> 00:22:06.780 Testing of his tumor revealed  
NOTE Confidence: 0.98435867  
00:22:06.780 --> 00:22:07.840 class two b.  
NOTE Confidence: 0.9948007  
00:22:08.140 --> 00:22:10.080 So two very similar appearing,  
NOTE Confidence: 0.98744035  
00:22:10.619 --> 00:22:11.840 kind of presentations,

NOTE Confidence: 0.9838923  
00:22:12.300 --> 00:22:13.740 but the biology of these  
NOTE Confidence: 0.9838923  
00:22:13.740 --> 00:22:15.840 tumors are dramatically different,  
NOTE Confidence: 0.99951017  
00:22:16.140 --> 00:22:17.520 and that does get detected  
NOTE Confidence: 0.9659501  
00:22:17.820 --> 00:22:19.740 on this forty, gene expression  
NOTE Confidence: 0.9659501  
00:22:19.740 --> 00:22:20.115 profile  
NOTE Confidence: 0.99724925  
00:22:20.994 --> 00:22:22.195 test. So ways that we  
NOTE Confidence: 0.99724925  
00:22:22.195 --> 00:22:23.795 can utilize this,  
NOTE Confidence: 0.91284704  
00:22:24.275 --> 00:22:25.875 for t or 2a and  
NOTE Confidence: 0.91284704  
00:22:25.875 --> 00:22:26.775 2b tumors,  
NOTE Confidence: 0.9904629  
00:22:27.395 --> 00:22:28.675 would be to consider additional  
NOTE Confidence: 0.9904629  
00:22:28.675 --> 00:22:30.035 workup to evaluate the nodal  
NOTE Confidence: 0.9904629  
00:22:30.035 --> 00:22:30.515 basin,  
NOTE Confidence: 0.84804195  
00:22:30.994 --> 00:22:32.295 CT NET with contrast.  
NOTE Confidence: 0.9442748  
00:22:32.990 --> 00:22:34.430 You could con also, if  
NOTE Confidence: 0.9442748  
00:22:34.430 --> 00:22:35.470 you're having any issues with  
NOTE Confidence: 0.9442748

00:22:35.470 --> 00:22:36.430 insurance, you could start with  
NOTE Confidence: 0.9442748

00:22:36.430 --> 00:22:37.170 an ultrasound,  
NOTE Confidence: 0.90649295

00:22:38.270 --> 00:22:39.390 and then assessing the nodal  
NOTE Confidence: 0.90649295

00:22:39.390 --> 00:22:40.590 basin with a lymph node  
NOTE Confidence: 0.90649295

00:22:40.590 --> 00:22:42.210 biopsy if there is lymphadenopathy  
NOTE Confidence: 0.89012706

00:22:42.590 --> 00:22:44.450 just proceeding with, neck dissection.  
NOTE Confidence: 0.89005613

00:22:45.494 --> 00:22:46.234 Also, potentially  
NOTE Confidence: 0.85560155

00:22:46.615 --> 00:22:47.595 a role for,  
NOTE Confidence: 0.997488

00:22:48.455 --> 00:22:50.155 adjuvant treatment decision making,  
NOTE Confidence: 0.9468825

00:22:50.695 --> 00:22:52.855 such as radiation therapy, and  
NOTE Confidence: 0.9468825

00:22:52.855 --> 00:22:53.355 doctor,  
NOTE Confidence: 0.9700164

00:22:53.975 --> 00:22:55.175 Young will speak about that,  
NOTE Confidence: 0.9700164

00:22:55.175 --> 00:22:56.535 and doctor Tran will speak  
NOTE Confidence: 0.9700164

00:22:56.535 --> 00:22:57.355 about chemotherapy.  
NOTE Confidence: 0.9436596

00:22:58.880 --> 00:23:00.340 And then also the frequency  
NOTE Confidence: 0.9436596

00:23:00.399 --> 00:23:01.779 of follow-up for these patients

NOTE Confidence: 0.9436596  
00:23:01.840 --> 00:23:03.600 could be increased based on  
NOTE Confidence: 0.9436596  
00:23:03.600 --> 00:23:04.480 their their,  
NOTE Confidence: 0.9884505  
00:23:04.880 --> 00:23:06.880 forty GEP results. So an  
NOTE Confidence: 0.9884505  
00:23:06.880 --> 00:23:08.399 example would be to escalate  
NOTE Confidence: 0.9884505  
00:23:08.399 --> 00:23:09.519 the care for a high  
NOTE Confidence: 0.9884505  
00:23:09.519 --> 00:23:10.000 risk,  
NOTE Confidence: 0.9151902  
00:23:10.480 --> 00:23:12.565 GEP even if the AJCC  
NOTE Confidence: 0.9151902  
00:23:12.625 --> 00:23:13.744 eighth edition has them as  
NOTE Confidence: 0.9151902  
00:23:13.744 --> 00:23:14.945 a as a t one.  
NOTE Confidence: 0.9151902  
00:23:14.945 --> 00:23:15.684 And similarly,  
NOTE Confidence: 0.98425996  
00:23:15.984 --> 00:23:17.424 consider de escalation. I would  
NOTE Confidence: 0.98425996  
00:23:17.424 --> 00:23:18.304 do that in the context  
NOTE Confidence: 0.98425996  
00:23:18.304 --> 00:23:19.125 of a multidisciplinary  
NOTE Confidence: 0.9767643  
00:23:19.505 --> 00:23:20.005 group,  
NOTE Confidence: 0.91733044  
00:23:20.385 --> 00:23:21.505 the care for low risk  
NOTE Confidence: 0.91733044

00:23:21.505 --> 00:23:22.865 GEP even if it was  
NOTE Confidence: 0.91733044

00:23:22.865 --> 00:23:24.085 a, like, a t three.  
NOTE Confidence: 0.96997416

00:23:24.769 --> 00:23:26.710 So takeaway points from this,  
NOTE Confidence: 0.98247784

00:23:27.250 --> 00:23:29.190 this was this, gene,  
NOTE Confidence: 0.96761084

00:23:29.649 --> 00:23:32.470 forty, GEP test was validated,  
NOTE Confidence: 0.829768

00:23:34.289 --> 00:23:34.789 retrospectively.  
NOTE Confidence: 0.99069786

00:23:35.250 --> 00:23:36.450 And I would say with,  
NOTE Confidence: 0.99069786

00:23:36.850 --> 00:23:38.630 some advanced stage tumors underrepresented,  
NOTE Confidence: 0.98300743

00:23:39.645 --> 00:23:41.565 further prospective studies are certainly  
NOTE Confidence: 0.98300743

00:23:41.565 --> 00:23:42.765 needed for us to have  
NOTE Confidence: 0.98300743

00:23:42.765 --> 00:23:43.885 a better handle on how  
NOTE Confidence: 0.98300743

00:23:43.885 --> 00:23:45.805 this can impact, future treatment  
NOTE Confidence: 0.98300743

00:23:45.805 --> 00:23:46.865 and patient outcomes.  
NOTE Confidence: 0.9828138

00:23:47.965 --> 00:23:48.765 There is a role, I  
NOTE Confidence: 0.9828138

00:23:48.765 --> 00:23:49.965 think, for using it as  
NOTE Confidence: 0.9828138

00:23:49.965 --> 00:23:51.085 an adjunct to our current

NOTE Confidence: 0.9828138  
00:23:51.085 --> 00:23:52.590 guidelines, but not to replace  
NOTE Confidence: 0.9828138  
00:23:52.590 --> 00:23:53.630 them and to have it  
NOTE Confidence: 0.9828138  
00:23:53.630 --> 00:23:54.690 be part of a multidisciplinary,  
NOTE Confidence: 0.97984695  
00:23:55.549 --> 00:23:56.049 discussion.  
NOTE Confidence: 0.91100985  
00:23:57.150 --> 00:23:58.429 And again, used could be  
NOTE Confidence: 0.91100985  
00:23:58.429 --> 00:23:59.869 used to escalate care. So  
NOTE Confidence: 0.91100985  
00:23:59.869 --> 00:24:01.570 that first case presentation,  
NOTE Confidence: 0.9641589  
00:24:02.029 --> 00:24:03.150 perhaps that I'm sorry, the  
NOTE Confidence: 0.9641589  
00:24:03.150 --> 00:24:04.510 second case presentation where he  
NOTE Confidence: 0.9641589  
00:24:04.510 --> 00:24:05.570 had a rapid recurrence,  
NOTE Confidence: 0.9959372  
00:24:06.145 --> 00:24:07.665 perhaps he's somebody that could  
NOTE Confidence: 0.9959372  
00:24:07.665 --> 00:24:09.285 have gone quickly to radiation,  
NOTE Confidence: 0.9500813  
00:24:10.865 --> 00:24:11.365 to,  
NOTE Confidence: 0.9849043  
00:24:11.984 --> 00:24:13.345 as a response to that  
NOTE Confidence: 0.9849043  
00:24:13.345 --> 00:24:13.845 T2,  
NOTE Confidence: 0.8867686

00:24:14.625 --> 00:24:16.705 or the the 2b class  
NOTE Confidence: 0.8867686

00:24:16.705 --> 00:24:18.005 from the forty GEP.  
NOTE Confidence: 0.9822885

00:24:18.910 --> 00:24:19.790 And I think it's also  
NOTE Confidence: 0.9822885

00:24:19.790 --> 00:24:20.830 important to note that,  
NOTE Confidence: 0.9559564

00:24:21.550 --> 00:24:22.990 of the studies included here  
NOTE Confidence: 0.9559564

00:24:22.990 --> 00:24:23.950 and a majority of the  
NOTE Confidence: 0.9559564

00:24:23.950 --> 00:24:25.250 ones that have been published,  
NOTE Confidence: 0.9559564

00:24:25.310 --> 00:24:27.250 they are, industry funded,  
NOTE Confidence: 0.97317386

00:24:28.030 --> 00:24:28.910 in some way. So I  
NOTE Confidence: 0.97317386

00:24:28.910 --> 00:24:30.270 think it's just important to  
NOTE Confidence: 0.97317386

00:24:30.270 --> 00:24:31.470 to keep it to to  
NOTE Confidence: 0.97317386

00:24:31.470 --> 00:24:32.965 keep that in mind as  
NOTE Confidence: 0.97317386

00:24:32.965 --> 00:24:35.284 we continue to determine the  
NOTE Confidence: 0.97317386

00:24:35.284 --> 00:24:36.825 usability of these tests.  
NOTE Confidence: 0.9983138

00:24:37.764 --> 00:24:38.504 Thank you.  
NOTE Confidence: 0.98889464

00:24:42.965 --> 00:24:44.984 Alright. Thank you, Ansley. I'm



NOTE Confidence: 0.9913781  
00:24:45.740 --> 00:24:47.180 going to go ahead and  
NOTE Confidence: 0.9913781  
00:24:47.180 --> 00:24:49.520 present the, radiation oncologist  
NOTE Confidence: 0.96237576  
00:24:50.060 --> 00:24:50.560 perspective  
NOTE Confidence: 0.98681974  
00:24:50.940 --> 00:24:51.420 on,  
NOTE Confidence: 0.99297667  
00:24:51.980 --> 00:24:53.680 our approaches to cutaneous,  
NOTE Confidence: 0.79648113  
00:24:54.540 --> 00:24:55.040 squain.  
NOTE Confidence: 0.97085655  
00:24:56.859 --> 00:24:57.740 Let me just get these  
NOTE Confidence: 0.97085655  
00:24:57.740 --> 00:24:58.640 slides going.  
NOTE Confidence: 0.99748623  
00:25:00.345 --> 00:25:00.845 Alright.  
NOTE Confidence: 0.9967283  
00:25:01.385 --> 00:25:01.785 So,  
NOTE Confidence: 0.9705742  
00:25:02.185 --> 00:25:04.185 I'm Melissa Young. I'm, the  
NOTE Confidence: 0.9705742  
00:25:04.185 --> 00:25:05.865 radiation oncologist on the panel  
NOTE Confidence: 0.9705742  
00:25:05.865 --> 00:25:06.365 today,  
NOTE Confidence: 0.9926453  
00:25:06.905 --> 00:25:08.105 one of the specialists in  
NOTE Confidence: 0.9926453  
00:25:08.105 --> 00:25:08.265 our,  
NOTE Confidence: 0.86285526

00:25:09.225 --> 00:25:10.105 head and neck,  
NOTE Confidence: 0.8809831  
00:25:11.225 --> 00:25:13.065 department within the the department  
NOTE Confidence: 0.8809831  
00:25:13.065 --> 00:25:14.125 of radiation oncology.  
NOTE Confidence: 0.9506055  
00:25:14.539 --> 00:25:15.419 And I just want really  
NOTE Confidence: 0.9506055  
00:25:15.419 --> 00:25:17.760 wanted to focus specifically on,  
NOTE Confidence: 0.99846524  
00:25:18.779 --> 00:25:19.760 you know, how  
NOTE Confidence: 0.9922796  
00:25:20.140 --> 00:25:21.179 how we look at these  
NOTE Confidence: 0.9922796  
00:25:21.179 --> 00:25:22.380 high risk skin cancers and  
NOTE Confidence: 0.9922796  
00:25:22.380 --> 00:25:23.100 how we have to think  
NOTE Confidence: 0.9922796  
00:25:23.100 --> 00:25:24.380 about the use of adjuvant  
NOTE Confidence: 0.9922796  
00:25:24.380 --> 00:25:24.880 radiotherapy  
NOTE Confidence: 0.9874798  
00:25:25.260 --> 00:25:26.700 as a risk reductive strategy  
NOTE Confidence: 0.9874798  
00:25:26.700 --> 00:25:27.740 to to reduce risk of  
NOTE Confidence: 0.9874798  
00:25:27.740 --> 00:25:28.240 recurrence.  
NOTE Confidence: 0.9621108  
00:25:28.625 --> 00:25:30.085 We've already heard the data  
NOTE Confidence: 0.9621108  
00:25:30.225 --> 00:25:31.744 indicating that these high risk,

NOTE Confidence: 0.9621108

00:25:31.744 --> 00:25:33.105 very high risk cancers that

NOTE Confidence: 0.9621108

00:25:33.105 --> 00:25:34.725 have a, you know,

NOTE Confidence: 0.9646209

00:25:35.105 --> 00:25:37.185 potential risk for recurrence and

NOTE Confidence: 0.9646209

00:25:37.185 --> 00:25:38.065 how are we going to

NOTE Confidence: 0.9646209

00:25:38.065 --> 00:25:39.105 kind of use this data

NOTE Confidence: 0.9646209

00:25:39.105 --> 00:25:41.125 and potentially gene expression profiling

NOTE Confidence: 0.98182714

00:25:41.670 --> 00:25:43.130 to to kind of refine

NOTE Confidence: 0.98182714

00:25:43.270 --> 00:25:44.950 our selection of who may

NOTE Confidence: 0.98182714

00:25:44.950 --> 00:25:46.630 warrant adjuvant treatment and who

NOTE Confidence: 0.98182714

00:25:46.630 --> 00:25:47.450 could potentially,

NOTE Confidence: 0.9107423

00:25:48.710 --> 00:25:50.250 forego adjuvant treatment.

NOTE Confidence: 0.97963345

00:25:50.950 --> 00:25:51.450 So,

NOTE Confidence: 0.940883

00:25:52.070 --> 00:25:53.930 as has already been demonstrated

NOTE Confidence: 0.940883

00:25:54.150 --> 00:25:55.845 that the mainstay of treatment

NOTE Confidence: 0.940883

00:25:55.845 --> 00:25:56.825 for skin cancer,

NOTE Confidence: 0.948767

00:25:57.365 --> 00:25:59.065 is for surgery upfront.  
NOTE Confidence: 0.9693674

00:26:00.085 --> 00:26:01.365 There are situations in where  
NOTE Confidence: 0.9693674

00:26:01.365 --> 00:26:03.205 radiotherapy might be used in  
NOTE Confidence: 0.9693674

00:26:03.205 --> 00:26:05.065 the definitive setting. It's usually,  
NOTE Confidence: 0.99766016

00:26:05.765 --> 00:26:07.045 reserved for patients who are  
NOTE Confidence: 0.99766016

00:26:07.045 --> 00:26:08.345 either deemed unresectable  
NOTE Confidence: 0.9848693

00:26:09.125 --> 00:26:10.984 or are refusing surgery itself.  
NOTE Confidence: 0.9882151

00:26:12.059 --> 00:26:12.940 When it comes to early  
NOTE Confidence: 0.9882151

00:26:12.940 --> 00:26:13.919 stage cutaneous,  
NOTE Confidence: 0.8216653

00:26:14.859 --> 00:26:15.359 squamous,  
NOTE Confidence: 0.9865479

00:26:15.980 --> 00:26:17.820 radiation has equivalent cure rates  
NOTE Confidence: 0.9865479

00:26:17.820 --> 00:26:19.020 to that of surgery, but  
NOTE Confidence: 0.9865479

00:26:19.020 --> 00:26:20.799 it is time intensive. Radiation  
NOTE Confidence: 0.9865479

00:26:20.940 --> 00:26:22.059 is not a single treatment,  
NOTE Confidence: 0.9865479

00:26:22.059 --> 00:26:23.179 much like surgery can be  
NOTE Confidence: 0.9865479

00:26:23.179 --> 00:26:24.135 done in a single office

NOTE Confidence: 0.9865479

00:26:24.215 --> 00:26:25.494 visit. This is eight sessions

NOTE Confidence: 0.9865479

00:26:25.494 --> 00:26:26.295 over the course of a

NOTE Confidence: 0.9865479

00:26:26.295 --> 00:26:27.275 month at minimum,

NOTE Confidence: 0.97331995

00:26:27.734 --> 00:26:29.015 but many may require thirty

NOTE Confidence: 0.97331995

00:26:29.015 --> 00:26:30.215 to thirty five sessions over

NOTE Confidence: 0.97331995

00:26:30.215 --> 00:26:31.575 six to seven weeks. And

NOTE Confidence: 0.97331995

00:26:31.575 --> 00:26:32.775 there also are going to

NOTE Confidence: 0.97331995

00:26:32.775 --> 00:26:34.775 be, morbidity and side effects

NOTE Confidence: 0.97331995

00:26:34.775 --> 00:26:36.635 associated with radiation treatment.

NOTE Confidence: 0.961875

00:26:37.710 --> 00:26:39.190 So it's not necessarily going

NOTE Confidence: 0.961875

00:26:39.190 --> 00:26:40.030 to be our go to

NOTE Confidence: 0.961875

00:26:40.030 --> 00:26:41.470 for upfront management and it

NOTE Confidence: 0.961875

00:26:41.470 --> 00:26:43.070 could potentially preclude the use

NOTE Confidence: 0.961875

00:26:43.070 --> 00:26:44.270 of radiation if the patient

NOTE Confidence: 0.961875

00:26:44.270 --> 00:26:45.390 were to ever have a

NOTE Confidence: 0.961875

00:26:45.390 --> 00:26:46.830 second cancer because you really

NOTE Confidence: 0.961875

00:26:46.830 --> 00:26:48.350 can't, shouldn't give radiation to

NOTE Confidence: 0.961875

00:26:48.350 --> 00:26:49.070 the same part of the

NOTE Confidence: 0.961875

00:26:49.070 --> 00:26:49.890 body twice.

NOTE Confidence: 0.99057835

00:26:50.415 --> 00:26:50.915 So

NOTE Confidence: 0.90910864

00:26:51.295 --> 00:26:52.735 therefore radiation is really an

NOTE Confidence: 0.90910864

00:26:52.735 --> 00:26:54.835 adjunct, in the adjuvant setting

NOTE Confidence: 0.90910864

00:26:54.895 --> 00:26:56.255 for high risk or very

NOTE Confidence: 0.90910864

00:26:56.255 --> 00:26:57.475 high risk skin cancers.

NOTE Confidence: 0.9584797

00:26:58.175 --> 00:26:58.975 Now I know that this

NOTE Confidence: 0.9584797

00:26:58.975 --> 00:27:00.895 has already been reviewed to

NOTE Confidence: 0.9584797

00:27:00.895 --> 00:27:02.735 some degree. This is just

NOTE Confidence: 0.9584797

00:27:02.735 --> 00:27:04.095 NCCN guidelines of kind of

NOTE Confidence: 0.9584797

00:27:04.095 --> 00:27:04.835 where radiation

NOTE Confidence: 0.9985327

00:27:05.190 --> 00:27:06.570 therapy may play in

NOTE Confidence: 0.83446133

00:27:06.950 --> 00:27:08.169 in, the

NOTE Confidence: 0.93847954

00:27:09.269 --> 00:27:10.789 care for a patient with

NOTE Confidence: 0.93847954

00:27:10.789 --> 00:27:11.750 a high risk or very

NOTE Confidence: 0.93847954

00:27:11.750 --> 00:27:12.789 high risk skin cancer. And

NOTE Confidence: 0.93847954

00:27:12.789 --> 00:27:13.830 again, just pointing out that

NOTE Confidence: 0.93847954

00:27:13.830 --> 00:27:14.789 this is really at the

NOTE Confidence: 0.93847954

00:27:14.789 --> 00:27:15.609 end of treatment,

NOTE Confidence: 0.9792034

00:27:16.230 --> 00:27:17.990 surgeries performed, you're looking at

NOTE Confidence: 0.9792034

00:27:17.990 --> 00:27:19.450 patients who have positive margins

NOTE Confidence: 0.9792034

00:27:19.510 --> 00:27:21.705 or other pathologic risk factors

NOTE Confidence: 0.9792034

00:27:21.705 --> 00:27:23.145 for those with negative margins

NOTE Confidence: 0.9792034

00:27:23.145 --> 00:27:24.925 that may warrant consideration

NOTE Confidence: 0.9435509

00:27:25.385 --> 00:27:26.685 of radiation therapy.

NOTE Confidence: 0.961782

00:27:28.025 --> 00:27:29.305 We've already seen the risk

NOTE Confidence: 0.961782

00:27:29.305 --> 00:27:29.805 stratification,

NOTE Confidence: 0.91754377

00:27:31.225 --> 00:27:32.105 data that's,

NOTE Confidence: 0.89133

00:27:32.425 --> 00:27:33.869 in the previous presentation, so

NOTE Confidence: 0.89133

00:27:33.869 --> 00:27:34.990 I won't belabor that. But

NOTE Confidence: 0.89133

00:27:34.990 --> 00:27:36.609 again, NCCN has,

NOTE Confidence: 0.9243202

00:27:37.710 --> 00:27:38.990 low risk, high risk, and

NOTE Confidence: 0.9243202

00:27:38.990 --> 00:27:40.050 very high risk,

NOTE Confidence: 0.90974504

00:27:40.430 --> 00:27:42.290 and Brigham and Women similarly

NOTE Confidence: 0.90974504

00:27:42.430 --> 00:27:42.930 has

NOTE Confidence: 0.9164408

00:27:43.310 --> 00:27:45.070 similar pathologic features that would

NOTE Confidence: 0.9164408

00:27:45.070 --> 00:27:46.510 also can be considered as

NOTE Confidence: 0.9164408

00:27:46.510 --> 00:27:47.250 risk factors

NOTE Confidence: 0.9984465

00:27:47.575 --> 00:27:48.855 to maybe help guide those

NOTE Confidence: 0.9984465

00:27:48.855 --> 00:27:49.734 patients who are at higher

NOTE Confidence: 0.9984465

00:27:49.734 --> 00:27:50.795 risk for recurrence.

NOTE Confidence: 0.9629821

00:27:53.095 --> 00:27:54.135 When it comes to adjuvant

NOTE Confidence: 0.9629821

00:27:54.135 --> 00:27:55.895 radiation, again, we're really reserving

NOTE Confidence: 0.9629821

00:27:55.895 --> 00:27:57.015 this usually to our very



NOTE Confidence: 0.9629821  
00:27:57.015 --> 00:27:58.615 high risk patients or certain  
NOTE Confidence: 0.9629821  
00:27:58.615 --> 00:27:59.835 high risk situations  
NOTE Confidence: 0.96651983  
00:28:00.295 --> 00:28:02.420 like recurrent tumors, patients who  
NOTE Confidence: 0.96651983  
00:28:02.420 --> 00:28:03.700 are immune suppressed and have  
NOTE Confidence: 0.96651983  
00:28:03.700 --> 00:28:05.640 higher local recurrence risk,  
NOTE Confidence: 0.9883885  
00:28:06.180 --> 00:28:07.859 or those with T2B or  
NOTE Confidence: 0.9883885  
00:28:07.859 --> 00:28:08.680 higher tumors.  
NOTE Confidence: 0.9614632  
00:28:09.619 --> 00:28:10.119 Interestingly,  
NOTE Confidence: 0.9993117  
00:28:10.420 --> 00:28:12.680 despite how common cutaneous  
NOTE Confidence: 0.9265677  
00:28:13.494 --> 00:28:15.355 squamous are, the data,  
NOTE Confidence: 0.9770638  
00:28:16.135 --> 00:28:17.575 prospective data in terms of  
NOTE Confidence: 0.9770638  
00:28:17.575 --> 00:28:19.415 the efficacy of adjuvant radiation  
NOTE Confidence: 0.9770638  
00:28:19.415 --> 00:28:20.875 is really lacking.  
NOTE Confidence: 0.927643  
00:28:21.415 --> 00:28:22.615 We really much much of  
NOTE Confidence: 0.927643  
00:28:22.615 --> 00:28:23.415 the data has just been  
NOTE Confidence: 0.927643

00:28:23.415 --> 00:28:25.195 derived from retrospective reports,  
NOTE Confidence: 0.9247024

00:28:25.575 --> 00:28:26.475 and therefore,  
NOTE Confidence: 0.9755883

00:28:27.820 --> 00:28:29.419 really truly teasing out who  
NOTE Confidence: 0.9755883

00:28:29.419 --> 00:28:31.019 might truly benefit from treatment  
NOTE Confidence: 0.9755883

00:28:31.019 --> 00:28:32.799 or not is is not  
NOTE Confidence: 0.9755883

00:28:33.019 --> 00:28:33.919 well defined.  
NOTE Confidence: 0.99744356

00:28:34.460 --> 00:28:34.960 Similarly,  
NOTE Confidence: 0.9556923

00:28:35.340 --> 00:28:36.559 when it comes to radiation,  
NOTE Confidence: 0.9556923

00:28:36.619 --> 00:28:38.480 I'm someone who's offering radiation  
NOTE Confidence: 0.9556923

00:28:38.539 --> 00:28:39.500 to a certain part of  
NOTE Confidence: 0.9556923

00:28:39.500 --> 00:28:40.885 the body, much like a  
NOTE Confidence: 0.9556923

00:28:40.885 --> 00:28:41.925 surgeon is gonna remove the  
NOTE Confidence: 0.9556923

00:28:41.925 --> 00:28:42.805 area of the tumor.  
NOTE Confidence: 0.9743027

00:28:43.525 --> 00:28:44.345 So radiation,  
NOTE Confidence: 0.91634244

00:28:45.925 --> 00:28:46.725 can either be,  
NOTE Confidence: 0.97438645

00:28:47.285 --> 00:28:48.725 administered just to the primary

NOTE Confidence: 0.97438645

00:28:48.725 --> 00:28:50.085 site where the where the

NOTE Confidence: 0.97438645

00:28:50.085 --> 00:28:50.585 surgery,

NOTE Confidence: 0.87762195

00:28:51.765 --> 00:28:53.065 removed the tumor itself,

NOTE Confidence: 0.96205825

00:28:53.870 --> 00:28:55.230 especially in a clinically node

NOTE Confidence: 0.96205825

00:28:55.230 --> 00:28:57.550 negative patient, although radiation may

NOTE Confidence: 0.96205825

00:28:57.550 --> 00:28:59.090 also include draining lymphatics.

NOTE Confidence: 0.9341682

00:28:59.710 --> 00:29:01.550 And in these retrospective reports,

NOTE Confidence: 0.9341682

00:29:01.550 --> 00:29:02.590 it's very hard to kinda

NOTE Confidence: 0.9341682

00:29:02.590 --> 00:29:04.030 tease out was this primary

NOTE Confidence: 0.9341682

00:29:04.030 --> 00:29:05.470 site radiation, was it primary

NOTE Confidence: 0.9341682

00:29:05.470 --> 00:29:06.990 plus regional radiation, and so

NOTE Confidence: 0.9341682

00:29:06.990 --> 00:29:08.110 kinda how can we also

NOTE Confidence: 0.9341682

00:29:08.110 --> 00:29:09.605 tease out the efficacy based

NOTE Confidence: 0.9341682

00:29:09.605 --> 00:29:10.965 on our target of the

NOTE Confidence: 0.9341682

00:29:10.965 --> 00:29:13.225 radiation is also less clear.

NOTE Confidence: 0.9372206

00:29:13.685 --> 00:29:14.485 I also want to point  
NOTE Confidence: 0.9372206

00:29:14.485 --> 00:29:16.005 out that, you know, we  
NOTE Confidence: 0.9372206

00:29:16.005 --> 00:29:17.865 don't want to overdo radiation  
NOTE Confidence: 0.9372206

00:29:17.925 --> 00:29:19.045 in every patient who comes  
NOTE Confidence: 0.9372206

00:29:19.045 --> 00:29:20.325 to our practice because the  
NOTE Confidence: 0.9372206

00:29:20.325 --> 00:29:21.685 more of someone you radiate  
NOTE Confidence: 0.9372206

00:29:21.685 --> 00:29:22.645 the more side effects you're  
NOTE Confidence: 0.9372206

00:29:22.645 --> 00:29:24.600 gonna then kind of subject  
NOTE Confidence: 0.9372206

00:29:24.600 --> 00:29:26.280 that patient to that can  
NOTE Confidence: 0.9372206

00:29:26.280 --> 00:29:27.480 affect life on quality of  
NOTE Confidence: 0.9372206

00:29:27.480 --> 00:29:27.880 life,  
NOTE Confidence: 0.9808006

00:29:28.360 --> 00:29:29.400 especially if you're talking about  
NOTE Confidence: 0.9808006

00:29:29.400 --> 00:29:30.200 things in the head and  
NOTE Confidence: 0.9808006

00:29:30.200 --> 00:29:31.400 neck region where you're talking  
NOTE Confidence: 0.9808006

00:29:31.400 --> 00:29:33.400 about salivary gland exposure, dry  
NOTE Confidence: 0.9808006

00:29:33.400 --> 00:29:34.700 mouth, lymphedema,

NOTE Confidence: 0.9600466

00:29:35.000 --> 00:29:36.975 scar tissue, and also potentially

NOTE Confidence: 0.9600466

00:29:36.975 --> 00:29:38.735 again eliminating radiation as an

NOTE Confidence: 0.9600466

00:29:38.735 --> 00:29:39.934 option should there be another

NOTE Confidence: 0.9600466

00:29:39.934 --> 00:29:41.555 cancer in this person's lifetime.

NOTE Confidence: 0.93489045

00:29:43.934 --> 00:29:45.155 Kind of to the point

NOTE Confidence: 0.93489045

00:29:45.375 --> 00:29:45.875 of

NOTE Confidence: 0.87799484

00:29:46.255 --> 00:29:48.595 the limited prospective data regarding

NOTE Confidence: 0.87799484

00:29:48.735 --> 00:29:50.175 the efficacy of adjuvant radiation

NOTE Confidence: 0.87799484

00:29:50.175 --> 00:29:51.295 we really don't have much

NOTE Confidence: 0.87799484

00:29:51.295 --> 00:29:52.035 but there

NOTE Confidence: 0.96490777

00:29:52.600 --> 00:29:53.960 just in the last few

NOTE Confidence: 0.96490777

00:29:53.960 --> 00:29:55.980 months another very large retrospective

NOTE Confidence: 0.96490777

00:29:56.279 --> 00:29:58.759 cohort was described with patients

NOTE Confidence: 0.96490777

00:29:58.759 --> 00:30:00.220 with very high risk disease,

NOTE Confidence: 0.9515292

00:30:01.240 --> 00:30:03.980 including multiple institutions where they

NOTE Confidence: 0.9515292

00:30:04.039 --> 00:30:05.559 looked into their databases finding

NOTE Confidence: 0.9515292

00:30:05.559 --> 00:30:07.184 twelve sixty seven patients who

NOTE Confidence: 0.9515292

00:30:07.184 --> 00:30:08.705 met high risk criteria but

NOTE Confidence: 0.9515292

00:30:08.705 --> 00:30:10.404 of note only twelve percent

NOTE Confidence: 0.9515292

00:30:10.544 --> 00:30:12.144 or so are receiving adjuvant

NOTE Confidence: 0.9515292

00:30:12.144 --> 00:30:13.205 radiation treatment.

NOTE Confidence: 0.9621716

00:30:14.065 --> 00:30:16.304 But in this retrospective cohort

NOTE Confidence: 0.9621716

00:30:16.304 --> 00:30:17.184 what we do find is

NOTE Confidence: 0.9621716

00:30:17.184 --> 00:30:18.865 adjuvant radiation does reduce the

NOTE Confidence: 0.9621716

00:30:18.865 --> 00:30:20.304 risk of both local, local

NOTE Confidence: 0.9621716

00:30:20.304 --> 00:30:21.700 regional as well as nodal

NOTE Confidence: 0.9621716

00:30:21.700 --> 00:30:23.460 recurrence by fifty percent. And

NOTE Confidence: 0.9621716

00:30:23.460 --> 00:30:24.500 here are just the Kaplan

NOTE Confidence: 0.9621716

00:30:24.500 --> 00:30:26.279 Meier curves demonstrating that.

NOTE Confidence: 0.9637089

00:30:26.980 --> 00:30:28.580 Importantly, and I think where

NOTE Confidence: 0.9637089

00:30:28.580 --> 00:30:29.940 we, you know, where gene

NOTE Confidence: 0.9637089  
00:30:29.940 --> 00:30:31.460 expression profiling might come in,  
NOTE Confidence: 0.9637089  
00:30:31.700 --> 00:30:33.139 to help sub stratify is  
NOTE Confidence: 0.9637089  
00:30:33.139 --> 00:30:34.904 is we're not seeing overall  
NOTE Confidence: 0.9637089  
00:30:34.904 --> 00:30:36.585 survival benefit. We're definitely seeing  
NOTE Confidence: 0.9637089  
00:30:36.585 --> 00:30:38.505 local control benefit and there's  
NOTE Confidence: 0.9637089  
00:30:38.505 --> 00:30:39.465 value to that but we're  
NOTE Confidence: 0.9637089  
00:30:39.465 --> 00:30:41.065 not necessarily seeing a survival  
NOTE Confidence: 0.9637089  
00:30:41.065 --> 00:30:41.945 benefit. So if we can  
NOTE Confidence: 0.9637089  
00:30:41.945 --> 00:30:43.385 identify those patients who could  
NOTE Confidence: 0.9637089  
00:30:43.385 --> 00:30:45.304 potentially have a survival benefit  
NOTE Confidence: 0.9637089  
00:30:45.304 --> 00:30:46.265 it might also help us  
NOTE Confidence: 0.9637089  
00:30:46.265 --> 00:30:47.580 prevent that patient who may  
NOTE Confidence: 0.9637089  
00:30:47.820 --> 00:30:49.100 ultimately succumb as the second  
NOTE Confidence: 0.9637089  
00:30:49.100 --> 00:30:50.480 case in the previous presentation.  
NOTE Confidence: 0.899041  
00:30:51.820 --> 00:30:53.200 So within this this  
NOTE Confidence: 0.92836255

00:30:53.580 --> 00:30:55.500 particular retrospective series they did

NOTE Confidence: 0.92836255

00:30:55.500 --> 00:30:56.539 want to look at patients

NOTE Confidence: 0.92836255

00:30:56.539 --> 00:30:57.740 who may have higher risk

NOTE Confidence: 0.92836255

00:30:57.740 --> 00:30:59.019 disease and they kind of

NOTE Confidence: 0.92836255

00:30:59.019 --> 00:31:00.779 sub stratified this by patients

NOTE Confidence: 0.92836255

00:31:00.779 --> 00:31:02.059 who are t2b but with

NOTE Confidence: 0.92836255

00:31:02.059 --> 00:31:03.120 three of the criteria,

NOTE Confidence: 0.9708246

00:31:04.195 --> 00:31:04.935 the T3s

NOTE Confidence: 0.9393389

00:31:05.235 --> 00:31:06.435 as well as those with

NOTE Confidence: 0.9393389

00:31:06.435 --> 00:31:07.955 LVI and they found within

NOTE Confidence: 0.9393389

00:31:07.955 --> 00:31:09.715 that twelve hundred patients, two

NOTE Confidence: 0.9393389

00:31:09.715 --> 00:31:11.395 forty six, that met this

NOTE Confidence: 0.9393389

00:31:11.395 --> 00:31:12.695 higher risk subtype,

NOTE Confidence: 0.99363256

00:31:13.155 --> 00:31:14.775 thirty percent of that population

NOTE Confidence: 0.99363256

00:31:14.835 --> 00:31:16.375 did receive adjuvant treatment.

NOTE Confidence: 0.9584459

00:31:16.830 --> 00:31:19.409 And we're, we're still seeing



NOTE Confidence: 0.9584459  
00:31:19.630 --> 00:31:21.150 similarly a fifty percent reduction  
NOTE Confidence: 0.9584459  
00:31:21.150 --> 00:31:22.590 in local recurrence but certainly  
NOTE Confidence: 0.9584459  
00:31:22.590 --> 00:31:24.190 that absolute benefit is better  
NOTE Confidence: 0.9584459  
00:31:24.190 --> 00:31:25.630 because you've now identified a  
NOTE Confidence: 0.9584459  
00:31:25.630 --> 00:31:27.309 potentially higher risk subgroup so  
NOTE Confidence: 0.9584459  
00:31:27.309 --> 00:31:28.510 those patients are more likely  
NOTE Confidence: 0.9584459  
00:31:28.510 --> 00:31:30.015 to benefit. Still not seeing  
NOTE Confidence: 0.9584459  
00:31:30.015 --> 00:31:31.235 a disease specific,  
NOTE Confidence: 0.96293026  
00:31:31.775 --> 00:31:33.155 survival benefit, however.  
NOTE Confidence: 0.9973664  
00:31:35.215 --> 00:31:36.735 This is where, you know,  
NOTE Confidence: 0.9973664  
00:31:36.735 --> 00:31:38.735 gene expression profiling is is  
NOTE Confidence: 0.9973664  
00:31:38.895 --> 00:31:40.095 there's a lot of optimism  
NOTE Confidence: 0.9973664  
00:31:40.095 --> 00:31:41.375 that this could potentially help  
NOTE Confidence: 0.9973664  
00:31:41.375 --> 00:31:42.975 further identify subgroups that may  
NOTE Confidence: 0.9973664  
00:31:42.975 --> 00:31:44.115 benefit from radiotherapy.  
NOTE Confidence: 0.823434

00:31:46.040 --> 00:31:46.620 So, you  
NOTE Confidence: 0.95034724

00:31:47.240 --> 00:31:48.920 know, in incorporating this in  
NOTE Confidence: 0.95034724

00:31:48.920 --> 00:31:50.200 future randomized trials I think  
NOTE Confidence: 0.95034724

00:31:50.200 --> 00:31:51.480 will also really be important  
NOTE Confidence: 0.95034724

00:31:51.480 --> 00:31:52.700 of trying to help delineate,  
NOTE Confidence: 0.94990313

00:31:53.320 --> 00:31:54.300 without bias,  
NOTE Confidence: 0.90388095

00:31:54.840 --> 00:31:56.600 how radiation therapy may may  
NOTE Confidence: 0.90388095

00:31:56.600 --> 00:31:57.260 be beneficial,  
NOTE Confidence: 0.9963746

00:31:57.720 --> 00:31:58.940 in this group of patients.  
NOTE Confidence: 0.97348386

00:32:00.735 --> 00:32:01.715 I wanted to  
NOTE Confidence: 0.9993655

00:32:02.015 --> 00:32:02.515 present  
NOTE Confidence: 0.9864706

00:32:03.855 --> 00:32:04.815 the same group that has  
NOTE Confidence: 0.9864706

00:32:04.815 --> 00:32:06.595 this forty gene expression profile  
NOTE Confidence: 0.9864706

00:32:06.735 --> 00:32:07.235 panel  
NOTE Confidence: 0.9166836

00:32:07.535 --> 00:32:09.075 also looked at their database  
NOTE Confidence: 0.9166836

00:32:09.135 --> 00:32:10.815 of the patients comparing those

NOTE Confidence: 0.9166836  
00:32:10.815 --> 00:32:12.495 who had radiation and who  
NOTE Confidence: 0.9166836  
00:32:12.495 --> 00:32:13.235 did not.  
NOTE Confidence: 0.9338859  
00:32:13.919 --> 00:32:15.200 And they are seeing a  
NOTE Confidence: 0.9338859  
00:32:15.200 --> 00:32:15.700 benefit  
NOTE Confidence: 0.9691408  
00:32:16.399 --> 00:32:17.279 or being able to use  
NOTE Confidence: 0.9691408  
00:32:17.279 --> 00:32:18.559 their class system to help  
NOTE Confidence: 0.9691408  
00:32:18.559 --> 00:32:20.320 identify subgroups of patients that  
NOTE Confidence: 0.9691408  
00:32:20.320 --> 00:32:21.759 may actually truly benefit from  
NOTE Confidence: 0.9691408  
00:32:21.759 --> 00:32:22.259 radiotherapy  
NOTE Confidence: 0.98856664  
00:32:22.559 --> 00:32:23.360 and those who may have  
NOTE Confidence: 0.98856664  
00:32:23.360 --> 00:32:24.340 lower risk disease  
NOTE Confidence: 0.98107326  
00:32:24.720 --> 00:32:27.039 despite classically being considered high  
NOTE Confidence: 0.98107326  
00:32:27.039 --> 00:32:28.419 risk or very high risk  
NOTE Confidence: 0.9286401  
00:32:28.835 --> 00:32:30.215 who could potentially  
NOTE Confidence: 0.97265244  
00:32:30.595 --> 00:32:32.275 omit radiotherapy as part of  
NOTE Confidence: 0.97265244

00:32:32.275 --> 00:32:32.935 their care.  
NOTE Confidence: 0.9775853

00:32:33.475 --> 00:32:33.975 So  
NOTE Confidence: 0.79555035

00:32:35.075 --> 00:32:36.755 specifically they again this is  
NOTE Confidence: 0.79555035

00:32:36.755 --> 00:32:37.895 a gene expression profiling  
NOTE Confidence: 0.9742888

00:32:38.835 --> 00:32:40.515 looking at in total about  
NOTE Confidence: 0.9742888

00:32:40.515 --> 00:32:41.955 four hundred and some patients  
NOTE Confidence: 0.9742888

00:32:41.955 --> 00:32:42.775 in this particular  
NOTE Confidence: 0.98852587

00:32:43.710 --> 00:32:44.830 cohort of patients that they  
NOTE Confidence: 0.98852587

00:32:44.830 --> 00:32:46.990 evaluated who had classically high  
NOTE Confidence: 0.98852587

00:32:46.990 --> 00:32:48.590 risk disease or very high  
NOTE Confidence: 0.98852587

00:32:48.590 --> 00:32:49.409 risk disease  
NOTE Confidence: 0.7636641

00:32:49.870 --> 00:32:50.690 but subclassifying  
NOTE Confidence: 0.9372527

00:32:51.070 --> 00:32:52.350 them into the class I,  
NOTE Confidence: 0.9372527

00:32:52.350 --> 00:32:53.390 the class IIA or the  
NOTE Confidence: 0.9372527

00:32:53.390 --> 00:32:54.510 class IIB based on the  
NOTE Confidence: 0.9372527

00:32:54.510 --> 00:32:55.809 gene expression profiling.

NOTE Confidence: 0.9054027

00:32:56.565 --> 00:32:58.085 Again small numbers only about

NOTE Confidence: 0.9054027

00:32:58.085 --> 00:32:59.524 thirteen twelve twelve to thirteen

NOTE Confidence: 0.9054027

00:32:59.524 --> 00:33:00.804 percent of patients actually receiving

NOTE Confidence: 0.9054027

00:33:00.804 --> 00:33:02.085 adjuvant treatment in this group

NOTE Confidence: 0.9054027

00:33:02.085 --> 00:33:03.365 but kind of spread across

NOTE Confidence: 0.9054027

00:33:03.365 --> 00:33:04.885 class 1a, class 2a and

NOTE Confidence: 0.9054027

00:33:04.885 --> 00:33:05.705 class 2b.

NOTE Confidence: 0.96719426

00:33:06.245 --> 00:33:07.284 And when they again look

NOTE Confidence: 0.96719426

00:33:07.284 --> 00:33:08.580 at the Kaplan Meier curves

NOTE Confidence: 0.96719426

00:33:08.580 --> 00:33:09.779 where we're seeing the largest

NOTE Confidence: 0.96719426

00:33:09.779 --> 00:33:11.059 benefit in the left side

NOTE Confidence: 0.96719426

00:33:11.059 --> 00:33:12.520 of the screen here are

NOTE Confidence: 0.96719426

00:33:12.580 --> 00:33:14.340 the class 2b patients. Their

NOTE Confidence: 0.96719426

00:33:14.340 --> 00:33:15.720 risk of metastasis

NOTE Confidence: 0.7443925

00:33:16.820 --> 00:33:17.220 with,

NOTE Confidence: 0.9991143

00:33:18.020 --> 00:33:19.000 without radiotherapy  
NOTE Confidence: 0.9606346

00:33:19.700 --> 00:33:21.220 are indicated by that dotted  
NOTE Confidence: 0.9606346

00:33:21.220 --> 00:33:22.200 line in red.  
NOTE Confidence: 0.9930747

00:33:22.575 --> 00:33:24.095 Whereas those that did receive  
NOTE Confidence: 0.9930747

00:33:24.095 --> 00:33:24.595 radiotherapy  
NOTE Confidence: 0.9941157

00:33:24.895 --> 00:33:26.515 actually had a dramatic benefit  
NOTE Confidence: 0.9564004

00:33:26.895 --> 00:33:28.174 reduction in risk of recurrence.  
NOTE Confidence: 0.9564004

00:33:28.174 --> 00:33:29.534 Now these are low numbers  
NOTE Confidence: 0.9564004

00:33:29.534 --> 00:33:30.735 but it does you know  
NOTE Confidence: 0.9564004

00:33:30.735 --> 00:33:32.015 suggest that we could identify  
NOTE Confidence: 0.9564004

00:33:32.015 --> 00:33:33.135 a group that's more likely  
NOTE Confidence: 0.9564004

00:33:33.135 --> 00:33:34.515 to benefit from radiotherapy.  
NOTE Confidence: 0.922159

00:33:36.010 --> 00:33:37.450 The right sided panel really  
NOTE Confidence: 0.922159

00:33:37.450 --> 00:33:39.050 just kind of shows this  
NOTE Confidence: 0.922159

00:33:39.050 --> 00:33:40.250 this benefit in in a  
NOTE Confidence: 0.922159

00:33:40.250 --> 00:33:42.010 different graphical way where class

NOTE Confidence: 0.922159  
00:33:42.010 --> 00:33:42.910 one a patients,  
NOTE Confidence: 0.99918336  
00:33:43.450 --> 00:33:45.470 despite meeting high risk criteria  
NOTE Confidence: 0.96707785  
00:33:45.770 --> 00:33:47.470 based on gene expression profiling  
NOTE Confidence: 0.96310055  
00:33:47.975 --> 00:33:48.935 from the small group of  
NOTE Confidence: 0.96310055  
00:33:48.935 --> 00:33:50.235 patients may not necessarily  
NOTE Confidence: 0.9767514  
00:33:50.615 --> 00:33:52.295 benefit from adjuvant treatment because  
NOTE Confidence: 0.9767514  
00:33:52.295 --> 00:33:53.735 their risk seems to already  
NOTE Confidence: 0.9767514  
00:33:53.735 --> 00:33:54.855 be so low of recurrence  
NOTE Confidence: 0.9767514  
00:33:54.855 --> 00:33:55.355 already.  
NOTE Confidence: 0.9315859  
00:33:55.735 --> 00:33:57.015 Whereas those with class two  
NOTE Confidence: 0.9315859  
00:33:57.015 --> 00:33:58.055 a are those where we  
NOTE Confidence: 0.9315859  
00:33:58.055 --> 00:33:59.355 might consider radiotherapy.  
NOTE Confidence: 0.96861076  
00:33:59.735 --> 00:34:00.535 There does seem to be  
NOTE Confidence: 0.96861076  
00:34:00.535 --> 00:34:02.710 some potential benefit there, but  
NOTE Confidence: 0.96861076  
00:34:02.710 --> 00:34:03.670 not quite as much of  
NOTE Confidence: 0.96861076

00:34:03.670 --> 00:34:04.630 a benefit as what we're  
NOTE Confidence: 0.96861076

00:34:04.630 --> 00:34:05.670 seeing in in that small  
NOTE Confidence: 0.96861076

00:34:05.670 --> 00:34:06.870 group of two class two  
NOTE Confidence: 0.96861076

00:34:06.870 --> 00:34:07.530 b patients.  
NOTE Confidence: 0.974698

00:34:09.270 --> 00:34:10.150 So some of the take  
NOTE Confidence: 0.974698

00:34:10.150 --> 00:34:11.430 home points I take from  
NOTE Confidence: 0.974698

00:34:11.430 --> 00:34:13.190 from the the forty, you  
NOTE Confidence: 0.974698

00:34:13.190 --> 00:34:14.870 know, gene expression panel that's  
NOTE Confidence: 0.974698

00:34:14.870 --> 00:34:16.230 available out there is is  
NOTE Confidence: 0.974698

00:34:16.230 --> 00:34:17.424 that I think we need  
NOTE Confidence: 0.974698

00:34:17.424 --> 00:34:19.285 prospective trials to better understand,  
NOTE Confidence: 0.9742615

00:34:19.984 --> 00:34:21.344 you know, how we can  
NOTE Confidence: 0.9742615

00:34:21.344 --> 00:34:23.744 identify patients who benefit from  
NOTE Confidence: 0.9742615

00:34:23.744 --> 00:34:25.424 this tool to help us  
NOTE Confidence: 0.9742615

00:34:25.424 --> 00:34:26.864 better stratify our patients in  
NOTE Confidence: 0.9742615

00:34:26.864 --> 00:34:28.565 terms of risk reductive adjuvant



NOTE Confidence: 0.9742615  
00:34:28.625 --> 00:34:29.125 strategies.  
NOTE Confidence: 0.9810977  
00:34:30.300 --> 00:34:32.060 In this retrospective cohort of  
NOTE Confidence: 0.9810977  
00:34:32.060 --> 00:34:32.560 patients,  
NOTE Confidence: 0.9507538  
00:34:33.100 --> 00:34:34.700 against small numbers, but it  
NOTE Confidence: 0.9507538  
00:34:34.700 --> 00:34:36.540 would seem that they have  
NOTE Confidence: 0.9507538  
00:34:36.540 --> 00:34:37.040 identified  
NOTE Confidence: 0.94275194  
00:34:37.660 --> 00:34:39.440 a class one gene expression  
NOTE Confidence: 0.94275194  
00:34:39.500 --> 00:34:40.400 profile that  
NOTE Confidence: 0.99926907  
00:34:41.100 --> 00:34:41.600 may  
NOTE Confidence: 0.9990584  
00:34:42.060 --> 00:34:42.560 help  
NOTE Confidence: 0.9852717  
00:34:43.005 --> 00:34:44.224 determine patients that  
NOTE Confidence: 0.954978  
00:34:44.924 --> 00:34:46.625 radiation could be safely omitted,  
NOTE Confidence: 0.954978  
00:34:46.684 --> 00:34:47.885 it could help reduce cost  
NOTE Confidence: 0.954978  
00:34:47.885 --> 00:34:49.164 of the healthcare system, but  
NOTE Confidence: 0.954978  
00:34:49.164 --> 00:34:50.924 also importantly prevent putting someone  
NOTE Confidence: 0.954978

00:34:50.924 --> 00:34:52.045 through side effects that could

NOTE Confidence: 0.954978

00:34:52.045 --> 00:34:53.244 affect quality of life moving

NOTE Confidence: 0.954978

00:34:53.244 --> 00:34:54.285 forward because of the side

NOTE Confidence: 0.954978

00:34:54.285 --> 00:34:56.385 effects radiation can cause.

NOTE Confidence: 0.96982974

00:34:57.530 --> 00:34:58.570 I think what's gonna be

NOTE Confidence: 0.96982974

00:34:58.570 --> 00:34:59.609 an important question to be

NOTE Confidence: 0.96982974

00:34:59.609 --> 00:35:01.050 answered is how do I

NOTE Confidence: 0.96982974

00:35:01.130 --> 00:35:02.090 how do we know what

NOTE Confidence: 0.96982974

00:35:02.090 --> 00:35:03.290 the benefit of radiation is

NOTE Confidence: 0.96982974

00:35:03.290 --> 00:35:04.410 in terms of what part

NOTE Confidence: 0.96982974

00:35:04.410 --> 00:35:05.630 of the body we're treating?

NOTE Confidence: 0.96982974

00:35:05.849 --> 00:35:07.530 So I mentioned earlier, there's

NOTE Confidence: 0.96982974

00:35:07.530 --> 00:35:08.730 no clear guidance in terms

NOTE Confidence: 0.96982974

00:35:08.730 --> 00:35:09.530 of do you treat the

NOTE Confidence: 0.96982974

00:35:09.530 --> 00:35:10.969 tumors tumor bed only or

NOTE Confidence: 0.96982974

00:35:10.969 --> 00:35:11.770 do you treat the tumor

NOTE Confidence: 0.96982974

00:35:11.770 --> 00:35:12.910 bed plus the nodes?

NOTE Confidence: 0.9974878

00:35:13.505 --> 00:35:14.705 I do know that there

NOTE Confidence: 0.9974878

00:35:14.705 --> 00:35:15.985 is interest in a,

NOTE Confidence: 0.7995587

00:35:16.545 --> 00:35:17.045 in,

NOTE Confidence: 0.98098385

00:35:17.985 --> 00:35:19.425 randomized trial to be designed

NOTE Confidence: 0.98098385

00:35:19.425 --> 00:35:21.105 where they would stratify patients

NOTE Confidence: 0.98098385

00:35:21.105 --> 00:35:22.225 based on class two a

NOTE Confidence: 0.98098385

00:35:22.225 --> 00:35:23.364 or class two b,

NOTE Confidence: 0.99880624

00:35:23.665 --> 00:35:24.165 randomizing

NOTE Confidence: 0.96095395

00:35:24.465 --> 00:35:26.250 them to radiation to the

NOTE Confidence: 0.96095395

00:35:26.250 --> 00:35:28.250 tumor bed only versus tumor

NOTE Confidence: 0.96095395

00:35:28.250 --> 00:35:30.090 bed plus nodal radiation, and

NOTE Confidence: 0.96095395

00:35:30.090 --> 00:35:31.050 c, are we seeing a

NOTE Confidence: 0.96095395

00:35:31.050 --> 00:35:32.489 benefit? Because it's not clear

NOTE Confidence: 0.96095395

00:35:32.489 --> 00:35:33.370 if you just radiate the

NOTE Confidence: 0.96095395

00:35:33.370 --> 00:35:34.810 primary site. Maybe we're preventing

NOTE Confidence: 0.96095395

00:35:34.810 --> 00:35:36.170 cancer cells from spreading to

NOTE Confidence: 0.96095395

00:35:36.170 --> 00:35:37.130 the nodes, and and maybe

NOTE Confidence: 0.96095395

00:35:37.130 --> 00:35:38.090 all the benefit is just

NOTE Confidence: 0.96095395

00:35:38.090 --> 00:35:39.465 treating the tumor bed. So

NOTE Confidence: 0.96095395

00:35:39.545 --> 00:35:40.745 so this trial is hoping

NOTE Confidence: 0.96095395

00:35:40.745 --> 00:35:41.325 to to

NOTE Confidence: 0.99208456

00:35:41.705 --> 00:35:42.925 kind of identify

NOTE Confidence: 0.97674805

00:35:43.225 --> 00:35:44.505 where where the benefit comes

NOTE Confidence: 0.97674805

00:35:44.505 --> 00:35:46.445 because if radiation is important

NOTE Confidence: 0.97674805

00:35:46.585 --> 00:35:48.125 as a risk reductive strategy,

NOTE Confidence: 0.97674805

00:35:48.344 --> 00:35:49.705 but we can identify a

NOTE Confidence: 0.97674805

00:35:49.705 --> 00:35:51.705 more localized radiation field that

NOTE Confidence: 0.97674805

00:35:51.705 --> 00:35:52.825 has less side effects for

NOTE Confidence: 0.97674805

00:35:52.825 --> 00:35:53.785 a patient with the same

NOTE Confidence: 0.97674805

00:35:53.785 --> 00:35:54.285 benefit,

NOTE Confidence: 0.96310616  
00:35:54.869 --> 00:35:55.989 I I think that's important  
NOTE Confidence: 0.96310616  
00:35:55.989 --> 00:35:57.289 for us to to understand.  
NOTE Confidence: 0.957676  
00:35:57.750 --> 00:35:59.349 And also this prospective trial  
NOTE Confidence: 0.957676  
00:35:59.349 --> 00:36:01.989 would theoretically also help confirm  
NOTE Confidence: 0.957676  
00:36:01.989 --> 00:36:03.430 in a prospective manner class  
NOTE Confidence: 0.957676  
00:36:03.430 --> 00:36:04.950 one patients could safely have  
NOTE Confidence: 0.957676  
00:36:04.950 --> 00:36:06.089 radiation omitted.  
NOTE Confidence: 0.97857815  
00:36:06.630 --> 00:36:07.989 And then long long, you  
NOTE Confidence: 0.97857815  
00:36:07.989 --> 00:36:09.369 know, big picture is  
NOTE Confidence: 0.97629184  
00:36:10.485 --> 00:36:11.765 a small number, only about  
NOTE Confidence: 0.97629184  
00:36:11.765 --> 00:36:12.885 twelve percent of patients based  
NOTE Confidence: 0.97629184  
00:36:12.885 --> 00:36:13.525 on a lot of these,  
NOTE Confidence: 0.97629184  
00:36:13.525 --> 00:36:14.885 you know, retrospective studies are  
NOTE Confidence: 0.97629184  
00:36:14.885 --> 00:36:16.185 actually receiving radiotherapy  
NOTE Confidence: 0.9094516  
00:36:16.485 --> 00:36:17.845 despite meeting a high risk,  
NOTE Confidence: 0.9094516

00:36:17.845 --> 00:36:18.985 very high risk categories.

NOTE Confidence: 0.9734986

00:36:20.885 --> 00:36:22.585 Can this gene expression profiling

NOTE Confidence: 0.9734986

00:36:22.885 --> 00:36:24.660 help, again, identify those patients

NOTE Confidence: 0.9734986

00:36:24.660 --> 00:36:25.780 who do have higher risk,

NOTE Confidence: 0.9734986

00:36:25.780 --> 00:36:26.739 who would have a greater

NOTE Confidence: 0.9734986

00:36:26.739 --> 00:36:27.700 benefit so that we could

NOTE Confidence: 0.9734986

00:36:27.700 --> 00:36:29.480 help prevent morbidity of recurrence?

NOTE Confidence: 0.9939175

00:36:30.180 --> 00:36:31.300 Are those the patients that

NOTE Confidence: 0.9939175

00:36:31.300 --> 00:36:32.500 it's worth putting through side

NOTE Confidence: 0.9939175

00:36:32.500 --> 00:36:33.619 effects and making sure we're

NOTE Confidence: 0.9939175

00:36:33.619 --> 00:36:34.900 kind of funneling into the

NOTE Confidence: 0.9939175

00:36:34.900 --> 00:36:35.880 radiation oncology,

NOTE Confidence: 0.94050586

00:36:36.420 --> 00:36:37.800 you know, adjuvant therapy?

NOTE Confidence: 0.98675656

00:36:38.645 --> 00:36:40.165 And having that shared decision

NOTE Confidence: 0.98675656

00:36:40.165 --> 00:36:41.844 making, discussion with the patient

NOTE Confidence: 0.98675656

00:36:41.844 --> 00:36:43.125 is also really helpful. Having

NOTE Confidence: 0.98675656

00:36:43.125 --> 00:36:44.825 this gene profile class

NOTE Confidence: 0.98443985

00:36:45.125 --> 00:36:46.805 stratification might help a patient

NOTE Confidence: 0.98443985

00:36:46.805 --> 00:36:47.945 make an informed decision.

NOTE Confidence: 0.9941731

00:36:48.565 --> 00:36:49.685 Since we're not seeing a

NOTE Confidence: 0.9941731

00:36:49.685 --> 00:36:51.685 survival benefit necessarily based on

NOTE Confidence: 0.9941731

00:36:51.685 --> 00:36:52.665 the small numbers,

NOTE Confidence: 0.9847354

00:36:53.100 --> 00:36:54.540 It's really coming down to

NOTE Confidence: 0.9847354

00:36:54.540 --> 00:36:55.660 how much do they value

NOTE Confidence: 0.9847354

00:36:55.660 --> 00:36:57.440 preventing a local recurrence potentially.

NOTE Confidence: 0.99627066

00:36:58.380 --> 00:36:59.980 And how we view these

NOTE Confidence: 0.99627066

00:36:59.980 --> 00:37:01.580 gene expression panels and how

NOTE Confidence: 0.99627066

00:37:01.580 --> 00:37:03.739 we incorporate our medical decision

NOTE Confidence: 0.99627066

00:37:03.739 --> 00:37:05.420 making about adjuvant radiation is

NOTE Confidence: 0.99627066

00:37:05.420 --> 00:37:06.780 probably also going to be

NOTE Confidence: 0.99627066

00:37:06.780 --> 00:37:07.920 ultimately influenced

NOTE Confidence: 0.9843912

00:37:08.625 --> 00:37:10.545 by systemic therapy options becoming

NOTE Confidence: 0.9843912

00:37:10.545 --> 00:37:11.045 available.

NOTE Confidence: 0.95564103

00:37:11.344 --> 00:37:12.465 Doctor. Tramm will talk about

NOTE Confidence: 0.95564103

00:37:12.465 --> 00:37:13.185 this kind of at the

NOTE Confidence: 0.95564103

00:37:13.185 --> 00:37:15.025 end summarizing this, but, you

NOTE Confidence: 0.95564103

00:37:15.025 --> 00:37:16.545 know, other systemic therapies that

NOTE Confidence: 0.95564103

00:37:16.545 --> 00:37:18.145 are available, other risk reductive

NOTE Confidence: 0.95564103

00:37:18.145 --> 00:37:19.344 strategies that may have a

NOTE Confidence: 0.95564103

00:37:19.344 --> 00:37:20.645 different side effect profile

NOTE Confidence: 0.955302

00:37:20.980 --> 00:37:22.500 may also frame how we

NOTE Confidence: 0.955302

00:37:22.500 --> 00:37:24.340 offer adjuvant treatment even in

NOTE Confidence: 0.955302

00:37:24.340 --> 00:37:25.300 the gene expression,

NOTE Confidence: 0.9943783

00:37:25.620 --> 00:37:26.680 profiling era.

NOTE Confidence: 0.9749109

00:37:31.060 --> 00:37:32.580 That's wonderful. I don't see

NOTE Confidence: 0.9749109

00:37:32.580 --> 00:37:34.260 any questions in the chat

NOTE Confidence: 0.9749109

00:37:34.260 --> 00:37:35.219 or the Q and A,



NOTE Confidence: 0.9749109  
00:37:35.219 --> 00:37:36.440 but just want to remind  
NOTE Confidence: 0.9970696  
00:37:36.825 --> 00:37:37.964 everyone to please  
NOTE Confidence: 0.99774337  
00:37:38.265 --> 00:37:39.244 ask us questions.  
NOTE Confidence: 0.8592836  
00:37:40.265 --> 00:37:41.625 You know, doctor Roche, I  
NOTE Confidence: 0.8592836  
00:37:41.625 --> 00:37:43.145 was curious, and also doctor  
NOTE Confidence: 0.8592836  
00:37:43.145 --> 00:37:43.645 Susie,  
NOTE Confidence: 0.92697746  
00:37:44.025 --> 00:37:45.505 if you had had received  
NOTE Confidence: 0.92697746  
00:37:45.705 --> 00:37:46.825 and I asked doctor Roche  
NOTE Confidence: 0.92697746  
00:37:46.825 --> 00:37:48.265 as she's our our PI  
NOTE Confidence: 0.92697746  
00:37:48.265 --> 00:37:49.864 locally of the NRG Neo  
NOTE Confidence: 0.92697746  
00:37:49.864 --> 00:37:50.364 adjuvant  
NOTE Confidence: 0.99869746  
00:37:50.790 --> 00:37:53.450 cutaneous squamous cell carcinoma trial.  
NOTE Confidence: 0.99892473  
00:37:54.070 --> 00:37:55.110 Would you be more or  
NOTE Confidence: 0.99892473  
00:37:55.110 --> 00:37:57.030 less likely to enroll a  
NOTE Confidence: 0.99892473  
00:37:57.030 --> 00:37:58.469 patient that maybe had a  
NOTE Confidence: 0.99892473

00:37:58.469 --> 00:37:58.969 smaller  
NOTE Confidence: 0.9665803

00:37:59.670 --> 00:38:00.870 tumor that you may not  
NOTE Confidence: 0.9665803

00:38:00.870 --> 00:38:02.570 have been as suspicious about  
NOTE Confidence: 0.99209493

00:38:02.950 --> 00:38:04.250 if they had a category  
NOTE Confidence: 0.99209493

00:38:04.390 --> 00:38:05.670 two a or b on  
NOTE Confidence: 0.99209493

00:38:05.670 --> 00:38:06.489 your trial?  
NOTE Confidence: 0.94356924

00:38:07.535 --> 00:38:08.575 Yep. You're referring to the  
NOTE Confidence: 0.94356924

00:38:08.575 --> 00:38:11.295 neoadjuvant simlopinab trial? That's yep.  
NOTE Confidence: 0.94356924

00:38:11.295 --> 00:38:11.795 Yeah.  
NOTE Confidence: 0.96999216

00:38:12.095 --> 00:38:14.255 So a smaller tumor, but  
NOTE Confidence: 0.96999216

00:38:14.255 --> 00:38:15.555 a higher higher,  
NOTE Confidence: 0.97003204

00:38:16.415 --> 00:38:18.575 biological class on the gene  
NOTE Confidence: 0.97003204

00:38:18.575 --> 00:38:19.075 panel.  
NOTE Confidence: 0.9627186

00:38:19.989 --> 00:38:20.950 I would I you know,  
NOTE Confidence: 0.9627186

00:38:20.950 --> 00:38:22.550 it's interesting because we as  
NOTE Confidence: 0.9627186

00:38:22.550 --> 00:38:23.050 we're

NOTE Confidence: 0.98541623  
00:38:23.590 --> 00:38:25.030 accruing for this trial and  
NOTE Confidence: 0.98541623  
00:38:25.030 --> 00:38:26.870 seeing how patients do, you  
NOTE Confidence: 0.98541623  
00:38:26.870 --> 00:38:28.390 know, it overall has a  
NOTE Confidence: 0.98541623  
00:38:28.390 --> 00:38:30.010 has a very substantial  
NOTE Confidence: 0.9736475  
00:38:31.635 --> 00:38:33.495 success rate in previous studies,  
NOTE Confidence: 0.99660605  
00:38:34.195 --> 00:38:35.235 but we are seeing some  
NOTE Confidence: 0.99660605  
00:38:35.235 --> 00:38:36.295 patients progressing.  
NOTE Confidence: 0.9847063  
00:38:36.915 --> 00:38:38.295 And so I do wonder,  
NOTE Confidence: 0.9847063  
00:38:38.355 --> 00:38:39.555 and I've you know, as  
NOTE Confidence: 0.9847063  
00:38:39.555 --> 00:38:40.755 as we've been talking about  
NOTE Confidence: 0.9847063  
00:38:40.755 --> 00:38:42.375 this, I've I was thinking,  
NOTE Confidence: 0.9847063  
00:38:42.515 --> 00:38:43.795 is is this something that  
NOTE Confidence: 0.9847063  
00:38:43.795 --> 00:38:45.395 could be added to an  
NOTE Confidence: 0.9847063  
00:38:45.395 --> 00:38:46.855 existing clinical trial,  
NOTE Confidence: 0.9799761  
00:38:47.500 --> 00:38:49.100 as an additional piece of  
NOTE Confidence: 0.9799761

00:38:49.100 --> 00:38:50.300 information to have about these  
NOTE Confidence: 0.9799761

00:38:50.300 --> 00:38:50.800 tumors,  
NOTE Confidence: 0.9650616

00:38:51.660 --> 00:38:53.420 we have patients that respond  
NOTE Confidence: 0.9650616

00:38:53.420 --> 00:38:54.480 very well to suniplumab,  
NOTE Confidence: 0.98431104

00:38:54.780 --> 00:38:56.140 and then we're seeing patients  
NOTE Confidence: 0.98431104

00:38:56.140 --> 00:38:57.260 that don't respond and that  
NOTE Confidence: 0.98431104

00:38:57.260 --> 00:38:57.920 they progress.  
NOTE Confidence: 0.98627913

00:38:58.940 --> 00:39:00.540 So this could be, you  
NOTE Confidence: 0.98627913

00:39:00.540 --> 00:39:02.480 know, provide some missing information.  
NOTE Confidence: 0.98921025

00:39:03.075 --> 00:39:04.594 But having that information to  
NOTE Confidence: 0.98921025

00:39:04.594 --> 00:39:05.335 your point,  
NOTE Confidence: 0.985822

00:39:05.635 --> 00:39:07.315 you know, might might raise  
NOTE Confidence: 0.985822

00:39:07.315 --> 00:39:08.835 some questions about maybe they  
NOTE Confidence: 0.985822

00:39:08.835 --> 00:39:09.635 should just go ahead and  
NOTE Confidence: 0.985822

00:39:09.635 --> 00:39:10.375 have surgery,  
NOTE Confidence: 0.9588481

00:39:11.474 --> 00:39:12.375 rather than,

NOTE Confidence: 0.9779666  
00:39:13.075 --> 00:39:14.035 rather than enroll in a  
NOTE Confidence: 0.9779666  
00:39:14.035 --> 00:39:14.935 clinical trial.  
NOTE Confidence: 0.99473035  
00:39:15.520 --> 00:39:16.960 I would also say that,  
NOTE Confidence: 0.9597996  
00:39:19.120 --> 00:39:20.320 in response to that question  
NOTE Confidence: 0.9597996  
00:39:20.320 --> 00:39:22.000 about enrollment in the clinical  
NOTE Confidence: 0.9597996  
00:39:22.000 --> 00:39:23.280 trial is that one of  
NOTE Confidence: 0.9597996  
00:39:23.280 --> 00:39:24.320 the issues is sometimes we  
NOTE Confidence: 0.9597996  
00:39:24.320 --> 00:39:25.600 don't have the full staging  
NOTE Confidence: 0.9597996  
00:39:25.600 --> 00:39:27.200 picture until after they have  
NOTE Confidence: 0.9597996  
00:39:27.200 --> 00:39:28.560 the MOSE procedure. Right? If  
NOTE Confidence: 0.9597996  
00:39:28.560 --> 00:39:30.580 the perineural invasion is not  
NOTE Confidence: 0.9970377  
00:39:30.945 --> 00:39:32.565 captured in the original biopsy,  
NOTE Confidence: 0.9970377  
00:39:32.625 --> 00:39:33.844 we're not realizing  
NOTE Confidence: 0.9963707  
00:39:34.145 --> 00:39:34.645 until,  
NOTE Confidence: 0.73888713  
00:39:35.344 --> 00:39:36.405 their full stage  
NOTE Confidence: 0.9460439

00:39:36.705 --> 00:39:38.305 until after they've had surgery.

NOTE Confidence: 0.9460439

00:39:38.305 --> 00:39:40.065 So having that GEP class

NOTE Confidence: 0.9460439

00:39:40.065 --> 00:39:41.045 prior to surgery,

NOTE Confidence: 0.9712155

00:39:41.905 --> 00:39:43.125 can help restratify,

NOTE Confidence: 0.9990504

00:39:44.145 --> 00:39:45.265 when you may not have

NOTE Confidence: 0.9990504

00:39:45.265 --> 00:39:46.450 all of the high risk

NOTE Confidence: 0.9990504

00:39:46.450 --> 00:39:47.430 features identified

NOTE Confidence: 0.93907565

00:39:48.050 --> 00:39:49.190 prior pre op.

NOTE Confidence: 0.99711823

00:39:52.130 --> 00:39:52.630 Okay.

NOTE Confidence: 0.9966122

00:39:53.810 --> 00:39:55.750 So we're gonna shift gears

NOTE Confidence: 0.86842954

00:39:56.210 --> 00:39:56.450 and,

NOTE Confidence: 0.9935365

00:39:57.170 --> 00:39:58.530 go into the magical world

NOTE Confidence: 0.9935365

00:39:58.530 --> 00:39:59.190 of melanoma.

NOTE Confidence: 0.9545364

00:40:02.214 --> 00:40:03.175 But, you know, some of

NOTE Confidence: 0.9545364

00:40:03.175 --> 00:40:04.855 my introduction is really gonna

NOTE Confidence: 0.9545364

00:40:04.855 --> 00:40:05.355 amplify

NOTE Confidence: 0.9987147  
00:40:05.734 --> 00:40:06.795 some incredibly  
NOTE Confidence: 0.9997286  
00:40:07.335 --> 00:40:07.835 important  
NOTE Confidence: 0.9099519  
00:40:08.135 --> 00:40:09.675 points that have already been  
NOTE Confidence: 0.9099519  
00:40:09.815 --> 00:40:11.675 made by doctor Young.  
NOTE Confidence: 0.96491313  
00:40:12.535 --> 00:40:13.915 I'll share my screen.  
NOTE Confidence: 0.4472357  
00:40:20.980 --> 00:40:21.480 Screen,  
NOTE Confidence: 0.9449503  
00:40:22.820 --> 00:40:23.960 it's visible, everyone?  
NOTE Confidence: 0.9988291  
00:40:24.660 --> 00:40:25.160 Okay.  
NOTE Confidence: 0.9987349  
00:40:26.180 --> 00:40:26.680 So  
NOTE Confidence: 0.9978935  
00:40:28.100 --> 00:40:28.600 the  
NOTE Confidence: 0.99880254  
00:40:29.465 --> 00:40:31.325 current landscape for melanoma  
NOTE Confidence: 0.99605787  
00:40:31.705 --> 00:40:33.385 about how we determine high  
NOTE Confidence: 0.99605787  
00:40:33.385 --> 00:40:35.325 risk disease is very different  
NOTE Confidence: 0.99605787  
00:40:35.545 --> 00:40:36.045 than  
NOTE Confidence: 0.9707799  
00:40:36.505 --> 00:40:38.125 where we are with cutaneous  
NOTE Confidence: 0.9707799

00:40:38.265 --> 00:40:40.585 squamous cell. So again, mostly  
NOTE Confidence: 0.9707799

00:40:40.585 --> 00:40:41.965 based on clinical pathologic  
NOTE Confidence: 0.71437615

00:40:42.265 --> 00:40:42.765 features.  
NOTE Confidence: 0.9433182

00:40:43.350 --> 00:40:45.290 And, really importantly, for melanoma,  
NOTE Confidence: 0.97907597

00:40:45.590 --> 00:40:47.830 we really routinely use sentinel  
NOTE Confidence: 0.97907597

00:40:47.830 --> 00:40:49.830 node biopsy based on the  
NOTE Confidence: 0.97907597

00:40:49.830 --> 00:40:51.050 MSLT one  
NOTE Confidence: 0.95873547

00:40:52.390 --> 00:40:54.070 trial. And the clinical path  
NOTE Confidence: 0.95873547

00:40:54.070 --> 00:40:55.430 features, many of which, you  
NOTE Confidence: 0.95873547

00:40:55.430 --> 00:40:56.550 know, similar to what doctor  
NOTE Confidence: 0.95873547

00:40:56.550 --> 00:40:58.410 Suzy had begun the conversation  
NOTE Confidence: 0.95873547

00:40:58.550 --> 00:40:59.775 with, are are some very,  
NOTE Confidence: 0.95873547

00:40:59.775 --> 00:41:00.994 very well validated,  
NOTE Confidence: 0.9728546

00:41:03.135 --> 00:41:03.635 nomograms.  
NOTE Confidence: 0.99935

00:41:04.335 --> 00:41:05.454 And some of the recent  
NOTE Confidence: 0.99935

00:41:05.454 --> 00:41:05.954 changes



NOTE Confidence: 0.9984423  
00:41:06.255 --> 00:41:07.474 to the  
NOTE Confidence: 0.995121  
00:41:07.934 --> 00:41:09.155 NCCN guidelines  
NOTE Confidence: 0.9657033  
00:41:10.015 --> 00:41:12.675 are incorporating actually using nomogram  
NOTE Confidence: 0.9657033  
00:41:12.734 --> 00:41:14.849 driven risk factors instead of  
NOTE Confidence: 0.9657033  
00:41:14.849 --> 00:41:15.589 the classic  
NOTE Confidence: 0.9958793  
00:41:16.130 --> 00:41:17.029 clinical pathologic  
NOTE Confidence: 0.99547654  
00:41:17.410 --> 00:41:18.770 features that had driven those  
NOTE Confidence: 0.99547654  
00:41:18.770 --> 00:41:19.750 decision making  
NOTE Confidence: 0.8758049  
00:41:20.450 --> 00:41:21.750 processes. But universally,  
NOTE Confidence: 0.9994023  
00:41:22.289 --> 00:41:22.789 as  
NOTE Confidence: 0.9592367  
00:41:23.089 --> 00:41:24.130 a as a group, we've  
NOTE Confidence: 0.9592367  
00:41:24.130 --> 00:41:24.950 agreed that  
NOTE Confidence: 0.9785118  
00:41:25.250 --> 00:41:26.950 a sentinel lymph node biopsy  
NOTE Confidence: 0.9785118  
00:41:27.010 --> 00:41:28.609 risk between five to ten  
NOTE Confidence: 0.9785118  
00:41:28.609 --> 00:41:29.085 percent  
NOTE Confidence: 0.9030574

00:41:29.565 --> 00:41:30.945 requires a discussion,  
NOTE Confidence: 0.9846792

00:41:31.484 --> 00:41:32.785 and ten or above  
NOTE Confidence: 0.9961709

00:41:33.484 --> 00:41:35.425 usually will be typically recommended  
NOTE Confidence: 0.9961709

00:41:35.484 --> 00:41:37.185 for a medically fit patient  
NOTE Confidence: 0.9946211

00:41:37.645 --> 00:41:38.925 in which the results of  
NOTE Confidence: 0.9946211

00:41:38.925 --> 00:41:40.525 the sentinel node are actually  
NOTE Confidence: 0.9946211

00:41:40.525 --> 00:41:41.665 going to be impactful.  
NOTE Confidence: 0.796526

00:41:42.150 --> 00:41:42.650 And  
NOTE Confidence: 0.98701054

00:41:43.029 --> 00:41:44.549 remember, the sentinel node is  
NOTE Confidence: 0.98701054

00:41:44.549 --> 00:41:45.989 what we use for risk  
NOTE Confidence: 0.98701054

00:41:45.989 --> 00:41:46.489 prognostication  
NOTE Confidence: 0.9143166

00:41:46.869 --> 00:41:47.369 to  
NOTE Confidence: 0.99992573

00:41:48.309 --> 00:41:48.809 better  
NOTE Confidence: 0.9993119

00:41:49.109 --> 00:41:49.609 delineate  
NOTE Confidence: 0.9771616

00:41:49.989 --> 00:41:51.430 where we are. Are we  
NOTE Confidence: 0.9771616

00:41:51.430 --> 00:41:52.710 stage one? Are we stage

NOTE Confidence: 0.9771616

00:41:52.710 --> 00:41:54.089 three? Where are we in

NOTE Confidence: 0.9771616

00:41:54.230 --> 00:41:55.910 between? And it really has

NOTE Confidence: 0.9771616

00:41:55.910 --> 00:41:56.890 a great discriminatory

NOTE Confidence: 0.8856238

00:41:57.270 --> 00:41:57.770 value.

NOTE Confidence: 0.9485425

00:41:58.125 --> 00:41:59.805 However, we're always faced with

NOTE Confidence: 0.9485425

00:41:59.805 --> 00:42:01.505 the challenges. You know,

NOTE Confidence: 0.97506535

00:42:01.885 --> 00:42:04.045 our overtreated patient. Right? There's

NOTE Confidence: 0.97506535

00:42:04.045 --> 00:42:05.565 gonna be some patients in

NOTE Confidence: 0.97506535

00:42:05.565 --> 00:42:07.005 melanoma that are gonna be

NOTE Confidence: 0.97506535

00:42:07.005 --> 00:42:08.065 cured by surgery

NOTE Confidence: 0.9992761

00:42:08.605 --> 00:42:10.285 alone. They don't gain anything

NOTE Confidence: 0.9992761

00:42:10.285 --> 00:42:11.940 by watching them closer. They

NOTE Confidence: 0.9992761

00:42:11.940 --> 00:42:12.839 don't gain anything

NOTE Confidence: 0.9713555

00:42:13.380 --> 00:42:15.079 from getting adjuvant therapy,

NOTE Confidence: 0.94957525

00:42:15.540 --> 00:42:17.160 but they bear real financial

NOTE Confidence: 0.94957525

00:42:17.300 --> 00:42:18.980 and emotional cost as well  
NOTE Confidence: 0.94957525

00:42:18.980 --> 00:42:19.719 as toxicity.  
NOTE Confidence: 0.9893172

00:42:21.140 --> 00:42:22.180 Then we have the other  
NOTE Confidence: 0.9893172

00:42:22.180 --> 00:42:23.540 patients that we're missing, the  
NOTE Confidence: 0.9893172

00:42:23.540 --> 00:42:25.700 undertreated patients. And, you know,  
NOTE Confidence: 0.9893172

00:42:25.700 --> 00:42:26.739 we worry a lot about  
NOTE Confidence: 0.9893172

00:42:26.739 --> 00:42:28.385 these in our most common  
NOTE Confidence: 0.9893172

00:42:28.445 --> 00:42:30.364 presentation for melanoma, which is  
NOTE Confidence: 0.9893172

00:42:30.364 --> 00:42:31.905 our earlier stage patients.  
NOTE Confidence: 0.94502974

00:42:32.205 --> 00:42:33.165 We know there's a small  
NOTE Confidence: 0.94502974

00:42:33.165 --> 00:42:34.844 percentage of these patients that  
NOTE Confidence: 0.94502974

00:42:34.844 --> 00:42:35.585 are recur  
NOTE Confidence: 0.7128343

00:42:36.125 --> 00:42:36.625 and  
NOTE Confidence: 0.9997461

00:42:36.925 --> 00:42:37.825 they go untreated  
NOTE Confidence: 0.9216212

00:42:38.125 --> 00:42:39.745 and that group gets missed.  
NOTE Confidence: 0.98612165

00:42:40.380 --> 00:42:41.339 And when we think about

NOTE Confidence: 0.98612165  
00:42:41.339 --> 00:42:42.719 it, it becomes an amplified  
NOTE Confidence: 0.98612165  
00:42:42.779 --> 00:42:43.819 problem. So we have a  
NOTE Confidence: 0.98612165  
00:42:43.819 --> 00:42:45.420 very small percentage, but that  
NOTE Confidence: 0.98612165  
00:42:45.420 --> 00:42:45.920 percentage  
NOTE Confidence: 0.9877628  
00:42:46.619 --> 00:42:47.119 absolutely  
NOTE Confidence: 0.9712384  
00:42:47.900 --> 00:42:49.339 represents a large group of  
NOTE Confidence: 0.9712384  
00:42:49.339 --> 00:42:50.859 patients because if, you know,  
NOTE Confidence: 0.9712384  
00:42:50.859 --> 00:42:52.059 over eighty percent of our  
NOTE Confidence: 0.9712384  
00:42:52.059 --> 00:42:53.099 patients are going to be  
NOTE Confidence: 0.9712384  
00:42:53.099 --> 00:42:54.719 early, even a small percentage  
NOTE Confidence: 0.9712384  
00:42:54.859 --> 00:42:56.665 of that becomes a bigger  
NOTE Confidence: 0.9712384  
00:42:56.665 --> 00:42:57.165 problem.  
NOTE Confidence: 0.9766441  
00:42:57.704 --> 00:42:58.984 And, again, our overall goal  
NOTE Confidence: 0.9766441  
00:42:58.984 --> 00:43:00.025 is we only want to  
NOTE Confidence: 0.9766441  
00:43:00.025 --> 00:43:01.224 treat patients that are going  
NOTE Confidence: 0.9766441

00:43:01.224 --> 00:43:02.585 to relapse. We want to  
NOTE Confidence: 0.9766441

00:43:02.585 --> 00:43:03.944 spare anyone that would be  
NOTE Confidence: 0.9766441

00:43:03.944 --> 00:43:05.385 cured with surgery. And in  
NOTE Confidence: 0.9766441

00:43:05.385 --> 00:43:06.344 order to do this, we  
NOTE Confidence: 0.9766441

00:43:06.344 --> 00:43:07.464 have to try to be  
NOTE Confidence: 0.9766441

00:43:07.464 --> 00:43:07.964 better  
NOTE Confidence: 0.9952738

00:43:08.265 --> 00:43:09.964 at accurate risk stratification.  
NOTE Confidence: 0.89113235

00:43:11.719 --> 00:43:12.859 So again, our AJCC  
NOTE Confidence: 0.9779466

00:43:13.160 --> 00:43:15.079 staging, it's it's good, but  
NOTE Confidence: 0.9779466

00:43:15.079 --> 00:43:17.000 it's not sufficient. We're striving  
NOTE Confidence: 0.9779466

00:43:17.000 --> 00:43:17.960 to keep doing that. That's  
NOTE Confidence: 0.9779466

00:43:17.960 --> 00:43:19.559 why it's always iterative, why  
NOTE Confidence: 0.9779466

00:43:19.559 --> 00:43:20.460 it gets improved.  
NOTE Confidence: 0.93415344

00:43:20.839 --> 00:43:22.200 So it does provide some  
NOTE Confidence: 0.93415344

00:43:22.200 --> 00:43:23.660 valuable baseline prognostication,  
NOTE Confidence: 0.9673

00:43:24.695 --> 00:43:25.335 but there's a lot of

NOTE Confidence: 0.9673  
00:43:25.335 --> 00:43:25.835 heterogeneity,  
NOTE Confidence: 0.96833384  
00:43:26.295 --> 00:43:27.494 there's a lot of overlap  
NOTE Confidence: 0.96833384  
00:43:27.494 --> 00:43:29.094 within these categories that we're  
NOTE Confidence: 0.96833384  
00:43:29.094 --> 00:43:30.695 working to parse out. And  
NOTE Confidence: 0.96833384  
00:43:30.695 --> 00:43:32.455 again, that's the question about  
NOTE Confidence: 0.96833384  
00:43:32.455 --> 00:43:34.135 not only nomograms, but does  
NOTE Confidence: 0.96833384  
00:43:34.135 --> 00:43:35.275 the GEP testing  
NOTE Confidence: 0.99955124  
00:43:36.055 --> 00:43:37.175 help us to get a  
NOTE Confidence: 0.99955124  
00:43:37.175 --> 00:43:37.915 more individualized  
NOTE Confidence: 0.9769976  
00:43:38.295 --> 00:43:39.594 risk for these patients?  
NOTE Confidence: 0.93624485  
00:43:41.170 --> 00:43:42.710 Again, that stage 1b2a  
NOTE Confidence: 0.9589772  
00:43:43.570 --> 00:43:44.770 patient group is really where  
NOTE Confidence: 0.9589772  
00:43:44.770 --> 00:43:46.050 I think that this is  
NOTE Confidence: 0.9589772  
00:43:46.050 --> 00:43:48.050 a real unmet need where  
NOTE Confidence: 0.9589772  
00:43:48.050 --> 00:43:49.330 we may be under treating  
NOTE Confidence: 0.9589772

00:43:49.330 --> 00:43:50.310 but also overtreating  
NOTE Confidence: 0.9555136

00:43:50.610 --> 00:43:51.750 part of that population,  
NOTE Confidence: 0.9989309

00:43:52.770 --> 00:43:53.270 so  
NOTE Confidence: 0.9997818

00:43:53.964 --> 00:43:54.844 we really need to be  
NOTE Confidence: 0.9997818

00:43:54.844 --> 00:43:56.545 able to distinguish these groups  
NOTE Confidence: 0.95899975

00:43:58.204 --> 00:44:00.125 so gene expression profile arrays  
NOTE Confidence: 0.95899975

00:44:00.125 --> 00:44:01.645 have been around for almost  
NOTE Confidence: 0.95899975

00:44:01.645 --> 00:44:03.744 fifteen years now in melanoma,  
NOTE Confidence: 0.95899975

00:44:03.885 --> 00:44:05.405 again much earlier in their  
NOTE Confidence: 0.95899975

00:44:05.405 --> 00:44:07.025 inception and use for cutaneous  
NOTE Confidence: 0.95899975

00:44:07.165 --> 00:44:08.920 squamous cell And there's three  
NOTE Confidence: 0.95899975

00:44:08.920 --> 00:44:10.200 main ones that are commercially  
NOTE Confidence: 0.95899975

00:44:10.200 --> 00:44:10.700 available,  
NOTE Confidence: 0.92641586

00:44:11.480 --> 00:44:13.160 two available in the States.  
NOTE Confidence: 0.92641586

00:44:13.160 --> 00:44:14.760 One is only available in  
NOTE Confidence: 0.92641586

00:44:14.760 --> 00:44:16.460 Germany, so the Castle Bioscience



NOTE Confidence: 0.92641586  
00:44:16.600 --> 00:44:17.260 is probably  
NOTE Confidence: 0.9650706  
00:44:17.560 --> 00:44:18.760 the oldest one that had  
NOTE Confidence: 0.9650706  
00:44:18.760 --> 00:44:20.520 been used. The more recent  
NOTE Confidence: 0.9650706  
00:44:20.520 --> 00:44:21.739 one is the,  
NOTE Confidence: 0.909567  
00:44:22.445 --> 00:44:23.185 the CPGEP,  
NOTE Confidence: 0.98042995  
00:44:23.805 --> 00:44:25.185 commonly known as the Merlin  
NOTE Confidence: 0.89494693  
00:44:25.565 --> 00:44:26.065 assay,  
NOTE Confidence: 0.9438585  
00:44:27.165 --> 00:44:28.765 which will speak in great  
NOTE Confidence: 0.9438585  
00:44:28.765 --> 00:44:30.364 detail, both myself and Doctor.  
NOTE Confidence: 0.9438585  
00:44:30.364 --> 00:44:30.864 Christiansen.  
NOTE Confidence: 0.97474796  
00:44:31.405 --> 00:44:33.105 And then an eleven gene  
NOTE Confidence: 0.9631763  
00:44:33.405 --> 00:44:35.165 GEP, the Melligenics, and that's  
NOTE Confidence: 0.9631763  
00:44:35.165 --> 00:44:36.465 used over in Germany.  
NOTE Confidence: 0.9763998  
00:44:37.349 --> 00:44:38.950 Each of them actually use  
NOTE Confidence: 0.9763998  
00:44:38.950 --> 00:44:41.130 completely different genes. So within  
NOTE Confidence: 0.9763998

00:44:41.190 --> 00:44:42.390 all of these,  
NOTE Confidence: 0.9933293

00:44:42.789 --> 00:44:44.549 prognostic and reference genes, they  
NOTE Confidence: 0.9933293

00:44:44.549 --> 00:44:45.930 actually do not overlap.  
NOTE Confidence: 0.94780844

00:44:47.509 --> 00:44:48.569 Some use clinical  
NOTE Confidence: 0.9409482

00:44:49.075 --> 00:44:50.515 pathologic variables, so that's in  
NOTE Confidence: 0.9409482

00:44:50.515 --> 00:44:52.515 the DECISION DX as well  
NOTE Confidence: 0.9409482

00:44:52.515 --> 00:44:53.955 as the Merlin assay, but  
NOTE Confidence: 0.9409482

00:44:53.955 --> 00:44:55.094 not in the melaninics.  
NOTE Confidence: 0.9630313

00:44:56.355 --> 00:44:58.755 The output in the DECISION  
NOTE Confidence: 0.9630313

00:44:58.755 --> 00:45:00.455 DX, the thirty one GEP,  
NOTE Confidence: 0.9630313

00:45:00.675 --> 00:45:02.535 when it includes clinical pathologic,  
NOTE Confidence: 0.9630313

00:45:02.594 --> 00:45:03.849 that makes it the I  
NOTE Confidence: 0.9630313

00:45:03.849 --> 00:45:04.910 thirty one GEP.  
NOTE Confidence: 0.91668946

00:45:05.210 --> 00:45:07.130 That's broken into four different  
NOTE Confidence: 0.91668946

00:45:07.130 --> 00:45:08.650 classes versus the other two  
NOTE Confidence: 0.91668946

00:45:08.650 --> 00:45:10.489 are really higher low risk

NOTE Confidence: 0.91668946  
00:45:10.489 --> 00:45:11.550 binary categories.  
NOTE Confidence: 0.9991773  
00:45:12.890 --> 00:45:13.390 The  
NOTE Confidence: 0.9954693  
00:45:13.690 --> 00:45:14.830 thirty one GEP,  
NOTE Confidence: 0.96450984  
00:45:15.295 --> 00:45:17.135 that was initially developed actually  
NOTE Confidence: 0.96450984  
00:45:17.135 --> 00:45:18.515 for overall prognosis,  
NOTE Confidence: 0.99576336  
00:45:18.895 --> 00:45:20.094 but then is now more  
NOTE Confidence: 0.99576336  
00:45:20.094 --> 00:45:21.395 developed towards giving  
NOTE Confidence: 0.9766879  
00:45:21.855 --> 00:45:22.975 some guidance for who we  
NOTE Confidence: 0.9766879  
00:45:22.975 --> 00:45:24.594 should be doing sentinel nodes.  
NOTE Confidence: 0.9766879  
00:45:24.655 --> 00:45:26.255 Merlin assay was really more  
NOTE Confidence: 0.9766879  
00:45:26.255 --> 00:45:27.855 developed with sentinel nodes, although  
NOTE Confidence: 0.9766879  
00:45:27.855 --> 00:45:29.955 there is perhaps some prognostic  
NOTE Confidence: 0.9650008  
00:45:30.590 --> 00:45:31.630 cation that can be done  
NOTE Confidence: 0.9650008  
00:45:31.630 --> 00:45:32.910 versus the g e the  
NOTE Confidence: 0.9650008  
00:45:32.910 --> 00:45:34.430 eleven g e p is  
NOTE Confidence: 0.9650008

00:45:34.430 --> 00:45:36.510 really focused on stage two  
NOTE Confidence: 0.9650008  
00:45:36.510 --> 00:45:37.010 disease  
NOTE Confidence: 0.9974237  
00:45:37.469 --> 00:45:38.370 and prognostic  
NOTE Confidence: 0.9876342  
00:45:38.830 --> 00:45:39.330 variables.  
NOTE Confidence: 0.9966446  
00:45:40.270 --> 00:45:41.410 These can be variably  
NOTE Confidence: 0.9533157  
00:45:41.870 --> 00:45:42.910 reimbursed. If we look at  
NOTE Confidence: 0.9533157  
00:45:42.910 --> 00:45:44.190 the cost of a sentinel  
NOTE Confidence: 0.9533157  
00:45:44.190 --> 00:45:45.315 node, that can range from  
NOTE Confidence: 0.9533157  
00:45:45.315 --> 00:45:46.994 nine to eleven thousand dollars  
NOTE Confidence: 0.9533157  
00:45:46.994 --> 00:45:47.815 in the states,  
NOTE Confidence: 0.9930105  
00:45:48.594 --> 00:45:50.214 and some of these GEP  
NOTE Confidence: 0.9930105  
00:45:50.355 --> 00:45:51.954 assays can cost, if they're  
NOTE Confidence: 0.9930105  
00:45:51.954 --> 00:45:53.974 not covered by insurance, anywhere  
NOTE Confidence: 0.9930105  
00:45:54.035 --> 00:45:54.535 from,  
NOTE Confidence: 0.92165685  
00:45:55.075 --> 00:45:56.835 three to seven thousand dollars  
NOTE Confidence: 0.92165685  
00:45:56.835 --> 00:45:58.695 depending upon insurance status.

NOTE Confidence: 0.9611006  
00:45:59.360 --> 00:46:00.640 So and right now, the  
NOTE Confidence: 0.9611006  
00:46:00.640 --> 00:46:02.480 thirty one GEP has not  
NOTE Confidence: 0.9611006  
00:46:02.480 --> 00:46:03.219 been recommended  
NOTE Confidence: 0.99823594  
00:46:03.680 --> 00:46:05.219 by any of the major  
NOTE Confidence: 0.99823594  
00:46:05.280 --> 00:46:05.780 societies.  
NOTE Confidence: 0.95564806  
00:46:06.480 --> 00:46:08.180 Just this year, the NCCN  
NOTE Confidence: 0.95564806  
00:46:08.400 --> 00:46:09.920 on the basis of the,  
NOTE Confidence: 0.95564806  
00:46:10.239 --> 00:46:11.860 Merlin o o one randomized  
NOTE Confidence: 0.95564806  
00:46:11.920 --> 00:46:12.820 clinical trial,  
NOTE Confidence: 0.9486222  
00:46:13.364 --> 00:46:14.665 has included this.  
NOTE Confidence: 0.96961516  
00:46:15.364 --> 00:46:16.805 And there is actually and  
NOTE Confidence: 0.96961516  
00:46:16.805 --> 00:46:17.844 doctor Tran will talk a  
NOTE Confidence: 0.96961516  
00:46:17.844 --> 00:46:18.725 little bit more about the  
NOTE Confidence: 0.96961516  
00:46:18.725 --> 00:46:20.585 nivo mela phase three trial,  
NOTE Confidence: 0.96961516  
00:46:20.645 --> 00:46:22.085 which is actually doing a  
NOTE Confidence: 0.9627005

00:46:23.445 --> 00:46:24.885 identifying the high risk group

NOTE Confidence: 0.9627005

00:46:24.885 --> 00:46:25.945 and actually randomizing

NOTE Confidence: 0.99053174

00:46:26.550 --> 00:46:28.390 those patients to receive either

NOTE Confidence: 0.99053174

00:46:28.390 --> 00:46:29.450 adjuvant nivolumab

NOTE Confidence: 0.9988209

00:46:29.910 --> 00:46:30.650 or placebo

NOTE Confidence: 0.9930682

00:46:31.190 --> 00:46:32.550 for our high risk stage

NOTE Confidence: 0.9930682

00:46:32.550 --> 00:46:33.290 two patients.

NOTE Confidence: 0.9960973

00:46:34.710 --> 00:46:36.070 So looking a little bit

NOTE Confidence: 0.9960973

00:46:36.070 --> 00:46:37.430 into what is the best

NOTE Confidence: 0.9960973

00:46:37.430 --> 00:46:38.730 data that's available

NOTE Confidence: 0.942372

00:46:39.030 --> 00:46:40.310 to review, so for the

NOTE Confidence: 0.942372

00:46:40.310 --> 00:46:41.290 thirty one GEP,

NOTE Confidence: 0.87090546

00:46:41.715 --> 00:46:43.415 there was a prospective decide

NOTE Confidence: 0.87090546

00:46:43.475 --> 00:46:43.975 study,

NOTE Confidence: 0.957361

00:46:44.835 --> 00:46:45.335 again,

NOTE Confidence: 0.99370116

00:46:45.795 --> 00:46:47.075 for what it was looking

NOTE Confidence: 0.99370116  
00:46:47.075 --> 00:46:48.435 for. So the negative predictive  
NOTE Confidence: 0.99370116  
00:46:48.435 --> 00:46:49.715 value means how much can  
NOTE Confidence: 0.99370116  
00:46:49.715 --> 00:46:51.415 you trust when someone says  
NOTE Confidence: 0.9857334  
00:46:52.835 --> 00:46:54.215 that this is not gonna  
NOTE Confidence: 0.94951624  
00:46:54.760 --> 00:46:56.280 be a positive sentinel note,  
NOTE Confidence: 0.94951624  
00:46:56.280 --> 00:46:57.880 so very, very good negative  
NOTE Confidence: 0.94951624  
00:46:57.880 --> 00:46:58.380 predictive  
NOTE Confidence: 0.9891372  
00:46:58.760 --> 00:47:00.780 value in these low risk  
NOTE Confidence: 0.9891372  
00:47:00.920 --> 00:47:02.360 patients, which you want. There's  
NOTE Confidence: 0.9891372  
00:47:02.360 --> 00:47:03.720 a low prevalence. We don't  
NOTE Confidence: 0.9891372  
00:47:03.720 --> 00:47:04.520 wanna have a lot of  
NOTE Confidence: 0.9891372  
00:47:04.520 --> 00:47:06.520 people that have disease that  
NOTE Confidence: 0.9891372  
00:47:06.520 --> 00:47:07.580 we didn't detect.  
NOTE Confidence: 0.9952264  
00:47:08.520 --> 00:47:09.020 Now  
NOTE Confidence: 0.9185629  
00:47:09.714 --> 00:47:11.255 the problem though is that  
NOTE Confidence: 0.9643221

00:47:11.635 --> 00:47:12.915 it not very good at  
NOTE Confidence: 0.9643221

00:47:12.915 --> 00:47:15.094 identifying who are the outliers.  
NOTE Confidence: 0.98080194

00:47:15.474 --> 00:47:17.315 Right? If everybody in your  
NOTE Confidence: 0.98080194

00:47:17.315 --> 00:47:19.075 test, they can identify and  
NOTE Confidence: 0.98080194

00:47:19.075 --> 00:47:20.355 I we already said that  
NOTE Confidence: 0.98080194

00:47:20.355 --> 00:47:21.474 there are t one a  
NOTE Confidence: 0.98080194

00:47:21.474 --> 00:47:22.835 patients that are going to  
NOTE Confidence: 0.98080194

00:47:22.835 --> 00:47:23.335 relapse.  
NOTE Confidence: 0.97209525

00:47:23.850 --> 00:47:25.310 If your test can't discriminate  
NOTE Confidence: 0.97209525

00:47:25.450 --> 00:47:27.450 between that, you know, there  
NOTE Confidence: 0.97209525

00:47:27.450 --> 00:47:29.130 there becomes some issue. But,  
NOTE Confidence: 0.97209525

00:47:29.130 --> 00:47:30.970 again, if it's negative, that  
NOTE Confidence: 0.97209525

00:47:30.970 --> 00:47:33.050 negative predictive value seems to  
NOTE Confidence: 0.97209525

00:47:33.050 --> 00:47:34.750 be very good with this.  
NOTE Confidence: 0.8644496

00:47:35.844 --> 00:47:37.685 The MERLIN one is the  
NOTE Confidence: 0.8644496

00:47:37.685 --> 00:47:38.585 largest prospective



NOTE Confidence: 0.95520216  
00:47:38.885 --> 00:47:40.805 GEP trial to date, you  
NOTE Confidence: 0.95520216  
00:47:40.805 --> 00:47:42.344 know, seventeen hundred  
NOTE Confidence: 0.9605166  
00:47:42.645 --> 00:47:43.145 patients,  
NOTE Confidence: 0.9288656  
00:47:44.085 --> 00:47:46.405 looking from, again, T1a through  
NOTE Confidence: 0.9288656  
00:47:46.405 --> 00:47:46.905 T3.  
NOTE Confidence: 0.9372866  
00:47:47.605 --> 00:47:49.364 Again, at patients who we're  
NOTE Confidence: 0.9372866  
00:47:49.364 --> 00:47:50.880 the most worried about and  
NOTE Confidence: 0.9372866  
00:47:50.880 --> 00:47:52.160 I think that there's very  
NOTE Confidence: 0.9372866  
00:47:52.160 --> 00:47:53.359 little debate whether or not  
NOTE Confidence: 0.9372866  
00:47:53.359 --> 00:47:54.480 they should get a sentinel  
NOTE Confidence: 0.9372866  
00:47:54.480 --> 00:47:55.219 node biopsy,  
NOTE Confidence: 0.9372299  
00:47:55.839 --> 00:47:56.339 again,  
NOTE Confidence: 0.9371035  
00:47:57.680 --> 00:47:59.200 it's really not going to  
NOTE Confidence: 0.9371035  
00:47:59.200 --> 00:48:00.420 be that discriminatory.  
NOTE Confidence: 0.98454326  
00:48:01.119 --> 00:48:02.480 However, in the group of  
NOTE Confidence: 0.98454326

00:48:02.480 --> 00:48:04.215 patients here, these high risk  
NOTE Confidence: 0.98454326

00:48:04.215 --> 00:48:05.575 t one a's, t one  
NOTE Confidence: 0.98454326

00:48:05.575 --> 00:48:07.495 b's, t two a's, these  
NOTE Confidence: 0.98454326

00:48:07.495 --> 00:48:08.555 are our class,  
NOTE Confidence: 0.9742887

00:48:09.175 --> 00:48:11.114 clinical stage one b patients.  
NOTE Confidence: 0.9742887

00:48:11.175 --> 00:48:11.675 Right?  
NOTE Confidence: 0.99918056

00:48:12.455 --> 00:48:13.675 Really good utility  
NOTE Confidence: 0.94417

00:48:14.215 --> 00:48:15.515 that we're seeing here.  
NOTE Confidence: 0.99491024

00:48:18.210 --> 00:48:19.270 Very good discriminatory  
NOTE Confidence: 0.9407075

00:48:19.810 --> 00:48:21.250 capacity, and and this may  
NOTE Confidence: 0.9407075

00:48:21.250 --> 00:48:22.150 be its greatest  
NOTE Confidence: 0.9839914

00:48:22.770 --> 00:48:23.270 value.  
NOTE Confidence: 0.9851559

00:48:23.570 --> 00:48:24.770 The assay has a good  
NOTE Confidence: 0.9851559

00:48:24.770 --> 00:48:26.369 success rate from also getting  
NOTE Confidence: 0.9851559

00:48:26.369 --> 00:48:27.109 the FFPBE  
NOTE Confidence: 0.75912666

00:48:27.969 --> 00:48:28.469 tissue,

NOTE Confidence: 0.96229446  
00:48:29.090 --> 00:48:31.265 and in these important categories  
NOTE Confidence: 0.96229446  
00:48:31.265 --> 00:48:32.545 here, this clinical 1b, but  
NOTE Confidence: 0.96229446  
00:48:32.545 --> 00:48:34.085 also in our older patients,  
NOTE Confidence: 0.96229446  
00:48:34.385 --> 00:48:36.145 where risks of general anesthesia,  
NOTE Confidence: 0.96229446  
00:48:36.145 --> 00:48:37.105 which you have to have  
NOTE Confidence: 0.96229446  
00:48:37.105 --> 00:48:38.145 to have a central note,  
NOTE Confidence: 0.96229446  
00:48:38.145 --> 00:48:38.885 are different.  
NOTE Confidence: 0.99024254  
00:48:39.265 --> 00:48:40.465 So in these in the  
NOTE Confidence: 0.99024254  
00:48:40.465 --> 00:48:41.905 patients that are low risk,  
NOTE Confidence: 0.99024254  
00:48:41.905 --> 00:48:43.780 again, six point six percent  
NOTE Confidence: 0.99024254  
00:48:43.780 --> 00:48:44.980 versus these patients that are  
NOTE Confidence: 0.99024254  
00:48:44.980 --> 00:48:45.480 being  
NOTE Confidence: 0.9631238  
00:48:45.780 --> 00:48:47.619 identified at high risk and  
NOTE Confidence: 0.9631238  
00:48:47.619 --> 00:48:49.140 where we're actually confirming that  
NOTE Confidence: 0.9631238  
00:48:49.140 --> 00:48:50.500 that's the case, I think  
NOTE Confidence: 0.9631238

00:48:50.500 --> 00:48:51.859 that this is also a  
NOTE Confidence: 0.9631238

00:48:51.859 --> 00:48:53.719 group that's pretty powerful.  
NOTE Confidence: 0.9996333

00:48:56.695 --> 00:48:57.994 It's been validated  
NOTE Confidence: 0.9788122

00:48:58.295 --> 00:48:59.974 independently now. This is a  
NOTE Confidence: 0.9788122

00:48:59.974 --> 00:49:02.535 recent data from, a Dutch  
NOTE Confidence: 0.9788122

00:49:02.535 --> 00:49:04.075 trial. Again, sensitivity  
NOTE Confidence: 0.95878166

00:49:04.375 --> 00:49:05.895 about ninety two point five  
NOTE Confidence: 0.95878166

00:49:05.895 --> 00:49:07.515 percent, a good negative  
NOTE Confidence: 0.9599164

00:49:08.109 --> 00:49:09.630 predictive value at ninety four  
NOTE Confidence: 0.9599164

00:49:09.630 --> 00:49:10.130 percent.  
NOTE Confidence: 0.99623543

00:49:10.670 --> 00:49:11.570 Again, specifically  
NOTE Confidence: 0.9639834

00:49:12.270 --> 00:49:13.710 at that group where we  
NOTE Confidence: 0.9639834

00:49:13.710 --> 00:49:14.910 actually have a real gray  
NOTE Confidence: 0.9639834

00:49:14.910 --> 00:49:16.369 area, where we have real  
NOTE Confidence: 0.9639834

00:49:16.430 --> 00:49:18.450 focused conversations in the clinic.  
NOTE Confidence: 0.9725479

00:49:18.829 --> 00:49:20.369 And, again, we see discrimination

NOTE Confidence: 0.97775537  
00:49:20.750 --> 00:49:23.145 between the recurrence free, distant  
NOTE Confidence: 0.97775537  
00:49:23.145 --> 00:49:24.844 metastasis free, and the melanoma  
NOTE Confidence: 0.97775537  
00:49:24.985 --> 00:49:25.965 specific survival  
NOTE Confidence: 0.9851365  
00:49:26.505 --> 00:49:27.885 between these groups.  
NOTE Confidence: 0.94693947  
00:49:28.185 --> 00:49:30.425 Okay? And, again, the these  
NOTE Confidence: 0.94693947  
00:49:30.585 --> 00:49:31.885 as you draw them out,  
NOTE Confidence: 0.99973106  
00:49:32.425 --> 00:49:33.485 these are conversations  
NOTE Confidence: 0.9766091  
00:49:33.785 --> 00:49:34.825 that you wanna have with  
NOTE Confidence: 0.9766091  
00:49:34.825 --> 00:49:35.565 your patients,  
NOTE Confidence: 0.99633396  
00:49:35.880 --> 00:49:37.339 things that help us discriminate  
NOTE Confidence: 0.99633396  
00:49:37.559 --> 00:49:38.920 about what we're gonna do,  
NOTE Confidence: 0.99633396  
00:49:38.920 --> 00:49:40.599 what decisions that we're going  
NOTE Confidence: 0.99633396  
00:49:40.599 --> 00:49:41.260 to make.  
NOTE Confidence: 0.93903846  
00:49:44.200 --> 00:49:46.039 And and, again, this is,  
NOTE Confidence: 0.79649186  
00:49:46.599 --> 00:49:47.099 from,  
NOTE Confidence: 0.90605193

00:49:48.535 --> 00:49:50.075 Yu et al, from, again,  
NOTE Confidence: 0.90605193

00:49:50.215 --> 00:49:52.455 just recently published. Again, looking  
NOTE Confidence: 0.90605193

00:49:52.455 --> 00:49:53.815 more specifically at t one  
NOTE Confidence: 0.90605193

00:49:53.815 --> 00:49:55.515 a melanomas and graphically  
NOTE Confidence: 0.9161053

00:49:56.055 --> 00:49:57.015 over here, you can see  
NOTE Confidence: 0.9161053

00:49:57.015 --> 00:49:58.935 that the they're detecting some  
NOTE Confidence: 0.9161053

00:49:58.935 --> 00:49:59.915 of these outliers,  
NOTE Confidence: 0.9883878

00:50:00.670 --> 00:50:01.950 the very group of people  
NOTE Confidence: 0.9883878

00:50:01.950 --> 00:50:03.150 that may have high risk  
NOTE Confidence: 0.9883878

00:50:03.150 --> 00:50:04.590 features. Again, it's a low  
NOTE Confidence: 0.9883878

00:50:04.590 --> 00:50:06.030 prevalence. It's a low group  
NOTE Confidence: 0.9883878

00:50:06.030 --> 00:50:07.550 of patients. So, again, we'll  
NOTE Confidence: 0.9883878

00:50:07.550 --> 00:50:08.590 all have to benefit the  
NOTE Confidence: 0.9883878

00:50:08.590 --> 00:50:09.570 cost and benefit  
NOTE Confidence: 0.9502234

00:50:09.950 --> 00:50:10.989 of that as well as  
NOTE Confidence: 0.9502234

00:50:10.989 --> 00:50:11.950 when we think about if

NOTE Confidence: 0.9502234  
00:50:11.950 --> 00:50:13.010 it's a low prevalence,  
NOTE Confidence: 0.98272854  
00:50:14.165 --> 00:50:15.364 you may have more false  
NOTE Confidence: 0.98272854  
00:50:15.364 --> 00:50:16.805 positives. Right? So a lot  
NOTE Confidence: 0.98272854  
00:50:16.805 --> 00:50:17.844 of this is focused on,  
NOTE Confidence: 0.98272854  
00:50:17.844 --> 00:50:18.724 you know, if it's a  
NOTE Confidence: 0.98272854  
00:50:18.724 --> 00:50:20.244 negative test, can you trust  
NOTE Confidence: 0.98272854  
00:50:20.244 --> 00:50:21.765 that? Right? So things that  
NOTE Confidence: 0.98272854  
00:50:21.765 --> 00:50:22.724 we all have to think  
NOTE Confidence: 0.98272854  
00:50:22.724 --> 00:50:23.605 about. And, again, a lot  
NOTE Confidence: 0.98272854  
00:50:23.605 --> 00:50:24.885 of this data, you could  
NOTE Confidence: 0.98272854  
00:50:24.885 --> 00:50:26.665 spend hours delving into.  
NOTE Confidence: 0.9324816  
00:50:27.540 --> 00:50:29.080 For head and neck populations  
NOTE Confidence: 0.9324816  
00:50:29.219 --> 00:50:30.820 where we worry about false  
NOTE Confidence: 0.9324816  
00:50:30.820 --> 00:50:32.660 negatives in sentinel nodes, that  
NOTE Confidence: 0.9324816  
00:50:32.660 --> 00:50:33.620 that rate is higher than  
NOTE Confidence: 0.9324816

00:50:33.620 --> 00:50:34.260 what we have on the  
NOTE Confidence: 0.9324816

00:50:34.260 --> 00:50:35.480 trunk and extremities,  
NOTE Confidence: 0.8799142

00:50:36.100 --> 00:50:38.340 again, recent study just published,  
NOTE Confidence: 0.8799142

00:50:38.340 --> 00:50:39.640 again, looking to validate,  
NOTE Confidence: 0.8503565

00:50:40.580 --> 00:50:41.080 the  
NOTE Confidence: 0.9393371

00:50:41.664 --> 00:50:42.244 the CPGP,  
NOTE Confidence: 0.9957701

00:50:43.265 --> 00:50:44.885 again, seems to be  
NOTE Confidence: 0.97598714

00:50:45.424 --> 00:50:46.944 none not different than what  
NOTE Confidence: 0.97598714

00:50:46.944 --> 00:50:48.565 we're seeing in the extremities,  
NOTE Confidence: 0.97598714

00:50:48.785 --> 00:50:49.924 which is really important.  
NOTE Confidence: 0.99746346

00:50:52.545 --> 00:50:53.045 So  
NOTE Confidence: 0.8791274

00:50:53.799 --> 00:50:54.839 when we're looking just for  
NOTE Confidence: 0.8791274

00:50:54.839 --> 00:50:56.619 sentinel node and decision making,  
NOTE Confidence: 0.9982626

00:50:56.920 --> 00:50:57.420 again,  
NOTE Confidence: 0.9693978

00:50:57.799 --> 00:50:58.680 if we kind of look  
NOTE Confidence: 0.9693978

00:50:58.680 --> 00:51:00.140 at things head to head,



NOTE Confidence: 0.9693978  
00:51:00.359 --> 00:51:02.119 there's some benefits but detriments,  
NOTE Confidence: 0.9693978  
00:51:02.119 --> 00:51:03.079 I think, of each of  
NOTE Confidence: 0.9693978  
00:51:03.079 --> 00:51:04.599 the assays. The thirty one  
NOTE Confidence: 0.9693978  
00:51:04.599 --> 00:51:05.799 GEP and I thirty one  
NOTE Confidence: 0.9693978  
00:51:05.799 --> 00:51:07.260 GEP, which has been around  
NOTE Confidence: 0.9693978  
00:51:07.400 --> 00:51:08.140 the longest,  
NOTE Confidence: 0.9940058  
00:51:09.145 --> 00:51:10.665 you know, is not great  
NOTE Confidence: 0.9940058  
00:51:10.665 --> 00:51:11.405 at discriminating  
NOTE Confidence: 0.9830752  
00:51:11.945 --> 00:51:13.645 amongst that t one a  
NOTE Confidence: 0.9830752  
00:51:13.864 --> 00:51:14.364 category,  
NOTE Confidence: 0.9994529  
00:51:15.465 --> 00:51:17.245 where it hasn't been validated.  
NOTE Confidence: 0.9734657  
00:51:18.825 --> 00:51:19.325 There's  
NOTE Confidence: 0.9583389  
00:51:19.785 --> 00:51:20.985 with both of them, we're  
NOTE Confidence: 0.9583389  
00:51:20.985 --> 00:51:22.790 gonna see that there's decreasing  
NOTE Confidence: 0.9583389  
00:51:23.010 --> 00:51:24.450 the number of central lymph  
NOTE Confidence: 0.9583389

00:51:24.450 --> 00:51:25.489 nodes in theory that we  
NOTE Confidence: 0.9583389  
00:51:25.489 --> 00:51:26.230 would perform.  
NOTE Confidence: 0.9532217  
00:51:27.090 --> 00:51:28.210 Almost all of this except  
NOTE Confidence: 0.9532217  
00:51:28.210 --> 00:51:29.030 for the DECIDE  
NOTE Confidence: 0.99854416  
00:51:29.410 --> 00:51:30.930 trial was also done only  
NOTE Confidence: 0.99854416  
00:51:30.930 --> 00:51:31.750 in retrospective  
NOTE Confidence: 0.9716429  
00:51:32.450 --> 00:51:34.150 series and really wasn't powerfully  
NOTE Confidence: 0.9716429  
00:51:34.210 --> 00:51:35.810 paired like the MERLIN trial  
NOTE Confidence: 0.9716429  
00:51:35.810 --> 00:51:37.110 was with that assay.  
NOTE Confidence: 0.9533678  
00:51:39.335 --> 00:51:40.775 And that really becomes the  
NOTE Confidence: 0.9533678  
00:51:40.775 --> 00:51:41.994 difference why that  
NOTE Confidence: 0.98668104  
00:51:42.614 --> 00:51:44.375 got the nod from the  
NOTE Confidence: 0.98668104  
00:51:44.375 --> 00:51:44.875 NCCN,  
NOTE Confidence: 0.9992358  
00:51:45.335 --> 00:51:47.015 just the number and the  
NOTE Confidence: 0.9992358  
00:51:47.015 --> 00:51:48.395 work that went into  
NOTE Confidence: 0.9960144  
00:51:48.855 --> 00:51:49.355 prospectively

NOTE Confidence: 0.8214377  
00:51:49.815 --> 00:51:50.714 following this,  
NOTE Confidence: 0.99961203  
00:51:51.734 --> 00:51:52.234 internationally  
NOTE Confidence: 0.98482203  
00:51:53.060 --> 00:51:53.800 for this.  
NOTE Confidence: 0.9955857  
00:51:54.180 --> 00:51:54.680 Again,  
NOTE Confidence: 0.9996631  
00:51:55.060 --> 00:51:55.800 some important  
NOTE Confidence: 0.9959878  
00:51:56.180 --> 00:51:56.840 take homes  
NOTE Confidence: 0.9437556  
00:51:57.300 --> 00:51:58.660 to always think about with  
NOTE Confidence: 0.9437556  
00:51:58.660 --> 00:51:59.160 these.  
NOTE Confidence: 0.99502635  
00:51:59.619 --> 00:52:01.140 There is industry funding and  
NOTE Confidence: 0.99502635  
00:52:01.140 --> 00:52:01.640 authorship  
NOTE Confidence: 0.93811464  
00:52:02.020 --> 00:52:03.219 bias. Even the best of  
NOTE Confidence: 0.93811464  
00:52:03.219 --> 00:52:04.500 us when we when these  
NOTE Confidence: 0.93811464  
00:52:04.500 --> 00:52:05.859 are funded, there's a lot  
NOTE Confidence: 0.93811464  
00:52:05.859 --> 00:52:07.300 of input from these,  
NOTE Confidence: 0.73558354  
00:52:08.835 --> 00:52:09.335 particularly  
NOTE Confidence: 0.9287799

00:52:09.635 --> 00:52:10.135 for  
NOTE Confidence: 0.9343736

00:52:10.435 --> 00:52:11.094 the g,  
NOTE Confidence: 0.91473883

00:52:11.475 --> 00:52:13.734 the, thirty one gene GP.  
NOTE Confidence: 0.98173743

00:52:14.755 --> 00:52:15.715 A lot of the data,  
NOTE Confidence: 0.98173743

00:52:15.715 --> 00:52:16.594 if you look at it,  
NOTE Confidence: 0.98173743

00:52:16.594 --> 00:52:18.195 they've been republishing some of  
NOTE Confidence: 0.98173743

00:52:18.195 --> 00:52:19.335 the similar datasets,  
NOTE Confidence: 0.9330791

00:52:19.875 --> 00:52:21.635 and that's a practice that  
NOTE Confidence: 0.9330791

00:52:21.635 --> 00:52:22.515 one has to be wary  
NOTE Confidence: 0.9330791

00:52:22.515 --> 00:52:23.715 about. So it can it  
NOTE Confidence: 0.9330791

00:52:23.715 --> 00:52:24.375 can almost  
NOTE Confidence: 0.93104756

00:52:25.340 --> 00:52:26.540 the value of that because  
NOTE Confidence: 0.93104756

00:52:26.540 --> 00:52:27.580 if you're publishing on the  
NOTE Confidence: 0.93104756

00:52:27.580 --> 00:52:29.420 same data and including some  
NOTE Confidence: 0.93104756

00:52:29.420 --> 00:52:30.460 and the other, it just  
NOTE Confidence: 0.93104756

00:52:30.460 --> 00:52:31.660 becomes really tricky when you're

NOTE Confidence: 0.93104756

00:52:31.660 --> 00:52:32.700 actually trying to go through

NOTE Confidence: 0.93104756

00:52:32.700 --> 00:52:33.360 the literature.

NOTE Confidence: 0.9424467

00:52:34.540 --> 00:52:36.780 Again, the primary objective technically

NOTE Confidence: 0.9424467

00:52:36.780 --> 00:52:37.980 wasn't met in the Merlin

NOTE Confidence: 0.9424467

00:52:37.980 --> 00:52:38.864 o o one,

NOTE Confidence: 0.9698401

00:52:39.585 --> 00:52:40.864 and and that was a

NOTE Confidence: 0.9698401

00:52:40.864 --> 00:52:42.385 higher than expected rate, and

NOTE Confidence: 0.9698401

00:52:42.385 --> 00:52:44.165 the the low risk not

NOTE Confidence: 0.9698401

00:52:44.225 --> 00:52:45.905 keeping that below that five

NOTE Confidence: 0.9698401

00:52:45.905 --> 00:52:47.905 percent threshold that we've tried

NOTE Confidence: 0.9698401

00:52:47.905 --> 00:52:49.505 to, you know, carve out

NOTE Confidence: 0.9698401

00:52:49.505 --> 00:52:50.725 as when we should consider

NOTE Confidence: 0.9698401

00:52:50.864 --> 00:52:52.145 doing it. So seven point

NOTE Confidence: 0.9698401

00:52:52.145 --> 00:52:53.529 one, is a little bit

NOTE Confidence: 0.9698401

00:52:53.529 --> 00:52:54.730 higher than what they what

NOTE Confidence: 0.9698401

00:52:54.730 --> 00:52:55.950 they thought would be.  
NOTE Confidence: 0.968741

00:52:58.089 --> 00:53:00.170 There's no survival benefit. It's  
NOTE Confidence: 0.968741

00:53:00.170 --> 00:53:01.529 not paired yet. Again, a  
NOTE Confidence: 0.968741

00:53:01.529 --> 00:53:02.250 little bit out of the  
NOTE Confidence: 0.968741

00:53:02.250 --> 00:53:03.849 scope of the conversation. Again,  
NOTE Confidence: 0.968741

00:53:03.849 --> 00:53:05.789 we talked about largely retrospective  
NOTE Confidence: 0.968741

00:53:06.010 --> 00:53:07.210 with the exception of the  
NOTE Confidence: 0.968741

00:53:07.210 --> 00:53:08.190 Merlin trial.  
NOTE Confidence: 0.9108334

00:53:08.945 --> 00:53:09.445 Again,  
NOTE Confidence: 0.9693574

00:53:09.905 --> 00:53:11.205 really needs to discriminate  
NOTE Confidence: 0.96432626

00:53:11.665 --> 00:53:12.705 the very groups that we  
NOTE Confidence: 0.96432626

00:53:12.705 --> 00:53:13.665 wanna use them. And if  
NOTE Confidence: 0.96432626

00:53:13.665 --> 00:53:14.864 someone wants to use a  
NOTE Confidence: 0.96432626

00:53:14.864 --> 00:53:16.545 study, the threshold has to  
NOTE Confidence: 0.96432626

00:53:16.545 --> 00:53:18.225 be really high and how  
NOTE Confidence: 0.96432626

00:53:18.225 --> 00:53:19.185 well this is gonna be

NOTE Confidence: 0.96432626  
00:53:19.185 --> 00:53:20.545 to justify the cost that  
NOTE Confidence: 0.96432626  
00:53:20.545 --> 00:53:21.445 it would potentially  
NOTE Confidence: 0.9935105  
00:53:21.745 --> 00:53:22.245 be.  
NOTE Confidence: 0.96808034  
00:53:22.785 --> 00:53:23.960 And I think that, you  
NOTE Confidence: 0.96808034  
00:53:23.960 --> 00:53:24.839 know, I alluded to it  
NOTE Confidence: 0.96808034  
00:53:24.839 --> 00:53:25.900 a little bit earlier,  
NOTE Confidence: 0.99100107  
00:53:26.359 --> 00:53:27.500 there's high pulse  
NOTE Confidence: 0.9903671  
00:53:28.039 --> 00:53:29.319 false positive rates. And the  
NOTE Confidence: 0.9903671  
00:53:29.319 --> 00:53:30.359 very first time that I  
NOTE Confidence: 0.9903671  
00:53:30.359 --> 00:53:31.400 ever saw a patient come  
NOTE Confidence: 0.9903671  
00:53:31.400 --> 00:53:32.219 into clinic  
NOTE Confidence: 0.97610676  
00:53:32.839 --> 00:53:33.799 was when I was a  
NOTE Confidence: 0.97610676  
00:53:33.799 --> 00:53:35.339 fellow in twenty fourteen,  
NOTE Confidence: 0.99958944  
00:53:35.799 --> 00:53:37.000 and a woman was three  
NOTE Confidence: 0.99958944  
00:53:37.000 --> 00:53:37.900 months postpartum  
NOTE Confidence: 0.98337996

00:53:38.495 --> 00:53:39.535 and had had a one  
NOTE Confidence: 0.98337996

00:53:39.535 --> 00:53:41.635 point eight millimeter non ulcerated  
NOTE Confidence: 0.9909225

00:53:42.094 --> 00:53:44.015 nodular melanoma with a negative  
NOTE Confidence: 0.9909225

00:53:44.015 --> 00:53:45.935 sentinel node and walked into  
NOTE Confidence: 0.9909225

00:53:45.935 --> 00:53:47.614 clinic with a class two  
NOTE Confidence: 0.9909225

00:53:47.614 --> 00:53:48.114 result  
NOTE Confidence: 0.9791305

00:53:48.575 --> 00:53:49.555 on her GEP.  
NOTE Confidence: 0.9887555

00:53:50.735 --> 00:53:51.235 And  
NOTE Confidence: 0.99978113

00:53:52.200 --> 00:53:52.859 we were  
NOTE Confidence: 0.9698353

00:53:53.160 --> 00:53:54.440 at a loss about what  
NOTE Confidence: 0.9698353

00:53:54.440 --> 00:53:55.339 do we do.  
NOTE Confidence: 0.96098846

00:53:55.960 --> 00:53:57.580 Again, I I thankfully graduated  
NOTE Confidence: 0.96098846

00:53:57.640 --> 00:53:58.880 from fellowship, but I I  
NOTE Confidence: 0.96098846

00:53:58.880 --> 00:54:00.040 I do think about and  
NOTE Confidence: 0.96098846

00:54:00.040 --> 00:54:00.700 I wonder  
NOTE Confidence: 0.9450658

00:54:01.160 --> 00:54:03.080 about this young woman who



NOTE Confidence: 0.9450658  
00:54:03.080 --> 00:54:04.359 was thirty eight years old  
NOTE Confidence: 0.9450658  
00:54:04.359 --> 00:54:05.239 who had come into the  
NOTE Confidence: 0.9450658  
00:54:05.239 --> 00:54:05.739 clinic.  
NOTE Confidence: 0.9988256  
00:54:06.200 --> 00:54:06.700 And  
NOTE Confidence: 0.999629  
00:54:07.305 --> 00:54:08.045 that psychological  
NOTE Confidence: 0.99767035  
00:54:08.825 --> 00:54:10.525 cost was something that has  
NOTE Confidence: 0.999818  
00:54:10.905 --> 00:54:11.805 stuck with me  
NOTE Confidence: 0.99973696  
00:54:12.265 --> 00:54:13.645 for the last  
NOTE Confidence: 0.9999285  
00:54:14.105 --> 00:54:14.605 decade  
NOTE Confidence: 0.95120096  
00:54:15.065 --> 00:54:16.364 about just seeing  
NOTE Confidence: 0.99753267  
00:54:16.744 --> 00:54:17.944 what the cost is to  
NOTE Confidence: 0.99753267  
00:54:17.944 --> 00:54:18.605 our patients  
NOTE Confidence: 0.9841633  
00:54:19.065 --> 00:54:20.025 if they have a false  
NOTE Confidence: 0.9841633  
00:54:20.025 --> 00:54:21.704 positive. It's nice, you know,  
NOTE Confidence: 0.9841633  
00:54:21.704 --> 00:54:23.360 to have a really good  
NOTE Confidence: 0.9841633

00:54:23.360 --> 00:54:25.040 negative predictive value and say,  
NOTE Confidence: 0.9841633

00:54:25.040 --> 00:54:26.239 okay. If it's negative, you're  
NOTE Confidence: 0.9841633

00:54:26.239 --> 00:54:26.739 good.  
NOTE Confidence: 0.9989581

00:54:27.600 --> 00:54:29.700 But when we're not really  
NOTE Confidence: 0.9565363

00:54:30.239 --> 00:54:32.020 capturing or we're causing undue  
NOTE Confidence: 0.9565363

00:54:32.160 --> 00:54:34.160 cost to patients, and like  
NOTE Confidence: 0.9565363

00:54:34.160 --> 00:54:35.200 I said, it's not just  
NOTE Confidence: 0.9565363

00:54:35.200 --> 00:54:35.700 about  
NOTE Confidence: 0.96691686

00:54:36.055 --> 00:54:37.335 screening and so forth, it's  
NOTE Confidence: 0.96691686

00:54:37.335 --> 00:54:38.215 also about what does it  
NOTE Confidence: 0.96691686

00:54:38.215 --> 00:54:39.675 do to them, again,  
NOTE Confidence: 0.9854804

00:54:40.135 --> 00:54:41.255 we need to be really,  
NOTE Confidence: 0.9854804

00:54:41.255 --> 00:54:43.015 really thoughtful about that. And  
NOTE Confidence: 0.9854804

00:54:43.015 --> 00:54:44.155 and, again, just  
NOTE Confidence: 0.98552114

00:54:44.455 --> 00:54:45.975 echoing all of my colleagues,  
NOTE Confidence: 0.98552114

00:54:45.975 --> 00:54:46.635 you know,

NOTE Confidence: 0.90484285  
00:54:46.935 --> 00:54:48.475 GEP, I think it really  
NOTE Confidence: 0.99795705  
00:54:48.840 --> 00:54:51.080 should inform shared decision making.  
NOTE Confidence: 0.99795705  
00:54:51.080 --> 00:54:52.220 It doesn't replace  
NOTE Confidence: 0.9993819  
00:54:52.600 --> 00:54:53.340 the conversations  
NOTE Confidence: 0.9918661  
00:54:53.640 --> 00:54:55.580 that we have and continued  
NOTE Confidence: 0.9918661  
00:54:55.720 --> 00:54:56.860 thoughtful interaction  
NOTE Confidence: 0.9917907  
00:54:57.640 --> 00:54:59.560 or replace the other tools  
NOTE Confidence: 0.9917907  
00:54:59.560 --> 00:55:00.460 that we have.  
NOTE Confidence: 0.99646044  
00:55:01.640 --> 00:55:02.920 So with that, I will  
NOTE Confidence: 0.99646044  
00:55:02.920 --> 00:55:03.820 I will close.  
NOTE Confidence: 0.9281211  
00:55:06.494 --> 00:55:07.635 Stop my share.  
NOTE Confidence: 0.94955707  
00:55:14.895 --> 00:55:15.714 Sorry, guys.  
NOTE Confidence: 0.9897847  
00:55:16.015 --> 00:55:17.855 Can't stop sharing. Oh, there  
NOTE Confidence: 0.9897847  
00:55:17.855 --> 00:55:18.435 it is.  
NOTE Confidence: 0.99712354  
00:55:19.239 --> 00:55:21.340 Thanks, Kelly. That was great.  
NOTE Confidence: 0.9973436

00:55:22.760 --> 00:55:24.680 So I am up next.  
NOTE Confidence: 0.9973436

00:55:24.680 --> 00:55:25.480 Let me see if I  
NOTE Confidence: 0.9973436

00:55:25.480 --> 00:55:26.860 can figure out the  
NOTE Confidence: 0.99963707

00:55:27.480 --> 00:55:29.180 sharing process here.  
NOTE Confidence: 0.99976563

00:55:32.154 --> 00:55:33.055 Okay. Great.  
NOTE Confidence: 0.9493399

00:55:33.914 --> 00:55:35.594 So I'm Sean Christiansen. I'm  
NOTE Confidence: 0.9493399

00:55:35.594 --> 00:55:36.255 a dermatologist  
NOTE Confidence: 0.98132855

00:55:36.635 --> 00:55:38.234 and Mohs surgeon, and I'm  
NOTE Confidence: 0.98132855

00:55:38.234 --> 00:55:39.994 gonna shift gears slightly. And  
NOTE Confidence: 0.98132855

00:55:39.994 --> 00:55:41.614 instead of giving an overview  
NOTE Confidence: 0.98132855

00:55:41.914 --> 00:55:43.674 of GEPs, I'm gonna focus  
NOTE Confidence: 0.98132855

00:55:43.674 --> 00:55:44.894 on one  
NOTE Confidence: 0.9997823

00:55:45.270 --> 00:55:46.489 specific utilization  
NOTE Confidence: 0.9980023

00:55:46.870 --> 00:55:47.690 of GEP,  
NOTE Confidence: 0.9319632

00:55:48.150 --> 00:55:49.350 in a clinical trial, which  
NOTE Confidence: 0.9319632

00:55:49.350 --> 00:55:50.469 is the ICEFAN trial, which

NOTE Confidence: 0.9319632  
00:55:50.469 --> 00:55:51.690 I'll get to talk about,  
NOTE Confidence: 0.95764875  
00:55:52.070 --> 00:55:53.290 in just a couple minutes.  
NOTE Confidence: 0.98894846  
00:55:53.830 --> 00:55:55.050 So these are my disclosures,  
NOTE Confidence: 0.98894846  
00:55:55.110 --> 00:55:56.310 and they're not relevant to  
NOTE Confidence: 0.98894846  
00:55:56.310 --> 00:55:57.510 what I'm talking about today  
NOTE Confidence: 0.98894846  
00:55:57.510 --> 00:55:58.965 except for the last one.  
NOTE Confidence: 0.996517  
00:55:59.445 --> 00:56:00.405 I I will be an  
NOTE Confidence: 0.996517  
00:56:00.405 --> 00:56:00.905 investigator,  
NOTE Confidence: 0.97224075  
00:56:02.005 --> 00:56:03.364 on the the trial, which  
NOTE Confidence: 0.97224075  
00:56:03.364 --> 00:56:04.905 is sponsored by Skyline  
NOTE Confidence: 0.99119955  
00:56:05.205 --> 00:56:05.705 Diagnostics,  
NOTE Confidence: 0.9880788  
00:56:06.245 --> 00:56:07.364 the company that makes the  
NOTE Confidence: 0.9880788  
00:56:07.364 --> 00:56:07.864 Merlin  
NOTE Confidence: 0.998566  
00:56:08.245 --> 00:56:08.745 GEP.  
NOTE Confidence: 0.99648863  
00:56:10.245 --> 00:56:11.364 So I'll talk first about  
NOTE Confidence: 0.99648863

00:56:11.364 --> 00:56:13.045 principles of surgical management of

NOTE Confidence: 0.99648863

00:56:13.045 --> 00:56:14.105 localized melanoma.

NOTE Confidence: 0.9795777

00:56:14.645 --> 00:56:15.880 I'm gonna take a slight

NOTE Confidence: 0.9795777

00:56:15.880 --> 00:56:17.820 tangent to focus on pathologic

NOTE Confidence: 0.9795777

00:56:17.960 --> 00:56:19.480 margin analysis and why that's

NOTE Confidence: 0.9795777

00:56:19.480 --> 00:56:19.980 important.

NOTE Confidence: 0.9989745

00:56:20.600 --> 00:56:21.719 And then we'll talk about

NOTE Confidence: 0.9989745

00:56:21.719 --> 00:56:23.180 how we can use GEP

NOTE Confidence: 0.9899709

00:56:23.640 --> 00:56:25.180 for predicting nodal metastasis

NOTE Confidence: 0.96002704

00:56:25.480 --> 00:56:26.920 risk and how that influences

NOTE Confidence: 0.96002704

00:56:26.920 --> 00:56:28.540 our decision making and treatment.

NOTE Confidence: 0.9977858

00:56:29.195 --> 00:56:30.075 And then I'll tell you

NOTE Confidence: 0.9977858

00:56:30.075 --> 00:56:31.295 about the the trial,

NOTE Confidence: 0.9631939

00:56:31.675 --> 00:56:32.955 that we're starting up at

NOTE Confidence: 0.9631939

00:56:32.955 --> 00:56:34.975 Yale, hopefully, sometime soon.

NOTE Confidence: 0.9948324

00:56:36.075 --> 00:56:38.155 So surgical management is really

NOTE Confidence: 0.9948324  
00:56:38.155 --> 00:56:39.755 the primary treatment for localized  
NOTE Confidence: 0.9948324  
00:56:39.755 --> 00:56:41.055 and early stage melanoma.  
NOTE Confidence: 0.97654563  
00:56:41.594 --> 00:56:42.875 And just to review, the  
NOTE Confidence: 0.97654563  
00:56:42.875 --> 00:56:44.610 goals of surgical excision are  
NOTE Confidence: 0.97654563  
00:56:44.610 --> 00:56:46.290 are to accurately stage the  
NOTE Confidence: 0.97654563  
00:56:46.290 --> 00:56:47.890 tumor, which is just as  
NOTE Confidence: 0.97654563  
00:56:47.890 --> 00:56:49.090 important now as it ever  
NOTE Confidence: 0.97654563  
00:56:49.090 --> 00:56:50.790 was, especially in the era  
NOTE Confidence: 0.97654563  
00:56:50.850 --> 00:56:52.630 of targeted therapy and immunotherapy.  
NOTE Confidence: 0.98236716  
00:56:52.930 --> 00:56:53.890 We we really need to  
NOTE Confidence: 0.98236716  
00:56:53.890 --> 00:56:55.250 know what the risk factors  
NOTE Confidence: 0.98236716  
00:56:55.250 --> 00:56:56.470 are to make those decisions.  
NOTE Confidence: 0.9973288  
00:56:57.330 --> 00:56:58.850 We also wanna optimize local  
NOTE Confidence: 0.9973288  
00:56:58.850 --> 00:57:00.725 control by achieving complete tumor  
NOTE Confidence: 0.9973288  
00:57:00.725 --> 00:57:01.225 removal  
NOTE Confidence: 0.98988634

00:57:01.525 --> 00:57:03.385 while balancing that with optimizing  
NOTE Confidence: 0.98988634

00:57:03.605 --> 00:57:05.445 functional and cosmetic outcomes from  
NOTE Confidence: 0.98988634

00:57:05.445 --> 00:57:05.945 surgery.  
NOTE Confidence: 0.99219

00:57:06.325 --> 00:57:08.005 And about fifty years ago,  
NOTE Confidence: 0.99219

00:57:08.005 --> 00:57:09.125 the trend was to really  
NOTE Confidence: 0.99219

00:57:09.125 --> 00:57:10.085 just take as wide of  
NOTE Confidence: 0.99219

00:57:10.085 --> 00:57:11.305 a margin as possible.  
NOTE Confidence: 0.97227764

00:57:12.020 --> 00:57:13.140 But since then, we've had  
NOTE Confidence: 0.97227764

00:57:13.140 --> 00:57:14.420 some trials that have shown  
NOTE Confidence: 0.97227764

00:57:14.420 --> 00:57:16.099 that wider surgical margins are  
NOTE Confidence: 0.97227764

00:57:16.099 --> 00:57:17.400 not necessarily better.  
NOTE Confidence: 0.97202057

00:57:18.020 --> 00:57:19.619 So a large trial sponsored  
NOTE Confidence: 0.97202057

00:57:19.619 --> 00:57:20.520 by the WHO,  
NOTE Confidence: 0.9798589

00:57:21.619 --> 00:57:23.745 showed that one centimeter versus  
NOTE Confidence: 0.9798589

00:57:23.825 --> 00:57:25.745 three centimeter excision margins for  
NOTE Confidence: 0.9798589

00:57:25.745 --> 00:57:27.425 melanoma less than two millimeters



NOTE Confidence: 0.9798589

00:57:27.425 --> 00:57:27.925 in-depth,

NOTE Confidence: 0.99896234

00:57:28.545 --> 00:57:29.745 there was no difference in

NOTE Confidence: 0.99896234

00:57:29.745 --> 00:57:30.805 disease free survival.

NOTE Confidence: 0.90177983

00:57:31.425 --> 00:57:32.465 And then later on in

NOTE Confidence: 0.90177983

00:57:32.465 --> 00:57:33.365 another trial,

NOTE Confidence: 0.9312069

00:57:34.065 --> 00:57:35.825 a deeper melanoma greater than

NOTE Confidence: 0.9312069

00:57:35.825 --> 00:57:37.350 two millimeters in-depth showed that

NOTE Confidence: 0.9312069

00:57:37.430 --> 00:57:38.250 two centimeters

NOTE Confidence: 0.97511977

00:57:38.630 --> 00:57:40.070 was not inferior to four

NOTE Confidence: 0.97511977

00:57:40.070 --> 00:57:41.530 centimeters. So there's a trend

NOTE Confidence: 0.97511977

00:57:41.670 --> 00:57:43.270 for us taking narrower margins,

NOTE Confidence: 0.97511977

00:57:43.270 --> 00:57:44.790 which can still be curative

NOTE Confidence: 0.97511977

00:57:44.790 --> 00:57:45.530 for melanoma.

NOTE Confidence: 0.93923974

00:57:46.070 --> 00:57:47.350 And the question is how

NOTE Confidence: 0.93923974

00:57:47.350 --> 00:57:48.650 narrow can we go?

NOTE Confidence: 0.9997492

00:57:49.270 --> 00:57:50.870 Before we answer that question,  
NOTE Confidence: 0.9997492

00:57:50.870 --> 00:57:52.010 we have to recognize  
NOTE Confidence: 0.96992046

00:57:52.315 --> 00:57:53.995 that skin cancer often does  
NOTE Confidence: 0.96992046

00:57:53.995 --> 00:57:55.855 has have irregular extension.  
NOTE Confidence: 0.96109235

00:57:56.395 --> 00:57:57.275 So this is something that  
NOTE Confidence: 0.96109235

00:57:57.275 --> 00:57:58.715 came out of a, a  
NOTE Confidence: 0.96109235

00:57:58.715 --> 00:58:00.155 publication in Annals of Plastic  
NOTE Confidence: 0.96109235

00:58:00.155 --> 00:58:01.915 Surgery many years ago. They  
NOTE Confidence: 0.96109235

00:58:01.915 --> 00:58:04.095 actually mapped out the three-dimensional  
NOTE Confidence: 0.9710892

00:58:04.555 --> 00:58:05.835 extension of the skin cancer,  
NOTE Confidence: 0.9710892

00:58:05.835 --> 00:58:06.555 and you can see how  
NOTE Confidence: 0.9710892

00:58:06.555 --> 00:58:07.530 it has many of these  
NOTE Confidence: 0.9710892

00:58:07.770 --> 00:58:08.270 irregular  
NOTE Confidence: 0.9902586

00:58:08.890 --> 00:58:10.010 strands that penetrate through the  
NOTE Confidence: 0.9902586

00:58:10.010 --> 00:58:11.230 subcutaneous tissue.  
NOTE Confidence: 0.99375933

00:58:11.530 --> 00:58:13.370 And these irregular and occult

NOTE Confidence: 0.99375933  
00:58:13.370 --> 00:58:15.130 islands of tumor may not  
NOTE Confidence: 0.99375933  
00:58:15.130 --> 00:58:17.150 be detected with standard histologic  
NOTE Confidence: 0.99375933  
00:58:17.370 --> 00:58:17.870 sections.  
NOTE Confidence: 0.9994108  
00:58:18.730 --> 00:58:19.770 So this is why the  
NOTE Confidence: 0.9994108  
00:58:19.770 --> 00:58:21.130 way that we process things  
NOTE Confidence: 0.9994108  
00:58:21.130 --> 00:58:22.270 is actually really important.  
NOTE Confidence: 0.86139446  
00:58:22.765 --> 00:58:23.744 So with standard,  
NOTE Confidence: 0.95068324  
00:58:24.205 --> 00:58:26.145 perpendicular or bread loaf sections,  
NOTE Confidence: 0.99443895  
00:58:26.605 --> 00:58:28.705 an elliptical specimen like this  
NOTE Confidence: 0.99443895  
00:58:28.845 --> 00:58:30.305 is cut into these perpendicular  
NOTE Confidence: 0.99443895  
00:58:30.525 --> 00:58:32.045 slices. Right? So we're only  
NOTE Confidence: 0.99443895  
00:58:32.045 --> 00:58:33.165 looking at the areas where  
NOTE Confidence: 0.99443895  
00:58:33.165 --> 00:58:34.380 we happen to take slices.  
NOTE Confidence: 0.99113876  
00:58:34.779 --> 00:58:36.059 And if there is one  
NOTE Confidence: 0.99113876  
00:58:36.059 --> 00:58:37.180 focal area that has a  
NOTE Confidence: 0.99113876

00:58:37.180 --> 00:58:38.799 positive margin with an irregular  
NOTE Confidence: 0.99113876

00:58:38.859 --> 00:58:39.359 extension,  
NOTE Confidence: 0.9982718

00:58:39.740 --> 00:58:41.180 that might not be captured  
NOTE Confidence: 0.9982718

00:58:41.180 --> 00:58:42.720 on these representative sections.  
NOTE Confidence: 0.96924734

00:58:43.259 --> 00:58:44.779 In contrast, if we use  
NOTE Confidence: 0.96924734

00:58:44.779 --> 00:58:46.380 en face sections with complete  
NOTE Confidence: 0.96924734

00:58:46.380 --> 00:58:47.900 margin analysis, we're looking at  
NOTE Confidence: 0.96924734

00:58:47.900 --> 00:58:49.660 the entire peripheral and deep  
NOTE Confidence: 0.96924734

00:58:49.660 --> 00:58:50.160 margin.  
NOTE Confidence: 0.9997665

00:58:50.475 --> 00:58:51.855 So any small area  
NOTE Confidence: 0.9764842

00:58:52.235 --> 00:58:53.935 of positivity at the margin  
NOTE Confidence: 0.9764842

00:58:54.075 --> 00:58:55.615 would, in fact, be detected.  
NOTE Confidence: 0.9708754

00:58:56.235 --> 00:58:57.215 And this is the principle  
NOTE Confidence: 0.9708754

00:58:57.275 --> 00:58:59.375 behind Mohs skin cancer surgery.  
NOTE Confidence: 0.97053987

00:58:59.675 --> 00:59:00.875 Just to review this very,  
NOTE Confidence: 0.97053987

00:59:00.875 --> 00:59:02.315 very briefly, this is a

NOTE Confidence: 0.97053987  
00:59:02.315 --> 00:59:04.075 staged excision of skin cancer  
NOTE Confidence: 0.97053987  
00:59:04.075 --> 00:59:04.895 with intraoperative  
NOTE Confidence: 0.99917346  
00:59:05.195 --> 00:59:06.095 frozen sections  
NOTE Confidence: 0.9973686  
00:59:06.600 --> 00:59:08.600 examining the complete surgical margin,  
NOTE Confidence: 0.9973686  
00:59:08.760 --> 00:59:09.560 which are read by the  
NOTE Confidence: 0.9973686  
00:59:09.560 --> 00:59:10.700 surgeon as pathologist.  
NOTE Confidence: 0.9879041  
00:59:11.720 --> 00:59:13.160 And it's mostly used for  
NOTE Confidence: 0.9879041  
00:59:13.160 --> 00:59:14.860 basal and squamous cell carcinoma.  
NOTE Confidence: 0.97265947  
00:59:15.160 --> 00:59:16.440 It has not traditionally been  
NOTE Confidence: 0.97265947  
00:59:16.440 --> 00:59:17.340 used for melanoma  
NOTE Confidence: 0.98951995  
00:59:17.800 --> 00:59:19.320 because it has traditionally been  
NOTE Confidence: 0.98951995  
00:59:19.320 --> 00:59:20.060 more difficult  
NOTE Confidence: 0.99481946  
00:59:20.440 --> 00:59:22.665 to identify melanoma on frozen  
NOTE Confidence: 0.99481946  
00:59:22.665 --> 00:59:23.165 sections.  
NOTE Confidence: 0.97306347  
00:59:23.945 --> 00:59:25.545 But recently, that has slightly  
NOTE Confidence: 0.97306347

00:59:25.545 --> 00:59:26.045 changed.  
NOTE Confidence: 0.8772692

00:59:27.145 --> 00:59:28.265 So now we can actually  
NOTE Confidence: 0.8772692

00:59:28.265 --> 00:59:29.385 use Mart one or melan  
NOTE Confidence: 0.8772692

00:59:29.385 --> 00:59:30.125 a immunostains  
NOTE Confidence: 0.9996472

00:59:30.665 --> 00:59:32.265 on frozen sections to identify  
NOTE Confidence: 0.9996472

00:59:32.265 --> 00:59:32.765 melanocytes.  
NOTE Confidence: 0.97497195

00:59:33.300 --> 00:59:35.220 So, these two images here  
NOTE Confidence: 0.97497195

00:59:35.220 --> 00:59:36.820 are frozen sections of skin.  
NOTE Confidence: 0.97497195

00:59:36.820 --> 00:59:37.780 One of them is a  
NOTE Confidence: 0.97497195

00:59:37.780 --> 00:59:39.380 floor example of melanoma in  
NOTE Confidence: 0.97497195

00:59:39.380 --> 00:59:40.820 situ. The other one is  
NOTE Confidence: 0.97497195

00:59:40.820 --> 00:59:42.100 normal skin with some freeze  
NOTE Confidence: 0.97497195

00:59:42.100 --> 00:59:42.600 artifact.  
NOTE Confidence: 0.9892769

00:59:42.900 --> 00:59:44.420 Any pathologist in the audience  
NOTE Confidence: 0.9892769

00:59:44.420 --> 00:59:45.940 will immediately recognize that it's  
NOTE Confidence: 0.9892769

00:59:45.940 --> 00:59:46.740 the one on the left

NOTE Confidence: 0.9892769

00:59:46.740 --> 00:59:47.480 that's melanoma.

NOTE Confidence: 0.9910456

00:59:48.085 --> 00:59:48.805 But for the rest of

NOTE Confidence: 0.9910456

00:59:48.805 --> 00:59:49.765 us, it really helps to

NOTE Confidence: 0.9910456

00:59:49.765 --> 00:59:50.665 have the immunostain.

NOTE Confidence: 0.9798034

00:59:51.205 --> 00:59:52.505 So by using this immunostain,

NOTE Confidence: 0.9798034

00:59:52.645 --> 00:59:53.925 we can clearly see there's

NOTE Confidence: 0.9798034

00:59:53.925 --> 00:59:56.005 confluence, there's nesting, there's upward

NOTE Confidence: 0.9798034

00:59:56.005 --> 00:59:57.445 scatter of melanocytes in the

NOTE Confidence: 0.9798034

00:59:57.445 --> 00:59:59.125 melanoma in situ. But in

NOTE Confidence: 0.9798034

00:59:59.125 --> 01:00:00.245 normal skin, we just see

NOTE Confidence: 0.9798034

01:00:00.245 --> 01:00:01.145 a normal distribution.

NOTE Confidence: 0.9627502

01:00:02.600 --> 01:00:03.800 And a dual center study

NOTE Confidence: 0.9627502

01:00:03.800 --> 01:00:04.920 found that there's very high

NOTE Confidence: 0.9627502

01:00:04.920 --> 01:00:06.600 concordance between most sections and

NOTE Confidence: 0.9627502

01:00:06.600 --> 01:00:08.940 permanent pathology when using immunostains

NOTE Confidence: 0.9627502

01:00:09.160 --> 01:00:09.800 to detect,  
NOTE Confidence: 0.9999092  
01:00:10.200 --> 01:00:10.700 melanoma.  
NOTE Confidence: 0.9869756  
01:00:11.240 --> 01:00:12.680 So, at Yale, we've actually  
NOTE Confidence: 0.9869756  
01:00:12.680 --> 01:00:13.480 been doing this for a  
NOTE Confidence: 0.9869756  
01:00:13.480 --> 01:00:15.340 few years now. Mostly melanoma  
NOTE Confidence: 0.9869756  
01:00:15.400 --> 01:00:16.440 in situ, but a few  
NOTE Confidence: 0.9869756  
01:00:16.440 --> 01:00:18.365 superficially invasive melanoma cases.  
NOTE Confidence: 0.9702179  
01:00:18.745 --> 01:00:19.625 So this is a woman  
NOTE Confidence: 0.9702179  
01:00:19.625 --> 01:00:20.825 with a melanoma in situ  
NOTE Confidence: 0.9702179  
01:00:20.825 --> 01:00:22.585 in a very cosmetically sensitive  
NOTE Confidence: 0.9702179  
01:00:22.585 --> 01:00:23.865 location on the nose. And  
NOTE Confidence: 0.9702179  
01:00:23.865 --> 01:00:24.745 so we wanna try and  
NOTE Confidence: 0.9702179  
01:00:24.745 --> 01:00:25.625 take as narrow of a  
NOTE Confidence: 0.9702179  
01:00:25.625 --> 01:00:27.225 margin as possible. So I  
NOTE Confidence: 0.9702179  
01:00:27.225 --> 01:00:28.345 ended up taking a  
NOTE Confidence: 0.9702179  
01:00:28.345 --> 01:00:29.945 four millimeter margin around this



NOTE Confidence: 0.9702179  
01:00:29.945 --> 01:00:30.445 initially.  
NOTE Confidence: 0.9563027  
01:00:31.210 --> 01:00:32.490 And the area in red  
NOTE Confidence: 0.9563027  
01:00:32.490 --> 01:00:33.530 is where I processed a  
NOTE Confidence: 0.9563027  
01:00:33.530 --> 01:00:34.890 deep bulk specimen just to  
NOTE Confidence: 0.9563027  
01:00:34.890 --> 01:00:35.530 look at that and make  
NOTE Confidence: 0.9563027  
01:00:35.530 --> 01:00:36.890 sure there was no invasive  
NOTE Confidence: 0.9563027  
01:00:36.890 --> 01:00:37.390 tumor.  
NOTE Confidence: 0.9694353  
01:00:37.770 --> 01:00:38.810 There was, in fact, just  
NOTE Confidence: 0.9694353  
01:00:38.810 --> 01:00:40.250 melanoma in situ that was  
NOTE Confidence: 0.9694353  
01:00:40.250 --> 01:00:40.750 present.  
NOTE Confidence: 0.9953115  
01:00:41.130 --> 01:00:42.590 But on that first layer,  
NOTE Confidence: 0.9953115  
01:00:42.810 --> 01:00:44.250 there was a positive margin  
NOTE Confidence: 0.9953115  
01:00:44.250 --> 01:00:46.010 at the superior edge only.  
NOTE Confidence: 0.9953115  
01:00:46.010 --> 01:00:47.065 So I then was able  
NOTE Confidence: 0.9953115  
01:00:47.065 --> 01:00:48.425 to take an additional stage  
NOTE Confidence: 0.9953115

01:00:48.425 --> 01:00:49.165 from there,  
NOTE Confidence: 0.9670646

01:00:49.545 --> 01:00:50.685 which was clear.  
NOTE Confidence: 0.9927241

01:00:51.225 --> 01:00:52.185 And this was the patient's  
NOTE Confidence: 0.9927241

01:00:52.185 --> 01:00:53.785 defect in the end. So  
NOTE Confidence: 0.9927241

01:00:53.785 --> 01:00:55.705 in the area inferiorly towards  
NOTE Confidence: 0.9927241

01:00:55.705 --> 01:00:56.665 the alar rim, I was  
NOTE Confidence: 0.9927241

01:00:56.665 --> 01:00:57.785 actually able to take a  
NOTE Confidence: 0.9927241

01:00:57.785 --> 01:00:59.079 narrower margin than what is  
NOTE Confidence: 0.9927241

01:00:59.079 --> 01:01:00.380 recommended by the NCCN.  
NOTE Confidence: 0.98402995

01:01:00.920 --> 01:01:01.800 And yet in the area  
NOTE Confidence: 0.98402995

01:01:01.800 --> 01:01:03.400 where the melanoma was extending  
NOTE Confidence: 0.98402995

01:01:03.400 --> 01:01:05.000 farther superiorly, I was able  
NOTE Confidence: 0.98402995

01:01:05.000 --> 01:01:06.359 to take a wider margin  
NOTE Confidence: 0.98402995

01:01:06.359 --> 01:01:07.880 and capture the melanoma to  
NOTE Confidence: 0.98402995

01:01:07.880 --> 01:01:08.940 achieve clear margins.  
NOTE Confidence: 0.94495666

01:01:09.960 --> 01:01:10.920 And then we can actually

NOTE Confidence: 0.94495666  
01:01:10.920 --> 01:01:12.494 do a local flap repair  
NOTE Confidence: 0.94495666  
01:01:12.494 --> 01:01:13.615 and and spare her a  
NOTE Confidence: 0.94495666  
01:01:13.615 --> 01:01:15.295 staged interpolation flap from the  
NOTE Confidence: 0.94495666  
01:01:15.295 --> 01:01:15.795 forehead.  
NOTE Confidence: 0.9660581  
01:01:16.255 --> 01:01:17.694 So so far, we've done  
NOTE Confidence: 0.9660581  
01:01:17.694 --> 01:01:19.055 a hundred and eighty cases,  
NOTE Confidence: 0.9660581  
01:01:19.295 --> 01:01:20.654 of melanoma with Mohs here  
NOTE Confidence: 0.9660581  
01:01:20.654 --> 01:01:21.775 at Yale, and this number  
NOTE Confidence: 0.9660581  
01:01:21.775 --> 01:01:22.994 continues to grow.  
NOTE Confidence: 0.998121  
01:01:24.015 --> 01:01:24.515 Okay.  
NOTE Confidence: 0.9502154  
01:01:25.150 --> 01:01:26.350 The data supports the use  
NOTE Confidence: 0.9502154  
01:01:26.350 --> 01:01:27.550 of Mohs surgery both for  
NOTE Confidence: 0.9502154  
01:01:27.550 --> 01:01:29.310 melanoma in situ and for  
NOTE Confidence: 0.9502154  
01:01:29.310 --> 01:01:30.290 invasive melanoma.  
NOTE Confidence: 0.96467066  
01:01:30.750 --> 01:01:31.870 So far, our data is  
NOTE Confidence: 0.96467066

01:01:31.870 --> 01:01:33.390 only retrospective, so we don't  
NOTE Confidence: 0.96467066

01:01:33.390 --> 01:01:34.750 have prospective data. But the  
NOTE Confidence: 0.96467066

01:01:34.750 --> 01:01:36.430 retrospective data shows that there  
NOTE Confidence: 0.96467066

01:01:36.430 --> 01:01:38.155 is a a clear benefit  
NOTE Confidence: 0.96467066

01:01:38.155 --> 01:01:39.515 in terms of local recurrence  
NOTE Confidence: 0.96467066

01:01:39.515 --> 01:01:40.494 with Mohs surgery,  
NOTE Confidence: 0.997106

01:01:41.115 --> 01:01:42.494 being less than one percent  
NOTE Confidence: 0.997106

01:01:42.635 --> 01:01:44.015 compared to standard excision,  
NOTE Confidence: 0.99683917

01:01:44.315 --> 01:01:45.535 which is about eight percent.  
NOTE Confidence: 0.9548942

01:01:45.994 --> 01:01:47.275 And if we do staged  
NOTE Confidence: 0.9548942

01:01:47.275 --> 01:01:49.194 excision, not via Mohs with  
NOTE Confidence: 0.9548942

01:01:49.194 --> 01:01:51.035 permanent suction processing, but with  
NOTE Confidence: 0.9548942

01:01:51.035 --> 01:01:52.414 complete margin analysis,  
NOTE Confidence: 0.9851867

01:01:52.750 --> 01:01:54.450 we can achieve a comparable  
NOTE Confidence: 0.9851867

01:01:54.750 --> 01:01:56.190 low rate of local recurrence.  
NOTE Confidence: 0.9851867

01:01:56.190 --> 01:01:57.790 So, again, it's not magic

NOTE Confidence: 0.9851867  
01:01:57.790 --> 01:01:58.690 of Mohs surgery.  
NOTE Confidence: 0.99731755  
01:01:59.070 --> 01:02:00.030 It's the way that we  
NOTE Confidence: 0.99731755  
01:02:00.030 --> 01:02:01.890 examine the pathologic margin.  
NOTE Confidence: 0.9693402  
01:02:02.350 --> 01:02:03.410 And so we hypothesize  
NOTE Confidence: 0.99664694  
01:02:03.790 --> 01:02:05.550 that excision with complete margin  
NOTE Confidence: 0.99664694  
01:02:05.550 --> 01:02:07.550 analysis may allow for both  
NOTE Confidence: 0.99664694  
01:02:07.550 --> 01:02:08.210 more accurate  
NOTE Confidence: 0.95988506  
01:02:08.565 --> 01:02:10.265 and more complete tumor removal  
NOTE Confidence: 0.95988506  
01:02:10.484 --> 01:02:12.484 with narrower surgical margins and  
NOTE Confidence: 0.95988506  
01:02:12.484 --> 01:02:14.345 thereby decreased surgical morbidity.  
NOTE Confidence: 0.97548366  
01:02:16.005 --> 01:02:17.204 Okay. So we're gonna go  
NOTE Confidence: 0.97548366  
01:02:17.204 --> 01:02:18.565 back to our general principle  
NOTE Confidence: 0.97548366  
01:02:18.565 --> 01:02:20.565 here, of accurately staging a  
NOTE Confidence: 0.97548366  
01:02:20.565 --> 01:02:21.444 tumor, and this is why  
NOTE Confidence: 0.97548366  
01:02:21.444 --> 01:02:22.964 sentinel lymph node biopsy is  
NOTE Confidence: 0.97548366

01:02:22.964 --> 01:02:23.625 so critical.  
NOTE Confidence: 0.99117464

01:02:24.119 --> 01:02:25.500 It gives us that information  
NOTE Confidence: 0.99117464

01:02:25.799 --> 01:02:26.539 on micronodal  
NOTE Confidence: 0.91058725

01:02:27.079 --> 01:02:27.579 metastases,  
NOTE Confidence: 0.9994429

01:02:27.960 --> 01:02:29.880 which will influence adjuvant treatment  
NOTE Confidence: 0.9994429

01:02:29.880 --> 01:02:30.380 decisions.  
NOTE Confidence: 0.9996816

01:02:31.079 --> 01:02:31.579 However,  
NOTE Confidence: 0.91676074

01:02:32.119 --> 01:02:34.140 GEPs now offer potentially  
NOTE Confidence: 0.99204767

01:02:34.519 --> 01:02:36.200 another way to access the  
NOTE Confidence: 0.99204767

01:02:36.200 --> 01:02:37.019 same question.  
NOTE Confidence: 0.9742643

01:02:37.935 --> 01:02:39.635 So this is the CPGEP,  
NOTE Confidence: 0.9650429

01:02:40.095 --> 01:02:42.015 the clinical pathologic gene expression  
NOTE Confidence: 0.9650429

01:02:42.015 --> 01:02:42.515 profiling  
NOTE Confidence: 0.8226156

01:02:42.975 --> 01:02:43.775 Merlin test.  
NOTE Confidence: 0.87705153

01:02:44.415 --> 01:02:46.115 This is a large prospective  
NOTE Confidence: 0.9093314

01:02:46.575 --> 01:02:47.075 multicenter

NOTE Confidence: 0.9401287  
01:02:47.375 --> 01:02:48.435 blinded evaluation,  
NOTE Confidence: 0.94618076  
01:02:48.895 --> 01:02:50.675 that doctor Alino already presented.  
NOTE Confidence: 0.94618076  
01:02:50.895 --> 01:02:52.175 Just wanna highlight a couple  
NOTE Confidence: 0.94618076  
01:02:52.175 --> 01:02:53.155 features here.  
NOTE Confidence: 0.9914078  
01:02:53.680 --> 01:02:55.040 When I say blinded, it  
NOTE Confidence: 0.9914078  
01:02:55.040 --> 01:02:56.480 means that the surgeons doing  
NOTE Confidence: 0.9914078  
01:02:56.480 --> 01:02:58.100 the sentinel lymph node procedure  
NOTE Confidence: 0.9914078  
01:02:58.320 --> 01:02:59.700 did not know the patient's  
NOTE Confidence: 0.9914078  
01:02:59.840 --> 01:03:01.520 GEP results, so they were  
NOTE Confidence: 0.9914078  
01:03:01.520 --> 01:03:02.580 blinded to that.  
NOTE Confidence: 0.96409935  
01:03:03.680 --> 01:03:04.800 And, also, just to highlight  
NOTE Confidence: 0.96409935  
01:03:04.800 --> 01:03:06.720 that this GEP includes both  
NOTE Confidence: 0.96409935  
01:03:06.720 --> 01:03:08.240 the gene expression as well  
NOTE Confidence: 0.96409935  
01:03:08.240 --> 01:03:09.315 as the patient's age and  
NOTE Confidence: 0.96409935  
01:03:09.315 --> 01:03:10.375 Breslow death.  
NOTE Confidence: 0.98658705

01:03:10.755 --> 01:03:11.555 And that's part of the  
NOTE Confidence: 0.98658705

01:03:11.555 --> 01:03:13.075 reason why for these t  
NOTE Confidence: 0.98658705

01:03:13.075 --> 01:03:13.895 three tumors,  
NOTE Confidence: 0.9878288

01:03:14.515 --> 01:03:16.195 a very small fraction of  
NOTE Confidence: 0.9878288

01:03:16.195 --> 01:03:17.875 them are actually classified as  
NOTE Confidence: 0.9878288

01:03:17.875 --> 01:03:18.615 low risk,  
NOTE Confidence: 0.9069252

01:03:19.474 --> 01:03:20.595 both because they have an  
NOTE Confidence: 0.9069252

01:03:20.595 --> 01:03:21.095 increased,  
NOTE Confidence: 0.97755086

01:03:21.670 --> 01:03:23.030 sort of aggressiveness of their  
NOTE Confidence: 0.97755086

01:03:23.030 --> 01:03:24.570 gene expression, but also because  
NOTE Confidence: 0.9698271

01:03:25.030 --> 01:03:26.790 this test includes the Breslow  
NOTE Confidence: 0.9698271

01:03:26.790 --> 01:03:28.150 depth. So it's actually pretty  
NOTE Confidence: 0.9698271

01:03:28.150 --> 01:03:29.270 rare to get a low  
NOTE Confidence: 0.9698271

01:03:29.270 --> 01:03:30.090 risk result,  
NOTE Confidence: 0.9840414

01:03:30.550 --> 01:03:31.590 with these t three tumors,  
NOTE Confidence: 0.9840414

01:03:31.590 --> 01:03:32.390 and we can see that



NOTE Confidence: 0.9840414  
01:03:32.390 --> 01:03:34.170 it doesn't very accurately predict,  
NOTE Confidence: 0.97749233  
01:03:34.550 --> 01:03:36.070 sentinel lymph node status in  
NOTE Confidence: 0.97749233  
01:03:36.070 --> 01:03:37.395 these groups of patients.  
NOTE Confidence: 0.980537  
01:03:37.695 --> 01:03:38.655 However, if we go to  
NOTE Confidence: 0.980537  
01:03:38.655 --> 01:03:40.335 this stage, the stage one  
NOTE Confidence: 0.980537  
01:03:40.335 --> 01:03:41.615 b subgroup, which is t  
NOTE Confidence: 0.980537  
01:03:41.615 --> 01:03:42.575 one b and t two  
NOTE Confidence: 0.980537  
01:03:42.575 --> 01:03:43.695 a, and you'll note that  
NOTE Confidence: 0.980537  
01:03:43.695 --> 01:03:44.995 this is actually the largest  
NOTE Confidence: 0.980537  
01:03:45.055 --> 01:03:46.495 fraction of patients in this  
NOTE Confidence: 0.980537  
01:03:46.495 --> 01:03:46.995 study.  
NOTE Confidence: 0.99361676  
01:03:48.015 --> 01:03:49.375 About half of these patients  
NOTE Confidence: 0.99361676  
01:03:49.375 --> 01:03:51.180 overall were were classified as  
NOTE Confidence: 0.99361676  
01:03:51.180 --> 01:03:52.780 GEP low risk, and we  
NOTE Confidence: 0.99361676  
01:03:52.780 --> 01:03:54.140 see that it really did  
NOTE Confidence: 0.99361676

01:03:54.140 --> 01:03:55.580 impact the rate of sentinel

NOTE Confidence: 0.99361676

01:03:55.580 --> 01:03:56.560 lymph node positivity.

NOTE Confidence: 0.9794392

01:03:56.940 --> 01:03:57.820 So in the t one

NOTE Confidence: 0.9794392

01:03:57.820 --> 01:03:59.020 b's, if they were low

NOTE Confidence: 0.9794392

01:03:59.020 --> 01:04:00.060 risk, they were only five

NOTE Confidence: 0.9794392

01:04:00.060 --> 01:04:02.160 percent, sentinel lymph node positive

NOTE Confidence: 0.9794392

01:04:02.380 --> 01:04:03.900 compared to sixteen percent in

NOTE Confidence: 0.9794392

01:04:03.900 --> 01:04:04.720 the high risk,

NOTE Confidence: 0.9802465

01:04:05.505 --> 01:04:06.964 similar for t two a.

NOTE Confidence: 0.9802465

01:04:07.025 --> 01:04:08.224 So it's the stage one

NOTE Confidence: 0.9802465

01:04:08.224 --> 01:04:09.825 b subgroup where this test

NOTE Confidence: 0.9802465

01:04:09.825 --> 01:04:11.045 can be most useful.

NOTE Confidence: 0.99950993

01:04:11.345 --> 01:04:12.484 And this is asking

NOTE Confidence: 0.9586586

01:04:12.785 --> 01:04:14.785 only the specific question of

NOTE Confidence: 0.9586586

01:04:14.785 --> 01:04:16.545 can we predict sentinel lymph

NOTE Confidence: 0.9586586

01:04:16.545 --> 01:04:18.704 node status and thereby perhaps

NOTE Confidence: 0.9586586

01:04:18.704 --> 01:04:20.065 avoid sentinel lymph node in

NOTE Confidence: 0.9586586

01:04:20.065 --> 01:04:20.885 certain patients.

NOTE Confidence: 0.9923299

01:04:21.960 --> 01:04:23.080 So then that brings us

NOTE Confidence: 0.9923299

01:04:23.080 --> 01:04:24.060 to the trial.

NOTE Confidence: 0.9711472

01:04:24.360 --> 01:04:25.660 So this is the ICEMAN

NOTE Confidence: 0.9711472

01:04:25.720 --> 01:04:27.720 trial intelligent choice of excision

NOTE Confidence: 0.9711472

01:04:27.720 --> 01:04:29.740 margin. And the primary objective

NOTE Confidence: 0.9711472

01:04:29.880 --> 01:04:31.640 is to compare three year

NOTE Confidence: 0.9711472

01:04:31.640 --> 01:04:33.640 recurrence free survival in patients

NOTE Confidence: 0.9711472

01:04:33.640 --> 01:04:34.920 that are treated with narrow

NOTE Confidence: 0.9711472

01:04:34.920 --> 01:04:36.619 excision versus wide excision.

NOTE Confidence: 0.98146

01:04:37.205 --> 01:04:39.285 The secondary objective is to,

NOTE Confidence: 0.97071254

01:04:40.005 --> 01:04:42.165 assess disease free survival, especially

NOTE Confidence: 0.97071254

01:04:42.165 --> 01:04:43.705 looking at nodal disease

NOTE Confidence: 0.9583455

01:04:44.645 --> 01:04:46.085 in patients who were treated

NOTE Confidence: 0.9583455

01:04:46.085 --> 01:04:47.685 with nodal surveillance without a

NOTE Confidence: 0.9583455

01:04:47.685 --> 01:04:49.065 sentinel lymph node biopsy.

NOTE Confidence: 0.92589384

01:04:49.460 --> 01:04:50.339 So here's a setup of

NOTE Confidence: 0.92589384

01:04:50.339 --> 01:04:51.940 the trial. Patients with clinical

NOTE Confidence: 0.92589384

01:04:51.940 --> 01:04:53.240 stage one invasive melanoma

NOTE Confidence: 0.97489846

01:04:53.779 --> 01:04:55.400 that are classified as Merlin

NOTE Confidence: 0.97489846

01:04:55.460 --> 01:04:57.400 low risk. So all patients,

NOTE Confidence: 0.9700181

01:04:58.099 --> 01:04:59.539 are tested with the GEP,

NOTE Confidence: 0.9700181

01:04:59.539 --> 01:05:00.500 and only those that are

NOTE Confidence: 0.9700181

01:05:00.500 --> 01:05:02.019 low risk are enrolled in

NOTE Confidence: 0.9700181

01:05:02.019 --> 01:05:03.859 this study. They're randomized to

NOTE Confidence: 0.9700181

01:05:03.859 --> 01:05:05.325 either narrow excision or wide

NOTE Confidence: 0.9700181

01:05:05.325 --> 01:05:06.525 excision. And we can see

NOTE Confidence: 0.9700181

01:05:06.525 --> 01:05:07.885 what that actually means. Narrow

NOTE Confidence: 0.9700181

01:05:07.885 --> 01:05:09.405 excision is zero point five

NOTE Confidence: 0.9700181

01:05:09.405 --> 01:05:09.905 centimeters

NOTE Confidence: 0.9717204  
01:05:10.445 --> 01:05:12.285 with complete margin analysis for  
NOTE Confidence: 0.9717204  
01:05:12.285 --> 01:05:13.805 high risk locations or high  
NOTE Confidence: 0.9717204  
01:05:13.805 --> 01:05:14.545 risk pathology.  
NOTE Confidence: 0.9704975  
01:05:15.005 --> 01:05:16.125 And then the wide excision  
NOTE Confidence: 0.9704975  
01:05:16.125 --> 01:05:17.905 is standard treatment per NCCN  
NOTE Confidence: 0.9704975  
01:05:18.045 --> 01:05:18.545 guidelines.  
NOTE Confidence: 0.999625  
01:05:19.820 --> 01:05:20.960 And none of these patients  
NOTE Confidence: 0.97972035  
01:05:21.260 --> 01:05:22.780 will have a sentinel lymph  
NOTE Confidence: 0.97972035  
01:05:22.780 --> 01:05:24.140 node biopsy as part of  
NOTE Confidence: 0.97972035  
01:05:24.140 --> 01:05:24.800 the trial.  
NOTE Confidence: 0.9620287  
01:05:25.580 --> 01:05:26.780 And these are the inclusion  
NOTE Confidence: 0.9620287  
01:05:26.780 --> 01:05:27.280 criteria,  
NOTE Confidence: 0.96857005  
01:05:27.820 --> 01:05:29.260 only t one b, t  
NOTE Confidence: 0.96857005  
01:05:29.260 --> 01:05:30.000 two a,  
NOTE Confidence: 0.9968009  
01:05:30.460 --> 01:05:30.960 or  
NOTE Confidence: 0.9921977

01:05:31.260 --> 01:05:32.565 t one a with depth  
NOTE Confidence: 0.9921977

01:05:32.645 --> 01:05:33.845 depth greater than zero point  
NOTE Confidence: 0.9921977

01:05:33.845 --> 01:05:35.365 five and greater than one  
NOTE Confidence: 0.9921977

01:05:35.365 --> 01:05:37.204 high risk feature, which includes  
NOTE Confidence: 0.9921977

01:05:37.204 --> 01:05:37.704 lymphovascular  
NOTE Confidence: 0.92465657

01:05:38.085 --> 01:05:39.305 invasion or mitoses.  
NOTE Confidence: 0.9925767

01:05:40.165 --> 01:05:41.045 And they all have to  
NOTE Confidence: 0.9925767

01:05:41.045 --> 01:05:42.905 be GEP low risk.  
NOTE Confidence: 0.97411245

01:05:44.085 --> 01:05:45.285 In case you need to  
NOTE Confidence: 0.97411245

01:05:45.285 --> 01:05:46.885 remind yourself what these categories  
NOTE Confidence: 0.97411245

01:05:46.885 --> 01:05:47.845 are, these are the actual  
NOTE Confidence: 0.97411245

01:05:47.845 --> 01:05:48.540 preslow deaths.  
NOTE Confidence: 0.99710554

01:05:49.420 --> 01:05:50.460 And so I mentioned that  
NOTE Confidence: 0.99710554

01:05:50.460 --> 01:05:51.660 sentinel lymph node biopsy is  
NOTE Confidence: 0.99710554

01:05:51.660 --> 01:05:52.540 not part of the trial,  
NOTE Confidence: 0.99710554

01:05:52.540 --> 01:05:53.820 but it may be performed

NOTE Confidence: 0.99710554  
01:05:53.820 --> 01:05:55.180 at physician discretion, which is  
NOTE Confidence: 0.99710554  
01:05:55.180 --> 01:05:55.680 important.  
NOTE Confidence: 0.96926695  
01:05:55.980 --> 01:05:57.020 So if we feel that  
NOTE Confidence: 0.96926695  
01:05:57.020 --> 01:05:58.540 a patient really would benefit  
NOTE Confidence: 0.96926695  
01:05:58.540 --> 01:05:59.980 from having sentinel lymph node  
NOTE Confidence: 0.96926695  
01:05:59.980 --> 01:06:01.660 biopsy even with a GEP  
NOTE Confidence: 0.96926695  
01:06:01.660 --> 01:06:02.815 low risk score, then then  
NOTE Confidence: 0.96926695  
01:06:02.815 --> 01:06:03.695 we can still do that  
NOTE Confidence: 0.96926695  
01:06:03.695 --> 01:06:04.835 as part of this trial.  
NOTE Confidence: 0.95065284  
01:06:06.255 --> 01:06:07.135 This is a large study  
NOTE Confidence: 0.95065284  
01:06:07.135 --> 01:06:08.335 with the planned enrollment of  
NOTE Confidence: 0.95065284  
01:06:08.335 --> 01:06:09.775 a thousand patients at multiple  
NOTE Confidence: 0.95065284  
01:06:09.775 --> 01:06:11.375 sites. It is currently already  
NOTE Confidence: 0.95065284  
01:06:11.375 --> 01:06:12.655 enrolling in a few sites,  
NOTE Confidence: 0.95065284  
01:06:12.655 --> 01:06:13.855 and, hopefully, Yale will be  
NOTE Confidence: 0.95065284

01:06:13.855 --> 01:06:14.915 coming on soon.  
NOTE Confidence: 0.9878371

01:06:16.100 --> 01:06:17.700 For these early stage melanoma,  
NOTE Confidence: 0.9878371

01:06:17.700 --> 01:06:19.220 we expect a very good  
NOTE Confidence: 0.9878371

01:06:19.220 --> 01:06:20.740 recurrence free survival of ninety  
NOTE Confidence: 0.9878371

01:06:20.740 --> 01:06:21.860 eight percent at three years.  
NOTE Confidence: 0.9878371

01:06:21.860 --> 01:06:22.500 So we really have to  
NOTE Confidence: 0.9878371

01:06:22.500 --> 01:06:23.380 have a large study to  
NOTE Confidence: 0.9878371

01:06:23.380 --> 01:06:24.740 be able to detect any  
NOTE Confidence: 0.9878371

01:06:24.740 --> 01:06:26.580 potential difference here, and this  
NOTE Confidence: 0.9878371

01:06:26.580 --> 01:06:27.400 is a noninferiority  
NOTE Confidence: 0.99720025

01:06:27.940 --> 01:06:28.440 design.  
NOTE Confidence: 0.999253

01:06:29.065 --> 01:06:30.105 And we're also looking at  
NOTE Confidence: 0.999253

01:06:30.105 --> 01:06:31.965 secondary outcomes of surgical morbidity  
NOTE Confidence: 0.9915957

01:06:32.425 --> 01:06:33.865 and quality of life measures,  
NOTE Confidence: 0.9915957

01:06:33.865 --> 01:06:34.925 which we expect,  
NOTE Confidence: 0.99263054

01:06:35.385 --> 01:06:36.905 will be less in patients



NOTE Confidence: 0.99263054  
01:06:36.905 --> 01:06:38.265 that are randomized to narrow  
NOTE Confidence: 0.99263054  
01:06:38.265 --> 01:06:38.765 excision.  
NOTE Confidence: 0.9946516  
01:06:40.105 --> 01:06:41.325 So just to summarize,  
NOTE Confidence: 0.9989895  
01:06:42.380 --> 01:06:43.820 know, we're thinking about our  
NOTE Confidence: 0.9989895  
01:06:43.820 --> 01:06:45.280 goals of surgical management,  
NOTE Confidence: 0.9933135  
01:06:45.740 --> 01:06:47.520 including both staging the tumor  
NOTE Confidence: 0.9933135  
01:06:47.580 --> 01:06:49.440 and optimizing local control.  
NOTE Confidence: 0.9906512  
01:06:50.300 --> 01:06:52.140 Complete margin analysis may allow  
NOTE Confidence: 0.9906512  
01:06:52.140 --> 01:06:53.580 us to have less morbid  
NOTE Confidence: 0.9906512  
01:06:53.580 --> 01:06:55.280 and yet still complete surgical  
NOTE Confidence: 0.9906512  
01:06:55.340 --> 01:06:56.860 resection with a narrow initial  
NOTE Confidence: 0.9906512  
01:06:56.860 --> 01:06:57.360 margin.  
NOTE Confidence: 0.9663021  
01:06:57.935 --> 01:06:59.395 And then using a GEP  
NOTE Confidence: 0.98341626  
01:06:59.695 --> 01:07:00.895 can maybe help us do  
NOTE Confidence: 0.98341626  
01:07:00.895 --> 01:07:02.175 some of the staging without  
NOTE Confidence: 0.98341626

01:07:02.175 --> 01:07:03.555 a sentinel lymph node biopsy,  
NOTE Confidence: 0.9932467

01:07:04.095 --> 01:07:05.635 in select groups of patients,  
NOTE Confidence: 0.9932467

01:07:05.695 --> 01:07:07.215 especially t one b, t  
NOTE Confidence: 0.9932467

01:07:07.215 --> 01:07:08.115 two a melanomas,  
NOTE Confidence: 0.93980443

01:07:08.975 --> 01:07:10.575 that come back as as  
NOTE Confidence: 0.93980443

01:07:10.575 --> 01:07:12.095 low risk on their GEP  
NOTE Confidence: 0.93980443

01:07:12.095 --> 01:07:12.595 testing.  
NOTE Confidence: 0.9998526

01:07:13.440 --> 01:07:15.460 So I will stop there.  
NOTE Confidence: 0.9998526

01:07:15.520 --> 01:07:16.260 Thank you.  
NOTE Confidence: 0.9419149

01:07:22.640 --> 01:07:24.079 Thank you so much, doctor  
NOTE Confidence: 0.9419149

01:07:24.079 --> 01:07:25.140 Christiansen, sir.  
NOTE Confidence: 0.9748419

01:07:25.845 --> 01:07:27.605 It's nice everyone has already  
NOTE Confidence: 0.9748419

01:07:27.605 --> 01:07:29.224 kind of laid out the  
NOTE Confidence: 0.9793103

01:07:29.525 --> 01:07:30.025 groundwork,  
NOTE Confidence: 0.9867742

01:07:30.724 --> 01:07:32.585 about all these very fancy  
NOTE Confidence: 0.9867742

01:07:32.724 --> 01:07:35.045 gene expression profiling assays. And

NOTE Confidence: 0.9867742  
01:07:35.045 --> 01:07:36.165 so my job now is  
NOTE Confidence: 0.9867742  
01:07:36.165 --> 01:07:37.065 trying to  
NOTE Confidence: 0.98379064  
01:07:37.365 --> 01:07:38.645 take all of this new  
NOTE Confidence: 0.98379064  
01:07:38.645 --> 01:07:40.085 technology and how do we  
NOTE Confidence: 0.98379064  
01:07:40.085 --> 01:07:41.790 integrate it best into clinical  
NOTE Confidence: 0.98379064  
01:07:42.030 --> 01:07:43.250 practice to really  
NOTE Confidence: 0.9506708  
01:07:43.550 --> 01:07:44.590 move the needle in terms  
NOTE Confidence: 0.9506708  
01:07:44.590 --> 01:07:46.270 of improving patient outcomes while  
NOTE Confidence: 0.9506708  
01:07:46.270 --> 01:07:48.210 minimizing morbidity and overtreatment.  
NOTE Confidence: 0.9821655  
01:07:48.910 --> 01:07:49.550 And so one of the  
NOTE Confidence: 0.9821655  
01:07:49.550 --> 01:07:50.990 things that I'll talk briefly  
NOTE Confidence: 0.9821655  
01:07:50.990 --> 01:07:51.870 about is kind of the  
NOTE Confidence: 0.9821655  
01:07:51.870 --> 01:07:53.230 difference between how we use  
NOTE Confidence: 0.9821655  
01:07:53.230 --> 01:07:54.990 these assays in melanoma versus  
NOTE Confidence: 0.9821655  
01:07:54.990 --> 01:07:56.930 in cutaneous squamous cell carcinomas.  
NOTE Confidence: 0.9626394

01:07:57.545 --> 01:07:58.825 And really there are three  
NOTE Confidence: 0.9626394

01:07:58.825 --> 01:08:00.905 main goals of trying to  
NOTE Confidence: 0.9626394

01:08:00.905 --> 01:08:03.305 utilize GEPs in clinical decision  
NOTE Confidence: 0.9626394

01:08:03.305 --> 01:08:04.825 making. One is, you know,  
NOTE Confidence: 0.9626394

01:08:04.825 --> 01:08:06.345 the question is, can we  
NOTE Confidence: 0.9626394

01:08:06.345 --> 01:08:08.045 avoid central lymph node biopsies  
NOTE Confidence: 0.9626394

01:08:08.265 --> 01:08:09.625 in individuals who are at  
NOTE Confidence: 0.9626394

01:08:09.625 --> 01:08:11.350 low risk, and reduce the  
NOTE Confidence: 0.9626394

01:08:11.350 --> 01:08:13.290 morbidity of surgical resection?  
NOTE Confidence: 0.986006

01:08:13.750 --> 01:08:14.710 You know, how does that  
NOTE Confidence: 0.986006

01:08:14.710 --> 01:08:16.070 score really inform whether or  
NOTE Confidence: 0.986006

01:08:16.070 --> 01:08:17.610 not the patient needs adjuvant  
NOTE Confidence: 0.986006

01:08:17.750 --> 01:08:19.370 therapy to try to minimize  
NOTE Confidence: 0.986006

01:08:19.430 --> 01:08:20.489 the stomach toxicities  
NOTE Confidence: 0.9941591

01:08:20.790 --> 01:08:21.989 for people who don't need  
NOTE Confidence: 0.9941591

01:08:21.989 --> 01:08:23.590 additional treatment and will have

NOTE Confidence: 0.9941591  
01:08:23.590 --> 01:08:24.890 a good outcome regardless?  
NOTE Confidence: 0.9989565  
01:08:25.590 --> 01:08:27.104 And then how do we  
NOTE Confidence: 0.9991825  
01:08:27.405 --> 01:08:29.025 utilize this information  
NOTE Confidence: 0.98820996  
01:08:29.325 --> 01:08:30.145 about risk  
NOTE Confidence: 0.96376896  
01:08:30.445 --> 01:08:32.385 to guide surveillance? Do individuals  
NOTE Confidence: 0.96376896  
01:08:32.525 --> 01:08:33.985 who have high risk tumors  
NOTE Confidence: 0.96376896  
01:08:34.125 --> 01:08:35.265 need more surveillance,  
NOTE Confidence: 0.9773393  
01:08:35.725 --> 01:08:37.905 more frequent visits, more frequent  
NOTE Confidence: 0.9773393  
01:08:38.125 --> 01:08:39.965 examinations and scans as opposed  
NOTE Confidence: 0.9773393  
01:08:39.965 --> 01:08:41.165 to those with low risk  
NOTE Confidence: 0.9773393  
01:08:41.165 --> 01:08:41.665 disease?  
NOTE Confidence: 0.9339176  
01:08:43.380 --> 01:08:44.740 So this is just kind  
NOTE Confidence: 0.9339176  
01:08:44.740 --> 01:08:46.340 of comparing again the MERLIN  
NOTE Confidence: 0.9339176  
01:08:46.340 --> 01:08:48.600 and the CASEL bioscience testing.  
NOTE Confidence: 0.9861778  
01:08:49.060 --> 01:08:50.340 I really only focused on  
NOTE Confidence: 0.9861778

01:08:50.340 --> 01:08:51.780 the assays that are available  
NOTE Confidence: 0.9861778

01:08:51.780 --> 01:08:53.240 here in the United States.  
NOTE Confidence: 0.95319426

01:08:54.260 --> 01:08:55.755 But really, as, you know,  
NOTE Confidence: 0.95319426

01:08:55.755 --> 01:08:57.614 my colleagues have already discussed,  
NOTE Confidence: 0.8738388

01:08:58.314 --> 01:09:00.635 Merlin has two categories, high  
NOTE Confidence: 0.8738388

01:09:00.635 --> 01:09:02.655 versus low, whereas Cassell has  
NOTE Confidence: 0.945929

01:09:02.955 --> 01:09:05.215 four different categories, 1A, 1B,  
NOTE Confidence: 0.945929

01:09:05.275 --> 01:09:07.215 2A, 2Bs in melanoma.  
NOTE Confidence: 0.9636985

01:09:08.715 --> 01:09:10.235 Really the Merlin is kind  
NOTE Confidence: 0.9636985

01:09:10.235 --> 01:09:12.450 of geared towards looking at  
NOTE Confidence: 0.9636985

01:09:12.450 --> 01:09:14.310 predicting sentinel lymph node positivity  
NOTE Confidence: 0.9636985

01:09:14.610 --> 01:09:16.050 to guide decision making and  
NOTE Confidence: 0.9636985

01:09:16.050 --> 01:09:17.189 lower risk melanomas,  
NOTE Confidence: 0.9647566

01:09:17.650 --> 01:09:19.729 whereas CASEL really tries to  
NOTE Confidence: 0.9647566

01:09:19.729 --> 01:09:21.590 address the question about recurrence  
NOTE Confidence: 0.9647566

01:09:21.810 --> 01:09:22.950 risk and prognostication.

NOTE Confidence: 0.92500854  
01:09:26.745 --> 01:09:28.745 The real question is these  
NOTE Confidence: 0.92500854  
01:09:28.745 --> 01:09:30.125 tests are very expensive.  
NOTE Confidence: 0.99556124  
01:09:30.425 --> 01:09:30.925 They're  
NOTE Confidence: 0.9321167  
01:09:31.305 --> 01:09:32.905 time consuming. There's a lag  
NOTE Confidence: 0.9321167  
01:09:32.905 --> 01:09:34.185 time in before you get  
NOTE Confidence: 0.9321167  
01:09:34.185 --> 01:09:34.925 the results.  
NOTE Confidence: 0.99701923  
01:09:35.465 --> 01:09:37.165 And given the cost,  
NOTE Confidence: 0.9991805  
01:09:38.025 --> 01:09:39.945 does this information really add  
NOTE Confidence: 0.9991805  
01:09:39.945 --> 01:09:41.645 overall value to the care?  
NOTE Confidence: 0.94637066  
01:09:41.970 --> 01:09:43.010 You know, we talk about  
NOTE Confidence: 0.94637066  
01:09:43.010 --> 01:09:44.070 nomograms and,  
NOTE Confidence: 0.95487815  
01:09:45.650 --> 01:09:46.770 in determining whether or not  
NOTE Confidence: 0.95487815  
01:09:46.770 --> 01:09:47.810 patients have a high risk  
NOTE Confidence: 0.95487815  
01:09:47.810 --> 01:09:49.010 of the sentinel lymph node  
NOTE Confidence: 0.95487815  
01:09:49.010 --> 01:09:51.110 positivity to determine lymph node  
NOTE Confidence: 0.95487815

01:09:51.250 --> 01:09:51.750 biopsies.  
NOTE Confidence: 0.99532795

01:09:52.930 --> 01:09:54.290 We have very good long  
NOTE Confidence: 0.99532795

01:09:54.290 --> 01:09:54.790 term  
NOTE Confidence: 0.9411258

01:09:55.665 --> 01:09:56.165 AJCC  
NOTE Confidence: 0.9831516

01:09:57.104 --> 01:09:58.804 melanoma specific recurrence,  
NOTE Confidence: 0.9393283

01:10:00.224 --> 01:10:01.364 specific survival,  
NOTE Confidence: 0.9885684

01:10:01.824 --> 01:10:03.284 and all of these latter,  
NOTE Confidence: 0.9395237

01:10:04.625 --> 01:10:06.304 you know, statistics are free.  
NOTE Confidence: 0.9395237

01:10:06.304 --> 01:10:07.744 So, what exactly is the  
NOTE Confidence: 0.9395237

01:10:07.744 --> 01:10:09.204 GEP testing contributing?  
NOTE Confidence: 0.9188053

01:10:10.410 --> 01:10:12.010 In addition to this, you  
NOTE Confidence: 0.9188053

01:10:12.010 --> 01:10:13.770 know, we obviously from the  
NOTE Confidence: 0.9188053

01:10:13.770 --> 01:10:15.050 pros and cons about the  
NOTE Confidence: 0.9188053

01:10:15.050 --> 01:10:16.410 discussion and how these assays  
NOTE Confidence: 0.9188053

01:10:16.410 --> 01:10:17.850 were designed and whether geared  
NOTE Confidence: 0.9188053

01:10:17.850 --> 01:10:18.670 towards addressing,



NOTE Confidence: 0.9841813  
01:10:19.130 --> 01:10:20.590 there are obvious flaws.  
NOTE Confidence: 0.9872021  
01:10:21.050 --> 01:10:22.570 They're not perfect. No single  
NOTE Confidence: 0.9872021  
01:10:22.570 --> 01:10:24.410 assay is going to yield  
NOTE Confidence: 0.9872021  
01:10:24.410 --> 01:10:24.990 the exact  
NOTE Confidence: 0.9554922  
01:10:25.575 --> 01:10:27.255 data that is required. And  
NOTE Confidence: 0.9554922  
01:10:27.255 --> 01:10:27.995 there's always  
NOTE Confidence: 0.99968576  
01:10:28.535 --> 01:10:29.435 some stage  
NOTE Confidence: 0.93723756  
01:10:29.735 --> 01:10:32.235 or some factor clinical pathologically,  
NOTE Confidence: 0.99812  
01:10:33.495 --> 01:10:34.854 that may not be well  
NOTE Confidence: 0.99812  
01:10:34.854 --> 01:10:36.315 represented in the assay.  
NOTE Confidence: 0.85308725  
01:10:36.695 --> 01:10:38.295 So for example, this is  
NOTE Confidence: 0.85308725  
01:10:38.295 --> 01:10:39.815 the Castle Bio and Science  
NOTE Confidence: 0.85308725  
01:10:39.815 --> 01:10:40.315 testing,  
NOTE Confidence: 0.998897  
01:10:40.680 --> 01:10:42.360 looking at the estimated proportion  
NOTE Confidence: 0.998897  
01:10:42.360 --> 01:10:43.660 of patients with melanoma  
NOTE Confidence: 0.9270368

01:10:44.520 --> 01:10:46.199 who are correctly classified as  
NOTE Confidence: 0.9270368

01:10:46.199 --> 01:10:47.239 high risk. And you can  
NOTE Confidence: 0.9270368

01:10:47.239 --> 01:10:48.460 see the stage ones,  
NOTE Confidence: 0.96623254

01:10:49.479 --> 01:10:50.280 did worse,  
NOTE Confidence: 0.99216753

01:10:50.600 --> 01:10:52.695 in this setting. Whereas if  
NOTE Confidence: 0.99216753

01:10:52.695 --> 01:10:53.735 you kind of flip this  
NOTE Confidence: 0.99216753

01:10:53.735 --> 01:10:55.095 and look at the estimated  
NOTE Confidence: 0.99216753

01:10:55.095 --> 01:10:56.955 proportion of patients without melanoma  
NOTE Confidence: 0.99216753

01:10:57.095 --> 01:10:58.955 recurrence that were correctly classified  
NOTE Confidence: 0.99216753

01:10:59.015 --> 01:10:59.915 as low risk,  
NOTE Confidence: 0.94107145

01:11:00.615 --> 01:11:02.055 again, the stage twos in  
NOTE Confidence: 0.94107145

01:11:02.055 --> 01:11:03.275 this situation  
NOTE Confidence: 0.99545205

01:11:03.814 --> 01:11:05.015 did a little bit worse  
NOTE Confidence: 0.99545205

01:11:05.015 --> 01:11:06.155 based on the assay.  
NOTE Confidence: 0.94762105

01:11:06.890 --> 01:11:08.650 So I think in general,  
NOTE Confidence: 0.94762105

01:11:08.650 --> 01:11:10.410 when you kinda summarize these

NOTE Confidence: 0.94762105  
01:11:10.410 --> 01:11:12.590 different studies that led to,  
NOTE Confidence: 0.9112563  
01:11:13.370 --> 01:11:15.150 the evaluation of these  
NOTE Confidence: 0.9484104  
01:11:15.450 --> 01:11:17.790 clinical assays in in patients,  
NOTE Confidence: 0.97549385  
01:11:18.330 --> 01:11:20.330 really, the consensus is that  
NOTE Confidence: 0.97549385  
01:11:20.330 --> 01:11:22.035 maybe they're not quite ready  
NOTE Confidence: 0.97549385  
01:11:22.035 --> 01:11:23.814 yet for prime time usage.  
NOTE Confidence: 0.83617157  
01:11:25.395 --> 01:11:26.695 The Merlin has,  
NOTE Confidence: 0.97028655  
01:11:27.314 --> 01:11:28.614 a nod in the NCCN  
NOTE Confidence: 0.97028655  
01:11:28.835 --> 01:11:30.035 to consider it,  
NOTE Confidence: 0.9035613  
01:11:30.435 --> 01:11:32.354 but ultimately, it should not  
NOTE Confidence: 0.9035613  
01:11:32.354 --> 01:11:32.854 supersede,  
NOTE Confidence: 0.99193156  
01:11:34.090 --> 01:11:36.910 clinical pathological features, clinical staging,  
NOTE Confidence: 0.99039066  
01:11:37.690 --> 01:11:38.729 and really should be used  
NOTE Confidence: 0.99039066  
01:11:38.729 --> 01:11:40.090 in the context as an  
NOTE Confidence: 0.99039066  
01:11:40.090 --> 01:11:42.250 investigational tool because there's still  
NOTE Confidence: 0.99039066

01:11:42.250 --> 01:11:43.770 so much that we still  
NOTE Confidence: 0.99039066

01:11:43.770 --> 01:11:45.290 need to clarify in regards  
NOTE Confidence: 0.99039066

01:11:45.290 --> 01:11:46.890 to how best to implement  
NOTE Confidence: 0.99039066

01:11:46.890 --> 01:11:49.015 them, what they ultimately mean,  
NOTE Confidence: 0.99039066

01:11:49.015 --> 01:11:50.795 what the long term survival,  
NOTE Confidence: 0.99039066

01:11:50.854 --> 01:11:51.354 recurrence  
NOTE Confidence: 0.9115127

01:11:52.535 --> 01:11:54.535 risk factors, and overall survival  
NOTE Confidence: 0.9115127

01:11:54.535 --> 01:11:55.755 is for these individuals.  
NOTE Confidence: 0.9063572

01:11:56.375 --> 01:11:57.575 So really right now, they're  
NOTE Confidence: 0.9063572

01:11:57.575 --> 01:11:59.495 still geared towards the, as  
NOTE Confidence: 0.9063572

01:11:59.495 --> 01:12:00.235 an investigational  
NOTE Confidence: 0.99967015

01:12:00.535 --> 01:12:01.035 tool  
NOTE Confidence: 0.9775794

01:12:01.500 --> 01:12:02.960 as part of clinical trials  
NOTE Confidence: 0.9775794

01:12:03.099 --> 01:12:04.559 and in the research setting.  
NOTE Confidence: 0.9577004

01:12:05.900 --> 01:12:06.939 This is kind of the  
NOTE Confidence: 0.9577004

01:12:06.939 --> 01:12:09.739 melanoma specific survival breakdown by

NOTE Confidence: 0.9577004  
01:12:09.739 --> 01:12:10.239 stage  
NOTE Confidence: 0.9010483  
01:12:10.860 --> 01:12:12.219 at five years and ten  
NOTE Confidence: 0.9010483  
01:12:12.219 --> 01:12:13.900 years. And as you can  
NOTE Confidence: 0.9010483  
01:12:13.900 --> 01:12:15.420 see, really, we try to  
NOTE Confidence: 0.9010483  
01:12:15.420 --> 01:12:17.915 gear therapy, any additional adjuvant  
NOTE Confidence: 0.9010483  
01:12:17.975 --> 01:12:19.275 therapy post surgery  
NOTE Confidence: 0.93987674  
01:12:19.735 --> 01:12:21.335 in those individuals that have  
NOTE Confidence: 0.93987674  
01:12:21.335 --> 01:12:22.314 a higher risk  
NOTE Confidence: 0.89507055  
01:12:22.695 --> 01:12:25.755 of, morbidity, mortality for melanoma.  
NOTE Confidence: 0.8572183  
01:12:26.295 --> 01:12:27.415 And so really it's those  
NOTE Confidence: 0.8572183  
01:12:27.415 --> 01:12:29.335 stage IIBs and beyond even  
NOTE Confidence: 0.8572183  
01:12:29.335 --> 01:12:30.660 including oligometastatic stage four  
NOTE Confidence: 0.7473723  
01:12:34.820 --> 01:12:35.880 trying to decrease  
NOTE Confidence: 0.9239017  
01:12:36.260 --> 01:12:38.820 recurrence, improve overall survival long  
NOTE Confidence: 0.9239017  
01:12:38.820 --> 01:12:40.660 term. But it's really hard  
NOTE Confidence: 0.9239017

01:12:40.660 --> 01:12:42.260 just given the heterogeneity of  
NOTE Confidence: 0.9239017

01:12:42.260 --> 01:12:44.180 this population too to really  
NOTE Confidence: 0.9239017

01:12:44.180 --> 01:12:44.680 decipher  
NOTE Confidence: 0.98411167

01:12:45.064 --> 01:12:46.925 who really needs additional therapy  
NOTE Confidence: 0.98411167

01:12:46.985 --> 01:12:48.525 or who are we overtreating  
NOTE Confidence: 0.98411167

01:12:48.744 --> 01:12:51.165 and inducing potentially permanent toxicities,  
NOTE Confidence: 0.984079

01:12:51.784 --> 01:12:53.804 particularly with immune checkpoint inhibitors.  
NOTE Confidence: 0.9630214

01:12:54.665 --> 01:12:56.025 These days too, we're also  
NOTE Confidence: 0.9630214

01:12:56.025 --> 01:12:57.165 moving in the neoadjuvant  
NOTE Confidence: 0.8888568

01:12:57.545 --> 01:12:58.985 space too, and Doctor. Roche  
NOTE Confidence: 0.8888568

01:12:58.985 --> 01:12:59.885 has an energy  
NOTE Confidence: 0.92428136

01:13:00.620 --> 01:13:02.479 neoadjuvant study trying to evaluate  
NOTE Confidence: 0.92428136

01:13:02.540 --> 01:13:04.220 this in a re response  
NOTE Confidence: 0.92428136

01:13:04.220 --> 01:13:04.720 adaptive,  
NOTE Confidence: 0.9200072

01:13:05.420 --> 01:13:05.920 system.  
NOTE Confidence: 0.95878524

01:13:07.020 --> 01:13:08.560 But, really, can we also

NOTE Confidence: 0.9761574  
01:13:08.939 --> 01:13:11.100 help improve overall survival by  
NOTE Confidence: 0.9761574  
01:13:11.100 --> 01:13:13.600 moving systemic therapy earlier on?  
NOTE Confidence: 0.9761574  
01:13:13.895 --> 01:13:15.594 So where along the spectrum  
NOTE Confidence: 0.9761574  
01:13:15.655 --> 01:13:17.835 really does, GEP therapy,  
NOTE Confidence: 0.9899535  
01:13:18.614 --> 01:13:19.435 play a role?  
NOTE Confidence: 0.98295665  
01:13:19.895 --> 01:13:21.814 So as of right now,  
NOTE Confidence: 0.98295665  
01:13:21.814 --> 01:13:23.574 there really is no strong  
NOTE Confidence: 0.98295665  
01:13:23.574 --> 01:13:24.074 indication,  
NOTE Confidence: 0.977514  
01:13:25.655 --> 01:13:27.735 in clinical trial that really  
NOTE Confidence: 0.977514  
01:13:27.735 --> 01:13:28.235 supports  
NOTE Confidence: 0.99907  
01:13:28.614 --> 01:13:29.114 determining  
NOTE Confidence: 0.98659974  
01:13:29.590 --> 01:13:30.890 or utilizing GEP  
NOTE Confidence: 0.9795043  
01:13:31.350 --> 01:13:32.630 as a sole marker of  
NOTE Confidence: 0.9795043  
01:13:32.630 --> 01:13:33.990 whether or not we decide  
NOTE Confidence: 0.9795043  
01:13:33.990 --> 01:13:35.350 to do adjuvant therapy in  
NOTE Confidence: 0.9795043

01:13:35.350 --> 01:13:36.090 these individuals.  
NOTE Confidence: 0.94519246

01:13:36.710 --> 01:13:38.550 Again, there's some good clinical  
NOTE Confidence: 0.94519246

01:13:38.550 --> 01:13:40.330 trials in progress that unfortunately  
NOTE Confidence: 0.94519246

01:13:40.470 --> 01:13:41.670 we don't have the data  
NOTE Confidence: 0.94519246

01:13:41.670 --> 01:13:43.574 yet on. So the NIVOMELA  
NOTE Confidence: 0.95053977

01:13:43.875 --> 01:13:45.735 trial is currently ongoing,  
NOTE Confidence: 0.82719094

01:13:46.354 --> 01:13:47.255 is still enrolling,  
NOTE Confidence: 0.9354315

01:13:48.114 --> 01:13:50.114 but it's prospective randomized phase  
NOTE Confidence: 0.9354315

01:13:50.114 --> 01:13:51.795 three study. The question here  
NOTE Confidence: 0.9354315

01:13:51.795 --> 01:13:52.295 is,  
NOTE Confidence: 0.8957777

01:13:52.675 --> 01:13:53.814 looking at melanogenics  
NOTE Confidence: 0.9882852

01:13:55.074 --> 01:13:56.755 to see if that can,  
NOTE Confidence: 0.99986786

01:13:57.235 --> 01:13:58.454 adequately predict  
NOTE Confidence: 0.9946896

01:13:58.860 --> 01:14:00.300 in those individuals with high  
NOTE Confidence: 0.9946896

01:14:00.300 --> 01:14:01.040 risk disease  
NOTE Confidence: 0.9857713

01:14:01.580 --> 01:14:03.260 whether or not utilization of



NOTE Confidence: 0.9857713

01:14:03.260 --> 01:14:06.160 adjuvant nivolumab versus placebo improves

NOTE Confidence: 0.9857713

01:14:06.220 --> 01:14:07.900 outcomes in individuals with stage

NOTE Confidence: 0.9857713

01:14:07.900 --> 01:14:08.640 two melanoma.

NOTE Confidence: 0.9918573

01:14:09.260 --> 01:14:10.540 And so something for the

NOTE Confidence: 0.9918573

01:14:10.540 --> 01:14:11.740 future that we all should

NOTE Confidence: 0.9918573

01:14:11.740 --> 01:14:13.180 pay attention to once that

NOTE Confidence: 0.9918573

01:14:13.180 --> 01:14:14.594 data comes out and whether

NOTE Confidence: 0.9918573

01:14:14.594 --> 01:14:15.915 or not we can start

NOTE Confidence: 0.9918573

01:14:15.915 --> 01:14:17.435 integrating this in a more,

NOTE Confidence: 0.9962365

01:14:18.475 --> 01:14:20.875 evidence based fashion into our

NOTE Confidence: 0.9962365

01:14:20.875 --> 01:14:22.255 clinical decision making.

NOTE Confidence: 0.98500526

01:14:22.715 --> 01:14:23.835 Now the elephant in the

NOTE Confidence: 0.98500526

01:14:23.835 --> 01:14:25.594 room that we've not discussed

NOTE Confidence: 0.98500526

01:14:25.594 --> 01:14:27.354 yet this entire night is

NOTE Confidence: 0.98500526

01:14:27.354 --> 01:14:28.475 how do we factor in

NOTE Confidence: 0.98500526

01:14:28.475 --> 01:14:28.975 ctDNA  
NOTE Confidence: 0.80720866  
01:14:29.435 --> 01:14:29.935 too?  
NOTE Confidence: 0.99727  
01:14:30.520 --> 01:14:32.620 So there's more utilization  
NOTE Confidence: 0.99948895  
01:14:33.080 --> 01:14:33.979 for ctDNA  
NOTE Confidence: 0.9449212  
01:14:34.360 --> 01:14:35.660 in clinical management,  
NOTE Confidence: 0.916785  
01:14:36.200 --> 01:14:37.400 again, with,  
NOTE Confidence: 0.97298235  
01:14:37.960 --> 01:14:39.640 kind of caveats that this  
NOTE Confidence: 0.97298235  
01:14:39.640 --> 01:14:40.300 is also,  
NOTE Confidence: 0.98898184  
01:14:41.320 --> 01:14:42.300 semi understudied.  
NOTE Confidence: 0.9970315  
01:14:42.925 --> 01:14:44.365 There's a lot of ongoing  
NOTE Confidence: 0.9970315  
01:14:44.365 --> 01:14:45.885 clinical trials looking at this  
NOTE Confidence: 0.9970315  
01:14:45.885 --> 01:14:46.865 and risk stratifying  
NOTE Confidence: 0.99983203  
01:14:47.245 --> 01:14:47.745 individuals  
NOTE Confidence: 0.9952395  
01:14:48.365 --> 01:14:49.345 with ctDNA  
NOTE Confidence: 0.9798251  
01:14:49.725 --> 01:14:50.225 positivity,  
NOTE Confidence: 0.9092684  
01:14:50.685 --> 01:14:53.265 basically detectable circulating tumor DNA

NOTE Confidence: 0.9092684  
01:14:53.325 --> 01:14:53.825 postoperative,  
NOTE Confidence: 0.9757934  
01:14:54.445 --> 01:14:56.205 and whether those individuals need  
NOTE Confidence: 0.9757934  
01:14:56.205 --> 01:14:58.110 adjuvant therapy versus those who  
NOTE Confidence: 0.9757934  
01:14:58.270 --> 01:14:59.330 clear their ctDNA  
NOTE Confidence: 0.8761334  
01:14:59.790 --> 01:15:00.530 post op.  
NOTE Confidence: 0.97960395  
01:15:01.310 --> 01:15:02.510 One of the best clinical  
NOTE Confidence: 0.97960395  
01:15:02.510 --> 01:15:03.869 trials that has been published  
NOTE Confidence: 0.97960395  
01:15:03.869 --> 01:15:05.150 to date in this setting  
NOTE Confidence: 0.97960395  
01:15:05.150 --> 01:15:06.750 actually occurred in stage two  
NOTE Confidence: 0.97960395  
01:15:06.750 --> 01:15:07.570 colon cancers.  
NOTE Confidence: 0.8845035  
01:15:08.189 --> 01:15:09.489 So this was the dynamic  
NOTE Confidence: 0.9881503  
01:15:09.790 --> 01:15:11.409 trial looking at ctDNA  
NOTE Confidence: 0.99861336  
01:15:11.949 --> 01:15:13.630 to guide the decision on  
NOTE Confidence: 0.99861336  
01:15:13.630 --> 01:15:15.445 whether adjuvant therapy needs to  
NOTE Confidence: 0.99861336  
01:15:15.445 --> 01:15:16.185 be pursued.  
NOTE Confidence: 0.9952641

01:15:17.205 --> 01:15:18.885 The three year relapse free  
NOTE Confidence: 0.9952641

01:15:18.885 --> 01:15:20.564 survival was eighty six point  
NOTE Confidence: 0.9952641

01:15:20.564 --> 01:15:22.665 four percent amongst those with  
NOTE Confidence: 0.9952641

01:15:22.725 --> 01:15:23.225 ctDNA  
NOTE Confidence: 0.99732065

01:15:23.685 --> 01:15:24.185 positivity.  
NOTE Confidence: 0.95593786

01:15:25.685 --> 01:15:27.125 It was really randomized to  
NOTE Confidence: 0.95593786

01:15:27.125 --> 01:15:29.280 investigators' choice use that to  
NOTE Confidence: 0.95593786

01:15:29.280 --> 01:15:30.719 guide decision making whether or  
NOTE Confidence: 0.95593786

01:15:30.719 --> 01:15:32.500 not they received adjuvant chemotherapy.  
NOTE Confidence: 0.9053566

01:15:32.880 --> 01:15:34.020 Again, the regimen,  
NOTE Confidence: 0.8617992

01:15:34.719 --> 01:15:36.020 deferred to the investigator.  
NOTE Confidence: 0.99875903

01:15:36.960 --> 01:15:38.560 This was versus ninety two  
NOTE Confidence: 0.99875903

01:15:38.560 --> 01:15:39.540 point five percent  
NOTE Confidence: 0.9359332

01:15:40.400 --> 01:15:40.900 of  
NOTE Confidence: 0.974451

01:15:41.385 --> 01:15:43.864 recurrence free survival amongst the  
NOTE Confidence: 0.974451

01:15:43.864 --> 01:15:45.704 CTD negative patients who did

NOTE Confidence: 0.974451  
01:15:45.704 --> 01:15:47.485 not receive any additional therapy.  
NOTE Confidence: 0.98511434  
01:15:47.945 --> 01:15:48.925 So in the end,  
NOTE Confidence: 0.9664839  
01:15:49.465 --> 01:15:51.145 based on the CTD guided  
NOTE Confidence: 0.9664839  
01:15:51.145 --> 01:15:52.525 group, fewer patients,  
NOTE Confidence: 0.99152505  
01:15:53.304 --> 01:15:54.824 had to undergo and receive  
NOTE Confidence: 0.99152505  
01:15:54.824 --> 01:15:55.885 adjuvant chemotherapy,  
NOTE Confidence: 0.997133  
01:15:57.090 --> 01:15:59.650 and overall responses were very  
NOTE Confidence: 0.997133  
01:15:59.650 --> 01:16:00.150 similar.  
NOTE Confidence: 0.8771532  
01:16:01.330 --> 01:16:02.949 Now the COMBOAD  
NOTE Confidence: 0.97331774  
01:16:04.050 --> 01:16:05.969 trial was utilized to look  
NOTE Confidence: 0.97331774  
01:16:05.969 --> 01:16:08.229 at adjuvant dabrafenib and trametinib  
NOTE Confidence: 0.97331774  
01:16:08.369 --> 01:16:10.389 for individuals with BRAF mutated  
NOTE Confidence: 0.97331774  
01:16:10.449 --> 01:16:10.949 melanomas  
NOTE Confidence: 0.9988201  
01:16:12.025 --> 01:16:12.825 for a year in the  
NOTE Confidence: 0.9988201  
01:16:12.825 --> 01:16:13.805 adjuvant setting.  
NOTE Confidence: 0.97084653

01:16:14.265 --> 01:16:15.145 So what they did in  
NOTE Confidence: 0.97084653

01:16:15.145 --> 01:16:17.245 this study was actually also  
NOTE Confidence: 0.97084653

01:16:17.385 --> 01:16:18.985 evaluate, and they reported this  
NOTE Confidence: 0.97084653

01:16:18.985 --> 01:16:19.485 separately,  
NOTE Confidence: 0.8815334

01:16:19.785 --> 01:16:20.925 biomarker analysis,  
NOTE Confidence: 0.9697492

01:16:21.625 --> 01:16:24.045 looking at ctDNA post resection.  
NOTE Confidence: 0.9697492

01:16:24.185 --> 01:16:25.545 They found that in those  
NOTE Confidence: 0.9697492

01:16:25.545 --> 01:16:26.045 individuals,  
NOTE Confidence: 0.9886793

01:16:26.900 --> 01:16:28.740 post resection, thirteen percent of  
NOTE Confidence: 0.9886793

01:16:28.740 --> 01:16:31.240 patients had still detectable ctDNA,  
NOTE Confidence: 0.9383039

01:16:32.420 --> 01:16:34.180 and those were associated with  
NOTE Confidence: 0.9383039

01:16:34.180 --> 01:16:35.640 worse survival outcomes.  
NOTE Confidence: 0.89808446

01:16:36.100 --> 01:16:37.400 And so, again, ctDNA  
NOTE Confidence: 0.9356928

01:16:37.700 --> 01:16:38.600 has been utilized  
NOTE Confidence: 0.78654355

01:16:39.140 --> 01:16:41.265 and is emerging as prognostic  
NOTE Confidence: 0.78654355

01:16:41.265 --> 01:16:41.765 outcome

NOTE Confidence: 0.93385124  
01:16:42.065 --> 01:16:43.365 in individuals  
NOTE Confidence: 0.89171565  
01:16:44.064 --> 01:16:44.564 with,  
NOTE Confidence: 0.7970657  
01:16:44.945 --> 01:16:46.885 you know, high risk disease.  
NOTE Confidence: 0.7970657  
01:16:47.104 --> 01:16:47.604 Ultimately,  
NOTE Confidence: 0.9763449  
01:16:48.785 --> 01:16:49.525 if one  
NOTE Confidence: 0.876571  
01:16:49.905 --> 01:16:50.405 assay  
NOTE Confidence: 0.8908091  
01:16:51.025 --> 01:16:52.962 ctDNA versus GEP is going  
NOTE Confidence: 0.8908091  
01:16:52.962 --> 01:16:53.048 to be superior, inferior versus  
NOTE Confidence: 0.8908091  
01:16:53.048 --> 01:16:53.134 others yet to be determined.  
NOTE Confidence: 0.8908091  
01:16:53.134 --> 01:16:53.685 And I think really  
NOTE Confidence: 0.75420374  
01:16:54.305 --> 01:16:54.805 given  
NOTE Confidence: 0.8592658  
01:16:57.490 --> 01:16:58.630 determined. And I think really  
NOTE Confidence: 0.8592658  
01:16:58.930 --> 01:16:59.570 given kind of the limitations  
NOTE Confidence: 0.8592658  
01:16:59.570 --> 01:17:01.170 on some of the GEP  
NOTE Confidence: 0.8592658  
01:17:01.170 --> 01:17:02.630 assays and what they're designed  
NOTE Confidence: 0.8592658

01:17:02.850 --> 01:17:04.210 to question whether or not  
NOTE Confidence: 0.8592658

01:17:04.210 --> 01:17:06.229 that's sentinel lymph node biopsy  
NOTE Confidence: 0.8592658

01:17:06.450 --> 01:17:07.990 versus overall prognostication,  
NOTE Confidence: 0.9701539

01:17:09.650 --> 01:17:11.695 where that is aligned also  
NOTE Confidence: 0.9701539

01:17:11.695 --> 01:17:12.814 kind of depends on the  
NOTE Confidence: 0.9701539

01:17:12.814 --> 01:17:14.354 assay in question two.  
NOTE Confidence: 0.9987117

01:17:15.535 --> 01:17:17.795 Whether or not GEP impacts  
NOTE Confidence: 0.9715694

01:17:18.335 --> 01:17:19.715 how we surveil melanomas,  
NOTE Confidence: 0.9827977

01:17:20.094 --> 01:17:21.215 also we're still in the  
NOTE Confidence: 0.9827977

01:17:21.215 --> 01:17:22.655 primitive era of this as  
NOTE Confidence: 0.9827977

01:17:22.655 --> 01:17:23.155 well.  
NOTE Confidence: 0.9481043

01:17:24.130 --> 01:17:25.650 Really the guidelines and the  
NOTE Confidence: 0.9481043

01:17:25.650 --> 01:17:26.150 consensus  
NOTE Confidence: 0.9711341

01:17:26.530 --> 01:17:28.370 from individuals is that no  
NOTE Confidence: 0.9711341

01:17:28.370 --> 01:17:29.810 changes really should be made  
NOTE Confidence: 0.9711341

01:17:29.810 --> 01:17:30.630 at this point



NOTE Confidence: 0.9086638  
01:17:31.090 --> 01:17:32.229 based on GEP,  
NOTE Confidence: 0.86140627  
01:17:33.170 --> 01:17:34.770 high risk versus low risk  
NOTE Confidence: 0.86140627  
01:17:34.770 --> 01:17:35.017 expression.  
NOTE Confidence: 0.8851721  
01:17:39.185 --> 01:17:40.725 Pathologic staging and histologic  
NOTE Confidence: 0.68442476  
01:17:41.345 --> 01:17:41.845 criteria.  
NOTE Confidence: 0.94184434  
01:17:42.305 --> 01:17:43.765 And that should always still  
NOTE Confidence: 0.94184434  
01:17:43.825 --> 01:17:45.665 take precedence over GEP as  
NOTE Confidence: 0.94184434  
01:17:45.665 --> 01:17:47.185 we're trying to learn more  
NOTE Confidence: 0.94184434  
01:17:47.185 --> 01:17:48.805 and gain more data, particularly  
NOTE Confidence: 0.94184434  
01:17:48.865 --> 01:17:50.945 prospective clinical trial data to  
NOTE Confidence: 0.94184434  
01:17:50.945 --> 01:17:52.520 see whether or not long  
NOTE Confidence: 0.94184434  
01:17:52.520 --> 01:17:53.420 term outcomes,  
NOTE Confidence: 0.97335446  
01:17:54.200 --> 01:17:55.100 hold true.  
NOTE Confidence: 0.9457389  
01:17:56.040 --> 01:17:57.640 Now kind of switching gears  
NOTE Confidence: 0.9457389  
01:17:57.640 --> 01:17:59.660 to the squamous cell carcinoma  
NOTE Confidence: 0.9457389

01:17:59.800 --> 01:18:01.400 GEP space, so this is  
NOTE Confidence: 0.9457389

01:18:01.400 --> 01:18:03.240 the CASEL Decision DX for  
NOTE Confidence: 0.9457389

01:18:03.240 --> 01:18:04.460 squamous cell carcinomas.  
NOTE Confidence: 0.8511521

01:18:05.145 --> 01:18:06.445 Now unlike melanomas,  
NOTE Confidence: 0.9995577

01:18:07.224 --> 01:18:07.885 the testing  
NOTE Confidence: 0.8092192

01:18:08.264 --> 01:18:10.364 of in this particular disease  
NOTE Confidence: 0.9749864

01:18:10.905 --> 01:18:13.145 has is more mature compared  
NOTE Confidence: 0.9749864

01:18:13.145 --> 01:18:14.045 to in melanoma.  
NOTE Confidence: 0.9753873

01:18:14.505 --> 01:18:15.645 So this is the forty  
NOTE Confidence: 0.9753873

01:18:15.704 --> 01:18:16.844 GEP panel.  
NOTE Confidence: 0.8110061

01:18:17.570 --> 01:18:18.869 Again, as,  
NOTE Confidence: 0.8938675

01:18:19.570 --> 01:18:21.090 my prior colleagues already has  
NOTE Confidence: 0.8938675

01:18:21.090 --> 01:18:23.010 talked kind of three different  
NOTE Confidence: 0.8938675

01:18:23.010 --> 01:18:25.570 categories, which help to predict  
NOTE Confidence: 0.8938675

01:18:25.570 --> 01:18:27.110 metastasis free survival.  
NOTE Confidence: 0.9942704

01:18:28.130 --> 01:18:29.570 Really kind of the three

NOTE Confidence: 0.9942704  
01:18:29.570 --> 01:18:30.550 year metastasis  
NOTE Confidence: 0.9989864  
01:18:30.929 --> 01:18:31.590 free survival  
NOTE Confidence: 0.9461652  
01:18:32.415 --> 01:18:33.854 is much better in those  
NOTE Confidence: 0.9461652  
01:18:33.854 --> 01:18:34.995 with class one  
NOTE Confidence: 0.95239985  
01:18:35.375 --> 01:18:36.975 at ninety one percent versus  
NOTE Confidence: 0.95239985  
01:18:36.975 --> 01:18:38.495 class IIBs, which are about  
NOTE Confidence: 0.95239985  
01:18:38.495 --> 01:18:39.555 forty four percent.  
NOTE Confidence: 0.80385834  
01:18:40.495 --> 01:18:41.155 And again,  
NOTE Confidence: 0.97138315  
01:18:41.935 --> 01:18:43.854 as Doctor. Roche had mentioned,  
NOTE Confidence: 0.97138315  
01:18:43.854 --> 01:18:45.235 kind of the positive predictive  
NOTE Confidence: 0.97138315  
01:18:45.295 --> 01:18:47.295 value shows improvement over our  
NOTE Confidence: 0.97138315  
01:18:47.295 --> 01:18:47.795 standard  
NOTE Confidence: 0.8321712  
01:18:48.710 --> 01:18:49.210 AGCC  
NOTE Confidence: 0.87790275  
01:18:49.590 --> 01:18:50.550 staging and,  
NOTE Confidence: 0.97979903  
01:18:51.110 --> 01:18:53.030 Brigham and Women's Hospital staging  
NOTE Confidence: 0.97979903

01:18:53.030 --> 01:18:54.410 systems at this point.  
NOTE Confidence: 0.9619137

01:18:54.870 --> 01:18:56.229 So again, it was nice  
NOTE Confidence: 0.9619137

01:18:56.229 --> 01:18:57.910 to see that comparison of  
NOTE Confidence: 0.9619137

01:18:57.910 --> 01:18:58.410 GEP,  
NOTE Confidence: 0.9981979

01:18:59.750 --> 01:19:01.930 versus traditional staging algorithms.  
NOTE Confidence: 0.8886901

01:19:02.615 --> 01:19:04.375 Now the question here also  
NOTE Confidence: 0.8886901

01:19:04.375 --> 01:19:05.415 is, you know, how do  
NOTE Confidence: 0.8886901

01:19:05.415 --> 01:19:07.814 we utilize GEP, the Castle  
NOTE Confidence: 0.8886901

01:19:07.814 --> 01:19:10.055 Bion Science testing for squamous  
NOTE Confidence: 0.8886901

01:19:10.055 --> 01:19:11.735 cell carcinomas to determine whether  
NOTE Confidence: 0.8886901

01:19:11.735 --> 01:19:13.335 or not individuals need adjuvant  
NOTE Confidence: 0.8886901

01:19:13.335 --> 01:19:13.835 therapy?  
NOTE Confidence: 0.995094

01:19:14.935 --> 01:19:16.715 There was actually two recent  
NOTE Confidence: 0.74739397

01:19:17.415 --> 01:19:17.915 updates  
NOTE Confidence: 0.9704809

01:19:18.479 --> 01:19:19.700 over the past year,  
NOTE Confidence: 0.8518392

01:19:20.080 --> 01:19:21.760 C POST and keynote six

NOTE Confidence: 0.8518392  
01:19:21.760 --> 01:19:23.439 thirty, looking at adjuvant anti  
NOTE Confidence: 0.8518392  
01:19:23.439 --> 01:19:24.880 PD-one therapy in these high  
NOTE Confidence: 0.8518392  
01:19:24.880 --> 01:19:25.380 risk  
NOTE Confidence: 0.8285796  
01:19:25.760 --> 01:19:27.200 individuals. So these are high  
NOTE Confidence: 0.8285796  
01:19:27.200 --> 01:19:27.667 risk generally by the MCCN  
NOTE Confidence: 0.8285796  
01:19:27.667 --> 01:19:27.852 criteria. The one utilized for  
NOTE Confidence: 0.8285796  
01:19:27.852 --> 01:19:28.500 C POST is kind of  
NOTE Confidence: 0.75126046  
01:19:29.760 --> 01:19:30.260 listed  
NOTE Confidence: 0.9603317  
01:19:38.594 --> 01:19:40.135 evasion, in transit metastases,  
NOTE Confidence: 0.9771782  
01:19:41.395 --> 01:19:42.695 recurrence, etcetera.  
NOTE Confidence: 0.87435853  
01:19:43.550 --> 01:19:44.750 And so really for C  
NOTE Confidence: 0.87435853  
01:19:44.750 --> 01:19:45.729 post trial,  
NOTE Confidence: 0.9984891  
01:19:46.110 --> 01:19:47.390 they did not report any  
NOTE Confidence: 0.9984891  
01:19:47.390 --> 01:19:48.370 GEP utilization  
NOTE Confidence: 0.79617256  
01:19:48.830 --> 01:19:50.290 nor did keynote sixthirty.  
NOTE Confidence: 0.9659419

01:19:50.910 --> 01:19:52.110 So again, in this phase,  
NOTE Confidence: 0.9659419

01:19:52.110 --> 01:19:53.150 it's kind of hard to  
NOTE Confidence: 0.9659419

01:19:53.150 --> 01:19:55.150 compare the utility of adjuvant  
NOTE Confidence: 0.9659419

01:19:55.150 --> 01:19:55.650 therapy,  
NOTE Confidence: 0.9991098

01:19:56.430 --> 01:19:57.410 at this time.  
NOTE Confidence: 0.85267043

01:19:58.335 --> 01:19:59.455 Now when we look at  
NOTE Confidence: 0.85267043

01:19:59.455 --> 01:19:59.955 surveillance,  
NOTE Confidence: 0.9725311

01:20:00.895 --> 01:20:02.175 we know that in terms  
NOTE Confidence: 0.9725311

01:20:02.175 --> 01:20:03.935 of metastases, the class I  
NOTE Confidence: 0.9725311

01:20:03.935 --> 01:20:05.455 patients had less than ten  
NOTE Confidence: 0.9725311

01:20:05.455 --> 01:20:07.455 percent risk of metastases versus  
NOTE Confidence: 0.9725311

01:20:07.455 --> 01:20:09.555 the class IIb. Those individuals  
NOTE Confidence: 0.9900892

01:20:09.935 --> 01:20:11.215 had a greater than fifty  
NOTE Confidence: 0.9900892

01:20:11.215 --> 01:20:12.595 percent risk of metastases.  
NOTE Confidence: 0.9984567

01:20:13.620 --> 01:20:15.139 So when you have an  
NOTE Confidence: 0.9984567

01:20:15.139 --> 01:20:15.639 AJCC

NOTE Confidence: 0.9274342  
01:20:16.260 --> 01:20:17.880 that's a T3, T4  
NOTE Confidence: 0.8769209  
01:20:19.300 --> 01:20:20.739 or a similar kind of  
NOTE Confidence: 0.8769209  
01:20:20.739 --> 01:20:21.239 T2B,  
NOTE Confidence: 0.83749896  
01:20:21.860 --> 01:20:23.719 T3 and the, BHW  
NOTE Confidence: 0.99166965  
01:20:24.420 --> 01:20:24.920 classification,  
NOTE Confidence: 0.93778485  
01:20:26.245 --> 01:20:28.265 those are always kinda intermediate  
NOTE Confidence: 0.93778485  
01:20:28.325 --> 01:20:30.265 or high risk. It's really  
NOTE Confidence: 0.93778485  
01:20:30.325 --> 01:20:32.005 kinda discerning the T one,  
NOTE Confidence: 0.93778485  
01:20:32.005 --> 01:20:33.525 T twos and the T  
NOTE Confidence: 0.93778485  
01:20:33.525 --> 01:20:34.905 one, T two As,  
NOTE Confidence: 0.92640567  
01:20:36.085 --> 01:20:37.604 that really the class one,  
NOTE Confidence: 0.92640567  
01:20:37.604 --> 01:20:38.805 class two A, class two  
NOTE Confidence: 0.92640567  
01:20:38.805 --> 01:20:40.985 B designation kinda really helps  
NOTE Confidence: 0.97830486  
01:20:41.689 --> 01:20:44.110 to better delineate with granularity  
NOTE Confidence: 0.9851469  
01:20:44.650 --> 01:20:46.250 those individuals that will be  
NOTE Confidence: 0.9851469

01:20:46.250 --> 01:20:47.710 at higher risk for developing  
NOTE Confidence: 0.9851469

01:20:47.850 --> 01:20:49.790 metastatic disease in the future.  
NOTE Confidence: 0.9851469

01:20:50.010 --> 01:20:51.610 And so really, it's kind  
NOTE Confidence: 0.9851469

01:20:51.610 --> 01:20:53.550 of in those individuals where  
NOTE Confidence: 0.9851469

01:20:53.725 --> 01:20:54.465 the discussion about  
NOTE Confidence: 0.9970516

01:20:55.085 --> 01:20:56.785 how do you improve upon  
NOTE Confidence: 0.85652137

01:20:58.045 --> 01:20:59.564 local disease control with the  
NOTE Confidence: 0.85652137

01:20:59.564 --> 01:21:01.025 addition of adjuvant radiation,  
NOTE Confidence: 0.9723699

01:21:01.965 --> 01:21:03.324 as Doctor. Young had alluded  
NOTE Confidence: 0.9723699

01:21:03.324 --> 01:21:04.445 to, that really kind of  
NOTE Confidence: 0.9723699

01:21:04.445 --> 01:21:04.945 makes  
NOTE Confidence: 0.9778277

01:21:05.405 --> 01:21:06.844 a difference in long term  
NOTE Confidence: 0.9778277

01:21:06.844 --> 01:21:07.905 clinical responses.  
NOTE Confidence: 0.97704154

01:21:09.810 --> 01:21:11.270 So when we think about,  
NOTE Confidence: 0.97071755

01:21:11.729 --> 01:21:13.969 surveillance in cutaneous squamous cell  
NOTE Confidence: 0.97071755

01:21:13.969 --> 01:21:15.110 carcinomas too,



NOTE Confidence: 0.9751009  
01:21:15.729 --> 01:21:16.770 this was kind of an  
NOTE Confidence: 0.9751009  
01:21:16.770 --> 01:21:18.949 interesting paradigm that was presented  
NOTE Confidence: 0.9751009  
01:21:19.170 --> 01:21:20.610 by Farberg et al,  
NOTE Confidence: 0.9817447  
01:21:21.090 --> 01:21:22.770 looking at those individuals that  
NOTE Confidence: 0.9817447  
01:21:22.770 --> 01:21:24.975 are classically considered high risk  
NOTE Confidence: 0.9817447  
01:21:25.055 --> 01:21:27.075 for cutaneous squamous cell carcinoma.  
NOTE Confidence: 0.9817447  
01:21:27.135 --> 01:21:29.215 So considering and taking into  
NOTE Confidence: 0.9817447  
01:21:29.215 --> 01:21:31.635 factor the forty GEP expression,  
NOTE Confidence: 0.8924935  
01:21:32.415 --> 01:21:33.615 and then looking at class  
NOTE Confidence: 0.8924935  
01:21:33.615 --> 01:21:35.235 one individuals. In these,  
NOTE Confidence: 0.9975  
01:21:36.015 --> 01:21:38.040 class one groups, we know  
NOTE Confidence: 0.9975  
01:21:38.040 --> 01:21:39.479 that these patients do well  
NOTE Confidence: 0.9975  
01:21:39.479 --> 01:21:39.979 overall  
NOTE Confidence: 0.9880235  
01:21:40.360 --> 01:21:41.260 based on,  
NOTE Confidence: 0.99338096  
01:21:42.760 --> 01:21:44.119 kind of their three year  
NOTE Confidence: 0.99338096

01:21:44.119 --> 01:21:45.900 relapse free survival outcomes.  
NOTE Confidence: 0.96890146

01:21:46.439 --> 01:21:48.219 So if you have someone  
NOTE Confidence: 0.96890146

01:21:48.360 --> 01:21:49.639 who has is a class  
NOTE Confidence: 0.96890146

01:21:49.639 --> 01:21:51.719 one, potentially fifty to sixty  
NOTE Confidence: 0.96890146

01:21:51.719 --> 01:21:53.255 percent of those individuals  
NOTE Confidence: 0.99672765

01:21:53.875 --> 01:21:54.854 could be spared,  
NOTE Confidence: 0.9259147

01:21:55.475 --> 01:21:57.875 additional adjuvant anti PD one  
NOTE Confidence: 0.9259147

01:21:57.875 --> 01:21:58.375 therapy.  
NOTE Confidence: 0.99087274

01:21:58.675 --> 01:22:00.295 So you're minimizing toxicity.  
NOTE Confidence: 0.9599793

01:22:00.755 --> 01:22:01.955 You know these patients are  
NOTE Confidence: 0.9599793

01:22:01.955 --> 01:22:03.175 gonna do well overall.  
NOTE Confidence: 0.9786164

01:22:04.275 --> 01:22:06.180 And so there is more  
NOTE Confidence: 0.9786164

01:22:06.240 --> 01:22:08.160 equipoise than to say, okay,  
NOTE Confidence: 0.9786164

01:22:08.160 --> 01:22:09.920 maybe these individuals don't need  
NOTE Confidence: 0.9786164

01:22:09.920 --> 01:22:11.140 quite as much surveillance,  
NOTE Confidence: 0.95960283

01:22:12.240 --> 01:22:14.580 and don't need standard, scheduled

NOTE Confidence: 0.95960283

01:22:14.640 --> 01:22:15.140 imaging.

NOTE Confidence: 0.9494646

01:22:15.920 --> 01:22:17.439 In those individuals then on

NOTE Confidence: 0.9494646

01:22:17.439 --> 01:22:18.640 the opposite side who have

NOTE Confidence: 0.9494646

01:22:18.640 --> 01:22:20.020 a class 2b signature,

NOTE Confidence: 0.97138304

01:22:20.425 --> 01:22:21.385 those are the ones that

NOTE Confidence: 0.97138304

01:22:21.385 --> 01:22:22.745 you really wanna focus on

NOTE Confidence: 0.97138304

01:22:22.745 --> 01:22:23.405 and maximizing,

NOTE Confidence: 0.98574275

01:22:24.345 --> 01:22:25.564 all the therapies

NOTE Confidence: 0.84991175

01:22:25.945 --> 01:22:26.445 upfront,

NOTE Confidence: 0.9916602

01:22:27.225 --> 01:22:28.285 to try to minimize,

NOTE Confidence: 0.9797325

01:22:28.905 --> 01:22:29.805 distant metastasis,

NOTE Confidence: 0.98542756

01:22:30.585 --> 01:22:31.085 recurrence.

NOTE Confidence: 0.9942581

01:22:31.785 --> 01:22:33.245 And so for these individuals,

NOTE Confidence: 0.95747674

01:22:33.625 --> 01:22:35.805 you wanna consider adjuvant radiation.

NOTE Confidence: 0.895512

01:22:36.720 --> 01:22:38.000 And this is what Doctor.

NOTE Confidence: 0.895512

01:22:38.000 --> 01:22:39.520 Young had already alluded to  
NOTE Confidence: 0.895512

01:22:39.520 --> 01:22:40.660 too with these individuals,  
NOTE Confidence: 0.9563445

01:22:41.360 --> 01:22:42.900 who had adjuvant radiation.  
NOTE Confidence: 0.98469985

01:22:43.440 --> 01:22:45.120 Those individuals had a fifty  
NOTE Confidence: 0.98469985

01:22:45.120 --> 01:22:46.800 percent improvement in five year  
NOTE Confidence: 0.98469985

01:22:46.800 --> 01:22:48.340 metastasis free survival.  
NOTE Confidence: 0.9350266

01:22:48.705 --> 01:22:49.665 And again, this was something  
NOTE Confidence: 0.9350266

01:22:49.665 --> 01:22:50.785 that was not seen in  
NOTE Confidence: 0.9350266

01:22:50.785 --> 01:22:51.905 class one or the class  
NOTE Confidence: 0.9350266

01:22:51.905 --> 01:22:52.405 2a  
NOTE Confidence: 0.7313836

01:22:53.185 --> 01:22:53.685 GPs.  
NOTE Confidence: 0.94275886

01:22:54.385 --> 01:22:56.165 The moderate intensity, obviously,  
NOTE Confidence: 0.9072256

01:22:56.705 --> 01:22:57.925 we consider,  
NOTE Confidence: 0.9964083

01:22:58.865 --> 01:23:00.645 doing all the adjuvant treatments,  
NOTE Confidence: 0.9170172

01:23:01.330 --> 01:23:02.470 the adjuvant radiation,  
NOTE Confidence: 0.8738052

01:23:03.010 --> 01:23:04.330 but at that point too,

NOTE Confidence: 0.8738052  
01:23:04.330 --> 01:23:05.810 it's all you're just also  
NOTE Confidence: 0.8738052  
01:23:05.810 --> 01:23:07.650 equicosed to talk about, kind  
NOTE Confidence: 0.8738052  
01:23:07.650 --> 01:23:09.330 of risk factors and on  
NOTE Confidence: 0.8738052  
01:23:09.330 --> 01:23:11.350 a patient per case basis,  
NOTE Confidence: 0.96897334  
01:23:11.650 --> 01:23:12.770 you know, what are their  
NOTE Confidence: 0.96897334  
01:23:12.770 --> 01:23:14.305 goals, what are their morbidities  
NOTE Confidence: 0.96897334  
01:23:14.445 --> 01:23:15.885 and trying to factor this  
NOTE Confidence: 0.96897334  
01:23:15.885 --> 01:23:17.505 in on a more personalized  
NOTE Confidence: 0.96897334  
01:23:17.725 --> 01:23:18.225 approach.  
NOTE Confidence: 0.9930692  
01:23:19.485 --> 01:23:20.525 So again, kind of the  
NOTE Confidence: 0.9930692  
01:23:20.525 --> 01:23:21.645 summary of all of this  
NOTE Confidence: 0.9930692  
01:23:21.645 --> 01:23:22.785 is that it's complicated.  
NOTE Confidence: 0.9957953  
01:23:23.965 --> 01:23:25.325 There's still a lot that  
NOTE Confidence: 0.9957953  
01:23:25.325 --> 01:23:26.365 we still have yet to  
NOTE Confidence: 0.9957953  
01:23:26.365 --> 01:23:28.385 learn in trying to integrate  
NOTE Confidence: 0.96408576

01:23:28.989 --> 01:23:30.590 these new technologies in our  
NOTE Confidence: 0.96408576

01:23:30.590 --> 01:23:31.489 clinical practice,  
NOTE Confidence: 0.98916775

01:23:32.270 --> 01:23:33.550 a lot of clinical trials  
NOTE Confidence: 0.98916775

01:23:33.550 --> 01:23:34.830 that are forthcoming that may  
NOTE Confidence: 0.98916775

01:23:34.830 --> 01:23:36.270 help to elucidate these,  
NOTE Confidence: 0.95256376

01:23:36.670 --> 01:23:37.810 questions and answers.  
NOTE Confidence: 0.68650293

01:23:39.790 --> 01:23:40.929 But really,  
NOTE Confidence: 0.9851989

01:23:41.469 --> 01:23:42.909 and, you know, trying to  
NOTE Confidence: 0.9851989

01:23:42.909 --> 01:23:44.755 figure out how do we  
NOTE Confidence: 0.9851989

01:23:44.755 --> 01:23:47.335 also then reconcile ctDNA data  
NOTE Confidence: 0.9851989

01:23:47.395 --> 01:23:49.395 with GEP data to best  
NOTE Confidence: 0.9851989

01:23:49.395 --> 01:23:50.695 guide decision making.  
NOTE Confidence: 0.97110504

01:23:51.715 --> 01:23:53.335 You know, there may be  
NOTE Confidence: 0.97110504

01:23:53.475 --> 01:23:53.975 forthcoming  
NOTE Confidence: 0.8050505

01:23:54.755 --> 01:23:55.255 GEP  
NOTE Confidence: 0.92289656

01:23:55.555 --> 01:23:56.835 like two point zero at

NOTE Confidence: 0.92289656  
01:23:56.835 --> 01:23:57.575 some point  
NOTE Confidence: 0.9919668  
01:23:57.880 --> 01:23:59.400 that will also help not  
NOTE Confidence: 0.9919668  
01:23:59.400 --> 01:24:01.320 only look at metastases, local  
NOTE Confidence: 0.9919668  
01:24:01.320 --> 01:24:03.020 recurrence, lymph node positivity,  
NOTE Confidence: 0.9764438  
01:24:03.560 --> 01:24:05.340 but overall survival too.  
NOTE Confidence: 0.9825855  
01:24:06.040 --> 01:24:07.160 And so I know there's  
NOTE Confidence: 0.9825855  
01:24:07.160 --> 01:24:09.400 individuals already working on this  
NOTE Confidence: 0.9825855  
01:24:09.400 --> 01:24:10.140 and emerging  
NOTE Confidence: 0.95196056  
01:24:10.440 --> 01:24:12.620 technologies in this regard too.  
NOTE Confidence: 0.9836533  
01:24:13.604 --> 01:24:14.664 With that, I think  
NOTE Confidence: 0.9931304  
01:24:15.045 --> 01:24:16.344 we are done.  
NOTE Confidence: 0.9465908  
01:24:16.965 --> 01:24:17.465 So,  
NOTE Confidence: 0.98543316  
01:24:18.405 --> 01:24:19.604 let me stop sharing, and  
NOTE Confidence: 0.98543316  
01:24:19.604 --> 01:24:20.564 maybe we can go back  
NOTE Confidence: 0.98543316  
01:24:20.564 --> 01:24:21.764 to the chat if anyone  
NOTE Confidence: 0.98543316

01:24:21.764 --> 01:24:22.744 has any questions.  
NOTE Confidence: 0.817202

01:24:45.594 --> 01:24:46.094 Okay.  
NOTE Confidence: 0.9614346

01:24:49.034 --> 01:24:49.675 We had,  
NOTE Confidence: 0.97177094

01:24:50.554 --> 01:24:52.074 Barb Barbara Johnson had a  
NOTE Confidence: 0.97177094

01:24:52.074 --> 01:24:53.675 question about how long the  
NOTE Confidence: 0.97177094

01:24:53.675 --> 01:24:55.054 assays take to  
NOTE Confidence: 0.8828219

01:24:55.810 --> 01:24:56.870 result to,  
NOTE Confidence: 0.896507

01:24:57.330 --> 01:24:58.150 doctor Christiansen.  
NOTE Confidence: 0.9858322

01:24:58.610 --> 01:24:59.090 Do you have a  
NOTE Confidence: 0.9947289

01:25:00.210 --> 01:25:01.250 you've been using this, I  
NOTE Confidence: 0.9947289

01:25:01.250 --> 01:25:02.550 think, a little bit more.  
NOTE Confidence: 0.9947289

01:25:02.770 --> 01:25:04.130 Yeah. So it's it's usually  
NOTE Confidence: 0.9947289

01:25:04.130 --> 01:25:05.030 about a week  
NOTE Confidence: 0.9925448

01:25:05.410 --> 01:25:07.010 turnaround time, and most of  
NOTE Confidence: 0.9925448

01:25:07.010 --> 01:25:09.505 that is from shipping. So  
NOTE Confidence: 0.98539466

01:25:09.885 --> 01:25:11.505 the the assay is done



NOTE Confidence: 0.93790954  
01:25:11.965 --> 01:25:13.885 on formalum fixed slides from  
NOTE Confidence: 0.93790954  
01:25:13.885 --> 01:25:14.945 the original biopsy,  
NOTE Confidence: 0.99801123  
01:25:15.724 --> 01:25:16.525 and that has to be  
NOTE Confidence: 0.99801123  
01:25:16.525 --> 01:25:17.965 shipped to the company. And  
NOTE Confidence: 0.99801123  
01:25:17.965 --> 01:25:19.085 then once they get it,  
NOTE Confidence: 0.99801123  
01:25:19.085 --> 01:25:19.965 then they can do that  
NOTE Confidence: 0.99801123  
01:25:19.965 --> 01:25:21.005 test within a day or  
NOTE Confidence: 0.99801123  
01:25:21.005 --> 01:25:21.505 so.  
NOTE Confidence: 0.99615246  
01:25:22.360 --> 01:25:23.640 So it's it's just the  
NOTE Confidence: 0.99615246  
01:25:23.640 --> 01:25:25.240 logistics of transferring it that  
NOTE Confidence: 0.99615246  
01:25:25.240 --> 01:25:26.040 takes a little bit of  
NOTE Confidence: 0.99615246  
01:25:26.040 --> 01:25:27.720 time. But since that's done  
NOTE Confidence: 0.99615246  
01:25:27.720 --> 01:25:30.060 on the original diagnostic biopsy,  
NOTE Confidence: 0.99615246  
01:25:30.280 --> 01:25:31.740 that can actually be initiated,  
NOTE Confidence: 0.994789  
01:25:32.680 --> 01:25:33.800 you know, while the patient  
NOTE Confidence: 0.994789

01:25:33.800 --> 01:25:34.840 is getting set up for  
NOTE Confidence: 0.994789

01:25:34.840 --> 01:25:36.460 their consultation and surgery.  
NOTE Confidence: 0.92110854

01:25:40.945 --> 01:25:42.064 I have a question for  
NOTE Confidence: 0.92110854

01:25:42.064 --> 01:25:43.684 doctor Christiansen maybe.  
NOTE Confidence: 0.96717536

01:25:45.264 --> 01:25:47.125 Sure. In terms of these  
NOTE Confidence: 0.96717536

01:25:47.184 --> 01:25:49.104 various assays, there's so many  
NOTE Confidence: 0.96717536

01:25:49.104 --> 01:25:51.184 companies that offer their own  
NOTE Confidence: 0.96717536

01:25:51.184 --> 01:25:51.684 proprietary  
NOTE Confidence: 0.9509034

01:25:52.145 --> 01:25:52.645 assay.  
NOTE Confidence: 0.9915508

01:25:53.830 --> 01:25:55.530 Sometimes tissue is quite precious.  
NOTE Confidence: 0.9915508

01:25:55.590 --> 01:25:57.030 So if you commit to  
NOTE Confidence: 0.9915508

01:25:57.030 --> 01:25:57.530 doing,  
NOTE Confidence: 0.96075684

01:25:58.630 --> 01:25:59.610 you know, formalin  
NOTE Confidence: 0.98582387

01:26:00.390 --> 01:26:02.550 submitting formalin fixed tissue to  
NOTE Confidence: 0.98582387

01:26:02.550 --> 01:26:04.170 a company for one particular  
NOTE Confidence: 0.98582387

01:26:04.229 --> 01:26:05.930 assay, for example, we do

NOTE Confidence: 0.98582387  
01:26:06.070 --> 01:26:07.835 a lot of Natera ctDNA  
NOTE Confidence: 0.98582387  
01:26:08.135 --> 01:26:08.635 monitoring.  
NOTE Confidence: 0.99352765  
01:26:10.055 --> 01:26:11.335 Do any of these companies  
NOTE Confidence: 0.99352765  
01:26:11.335 --> 01:26:12.395 ever work together  
NOTE Confidence: 0.9989667  
01:26:13.094 --> 01:26:13.594 to  
NOTE Confidence: 0.95984775  
01:26:14.295 --> 01:26:15.114 kind of maximize  
NOTE Confidence: 0.9234059  
01:26:15.895 --> 01:26:17.435 the DNA and  
NOTE Confidence: 0.8962195  
01:26:18.375 --> 01:26:19.594 the kind of the RNA  
NOTE Confidence: 0.8962195  
01:26:19.655 --> 01:26:21.575 so that they get as  
NOTE Confidence: 0.8962195  
01:26:21.575 --> 01:26:22.075 much  
NOTE Confidence: 0.9770368  
01:26:22.479 --> 01:26:24.079 out of such little tissue,  
NOTE Confidence: 0.9770368  
01:26:24.079 --> 01:26:25.360 particularly if we're talking about  
NOTE Confidence: 0.9770368  
01:26:25.360 --> 01:26:27.139 trying to prioritize looking at  
NOTE Confidence: 0.9770368  
01:26:27.280 --> 01:26:28.260 comparing ctDNA  
NOTE Confidence: 0.97381413  
01:26:28.560 --> 01:26:30.479 gene expression profiling in some  
NOTE Confidence: 0.97381413

01:26:30.479 --> 01:26:31.520 of these t one, t  
NOTE Confidence: 0.97381413

01:26:31.520 --> 01:26:33.040 two tumors where there's not  
NOTE Confidence: 0.97381413

01:26:33.040 --> 01:26:34.239 gonna be much to begin  
NOTE Confidence: 0.97381413

01:26:34.239 --> 01:26:34.739 with.  
NOTE Confidence: 0.97624373

01:26:36.555 --> 01:26:37.354 So I don't think I  
NOTE Confidence: 0.97624373

01:26:37.354 --> 01:26:38.895 know enough to accurately,  
NOTE Confidence: 0.96492445

01:26:39.195 --> 01:26:40.575 fully answer that question,  
NOTE Confidence: 0.9782506

01:26:40.955 --> 01:26:43.115 but my guess is probably  
NOTE Confidence: 0.9782506

01:26:43.115 --> 01:26:44.475 the answer is no. I  
NOTE Confidence: 0.9782506

01:26:44.475 --> 01:26:45.995 think these companies are all  
NOTE Confidence: 0.9782506

01:26:45.995 --> 01:26:46.495 independent,  
NOTE Confidence: 0.9746799

01:26:47.275 --> 01:26:48.155 and they all do their  
NOTE Confidence: 0.9746799

01:26:48.155 --> 01:26:49.275 own thing. I mean, I  
NOTE Confidence: 0.9746799

01:26:49.275 --> 01:26:50.155 think, you know, you you  
NOTE Confidence: 0.9746799

01:26:50.155 --> 01:26:51.835 presented the idea of using  
NOTE Confidence: 0.9746799

01:26:51.835 --> 01:26:53.349 GEP GEP and ctDNA

NOTE Confidence: 0.98178136

01:26:53.729 --> 01:26:55.329 together in a prospective trial.

NOTE Confidence: 0.98178136

01:26:55.329 --> 01:26:56.530 And if that were going

NOTE Confidence: 0.98178136

01:26:56.530 --> 01:26:57.809 to happen, then, you know,

NOTE Confidence: 0.98178136

01:26:57.809 --> 01:26:58.689 they would have to work

NOTE Confidence: 0.98178136

01:26:58.689 --> 01:26:59.189 together.

NOTE Confidence: 0.9464754

01:27:00.050 --> 01:27:01.010 But I think short of

NOTE Confidence: 0.9464754

01:27:01.010 --> 01:27:03.030 that right now, everybody's independent.

NOTE Confidence: 0.9632113

01:27:05.344 --> 01:27:06.705 I I believe that's that's

NOTE Confidence: 0.9632113

01:27:06.705 --> 01:27:08.304 correct. And and, actually, I

NOTE Confidence: 0.9632113

01:27:08.304 --> 01:27:10.465 believe that the Signatera slash

NOTE Confidence: 0.9632113

01:27:10.465 --> 01:27:12.304 Natera company is working on

NOTE Confidence: 0.9632113

01:27:12.304 --> 01:27:12.965 their own

NOTE Confidence: 0.9932131

01:27:13.425 --> 01:27:13.925 GEP.

NOTE Confidence: 0.979887

01:27:14.545 --> 01:27:15.045 So,

NOTE Confidence: 0.9432562

01:27:15.745 --> 01:27:16.705 and and to the point

NOTE Confidence: 0.9432562

01:27:16.705 --> 01:27:17.525 made earlier,  
NOTE Confidence: 0.99369514

01:27:18.010 --> 01:27:19.689 each one is proprietary. So  
NOTE Confidence: 0.99369514

01:27:19.689 --> 01:27:21.370 there's a reason that the  
NOTE Confidence: 0.99369514

01:27:21.370 --> 01:27:23.550 genes of interest don't overlap  
NOTE Confidence: 0.94536185

01:27:24.330 --> 01:27:26.010 with many of these even  
NOTE Confidence: 0.94536185

01:27:26.010 --> 01:27:27.310 though they're looking at  
NOTE Confidence: 0.9862129

01:27:27.850 --> 01:27:29.689 melanoma, which I always find  
NOTE Confidence: 0.9862129

01:27:29.689 --> 01:27:30.189 fascinating.  
NOTE Confidence: 0.9702662

01:27:30.729 --> 01:27:32.635 And you'll, unfortunately, I don't  
NOTE Confidence: 0.9702662

01:27:32.635 --> 01:27:33.915 know if we'll we'll ever  
NOTE Confidence: 0.9702662

01:27:33.915 --> 01:27:34.715 be able to get head  
NOTE Confidence: 0.9702662

01:27:34.715 --> 01:27:35.375 to head,  
NOTE Confidence: 0.9998584

01:27:36.314 --> 01:27:36.814 comparisons  
NOTE Confidence: 0.9703074

01:27:37.354 --> 01:27:38.795 for these because of the  
NOTE Confidence: 0.9703074

01:27:38.795 --> 01:27:40.235 reason that you said our  
NOTE Confidence: 0.9703074

01:27:40.235 --> 01:27:41.995 melanomas are small and the

NOTE Confidence: 0.9703074

01:27:41.995 --> 01:27:43.755 samples are precious. And,

NOTE Confidence: 0.9841064

01:27:44.475 --> 01:27:45.135 you know,

NOTE Confidence: 0.97101605

01:27:46.590 --> 01:27:48.110 it it'll be very, very

NOTE Confidence: 0.97101605

01:27:48.110 --> 01:27:50.030 interesting. But, again, we never

NOTE Confidence: 0.97101605

01:27:50.030 --> 01:27:52.110 thought companies would cooperate for

NOTE Confidence: 0.97101605

01:27:52.110 --> 01:27:53.950 systemic immune therapy and look

NOTE Confidence: 0.97101605

01:27:53.950 --> 01:27:55.490 where we are now. So

NOTE Confidence: 0.97101605

01:27:55.550 --> 01:27:56.450 I'm I'm hopeful.

NOTE Confidence: 0.86476105

01:28:01.275 --> 01:28:02.875 Maybe the sponsor of Iceman

NOTE Confidence: 0.86476105

01:28:02.875 --> 01:28:04.235 would like to do c

NOTE Confidence: 0.86476105

01:28:04.235 --> 01:28:04.974 two DNA.

NOTE Confidence: 0.9840501

01:28:06.715 --> 01:28:07.454 They might.

NOTE Confidence: 0.9283727

01:28:09.914 --> 01:28:10.795 We'll bring it up at

NOTE Confidence: 0.9283727

01:28:10.795 --> 01:28:12.414 the next investigators meeting.

NOTE Confidence: 0.99846584

01:28:14.770 --> 01:28:16.290 Alright. Well, for all of

NOTE Confidence: 0.99846584

01:28:16.290 --> 01:28:17.890 those folks, I can't believe  
NOTE Confidence: 0.99846584

01:28:17.890 --> 01:28:19.010 how many people have stayed  
NOTE Confidence: 0.99846584

01:28:19.010 --> 01:28:19.989 on the entire  
NOTE Confidence: 0.9878246

01:28:20.290 --> 01:28:21.489 time. So thank you so  
NOTE Confidence: 0.9878246

01:28:21.489 --> 01:28:23.090 much to your audience. Thank  
NOTE Confidence: 0.9878246

01:28:23.090 --> 01:28:25.250 you for questions, and thank  
NOTE Confidence: 0.9878246

01:28:25.250 --> 01:28:26.530 you to my colleagues that  
NOTE Confidence: 0.9878246

01:28:26.530 --> 01:28:27.750 I have the pleasure  
NOTE Confidence: 0.97305524

01:28:28.255 --> 01:28:29.614 to work with every day  
NOTE Confidence: 0.97305524

01:28:29.614 --> 01:28:31.155 and pick their brain about  
NOTE Confidence: 0.97305524

01:28:31.295 --> 01:28:32.435 just about anything.  
NOTE Confidence: 0.99442005

01:28:33.215 --> 01:28:34.915 So thank you to everyone  
NOTE Confidence: 0.9536131

01:28:35.375 --> 01:28:37.375 and, we're all open, very  
NOTE Confidence: 0.9536131

01:28:37.375 --> 01:28:38.995 easy to find via email.  
NOTE Confidence: 0.9536131

01:28:39.148 --> 01:28:40.748 If people had questions that  
NOTE Confidence: 0.9536131

01:28:40.748 --> 01:28:42.188 they come up with, even



NOTE Confidence: 0.9536131

01:28:42.188 --> 01:28:42.988 for those of you who

NOTE Confidence: 0.9536131

01:28:42.988 --> 01:28:44.508 may be later viewing this

NOTE Confidence: 0.9536131

01:28:44.508 --> 01:28:46.108 on YouTube. So thank you

NOTE Confidence: 0.9536131

01:28:46.108 --> 01:28:47.488 and have a wonderful evening.