

WEBVTT

NOTE duration: "01:10:49.770"

NOTE Confidence: 0.9838867

00:00:00.160 --> 00:00:01.439 Welcome, everyone. We have a

NOTE Confidence: 0.9838867

00:00:01.439 --> 00:00:01.939 wonderful

NOTE Confidence: 1

00:00:02.320 --> 00:00:02.820 session

NOTE Confidence: 0.9881836

00:00:03.199 --> 00:00:04.980 where we've decided to group,

NOTE Confidence: 0.99975586

00:00:05.519 --> 00:00:07.460 multiple diseases under one

NOTE Confidence: 0.9432817

00:00:07.839 --> 00:00:10.260 important theme, that being the

NOTE Confidence: 0.9432817

00:00:10.559 --> 00:00:13.184 growing importance of her cutaneous

NOTE Confidence: 0.9432817

00:00:13.405 --> 00:00:13.905 malignancies,

NOTE Confidence: 0.9694214

00:00:14.844 --> 00:00:16.765 giving our patients who seem

NOTE Confidence: 0.9694214

00:00:16.765 --> 00:00:17.585 to have advanced

NOTE Confidence: 1

00:00:18.125 --> 00:00:18.625 disease

NOTE Confidence: 0.914604

00:00:19.325 --> 00:00:21.564 consideration for neoadjuvant treatment. So

NOTE Confidence: 0.914604

00:00:21.564 --> 00:00:23.325 today you'll hear first from

NOTE Confidence: 0.914604

00:00:23.325 --> 00:00:25.425 from doctor Kathleen Souzy about

NOTE Confidence: 0.914604

00:00:25.645 --> 00:00:26.845 the role that she plays
NOTE Confidence: 0.914604

00:00:26.845 --> 00:00:28.340 as a as a highly
NOTE Confidence: 0.914604

00:00:28.340 --> 00:00:30.020 talented Mohs surgeon and seen
NOTE Confidence: 0.914604

00:00:30.020 --> 00:00:31.460 many of these advanced cases
NOTE Confidence: 0.914604

00:00:31.460 --> 00:00:32.600 and setting the stage
NOTE Confidence: 0.99054825

00:00:32.979 --> 00:00:34.680 for our high risk cutaneous
NOTE Confidence: 0.99054825

00:00:34.820 --> 00:00:36.760 squamous cell and really highlighting
NOTE Confidence: 0.99054825

00:00:37.060 --> 00:00:38.600 who those patients are
NOTE Confidence: 0.99501956

00:00:38.900 --> 00:00:40.600 that fit into that category,
NOTE Confidence: 0.9529261

00:00:41.284 --> 00:00:42.165 which can be a little
NOTE Confidence: 0.9529261

00:00:42.165 --> 00:00:44.005 complicated to begin with. And
NOTE Confidence: 0.9529261

00:00:44.005 --> 00:00:45.604 then Doctor. Ansely Roche has
NOTE Confidence: 0.9529261

00:00:45.604 --> 00:00:46.645 joined us as a as
NOTE Confidence: 0.9529261

00:00:46.645 --> 00:00:47.864 a head and neck surgeon,
NOTE Confidence: 0.9529261

00:00:48.085 --> 00:00:49.125 one of our main cancer
NOTE Confidence: 0.9529261

00:00:49.125 --> 00:00:50.325 surgeons here at the Smilow

NOTE Confidence: 0.9529261
00:00:50.325 --> 00:00:50.825 Hospital,
NOTE Confidence: 0.97502255
00:00:51.205 --> 00:00:52.405 to again talk about some
NOTE Confidence: 0.97502255
00:00:52.405 --> 00:00:53.845 of her experience and give
NOTE Confidence: 0.97502255
00:00:53.845 --> 00:00:55.225 us some cases
NOTE Confidence: 0.9461806
00:00:55.525 --> 00:00:56.665 with Doctor. Bhatia
NOTE Confidence: 0.9465332
00:00:57.020 --> 00:00:59.120 then joining us from medical
NOTE Confidence: 0.9465332
00:00:59.180 --> 00:01:00.620 oncology for many of these
NOTE Confidence: 0.9465332
00:01:00.620 --> 00:01:01.600 high risk patients,
NOTE Confidence: 0.9565615
00:01:01.980 --> 00:01:03.420 explaining the role not only
NOTE Confidence: 0.9565615
00:01:03.420 --> 00:01:05.420 of immunotherapy in general, but
NOTE Confidence: 0.9565615
00:01:05.420 --> 00:01:06.799 that in the new adjuvant
NOTE Confidence: 0.9565615
00:01:06.940 --> 00:01:08.479 setting where there's an increasingly
NOTE Confidence: 0.9565615
00:01:08.700 --> 00:01:09.680 important role.
NOTE Confidence: 0.94296736
00:01:10.060 --> 00:01:11.180 And then we have doctor
NOTE Confidence: 0.94296736
00:01:11.180 --> 00:01:12.540 Thuy Tran, who's one of
NOTE Confidence: 0.94296736

00:01:12.540 --> 00:01:12.915 our
NOTE Confidence: 0.9817959

00:01:13.475 --> 00:01:15.475 senior medical oncologists and an
NOTE Confidence: 0.9817959

00:01:15.475 --> 00:01:17.715 expert in cutaneous malignancies, particularly
NOTE Confidence: 0.9817959

00:01:17.715 --> 00:01:18.615 that in melanoma,
NOTE Confidence: 0.9959368

00:01:19.075 --> 00:01:20.694 who will, along with me,
NOTE Confidence: 0.9959368

00:01:20.834 --> 00:01:22.135 take us through our journey
NOTE Confidence: 0.9959368

00:01:22.194 --> 00:01:23.575 of where we've arrived
NOTE Confidence: 0.83081055

00:01:23.955 --> 00:01:24.435 towards,
NOTE Confidence: 0.94420266

00:01:24.755 --> 00:01:25.975 the role of new adjuvant
NOTE Confidence: 0.94420266

00:01:26.115 --> 00:01:28.459 treatment in cutaneous high risk
NOTE Confidence: 0.94420266

00:01:28.459 --> 00:01:28.959 melanoma.
NOTE Confidence: 0.9992676

00:01:29.500 --> 00:01:30.719 So with that, I'll
NOTE Confidence: 0.95440674

00:01:31.100 --> 00:01:32.640 have doctor Susie begin.
NOTE Confidence: 0.9995117

00:01:33.100 --> 00:01:33.600 Sure.
NOTE Confidence: 0.84851074

00:01:34.619 --> 00:01:35.340 I'm just,
NOTE Confidence: 0.9951782

00:01:35.899 --> 00:01:37.679 share my screen here.

NOTE Confidence: 0.92177737

00:01:47.645 --> 00:01:50.065 Hold on. Something happened there.

NOTE Confidence: 0.9973958

00:01:50.925 --> 00:01:51.825 There we go.

NOTE Confidence: 0.9995117

00:01:52.445 --> 00:01:52.945 Okay.

NOTE Confidence: 0.8815511

00:01:53.620 --> 00:01:55.140 Good evening, everyone. My name

NOTE Confidence: 0.8815511

00:01:55.140 --> 00:01:57.720 is Katie Swozzi, and I'm,

NOTE Confidence: 0.8815918

00:01:58.420 --> 00:02:00.520 section chief of dermatologic surgery

NOTE Confidence: 0.96551293

00:02:00.979 --> 00:02:03.000 and specialize in Mohs micrographic

NOTE Confidence: 0.96551293

00:02:03.140 --> 00:02:04.340 surgery. And today, we're gonna

NOTE Confidence: 0.96551293

00:02:04.340 --> 00:02:05.880 talk about high risk cutaneous

NOTE Confidence: 0.96551293

00:02:06.020 --> 00:02:07.159 squamous cell carcinoma.

NOTE Confidence: 0.7722168

00:02:07.460 --> 00:02:07.960 So,

NOTE Confidence: 0.99279785

00:02:08.974 --> 00:02:10.894 why does accurate staging matter?

NOTE Confidence: 0.99279785

00:02:10.894 --> 00:02:12.275 Well, we know that overall,

NOTE Confidence: 0.9674944

00:02:12.655 --> 00:02:14.174 cutaneous SCC has a very

NOTE Confidence: 0.9674944

00:02:14.174 --> 00:02:15.394 favorable prognosis.

NOTE Confidence: 0.9926758

00:02:16.655 --> 00:02:17.555 The incidence
NOTE Confidence: 0.98889804

00:02:17.935 --> 00:02:19.614 is about a million cases
NOTE Confidence: 0.98889804

00:02:19.614 --> 00:02:20.669 a year, so it's a
NOTE Confidence: 0.98889804

00:02:20.669 --> 00:02:22.450 very common tumor. And so
NOTE Confidence: 0.98889804

00:02:22.510 --> 00:02:23.569 the risk of unfavorable
NOTE Confidence: 0.9041341

00:02:23.870 --> 00:02:25.250 outcomes is low,
NOTE Confidence: 0.9989537

00:02:25.950 --> 00:02:27.310 less than five percent for
NOTE Confidence: 0.9989537

00:02:27.310 --> 00:02:28.129 local recurrence,
NOTE Confidence: 0.9739583

00:02:28.430 --> 00:02:29.549 less than four percent for
NOTE Confidence: 0.9739583

00:02:29.549 --> 00:02:31.069 nodal metastasis, and less than
NOTE Confidence: 0.9739583

00:02:31.069 --> 00:02:32.989 three percent for disease specific
NOTE Confidence: 0.9739583

00:02:32.989 --> 00:02:34.625 death. But when you have
NOTE Confidence: 0.9739583

00:02:34.764 --> 00:02:36.285 a tumor that is so
NOTE Confidence: 0.9739583

00:02:36.285 --> 00:02:36.785 common,
NOTE Confidence: 0.9905599

00:02:37.565 --> 00:02:38.445 you know, when we look
NOTE Confidence: 0.9905599

00:02:38.445 --> 00:02:38.764 at,

NOTE Confidence: 0.99424237
00:02:39.245 --> 00:02:41.105 annual estimated deaths with cutaneous
NOTE Confidence: 0.99424237
00:02:41.165 --> 00:02:42.145 squamous cell carcinoma,
NOTE Confidence: 0.99055177
00:02:42.764 --> 00:02:44.685 it's actually greater annually than
NOTE Confidence: 0.99055177
00:02:44.685 --> 00:02:45.965 melanoma. And there is, you
NOTE Confidence: 0.99055177
00:02:45.965 --> 00:02:47.245 know, some overlap with head
NOTE Confidence: 0.99055177
00:02:47.245 --> 00:02:48.705 and neck cancer where sometimes
NOTE Confidence: 0.9900642
00:02:49.010 --> 00:02:50.450 the lines are blurred between,
NOTE Confidence: 0.9900642
00:02:50.450 --> 00:02:51.329 you know, what is a
NOTE Confidence: 0.9900642
00:02:51.329 --> 00:02:51.829 cutaneous,
NOTE Confidence: 0.9689128
00:02:52.290 --> 00:02:53.650 SCC versus a head and
NOTE Confidence: 0.9689128
00:02:53.650 --> 00:02:55.090 neck SCC when we're talking
NOTE Confidence: 0.9689128
00:02:55.090 --> 00:02:55.909 about areas
NOTE Confidence: 0.968192
00:02:56.290 --> 00:02:57.730 like the lip or sometimes
NOTE Confidence: 0.968192
00:02:57.730 --> 00:02:58.469 for tumors,
NOTE Confidence: 0.95092773
00:02:59.010 --> 00:02:59.909 that arise,
NOTE Confidence: 0.9617608

00:03:00.769 --> 00:03:02.370 you know, within the parotid
NOTE Confidence: 0.9617608

00:03:02.370 --> 00:03:04.095 where we're not sure where
NOTE Confidence: 0.9617608

00:03:04.095 --> 00:03:06.194 the original primary was. So,
NOTE Confidence: 0.9617608

00:03:06.254 --> 00:03:07.294 really, the key is how
NOTE Confidence: 0.9617608

00:03:07.294 --> 00:03:08.415 do we predict these bad
NOTE Confidence: 0.9617608

00:03:08.415 --> 00:03:10.254 actors at diagnosis? So I'm
NOTE Confidence: 0.9617608

00:03:10.254 --> 00:03:11.614 gonna start just, with,
NOTE Confidence: 0.9492798

00:03:12.174 --> 00:03:13.855 case I actually shared with
NOTE Confidence: 0.9492798

00:03:13.855 --> 00:03:15.215 doctor Bhatia. So this was
NOTE Confidence: 0.9492798

00:03:15.215 --> 00:03:16.495 a patient who presented with
NOTE Confidence: 0.9492798

00:03:16.495 --> 00:03:17.555 a very routine
NOTE Confidence: 0.9078776

00:03:18.700 --> 00:03:19.200 cutaneous,
NOTE Confidence: 0.8680827

00:03:20.700 --> 00:03:22.139 swim cell carcinoma on the
NOTE Confidence: 0.8680827

00:03:22.139 --> 00:03:22.639 scalp,
NOTE Confidence: 0.9773569

00:03:22.940 --> 00:03:25.020 for Mohs micrographic surgery. So
NOTE Confidence: 0.9773569

00:03:25.020 --> 00:03:26.540 this is something that I'll

NOTE Confidence: 0.9773569
00:03:26.540 --> 00:03:27.660 see in my practice, walk
NOTE Confidence: 0.9773569
00:03:27.660 --> 00:03:29.099 in the door, you know,
NOTE Confidence: 0.9773569
00:03:29.099 --> 00:03:30.220 more than twenty times a
NOTE Confidence: 0.9773569
00:03:30.220 --> 00:03:31.835 week. And so this tumor
NOTE Confidence: 0.9773569
00:03:31.835 --> 00:03:33.135 was less than two centimeters.
NOTE Confidence: 0.9773569
00:03:33.275 --> 00:03:34.955 It was cleared on two
NOTE Confidence: 0.9773569
00:03:34.955 --> 00:03:36.655 stages and repaired linearly.
NOTE Confidence: 0.94628906
00:03:37.755 --> 00:03:38.255 About
NOTE Confidence: 0.98185223
00:03:38.715 --> 00:03:40.335 one month later, the patient
NOTE Confidence: 0.98185223
00:03:40.395 --> 00:03:40.895 presented,
NOTE Confidence: 0.80029297
00:03:41.675 --> 00:03:42.175 with,
NOTE Confidence: 0.97663975
00:03:42.955 --> 00:03:43.915 he called saying that he
NOTE Confidence: 0.97663975
00:03:43.915 --> 00:03:44.795 had a nodule on the
NOTE Confidence: 0.97663975
00:03:44.795 --> 00:03:45.989 scalp, and we thought maybe
NOTE Confidence: 0.97663975
00:03:45.989 --> 00:03:47.269 it was a spitting suture,
NOTE Confidence: 0.97663975

00:03:47.269 --> 00:03:48.629 hadn't come in and saw
NOTE Confidence: 0.97663975

00:03:48.629 --> 00:03:50.069 this. Still thought maybe this
NOTE Confidence: 0.97663975

00:03:50.069 --> 00:03:51.590 was just a suture reaction,
NOTE Confidence: 0.97663975

00:03:51.590 --> 00:03:53.209 but was suspicious enough for
NOTE Confidence: 0.98876953

00:03:53.510 --> 00:03:54.790 a recurrence that the lesion
NOTE Confidence: 0.98876953

00:03:54.790 --> 00:03:55.530 was biopsied.
NOTE Confidence: 0.95735675

00:03:56.230 --> 00:03:57.290 And it showed,
NOTE Confidence: 0.96877444

00:03:57.825 --> 00:03:59.605 and the biopsy confirmed recurrent
NOTE Confidence: 0.96877444

00:03:59.745 --> 00:04:02.245 SCC that was infiltrative histology
NOTE Confidence: 0.99405324

00:04:02.625 --> 00:04:03.825 with a depth of seven
NOTE Confidence: 0.99405324

00:04:03.825 --> 00:04:05.745 point five millimeters. So we'll
NOTE Confidence: 0.99405324

00:04:05.745 --> 00:04:06.785 pause that case for a
NOTE Confidence: 0.99405324

00:04:06.785 --> 00:04:07.825 second, and let's just talk
NOTE Confidence: 0.99405324

00:04:07.825 --> 00:04:09.505 about our staging criteria for
NOTE Confidence: 0.99405324

00:04:09.505 --> 00:04:10.565 cutaneous SCC.
NOTE Confidence: 0.9951172

00:04:11.110 --> 00:04:11.849 So AJCC

NOTE Confidence: 0.9814453
00:04:12.150 --> 00:04:12.550 eight,
NOTE Confidence: 0.995752
00:04:12.950 --> 00:04:14.730 is our current staging criteria,
NOTE Confidence: 0.9554492
00:04:15.430 --> 00:04:16.870 for, tumors of the head
NOTE Confidence: 0.9554492
00:04:16.870 --> 00:04:17.589 and neck. And it is
NOTE Confidence: 0.9554492
00:04:17.589 --> 00:04:18.870 important to note that these
NOTE Confidence: 0.9554492
00:04:18.870 --> 00:04:20.470 staging criteria is specific for,
NOTE Confidence: 0.9554492
00:04:20.870 --> 00:04:22.570 head and neck cutaneous SCC.
NOTE Confidence: 0.9838867
00:04:23.164 --> 00:04:23.485 And,
NOTE Confidence: 0.9204799
00:04:24.044 --> 00:04:25.164 the really, this is a
NOTE Confidence: 0.9204799
00:04:25.164 --> 00:04:25.904 big advancement,
NOTE Confidence: 0.970459
00:04:26.604 --> 00:04:28.145 from AJCC seven,
NOTE Confidence: 0.9869792
00:04:29.245 --> 00:04:30.845 now about, over seven years
NOTE Confidence: 0.9869792
00:04:30.845 --> 00:04:31.345 ago,
NOTE Confidence: 0.99609375
00:04:32.365 --> 00:04:32.865 where
NOTE Confidence: 0.98945314
00:04:33.245 --> 00:04:35.264 the two the tumor criteria
NOTE Confidence: 0.9850006

00:04:35.565 --> 00:04:37.060 moved from not just a
NOTE Confidence: 0.9850006
00:04:37.060 --> 00:04:38.820 designation by size, but also
NOTE Confidence: 0.9850006
00:04:38.820 --> 00:04:40.820 to include other high risk
NOTE Confidence: 0.9850006
00:04:40.820 --> 00:04:41.320 features.
NOTE Confidence: 0.9980469
00:04:41.779 --> 00:04:42.500 So this,
NOTE Confidence: 0.9985962
00:04:43.380 --> 00:04:45.080 t three group now includes,
NOTE Confidence: 0.9985962
00:04:45.380 --> 00:04:46.839 any tumor that has minor
NOTE Confidence: 0.9985962
00:04:46.900 --> 00:04:47.640 bone erosion
NOTE Confidence: 0.98296446
00:04:48.100 --> 00:04:49.720 or perineural invasion
NOTE Confidence: 0.99820966
00:04:50.315 --> 00:04:51.835 or deep invasion. And so
NOTE Confidence: 0.99820966
00:04:51.835 --> 00:04:53.514 deep invasion is defined as
NOTE Confidence: 0.99820966
00:04:53.514 --> 00:04:54.335 beyond subcutaneous
NOTE Confidence: 0.9930827
00:04:54.714 --> 00:04:56.714 fat or greater than six
NOTE Confidence: 0.9930827
00:04:56.714 --> 00:04:58.175 millimeters from the tumor,
NOTE Confidence: 0.97509766
00:04:59.115 --> 00:05:00.475 or from the, base of
NOTE Confidence: 0.97509766
00:05:00.475 --> 00:05:02.555 the adjacent normal epidermis to

NOTE Confidence: 0.97509766
00:05:02.555 --> 00:05:03.535 the base of the tumor.
NOTE Confidence: 0.9573296
00:05:03.860 --> 00:05:05.700 And perineural invasion is defined
NOTE Confidence: 0.9573296
00:05:05.700 --> 00:05:06.200 as,
NOTE Confidence: 0.9753418
00:05:06.980 --> 00:05:08.580 nerve caliber of greater than,
NOTE Confidence: 0.9753418
00:05:08.820 --> 00:05:09.800 point one millimeters
NOTE Confidence: 0.9902181
00:05:10.100 --> 00:05:11.620 or deep nerves below the
NOTE Confidence: 0.9902181
00:05:11.620 --> 00:05:13.779 dermis or radiographic evidence of
NOTE Confidence: 0.9902181
00:05:13.779 --> 00:05:15.400 nerve involvement, which is rare.
NOTE Confidence: 0.9902344
00:05:16.225 --> 00:05:17.045 And so,
NOTE Confidence: 0.97965497
00:05:17.985 --> 00:05:19.025 this really helped,
NOTE Confidence: 0.9784342
00:05:19.665 --> 00:05:20.565 to stratify,
NOTE Confidence: 0.9164632
00:05:21.345 --> 00:05:23.745 risk as in AJCC seven,
NOTE Confidence: 0.9164632
00:05:23.745 --> 00:05:24.065 the,
NOTE Confidence: 0.97663575
00:05:24.625 --> 00:05:26.545 the biggest proportion of poor
NOTE Confidence: 0.97663575
00:05:26.545 --> 00:05:28.230 outcomes occurred in t two,
NOTE Confidence: 0.9977214

00:05:28.630 --> 00:05:29.350 and this was a very
NOTE Confidence: 0.9977214

00:05:29.350 --> 00:05:29.850 heterogeneous
NOTE Confidence: 0.9463588

00:05:30.150 --> 00:05:32.150 group. So now, the greatest
NOTE Confidence: 0.9463588

00:05:32.150 --> 00:05:32.790 proportion of,
NOTE Confidence: 0.9970703

00:05:33.990 --> 00:05:34.730 poor outcomes
NOTE Confidence: 0.95196855

00:05:35.110 --> 00:05:36.550 occurs in t three as
NOTE Confidence: 0.95196855

00:05:36.550 --> 00:05:37.589 t four, you know, which
NOTE Confidence: 0.95196855

00:05:37.589 --> 00:05:39.110 is, gross bone invasion is
NOTE Confidence: 0.95196855

00:05:39.110 --> 00:05:40.970 a relatively restricted group.
NOTE Confidence: 0.93951285

00:05:41.764 --> 00:05:43.464 So the second staging criteria
NOTE Confidence: 0.93951285

00:05:43.605 --> 00:05:44.885 is the Brigham and Women's
NOTE Confidence: 0.93951285

00:05:44.885 --> 00:05:46.665 staging criteria, and this one's,
NOTE Confidence: 0.9992676

00:05:47.205 --> 00:05:48.825 relatively simple and straightforward.
NOTE Confidence: 0.9786865

00:05:49.285 --> 00:05:51.125 It's based, strictly on risk
NOTE Confidence: 0.9786865

00:05:51.125 --> 00:05:52.725 factors. So the risk factors
NOTE Confidence: 0.9786865

00:05:52.725 --> 00:05:54.245 that are considered are tumor

NOTE Confidence: 0.9786865

00:05:54.245 --> 00:05:56.025 size greater than two centimeters,

NOTE Confidence: 0.9637427

00:05:56.689 --> 00:05:59.349 tumor invasion beyond subcutaneous fat,

NOTE Confidence: 0.9637427

00:05:59.569 --> 00:06:01.330 again, perineural invasion with that

NOTE Confidence: 0.9637427

00:06:01.330 --> 00:06:03.009 point one millimeter cutoff, and

NOTE Confidence: 0.9637427

00:06:03.009 --> 00:06:05.889 poorly differentiated histology. So if

NOTE Confidence: 0.9637427

00:06:05.889 --> 00:06:07.250 you have zero risk factors,

NOTE Confidence: 0.9637427

00:06:07.250 --> 00:06:08.849 your t one, one risk

NOTE Confidence: 0.9637427

00:06:08.849 --> 00:06:10.229 factor t two a,

NOTE Confidence: 0.98945755

00:06:10.625 --> 00:06:11.745 two to three risk factors,

NOTE Confidence: 0.98945755

00:06:11.745 --> 00:06:13.505 t two b, and greater

NOTE Confidence: 0.98945755

00:06:13.505 --> 00:06:14.005 than,

NOTE Confidence: 0.9547974

00:06:14.545 --> 00:06:16.225 four risk factors for your,

NOTE Confidence: 0.9547974

00:06:16.465 --> 00:06:18.305 would be, t three. And

NOTE Confidence: 0.9547974

00:06:18.305 --> 00:06:19.345 so when we look at

NOTE Confidence: 0.9547974

00:06:19.345 --> 00:06:21.605 how the staging criteria compare,

NOTE Confidence: 0.97998047

00:06:22.145 --> 00:06:23.285 against each other,
NOTE Confidence: 0.92940027

00:06:24.089 --> 00:06:25.130 so note, Brigham and Women
NOTE Confidence: 0.92940027

00:06:25.130 --> 00:06:25.930 does not have a t
NOTE Confidence: 0.92940027

00:06:25.930 --> 00:06:27.449 four stage, so their t
NOTE Confidence: 0.92940027

00:06:27.449 --> 00:06:28.250 three tracks,
NOTE Confidence: 0.9866821

00:06:28.810 --> 00:06:30.810 along with, t four in
NOTE Confidence: 0.9866821

00:06:30.810 --> 00:06:32.650 AJCC eight. But Brigham and
NOTE Confidence: 0.9866821

00:06:32.650 --> 00:06:33.610 Women does have a little
NOTE Confidence: 0.9866821

00:06:33.610 --> 00:06:34.830 bit of a better differentiation
NOTE Confidence: 0.96456474

00:06:35.130 --> 00:06:36.570 in terms of outcomes here
NOTE Confidence: 0.96456474

00:06:36.570 --> 00:06:38.169 looking at local recurrence and
NOTE Confidence: 0.96456474

00:06:38.169 --> 00:06:40.205 nodal metastasis between the t
NOTE Confidence: 0.96456474

00:06:40.205 --> 00:06:41.165 two a and t two
NOTE Confidence: 0.96456474

00:06:41.165 --> 00:06:41.665 b,
NOTE Confidence: 0.9446479

00:06:42.605 --> 00:06:44.285 categories where, you know, in
NOTE Confidence: 0.9446479

00:06:44.285 --> 00:06:46.145 AJCC eight, those t two

NOTE Confidence: 0.9446479
00:06:46.285 --> 00:06:47.565 and t three still track
NOTE Confidence: 0.9446479
00:06:47.565 --> 00:06:48.705 pretty close together.
NOTE Confidence: 0.9805086
00:06:49.485 --> 00:06:50.365 But, you know, you can
NOTE Confidence: 0.9805086
00:06:50.365 --> 00:06:51.825 see here when we're looking
NOTE Confidence: 0.9805086
00:06:51.870 --> 00:06:53.010 for risk of nodal metastasis,
NOTE Confidence: 0.9805086
00:06:53.229 --> 00:06:54.270 it's, you know, less than
NOTE Confidence: 0.9805086
00:06:54.270 --> 00:06:55.229 ten percent in t two
NOTE Confidence: 0.9805086
00:06:55.229 --> 00:06:56.830 a jumping up to, greater
NOTE Confidence: 0.9805086
00:06:56.830 --> 00:06:57.949 than twenty percent in t
NOTE Confidence: 0.9805086
00:06:57.949 --> 00:06:59.229 two b. So this t
NOTE Confidence: 0.9805086
00:06:59.229 --> 00:07:00.430 two b category is really
NOTE Confidence: 0.9805086
00:07:00.430 --> 00:07:01.630 where our antenna is going
NOTE Confidence: 0.9805086
00:07:01.630 --> 00:07:02.130 up,
NOTE Confidence: 0.9961635
00:07:02.750 --> 00:07:03.790 you know, in terms of,
NOTE Confidence: 0.9961635
00:07:03.790 --> 00:07:04.190 you know,
NOTE Confidence: 0.99819946

00:07:04.985 --> 00:07:06.585 getting imaging for these patients,
NOTE Confidence: 0.99819946

00:07:06.585 --> 00:07:07.805 thinking about coordination
NOTE Confidence: 0.95043945

00:07:08.264 --> 00:07:08.585 for,
NOTE Confidence: 0.9980469

00:07:10.105 --> 00:07:11.325 recommendations for
NOTE Confidence: 0.9742025

00:07:11.705 --> 00:07:12.685 adjuvant radiation,
NOTE Confidence: 0.9710829

00:07:13.465 --> 00:07:14.825 or, you know, getting our
NOTE Confidence: 0.9710829

00:07:14.825 --> 00:07:16.365 other colleagues on board.
NOTE Confidence: 0.97579783

00:07:17.160 --> 00:07:18.120 But this is based at
NOTE Confidence: 0.97579783

00:07:18.120 --> 00:07:19.320 staging on biopsy, and I
NOTE Confidence: 0.97579783

00:07:19.320 --> 00:07:21.020 think that's really important because
NOTE Confidence: 0.97579783

00:07:21.320 --> 00:07:22.600 when we look at depth
NOTE Confidence: 0.97579783

00:07:22.600 --> 00:07:23.800 of invasion, this is not
NOTE Confidence: 0.97579783

00:07:23.800 --> 00:07:25.240 always gonna be reported. And
NOTE Confidence: 0.97579783

00:07:25.240 --> 00:07:26.200 sometimes we don't know the
NOTE Confidence: 0.97579783

00:07:26.200 --> 00:07:27.320 depth of invasion just on
NOTE Confidence: 0.97579783

00:07:27.320 --> 00:07:28.680 the biopsy alone because we're

NOTE Confidence: 0.97579783

00:07:28.680 --> 00:07:30.140 taking superficial shapes.

NOTE Confidence: 0.95532227

00:07:30.760 --> 00:07:30.920 So,

NOTE Confidence: 0.95598495

00:07:31.785 --> 00:07:33.145 you know, going back to

NOTE Confidence: 0.95598495

00:07:33.145 --> 00:07:34.585 our patient, if we put

NOTE Confidence: 0.95598495

00:07:34.585 --> 00:07:35.805 him in staging criteria,

NOTE Confidence: 0.98128253

00:07:36.585 --> 00:07:38.185 he would fit, t three

NOTE Confidence: 0.98128253

00:07:38.185 --> 00:07:39.145 based on that depth of

NOTE Confidence: 0.98128253

00:07:39.145 --> 00:07:40.585 invasion of seven point five

NOTE Confidence: 0.98128253

00:07:40.585 --> 00:07:41.085 millimeters.

NOTE Confidence: 0.9838603

00:07:41.625 --> 00:07:42.985 But with Brigham and Women,

NOTE Confidence: 0.9838603

00:07:42.985 --> 00:07:43.945 he'd be t two a.

NOTE Confidence: 0.9838603

00:07:43.945 --> 00:07:44.985 He really only had that

NOTE Confidence: 0.9838603

00:07:44.985 --> 00:07:46.169 one risk factor of depth.

NOTE Confidence: 0.9838603

00:07:46.169 --> 00:07:47.050 So you can see here

NOTE Confidence: 0.9838603

00:07:47.050 --> 00:07:48.729 that there's still discrepancy between

NOTE Confidence: 0.9838603

00:07:48.729 --> 00:07:50.090 our staging systems, and we're
NOTE Confidence: 0.9838603

00:07:50.090 --> 00:07:50.750 not always
NOTE Confidence: 0.9917457

00:07:51.210 --> 00:07:52.410 able to put our patients,
NOTE Confidence: 0.9917457

00:07:52.410 --> 00:07:53.530 you know, in in one
NOTE Confidence: 0.9917457

00:07:53.530 --> 00:07:55.770 box. And so in addition
NOTE Confidence: 0.9917457

00:07:55.770 --> 00:07:57.770 to so staging criteria take
NOTE Confidence: 0.9917457

00:07:57.770 --> 00:08:00.135 into account tumor factors only,
NOTE Confidence: 0.9917457

00:08:00.135 --> 00:08:01.335 but we know that patient
NOTE Confidence: 0.9917457

00:08:01.335 --> 00:08:03.415 factors are highly important when
NOTE Confidence: 0.9917457

00:08:03.415 --> 00:08:05.415 we're stratifying high risk squamous.
NOTE Confidence: 0.9917457

00:08:05.415 --> 00:08:06.155 And so,
NOTE Confidence: 0.99902344

00:08:06.775 --> 00:08:07.675 things here,
NOTE Confidence: 0.97394353

00:08:08.055 --> 00:08:09.975 like lesions, you know, off
NOTE Confidence: 0.97394353

00:08:09.975 --> 00:08:10.855 the head and neck, which
NOTE Confidence: 0.97394353

00:08:10.855 --> 00:08:11.355 AJCC
NOTE Confidence: 0.9532471

00:08:11.840 --> 00:08:13.600 eight does not, take into

NOTE Confidence: 0.9532471
00:08:13.600 --> 00:08:14.100 account.
NOTE Confidence: 0.8631999
00:08:14.720 --> 00:08:16.260 But also is the lesion
NOTE Confidence: 0.8631999
00:08:16.480 --> 00:08:16.980 recurrent?
NOTE Confidence: 0.99833983
00:08:17.440 --> 00:08:18.660 Is the patient immunosuppressed?
NOTE Confidence: 0.96014404
00:08:18.960 --> 00:08:20.160 This is a a key,
NOTE Confidence: 0.96014404
00:08:20.400 --> 00:08:21.620 patient risk factor.
NOTE Confidence: 0.92583007
00:08:22.240 --> 00:08:23.760 You know, sites of prior
NOTE Confidence: 0.92583007
00:08:23.760 --> 00:08:25.940 radiation, a rapidly growing tumor,
NOTE Confidence: 0.907284
00:08:27.264 --> 00:08:28.865 also important, but not taking
NOTE Confidence: 0.907284
00:08:28.865 --> 00:08:30.224 into account and staging criteria.
NOTE Confidence: 0.907284
00:08:30.224 --> 00:08:31.104 And we're thinking back to
NOTE Confidence: 0.907284
00:08:31.104 --> 00:08:31.764 this patient.
NOTE Confidence: 0.981369
00:08:32.145 --> 00:08:33.985 He's hitting these categories as
NOTE Confidence: 0.981369
00:08:33.985 --> 00:08:35.024 well as that depth of
NOTE Confidence: 0.981369
00:08:35.024 --> 00:08:36.625 invasion. So by eight by
NOTE Confidence: 0.981369

00:08:36.625 --> 00:08:37.125 NCCN,
NOTE Confidence: 0.99971515

00:08:37.825 --> 00:08:38.705 this patient would be in
NOTE Confidence: 0.99971515

00:08:38.705 --> 00:08:40.005 a very high risk category.
NOTE Confidence: 0.99971515

00:08:40.145 --> 00:08:40.804 In addition,
NOTE Confidence: 0.94965273

00:08:41.470 --> 00:08:42.690 you may give him immunosuppression
NOTE Confidence: 0.94965273

00:08:42.990 --> 00:08:44.030 too because of history of
NOTE Confidence: 0.94965273

00:08:44.030 --> 00:08:45.090 follicular lymphoma.
NOTE Confidence: 0.98102003

00:08:46.030 --> 00:08:47.950 So, and this histology question
NOTE Confidence: 0.98102003

00:08:47.950 --> 00:08:49.550 is also important because, you
NOTE Confidence: 0.98102003

00:08:49.550 --> 00:08:51.570 know, really, that poorly differentiated
NOTE Confidence: 0.98102003

00:08:51.790 --> 00:08:53.150 histology is the only risk
NOTE Confidence: 0.98102003

00:08:53.150 --> 00:08:54.429 factor that counts, but there
NOTE Confidence: 0.98102003

00:08:54.429 --> 00:08:55.730 are other high risk subtypes
NOTE Confidence: 0.98102003

00:08:55.790 --> 00:08:57.804 of cutaneous SCC. So when
NOTE Confidence: 0.98102003

00:08:57.804 --> 00:09:00.045 I see infiltrative histology, again,
NOTE Confidence: 0.98102003

00:09:00.045 --> 00:09:01.485 my antenna is up that

NOTE Confidence: 0.98102003
00:09:01.485 --> 00:09:02.605 this is a high risk,
NOTE Confidence: 0.98102003
00:09:02.925 --> 00:09:04.145 tumor even if
NOTE Confidence: 0.94297284
00:09:04.525 --> 00:09:06.065 it's not upstaging them,
NOTE Confidence: 1
00:09:06.525 --> 00:09:07.665 based on that criteria.
NOTE Confidence: 0.9399298
00:09:09.290 --> 00:09:11.210 So, here, I just wanted
NOTE Confidence: 0.9399298
00:09:11.210 --> 00:09:12.890 to show the, frozen section
NOTE Confidence: 0.9399298
00:09:12.890 --> 00:09:14.429 histology from this patient's,
NOTE Confidence: 0.9683258
00:09:14.970 --> 00:09:16.490 MOSE surgery, and you could
NOTE Confidence: 0.9683258
00:09:16.490 --> 00:09:17.690 see this was, on the
NOTE Confidence: 0.9683258
00:09:17.690 --> 00:09:18.970 second MOSE when he came
NOTE Confidence: 0.9683258
00:09:18.970 --> 00:09:20.490 back for that recurrence. And
NOTE Confidence: 0.9683258
00:09:20.490 --> 00:09:21.370 here, you can see that
NOTE Confidence: 0.9683258
00:09:21.370 --> 00:09:22.730 this tumor is set down
NOTE Confidence: 0.9683258
00:09:22.730 --> 00:09:23.710 below the subcutaneous
NOTE Confidence: 0.91503906
00:09:24.090 --> 00:09:24.590 fat,
NOTE Confidence: 0.92281085

00:09:25.765 --> 00:09:27.385 in the galea here,
NOTE Confidence: 0.9488231

00:09:27.845 --> 00:09:29.125 and the muscular layer of
NOTE Confidence: 0.9488231

00:09:29.125 --> 00:09:30.325 the scalp. And when we
NOTE Confidence: 0.9488231

00:09:30.325 --> 00:09:31.365 look up close, you can
NOTE Confidence: 0.9488231

00:09:31.365 --> 00:09:32.725 see, this I would call
NOTE Confidence: 0.9488231

00:09:32.725 --> 00:09:34.885 poorly differentiated histology with the
NOTE Confidence: 0.9488231

00:09:34.885 --> 00:09:36.825 high, nuclear to cytoplasmic
NOTE Confidence: 0.9684245

00:09:37.205 --> 00:09:38.804 ratio and almost forming these,
NOTE Confidence: 0.9684245

00:09:38.804 --> 00:09:40.769 like, pseudo glandular like structures
NOTE Confidence: 0.9684245

00:09:40.769 --> 00:09:43.190 and clearly losing, its differentiation
NOTE Confidence: 0.9995117

00:09:43.570 --> 00:09:44.070 pattern.
NOTE Confidence: 0.99853516

00:09:45.089 --> 00:09:45.589 So,
NOTE Confidence: 0.998291

00:09:46.290 --> 00:09:47.269 you know, this patient,
NOTE Confidence: 0.89948916

00:09:47.730 --> 00:09:49.009 after the second mose, again,
NOTE Confidence: 0.89948916

00:09:49.009 --> 00:09:51.009 repaired linearly, and then within
NOTE Confidence: 0.89948916

00:09:51.009 --> 00:09:52.389 weeks presented again,

NOTE Confidence: 0.99121094
00:09:53.009 --> 00:09:53.509 with
NOTE Confidence: 0.96747625
00:09:53.865 --> 00:09:55.065 nodules here. And at this
NOTE Confidence: 0.96747625
00:09:55.065 --> 00:09:56.184 point here where you're seeing
NOTE Confidence: 0.96747625
00:09:56.184 --> 00:09:57.625 nodule along the scar line,
NOTE Confidence: 0.96747625
00:09:57.625 --> 00:09:58.745 but then outside the scar
NOTE Confidence: 0.96747625
00:09:58.745 --> 00:10:00.025 line, this is,
NOTE Confidence: 0.92677414
00:10:01.065 --> 00:10:03.304 a clinical representation of satellite
NOTE Confidence: 0.92677414
00:10:03.304 --> 00:10:05.165 ptosis or in transit METs.
NOTE Confidence: 0.9975586
00:10:06.105 --> 00:10:06.845 And so
NOTE Confidence: 0.98245883
00:10:07.910 --> 00:10:09.830 for satellite ptosis, you know,
NOTE Confidence: 0.98245883
00:10:09.830 --> 00:10:11.350 here, this is really where
NOTE Confidence: 0.98245883
00:10:11.350 --> 00:10:11.850 multidisciplinary
NOTE Confidence: 0.98030597
00:10:12.390 --> 00:10:13.690 discussion is important.
NOTE Confidence: 0.9975586
00:10:14.710 --> 00:10:16.250 And, you know, for operable
NOTE Confidence: 0.9975586
00:10:16.309 --> 00:10:16.809 disease,
NOTE Confidence: 0.96505433

00:10:17.270 --> 00:10:18.230 where you really feel like
NOTE Confidence: 0.96505433

00:10:18.230 --> 00:10:19.510 those in transit METs are
NOTE Confidence: 0.96505433

00:10:19.510 --> 00:10:20.950 still contained within a region
NOTE Confidence: 0.96505433

00:10:20.950 --> 00:10:22.390 where wide local excision is
NOTE Confidence: 0.96505433

00:10:22.390 --> 00:10:23.815 an option, Here's where you
NOTE Confidence: 0.96505433

00:10:23.815 --> 00:10:25.434 may be considering the adjuvant
NOTE Confidence: 0.96505433

00:10:25.575 --> 00:10:27.415 therapy, and, I'm sure we're
NOTE Confidence: 0.96505433

00:10:27.415 --> 00:10:28.795 gonna talk about this later,
NOTE Confidence: 0.9477088

00:10:29.175 --> 00:10:31.175 versus for unresectable disease where
NOTE Confidence: 0.9477088

00:10:31.175 --> 00:10:32.615 really then you're looking into
NOTE Confidence: 0.9477088

00:10:32.615 --> 00:10:34.214 systemic options. And so here
NOTE Confidence: 0.9477088

00:10:34.214 --> 00:10:35.115 was this patient,
NOTE Confidence: 0.98750573

00:10:35.760 --> 00:10:37.040 While we were discussing what
NOTE Confidence: 0.98750573

00:10:37.040 --> 00:10:37.920 to do with him, this
NOTE Confidence: 0.98750573

00:10:37.920 --> 00:10:39.780 is how his tumor exploded
NOTE Confidence: 0.98750573

00:10:39.920 --> 00:10:40.740 really within,

NOTE Confidence: 0.9996745
00:10:41.280 --> 00:10:42.100 you know, within
NOTE Confidence: 0.7592163
00:10:42.560 --> 00:10:43.860 a couple weeks' time.
NOTE Confidence: 0.9959358
00:10:45.760 --> 00:10:46.720 So I just wanted to
NOTE Confidence: 0.9959358
00:10:46.720 --> 00:10:47.680 put in a plug for,
NOTE Confidence: 0.9959358
00:10:48.080 --> 00:10:50.160 this risk calculator. So this
NOTE Confidence: 0.9959358
00:10:50.160 --> 00:10:50.820 was developed
NOTE Confidence: 0.95177114
00:10:51.404 --> 00:10:52.625 by some of my colleagues
NOTE Confidence: 0.95177114
00:10:52.684 --> 00:10:54.205 in the Mose College, in
NOTE Confidence: 0.95177114
00:10:54.205 --> 00:10:54.705 conjunction
NOTE Confidence: 0.96798706
00:10:55.325 --> 00:10:57.005 with, colleagues in head and
NOTE Confidence: 0.96798706
00:10:57.005 --> 00:10:58.285 neck surgery and,
NOTE Confidence: 0.9783325
00:10:58.925 --> 00:11:00.065 radiation oncology,
NOTE Confidence: 0.89923966
00:11:01.005 --> 00:11:01.964 and med onc as well,
NOTE Confidence: 0.89923966
00:11:01.964 --> 00:11:02.545 I believe.
NOTE Confidence: 0.9909668
00:11:03.005 --> 00:11:04.865 And this, was just published
NOTE Confidence: 0.9909668

00:11:05.165 --> 00:11:05.665 in
NOTE Confidence: 0.8866781

00:11:06.770 --> 00:11:07.670 JAMA Dermatology
NOTE Confidence: 0.8898926

00:11:08.290 --> 00:11:08.770 in,
NOTE Confidence: 0.99890137

00:11:09.970 --> 00:11:11.350 February of this year.
NOTE Confidence: 0.96215045

00:11:12.050 --> 00:11:13.490 The QR codes here, if
NOTE Confidence: 0.96215045

00:11:13.490 --> 00:11:14.450 you wanna download it, it's
NOTE Confidence: 0.96215045

00:11:14.450 --> 00:11:15.330 an app, and it's really
NOTE Confidence: 0.96215045

00:11:15.330 --> 00:11:16.610 nice because it takes into
NOTE Confidence: 0.96215045

00:11:16.610 --> 00:11:18.610 account the staging criteria that
NOTE Confidence: 0.96215045

00:11:18.610 --> 00:11:19.894 I just just reviewed as
NOTE Confidence: 0.96215045

00:11:19.894 --> 00:11:21.095 well as many of the
NOTE Confidence: 0.96215045

00:11:21.095 --> 00:11:22.135 features that are in the
NOTE Confidence: 0.96215045

00:11:22.135 --> 00:11:23.355 NCCN guidelines
NOTE Confidence: 0.967041

00:11:24.135 --> 00:11:25.415 to, to,
NOTE Confidence: 1

00:11:25.894 --> 00:11:27.035 give you personalized
NOTE Confidence: 0.979934

00:11:27.495 --> 00:11:29.014 risk profiles for your patient.

NOTE Confidence: 0.979934
00:11:29.014 --> 00:11:30.135 So I think it's really
NOTE Confidence: 0.979934
00:11:30.135 --> 00:11:31.574 easy to use for anyone
NOTE Confidence: 0.979934
00:11:31.574 --> 00:11:32.454 to have on their phone,
NOTE Confidence: 0.979934
00:11:32.454 --> 00:11:32.855 and,
NOTE Confidence: 0.96186525
00:11:33.654 --> 00:11:35.170 I've found it very helpful.
NOTE Confidence: 0.96186525
00:11:35.170 --> 00:11:37.089 And the initial, data on
NOTE Confidence: 0.96186525
00:11:37.089 --> 00:11:39.029 this very large cohort multi
NOTE Confidence: 0.8430176
00:11:39.330 --> 00:11:40.149 multi institutional
NOTE Confidence: 0.9296875
00:11:40.450 --> 00:11:42.290 cohort shows that actually the
NOTE Confidence: 0.9296875
00:11:42.290 --> 00:11:42.790 predictive,
NOTE Confidence: 0.99088544
00:11:45.089 --> 00:11:46.230 the predictive ability,
NOTE Confidence: 0.93662107
00:11:46.610 --> 00:11:49.269 outperforms either staging criteria alone.
NOTE Confidence: 0.99321055
00:11:50.895 --> 00:11:52.015 So that's what I wanted
NOTE Confidence: 0.99321055
00:11:52.015 --> 00:11:53.615 to talk about. So now
NOTE Confidence: 0.99321055
00:11:53.615 --> 00:11:55.475 I'm gonna turn it over
NOTE Confidence: 0.99321055

00:11:55.535 --> 00:11:57.295 to doctor Badia. Is that
NOTE Confidence: 0.99321055
00:11:57.295 --> 00:11:57.795 right?
NOTE Confidence: 1
00:11:59.054 --> 00:12:00.835 Let me stop my share.
NOTE Confidence: 0.96287626
00:12:04.610 --> 00:12:05.809 I wasn't sure if doctor
NOTE Confidence: 0.96287626
00:12:05.809 --> 00:12:07.090 Roche was going next. Oh,
NOTE Confidence: 0.96287626
00:12:07.090 --> 00:12:09.090 sorry. Doctor Roche. I'm sorry.
NOTE Confidence: 0.96287626
00:12:09.090 --> 00:12:09.830 I missed.
NOTE Confidence: 0.9992327
00:12:10.770 --> 00:12:12.929 All good. All good. Alright.
NOTE Confidence: 0.9992327
00:12:12.929 --> 00:12:13.830 Let's see.
NOTE Confidence: 0.9829799
00:12:14.929 --> 00:12:16.050 Alright. I will share my
NOTE Confidence: 0.9829799
00:12:16.050 --> 00:12:16.950 slides now.
NOTE Confidence: 0.99560547
00:12:18.050 --> 00:12:18.550 Okay.
NOTE Confidence: 0.92285156
00:12:20.665 --> 00:12:22.665 Great. Can set you guys
NOTE Confidence: 0.92285156
00:12:22.665 --> 00:12:23.644 can see my slides?
NOTE Confidence: 0.998291
00:12:24.345 --> 00:12:25.565 Great. Okay.
NOTE Confidence: 0.94602966
00:12:26.105 --> 00:12:27.304 So I'm Ansley Roche. I'm

NOTE Confidence: 0.94602966
00:12:27.304 --> 00:12:28.125 a head, neck,
NOTE Confidence: 0.95305526
00:12:28.584 --> 00:12:30.264 cancer and reconstructive surgeon here
NOTE Confidence: 0.95305526
00:12:30.264 --> 00:12:30.925 at Yale.
NOTE Confidence: 0.9770508
00:12:31.304 --> 00:12:31.804 I
NOTE Confidence: 0.94244874
00:12:32.700 --> 00:12:33.740 take care of patients with
NOTE Confidence: 0.94244874
00:12:33.740 --> 00:12:35.100 cancers of the oral cavity,
NOTE Confidence: 0.94244874
00:12:35.100 --> 00:12:36.640 oral pharynx, the upper airdigestive
NOTE Confidence: 0.94244874
00:12:36.780 --> 00:12:38.480 tract, but also cutaneous malignancies,
NOTE Confidence: 0.945421
00:12:40.620 --> 00:12:41.900 salivary gland tumors.
NOTE Confidence: 0.97504133
00:12:42.300 --> 00:12:43.500 So I'll be talking about
NOTE Confidence: 0.97504133
00:12:43.500 --> 00:12:45.020 sort of the clinical some
NOTE Confidence: 0.97504133
00:12:45.020 --> 00:12:45.679 of the clinical,
NOTE Confidence: 0.9609375
00:12:46.300 --> 00:12:47.520 scenarios that we,
NOTE Confidence: 0.92389786
00:12:48.154 --> 00:12:49.754 come run into and the
NOTE Confidence: 0.92389786
00:12:49.754 --> 00:12:50.574 role of,
NOTE Confidence: 0.98774415

00:12:51.035 --> 00:12:53.214 neoadjuvant treatment for these patients.

NOTE Confidence: 0.9719336

00:12:53.915 --> 00:12:54.954 So I'll present a case

NOTE Confidence: 0.9719336

00:12:54.954 --> 00:12:56.074 and then I'll just discuss

NOTE Confidence: 0.9719336

00:12:56.074 --> 00:12:57.694 sort of the basis for

NOTE Confidence: 0.9719336

00:12:57.754 --> 00:12:59.355 how these how this treatment

NOTE Confidence: 0.9719336

00:12:59.355 --> 00:13:00.654 sort of came to be,

NOTE Confidence: 0.9849121

00:13:00.959 --> 00:13:02.800 generally quite well accepted for

NOTE Confidence: 0.9849121

00:13:02.800 --> 00:13:04.100 head and neck cancer patients.

NOTE Confidence: 0.9901678

00:13:05.040 --> 00:13:06.800 Let me there we go.

NOTE Confidence: 0.9901678

00:13:06.800 --> 00:13:08.240 Okay. So this is a

NOTE Confidence: 0.9901678

00:13:08.240 --> 00:13:08.740 patient,

NOTE Confidence: 0.7753906

00:13:09.360 --> 00:13:09.860 AR,

NOTE Confidence: 0.97908527

00:13:10.639 --> 00:13:11.600 I saw about a year

NOTE Confidence: 0.97908527

00:13:11.600 --> 00:13:12.420 and a half ago.

NOTE Confidence: 0.9831744

00:13:12.800 --> 00:13:14.865 Fairly sick gentleman, older, eighty

NOTE Confidence: 0.9831744

00:13:14.865 --> 00:13:16.385 six year old, with a

NOTE Confidence: 0.9831744

00:13:16.385 --> 00:13:18.385 pacemaker on eliquis, congestive heart

NOTE Confidence: 0.9831744

00:13:18.385 --> 00:13:20.865 failure, multiple medical comorbidities, had

NOTE Confidence: 0.9831744

00:13:20.865 --> 00:13:23.105 had multiple cutaneous malignancies, all

NOTE Confidence: 0.9831744

00:13:23.105 --> 00:13:25.024 basal cell, carcinoma of the

NOTE Confidence: 0.9831744

00:13:25.024 --> 00:13:25.524 torso,

NOTE Confidence: 0.9620019

00:13:26.145 --> 00:13:27.584 that were excised with Mose

NOTE Confidence: 0.9620019

00:13:27.584 --> 00:13:28.785 who developed the sort of

NOTE Confidence: 0.9620019

00:13:28.785 --> 00:13:30.660 rapidly growing mass in the

NOTE Confidence: 0.9620019

00:13:30.660 --> 00:13:32.740 left preauricular area, had been

NOTE Confidence: 0.9620019

00:13:32.740 --> 00:13:33.779 present for just a couple

NOTE Confidence: 0.9620019

00:13:33.779 --> 00:13:34.820 of months and just kept

NOTE Confidence: 0.9620019

00:13:34.820 --> 00:13:36.179 increasing in size sort of

NOTE Confidence: 0.9620019

00:13:36.179 --> 00:13:36.899 by the day,

NOTE Confidence: 0.9835675

00:13:37.459 --> 00:13:38.019 right in front of the

NOTE Confidence: 0.9835675

00:13:38.019 --> 00:13:39.059 family's eyes. They were quite

NOTE Confidence: 0.9835675

00:13:39.059 --> 00:13:40.500 troubled by it. So he
NOTE Confidence: 0.9835675

00:13:40.500 --> 00:13:41.779 had a biopsy of this,
NOTE Confidence: 0.9835675

00:13:41.779 --> 00:13:43.300 and it demonstrated squamous cell
NOTE Confidence: 0.9835675

00:13:43.300 --> 00:13:43.800 carcinoma.
NOTE Confidence: 0.9493408

00:13:45.915 --> 00:13:47.774 Of note on physical exam,
NOTE Confidence: 0.9493408

00:13:47.834 --> 00:13:48.235 his,
NOTE Confidence: 0.97088856

00:13:48.875 --> 00:13:51.194 facial nerve, was fully intact
NOTE Confidence: 0.97088856

00:13:51.194 --> 00:13:52.875 and really no other kind
NOTE Confidence: 0.97088856

00:13:52.875 --> 00:13:54.795 of significant findings, no cervical
NOTE Confidence: 0.97088856

00:13:54.795 --> 00:13:56.255 lymphadenopathy on exam.
NOTE Confidence: 0.96118164

00:13:57.610 --> 00:13:58.910 Cross sectional imaging,
NOTE Confidence: 0.9781669

00:13:59.529 --> 00:14:00.890 she can see this left
NOTE Confidence: 0.9781669

00:14:00.890 --> 00:14:02.190 preauricular lesion,
NOTE Confidence: 0.9883147

00:14:03.209 --> 00:14:05.370 two two sections here. This
NOTE Confidence: 0.9883147

00:14:05.370 --> 00:14:06.250 first one on the left,
NOTE Confidence: 0.9883147

00:14:06.250 --> 00:14:07.050 you can see it's, you

NOTE Confidence: 0.9883147
00:14:07.050 --> 00:14:08.110 know, superficial,
NOTE Confidence: 0.9822022
00:14:08.804 --> 00:14:10.085 the superficial extent of it.
NOTE Confidence: 0.9822022
00:14:10.085 --> 00:14:10.965 And then on the right,
NOTE Confidence: 0.9822022
00:14:10.965 --> 00:14:11.845 you can see that there
NOTE Confidence: 0.9822022
00:14:11.845 --> 00:14:13.545 is this sort of projection,
NOTE Confidence: 0.9922241
00:14:14.165 --> 00:14:15.365 of tumor heading into the
NOTE Confidence: 0.9922241
00:14:15.365 --> 00:14:16.665 deep lobe of the parotid,
NOTE Confidence: 0.98738605
00:14:18.085 --> 00:14:19.765 adjacent to where the facial
NOTE Confidence: 0.98738605
00:14:19.765 --> 00:14:21.845 nerve, leaves the skull base
NOTE Confidence: 0.98738605
00:14:21.845 --> 00:14:23.145 and heads into the parenchyma
NOTE Confidence: 0.98738605
00:14:23.285 --> 00:14:23.945 of the parotid.
NOTE Confidence: 0.97281903
00:14:25.200 --> 00:14:27.360 No cervical lymphadenopathy was visualized
NOTE Confidence: 0.97281903
00:14:27.360 --> 00:14:28.100 on CT.
NOTE Confidence: 0.9577637
00:14:28.959 --> 00:14:30.260 He then underwent,
NOTE Confidence: 0.9446899
00:14:31.040 --> 00:14:32.399 a PET scan as well
NOTE Confidence: 0.9446899

00:14:32.399 --> 00:14:34.000 that redemonstrated this lesion. And
NOTE Confidence: 0.9446899

00:14:34.000 --> 00:14:34.959 then you can see here
NOTE Confidence: 0.9446899

00:14:34.959 --> 00:14:36.420 it has this kind of
NOTE Confidence: 0.9914551

00:14:36.855 --> 00:14:37.755 crescent like
NOTE Confidence: 0.91503906

00:14:38.375 --> 00:14:38.875 projection
NOTE Confidence: 0.8688965

00:14:39.255 --> 00:14:39.834 and distribution.
NOTE Confidence: 0.9625777

00:14:41.415 --> 00:14:43.815 And no cervical lymphadenopathy was
NOTE Confidence: 0.9625777

00:14:43.815 --> 00:14:45.175 noted on the pet, nor
NOTE Confidence: 0.9625777

00:14:45.175 --> 00:14:46.315 any distant metastasis.
NOTE Confidence: 0.93639064

00:14:48.855 --> 00:14:50.315 So, I talked to him
NOTE Confidence: 0.93639064

00:14:50.375 --> 00:14:52.360 about what surgery would be.
NOTE Confidence: 0.93639064

00:14:52.600 --> 00:14:53.800 It would have obviously involve
NOTE Confidence: 0.93639064

00:14:53.800 --> 00:14:54.940 a wide local excision.
NOTE Confidence: 0.99930245

00:14:55.399 --> 00:14:57.320 Due to the location of
NOTE Confidence: 0.99930245

00:14:57.320 --> 00:14:58.540 this being
NOTE Confidence: 0.9987305

00:14:59.160 --> 00:15:01.260 superficial to the parotid gland,

NOTE Confidence: 0.9984538

00:15:01.800 --> 00:15:02.760 he would need a total

NOTE Confidence: 0.9984538

00:15:02.760 --> 00:15:03.260 parotidectomy

NOTE Confidence: 0.98495

00:15:04.355 --> 00:15:06.194 Depending on the the relationship

NOTE Confidence: 0.98495

00:15:06.194 --> 00:15:07.475 of this cancer to the

NOTE Confidence: 0.98495

00:15:07.475 --> 00:15:08.995 facial nerve, he would potentially

NOTE Confidence: 0.98495

00:15:08.995 --> 00:15:10.935 need facial nerve sacrifice, and

NOTE Confidence: 0.98495

00:15:10.995 --> 00:15:12.194 we would you know, that

NOTE Confidence: 0.98495

00:15:12.194 --> 00:15:13.235 happens from time to time,

NOTE Confidence: 0.98495

00:15:13.235 --> 00:15:14.435 and we reconstruct that with

NOTE Confidence: 0.98495

00:15:14.435 --> 00:15:15.654 nerve grafting or

NOTE Confidence: 0.9229167

00:15:17.220 --> 00:15:20.120 static and dynamic facial reanimation

NOTE Confidence: 0.53466797

00:15:20.500 --> 00:15:21.000 techniques,

NOTE Confidence: 0.9489624

00:15:24.100 --> 00:15:26.200 and potentially free tissue transfer,

NOTE Confidence: 0.9489624

00:15:26.260 --> 00:15:28.100 meaning, taking, you know, tissue

NOTE Confidence: 0.9489624

00:15:28.100 --> 00:15:28.899 from one part of the

NOTE Confidence: 0.9489624

00:15:28.899 --> 00:15:30.405 body and and kind of
NOTE Confidence: 0.9941406

00:15:31.045 --> 00:15:31.545 revascularizing
NOTE Confidence: 0.94879705

00:15:32.085 --> 00:15:32.885 it in the head and
NOTE Confidence: 0.94879705

00:15:32.885 --> 00:15:34.085 neck, to give a blood
NOTE Confidence: 0.94879705

00:15:34.085 --> 00:15:34.585 supply.
NOTE Confidence: 0.9933795

00:15:34.965 --> 00:15:36.005 All in all, a surgery
NOTE Confidence: 0.9933795

00:15:36.005 --> 00:15:37.285 that would take probably on
NOTE Confidence: 0.9933795

00:15:37.285 --> 00:15:38.165 the order of ten to
NOTE Confidence: 0.9933795

00:15:38.165 --> 00:15:38.985 twelve hours.
NOTE Confidence: 0.96495223

00:15:39.605 --> 00:15:40.965 So we presented him as
NOTE Confidence: 0.96495223

00:15:40.965 --> 00:15:41.945 always at our multidisciplinary
NOTE Confidence: 0.93706053

00:15:42.245 --> 00:15:43.465 head and neck tumor conference,
NOTE Confidence: 0.99630535

00:15:44.290 --> 00:15:45.730 and he was evaluated by
NOTE Confidence: 0.99630535

00:15:45.730 --> 00:15:47.110 all members of our multidisciplinary
NOTE Confidence: 0.9655762

00:15:47.650 --> 00:15:48.150 team.
NOTE Confidence: 0.99538577

00:15:48.770 --> 00:15:50.630 And considering his comorbidities,

NOTE Confidence: 0.9945313
00:15:52.130 --> 00:15:53.570 and the extent of what
NOTE Confidence: 0.9945313
00:15:53.570 --> 00:15:55.510 his surgery would be, the
NOTE Confidence: 0.96569824
00:15:56.205 --> 00:15:57.565 recommendation was to at least
NOTE Confidence: 0.96569824
00:15:57.565 --> 00:15:58.045 consider,
NOTE Confidence: 0.9630005
00:15:58.365 --> 00:15:59.585 neoadjuvant samiplimab.
NOTE Confidence: 0.965861
00:16:00.045 --> 00:16:00.845 And so he and his
NOTE Confidence: 0.965861
00:16:00.845 --> 00:16:01.345 family,
NOTE Confidence: 0.97280884
00:16:01.725 --> 00:16:03.565 agreed to proceed with this
NOTE Confidence: 0.97280884
00:16:03.565 --> 00:16:04.545 method of treatment.
NOTE Confidence: 0.9354248
00:16:04.925 --> 00:16:05.665 And he,
NOTE Confidence: 0.86950684
00:16:07.645 --> 00:16:08.385 was initiated.
NOTE Confidence: 0.982103
00:16:09.165 --> 00:16:10.285 And we have the baseline
NOTE Confidence: 0.982103
00:16:10.285 --> 00:16:11.245 picture on the left. And
NOTE Confidence: 0.982103
00:16:11.245 --> 00:16:12.420 then after just two months
NOTE Confidence: 0.982103
00:16:12.420 --> 00:16:13.160 of samiplimab,
NOTE Confidence: 0.99609375

00:16:13.780 --> 00:16:14.680 you can see
NOTE Confidence: 0.98063153

00:16:15.060 --> 00:16:16.360 a pretty dramatic
NOTE Confidence: 0.9702474

00:16:16.820 --> 00:16:18.520 response here of the lesion.
NOTE Confidence: 0.9090294

00:16:21.700 --> 00:16:23.220 And six months later, you
NOTE Confidence: 0.9090294

00:16:23.220 --> 00:16:24.820 can see a photograph here
NOTE Confidence: 0.9090294

00:16:24.820 --> 00:16:25.560 on the left.
NOTE Confidence: 0.78225374

00:16:26.260 --> 00:16:26.935 Really just essentially complete resolution.
NOTE Confidence: 0.78225374

00:16:27.024 --> 00:16:27.572 There's, you know, obviously some
NOTE Confidence: 0.78225374

00:16:27.572 --> 00:16:28.265 residual complete
NOTE Confidence: 0.8762354

00:16:29.605 --> 00:16:30.745 resolution. There's, you know, obviously
NOTE Confidence: 0.8762354

00:16:30.805 --> 00:16:32.725 some residual scar. And a
NOTE Confidence: 0.8762354

00:16:32.725 --> 00:16:33.925 PET scan done around that
NOTE Confidence: 0.8762354

00:16:33.925 --> 00:16:35.765 same time, showed no evidence
NOTE Confidence: 0.8762354

00:16:35.765 --> 00:16:36.425 of disease,
NOTE Confidence: 0.8668213

00:16:36.965 --> 00:16:37.625 kind of,
NOTE Confidence: 0.95496416

00:16:39.125 --> 00:16:41.145 FDG resolution of this lesion.

NOTE Confidence: 0.9660423
00:16:42.769 --> 00:16:44.610 At one year, he has
NOTE Confidence: 0.9660423
00:16:44.610 --> 00:16:45.970 essentially just a scar in
NOTE Confidence: 0.9660423
00:16:45.970 --> 00:16:47.170 this area and a PET
NOTE Confidence: 0.9660423
00:16:47.170 --> 00:16:49.010 scan that, again, continues to
NOTE Confidence: 0.9660423
00:16:49.010 --> 00:16:49.829 show no,
NOTE Confidence: 0.9996745
00:16:50.449 --> 00:16:51.510 evidence of disease.
NOTE Confidence: 0.95731026
00:16:52.769 --> 00:16:53.990 So he remained on samiplimab
NOTE Confidence: 0.95731026
00:16:54.290 --> 00:16:55.889 for an additional year, so
NOTE Confidence: 0.95731026
00:16:55.889 --> 00:16:57.625 two years total. And,
NOTE Confidence: 0.99050903
00:16:58.084 --> 00:16:58.964 he was felt to have
NOTE Confidence: 0.99050903
00:16:58.964 --> 00:17:00.644 developed a complete at least
NOTE Confidence: 0.99050903
00:17:00.644 --> 00:17:02.264 a complete clinical and radiographic
NOTE Confidence: 0.99050903
00:17:02.404 --> 00:17:02.904 response.
NOTE Confidence: 0.92567664
00:17:05.044 --> 00:17:06.085 Since this is sort of
NOTE Confidence: 0.92567664
00:17:06.085 --> 00:17:06.744 a novel
NOTE Confidence: 0.9555664

00:17:07.924 --> 00:17:09.285 strategy to treat these types
NOTE Confidence: 0.9555664

00:17:09.285 --> 00:17:10.744 of cancers, I
NOTE Confidence: 0.9571289

00:17:11.160 --> 00:17:12.359 recommended that he get just
NOTE Confidence: 0.9571289

00:17:12.359 --> 00:17:14.040 an excisional biopsy, so sort
NOTE Confidence: 0.9571289

00:17:14.040 --> 00:17:16.300 of confirm complete pathologic resolution.
NOTE Confidence: 0.95846355

00:17:17.640 --> 00:17:19.160 He and his family have
NOTE Confidence: 0.95846355

00:17:19.160 --> 00:17:20.600 refused. Again, I think having
NOTE Confidence: 0.95846355

00:17:20.600 --> 00:17:22.380 to do predominantly with his,
NOTE Confidence: 0.9850586

00:17:22.760 --> 00:17:24.060 multiple medical comorbidities.
NOTE Confidence: 0.88762206

00:17:25.320 --> 00:17:26.359 But as of now, he
NOTE Confidence: 0.88762206

00:17:26.359 --> 00:17:28.595 remains without evidence of disease.
NOTE Confidence: 0.974871

00:17:30.095 --> 00:17:31.615 So just a little bit
NOTE Confidence: 0.974871

00:17:31.615 --> 00:17:33.315 of background of this therapy.
NOTE Confidence: 0.974871

00:17:33.535 --> 00:17:35.695 So, in twenty twenty two,
NOTE Confidence: 0.974871

00:17:36.015 --> 00:17:37.375 a group at MD Anderson
NOTE Confidence: 0.974871

00:17:37.375 --> 00:17:37.875 published,

NOTE Confidence: 0.6446126
00:17:39.455 --> 00:17:40.910 a phase two,
NOTE Confidence: 0.8598633
00:17:41.770 --> 00:17:42.590 non randomized
NOTE Confidence: 0.9230957
00:17:43.450 --> 00:17:44.590 trial in
NOTE Confidence: 0.8547363
00:17:44.970 --> 00:17:46.190 the New England Journal
NOTE Confidence: 0.9082031
00:17:46.490 --> 00:17:47.790 where they selected
NOTE Confidence: 0.97402346
00:17:48.410 --> 00:17:50.030 about twenty or so patients
NOTE Confidence: 0.65234375
00:17:50.730 --> 00:17:51.230 to
NOTE Confidence: 0.91669923
00:17:52.335 --> 00:17:53.315 receive samiplimab.
NOTE Confidence: 0.9836588
00:17:53.695 --> 00:17:55.554 These were for resectable cutaneous
NOTE Confidence: 0.9144694
00:17:56.174 --> 00:17:57.234 squamous cell carcinomas
NOTE Confidence: 0.9462367
00:17:57.695 --> 00:17:58.895 squamous cell carcinomas of the
NOTE Confidence: 0.9462367
00:17:58.895 --> 00:18:00.015 head and neck that were
NOTE Confidence: 0.9462367
00:18:00.015 --> 00:18:01.234 stage two to four.
NOTE Confidence: 0.8317871
00:18:02.255 --> 00:18:02.734 And,
NOTE Confidence: 0.99853516
00:18:03.215 --> 00:18:03.955 they received
NOTE Confidence: 0.8023071

00:18:04.670 --> 00:18:05.809 neoadjuvant zenlopimab.
NOTE Confidence: 0.9729818

00:18:06.670 --> 00:18:08.270 They followed them both clinically
NOTE Confidence: 0.9729818

00:18:08.270 --> 00:18:09.010 and radiographically.
NOTE Confidence: 0.967041

00:18:09.710 --> 00:18:11.470 And then they ultimately did
NOTE Confidence: 0.967041

00:18:11.470 --> 00:18:12.609 have them all undergo,
NOTE Confidence: 0.9598796

00:18:13.470 --> 00:18:15.150 biopsy or excision of the
NOTE Confidence: 0.9598796

00:18:15.150 --> 00:18:17.570 remaining or, remnant lesion.
NOTE Confidence: 0.9803467

00:18:18.045 --> 00:18:19.484 And what they found was
NOTE Confidence: 0.9803467

00:18:19.484 --> 00:18:20.705 a pretty remarkable,
NOTE Confidence: 0.98217773

00:18:21.565 --> 00:18:22.065 response.
NOTE Confidence: 0.9946289

00:18:22.845 --> 00:18:24.045 The dark green here in
NOTE Confidence: 0.9946289

00:18:24.045 --> 00:18:25.805 this waterfall plot shows the
NOTE Confidence: 0.9946289

00:18:25.805 --> 00:18:26.785 number of patients
NOTE Confidence: 0.86653644

00:18:27.325 --> 00:18:28.785 that had, complete,
NOTE Confidence: 0.9926758

00:18:29.085 --> 00:18:29.585 pathologic
NOTE Confidence: 0.8967582

00:18:29.965 --> 00:18:31.770 response. Meaning, they they received

NOTE Confidence: 0.8967582

00:18:31.770 --> 00:18:33.210 samiplimab, they went to the

NOTE Confidence: 0.8967582

00:18:33.210 --> 00:18:35.130 operating room, excised the remaining

NOTE Confidence: 0.8967582

00:18:35.130 --> 00:18:36.570 lesion or what's left or

NOTE Confidence: 0.8967582

00:18:36.570 --> 00:18:37.609 the scar, and,

NOTE Confidence: 0.92616105

00:18:38.650 --> 00:18:40.250 quite the majority of them

NOTE Confidence: 0.92616105

00:18:40.250 --> 00:18:42.030 had complete pathologic response.

NOTE Confidence: 0.9770345

00:18:42.890 --> 00:18:44.330 And then, you know, more

NOTE Confidence: 0.9770345

00:18:44.330 --> 00:18:46.365 had major pathologic response, meaning

NOTE Confidence: 0.9770345

00:18:46.365 --> 00:18:48.225 there's still some tumor remaining.

NOTE Confidence: 0.9538737

00:18:49.484 --> 00:18:51.484 And, a very small portion

NOTE Confidence: 0.9538737

00:18:51.484 --> 00:18:53.105 had no kind of pathologic

NOTE Confidence: 0.9538737

00:18:53.165 --> 00:18:55.025 response and even smaller portion,

NOTE Confidence: 0.9851752

00:18:55.484 --> 00:18:56.845 patients did not agree to

NOTE Confidence: 0.9851752

00:18:56.845 --> 00:18:57.805 go to the operating room

NOTE Confidence: 0.9851752

00:18:57.805 --> 00:18:58.465 for excision.

NOTE Confidence: 0.9711914

00:18:59.480 --> 00:19:00.119 So this is sort of
NOTE Confidence: 0.9711914

00:19:00.119 --> 00:19:01.720 the foundation for kind of
NOTE Confidence: 0.9711914

00:19:01.720 --> 00:19:02.859 the next iteration
NOTE Confidence: 0.9680176

00:19:03.320 --> 00:19:03.720 of,
NOTE Confidence: 0.94469106

00:19:04.840 --> 00:19:05.800 what is we're trying to
NOTE Confidence: 0.94469106

00:19:05.800 --> 00:19:07.240 learn about this this new
NOTE Confidence: 0.94469106

00:19:07.240 --> 00:19:07.740 medication,
NOTE Confidence: 0.9970703

00:19:08.680 --> 00:19:09.580 fairly new.
NOTE Confidence: 0.99248046

00:19:10.119 --> 00:19:12.060 We are have we've just
NOTE Confidence: 0.7841797

00:19:12.965 --> 00:19:13.465 opened,
NOTE Confidence: 0.9927455

00:19:14.005 --> 00:19:15.445 as a site for a
NOTE Confidence: 0.9927455

00:19:15.445 --> 00:19:16.265 multi institutional
NOTE Confidence: 0.87280273

00:19:16.805 --> 00:19:17.305 trial,
NOTE Confidence: 0.95337814

00:19:18.965 --> 00:19:20.405 featured or funded by or
NOTE Confidence: 0.95337814

00:19:20.405 --> 00:19:21.625 sponsored by the NRG,
NOTE Confidence: 0.99726564

00:19:21.925 --> 00:19:23.465 where patients will be randomized

NOTE Confidence: 0.90670776

00:19:23.765 --> 00:19:25.945 to receive, neoadjuvant immunotherapy

NOTE Confidence: 0.9538574

00:19:27.460 --> 00:19:28.740 versus not. And then go

NOTE Confidence: 0.9538574

00:19:28.740 --> 00:19:30.659 on to receive a response

NOTE Confidence: 0.9538574

00:19:30.659 --> 00:19:31.159 adapted

NOTE Confidence: 0.9698893

00:19:31.460 --> 00:19:32.519 treatment modality.

NOTE Confidence: 0.9458496

00:19:32.820 --> 00:19:33.460 So this is just a

NOTE Confidence: 0.9458496

00:19:33.460 --> 00:19:35.399 quick diagram of the schema.

NOTE Confidence: 0.95628786

00:19:36.500 --> 00:19:38.019 Patients will be stratified whether

NOTE Confidence: 0.95628786

00:19:38.019 --> 00:19:39.619 they're immunosuppressed. And actually this

NOTE Confidence: 0.95628786

00:19:39.619 --> 00:19:41.665 protocol allows for patients to

NOTE Confidence: 0.95628786

00:19:41.665 --> 00:19:42.705 be on, if they're on

NOTE Confidence: 0.95628786

00:19:42.705 --> 00:19:43.905 a low dose of steroids

NOTE Confidence: 0.95628786

00:19:43.905 --> 00:19:45.345 for other medical issues, they

NOTE Confidence: 0.95628786

00:19:45.345 --> 00:19:48.065 are still eligible for involvement

NOTE Confidence: 0.95628786

00:19:48.065 --> 00:19:48.725 in the study.

NOTE Confidence: 0.9308364

00:19:49.984 --> 00:19:50.945 And then they'll be, and
NOTE Confidence: 0.9308364

00:19:50.945 --> 00:19:51.905 then also looking at their
NOTE Confidence: 0.9308364

00:19:51.905 --> 00:19:53.185 nodal disease and then they'll
NOTE Confidence: 0.9308364

00:19:53.185 --> 00:19:53.845 be randomized
NOTE Confidence: 0.9370575

00:19:54.380 --> 00:19:55.900 either to arm one or
NOTE Confidence: 0.9370575

00:19:55.900 --> 00:19:56.860 arm two where arm one
NOTE Confidence: 0.9370575

00:19:56.860 --> 00:19:58.060 is the standard of care
NOTE Confidence: 0.9370575

00:19:58.060 --> 00:19:58.560 surgery,
NOTE Confidence: 0.9988064

00:19:58.860 --> 00:19:59.980 being the standard of care
NOTE Confidence: 0.9988064

00:19:59.980 --> 00:20:01.440 for these cutaneous malignancies
NOTE Confidence: 0.8928304

00:20:02.060 --> 00:20:03.740 followed by adjuvant radiation is
NOTE Confidence: 0.8928304

00:20:03.740 --> 00:20:05.600 indicated from the final pathology.
NOTE Confidence: 0.97441405

00:20:06.220 --> 00:20:07.680 The second arm or the
NOTE Confidence: 0.99348956

00:20:09.544 --> 00:20:10.684 study arm is
NOTE Confidence: 0.85943604

00:20:10.984 --> 00:20:12.765 receipt of neoadjuvant salmipulumab.
NOTE Confidence: 0.99560547

00:20:13.465 --> 00:20:14.125 And then

NOTE Confidence: 0.95962065

00:20:15.225 --> 00:20:17.465 patients undergo what's been described

NOTE Confidence: 0.95962065

00:20:17.465 --> 00:20:19.244 as a response adapted oncologic

NOTE Confidence: 0.95962065

00:20:19.465 --> 00:20:19.965 surgery,

NOTE Confidence: 0.9980469

00:20:20.505 --> 00:20:21.005 meaning

NOTE Confidence: 0.95996094

00:20:22.025 --> 00:20:23.645 a surgery that is

NOTE Confidence: 0.9995117

00:20:24.530 --> 00:20:26.289 reflective of the response that

NOTE Confidence: 0.9995117

00:20:26.289 --> 00:20:27.909 patients have had to treatment.

NOTE Confidence: 0.98254395

00:20:28.210 --> 00:20:29.250 And so for the gentleman

NOTE Confidence: 0.98254395

00:20:29.250 --> 00:20:30.070 that I presented,

NOTE Confidence: 0.96625847

00:20:30.850 --> 00:20:31.809 we wouldn't go in and

NOTE Confidence: 0.96625847

00:20:31.809 --> 00:20:33.409 do a a wide local

NOTE Confidence: 0.96625847

00:20:33.409 --> 00:20:34.869 excision, total parotidectomy,

NOTE Confidence: 0.9897949

00:20:35.890 --> 00:20:37.830 you know, neck dissection reconstruction.

NOTE Confidence: 0.97887367

00:20:38.355 --> 00:20:40.355 We'd essentially excise the scar.

NOTE Confidence: 0.97887367

00:20:40.355 --> 00:20:42.035 So wherever there is clinical

NOTE Confidence: 0.97887367

00:20:42.035 --> 00:20:43.315 evidence of disease, you know,
NOTE Confidence: 0.97887367

00:20:43.315 --> 00:20:44.515 if he would get a
NOTE Confidence: 0.97887367

00:20:44.515 --> 00:20:46.595 CT scan before surgery, wherever
NOTE Confidence: 0.97887367

00:20:46.595 --> 00:20:48.195 there's clinical evidence of disease,
NOTE Confidence: 0.9973493

00:20:48.595 --> 00:20:50.195 including radiographic, that's what we
NOTE Confidence: 0.9973493

00:20:50.195 --> 00:20:50.855 would excise.
NOTE Confidence: 0.98668927

00:20:51.530 --> 00:20:52.570 And then those patients would
NOTE Confidence: 0.98668927

00:20:52.570 --> 00:20:53.770 go on to receive adjuvant
NOTE Confidence: 0.98668927

00:20:53.770 --> 00:20:55.130 radiation based on their final
NOTE Confidence: 0.98668927

00:20:55.130 --> 00:20:55.630 pathology.
NOTE Confidence: 0.9458008

00:20:56.650 --> 00:20:58.250 And, also additional,
NOTE Confidence: 0.8808594

00:20:58.809 --> 00:20:59.309 samiplimab.
NOTE Confidence: 0.99375

00:21:00.169 --> 00:21:01.609 Of note, if patients have
NOTE Confidence: 0.99375

00:21:01.609 --> 00:21:03.609 a complete pathologic response, they
NOTE Confidence: 0.99375

00:21:03.609 --> 00:21:05.369 will not receive any additional
NOTE Confidence: 0.99375

00:21:05.369 --> 00:21:05.869 samiplimab.

NOTE Confidence: 0.94816077

00:21:07.535 --> 00:21:08.655 And this is just sort

NOTE Confidence: 0.94816077

00:21:08.655 --> 00:21:09.615 of a description of what

NOTE Confidence: 0.94816077

00:21:09.615 --> 00:21:11.615 response adapted oncologic surgery is.

NOTE Confidence: 0.94816077

00:21:11.615 --> 00:21:13.695 It's controlling for margins, as

NOTE Confidence: 0.94816077

00:21:13.695 --> 00:21:14.755 we always do.

NOTE Confidence: 0.87609863

00:21:16.015 --> 00:21:18.035 Gross viable or visible tumor

NOTE Confidence: 0.87609863

00:21:18.095 --> 00:21:19.315 and any abnormality,

NOTE Confidence: 0.99421036

00:21:20.015 --> 00:21:20.895 that's seen at the time

NOTE Confidence: 0.99421036

00:21:20.895 --> 00:21:21.555 of surgery.

NOTE Confidence: 0.9564697

00:21:22.260 --> 00:21:23.780 We address the nodal basin

NOTE Confidence: 0.9564697

00:21:23.780 --> 00:21:25.960 based on the baseline imaging.

NOTE Confidence: 0.95478517

00:21:27.060 --> 00:21:28.180 And then where there's an,

NOTE Confidence: 0.95478517

00:21:28.500 --> 00:21:29.940 any sort of concern about

NOTE Confidence: 0.95478517

00:21:29.940 --> 00:21:31.480 function. So in this gentleman,

NOTE Confidence: 0.9865025

00:21:31.859 --> 00:21:33.140 the facial nerve being at

NOTE Confidence: 0.9865025

00:21:33.140 --> 00:21:33.855 high risk,
NOTE Confidence: 0.9772631

00:21:34.655 --> 00:21:36.595 you know, the study encourages
NOTE Confidence: 0.9772631

00:21:36.815 --> 00:21:38.494 that we not do the
NOTE Confidence: 0.9772631

00:21:38.494 --> 00:21:39.615 original surgery, which would have
NOTE Confidence: 0.9772631

00:21:39.615 --> 00:21:41.395 been a potential radical tonsillectomy,
NOTE Confidence: 0.9772631

00:21:41.695 --> 00:21:42.755 facial nerve sacrifice.
NOTE Confidence: 0.9459292

00:21:43.375 --> 00:21:44.655 And essentially for this gentleman,
NOTE Confidence: 0.9459292

00:21:44.655 --> 00:21:45.615 would have looked something like
NOTE Confidence: 0.9459292

00:21:45.615 --> 00:21:47.215 a wide local excision, possibly
NOTE Confidence: 0.9459292

00:21:47.215 --> 00:21:48.355 a superficial parotidectomy,
NOTE Confidence: 0.9529121

00:21:48.655 --> 00:21:49.570 where we would just peel
NOTE Confidence: 0.9529121

00:21:49.570 --> 00:21:50.609 the the parotid off of
NOTE Confidence: 0.9529121

00:21:50.609 --> 00:21:51.510 the facial nerve.
NOTE Confidence: 0.9179466

00:21:53.090 --> 00:21:54.130 So a lot of promise
NOTE Confidence: 0.9179466

00:21:54.130 --> 00:21:56.050 with this, study and we
NOTE Confidence: 0.9179466

00:21:56.050 --> 00:21:56.550 are,

NOTE Confidence: 0.8789411
00:21:57.090 --> 00:21:58.609 opening or if not, have
NOTE Confidence: 0.8789411
00:21:58.609 --> 00:21:59.350 already opened,
NOTE Confidence: 0.90757924
00:21:59.730 --> 00:22:01.570 and will start enrolling, very
NOTE Confidence: 0.90757924
00:22:01.570 --> 00:22:02.070 soon.
NOTE Confidence: 0.8938304
00:22:03.914 --> 00:22:05.275 But just a quick question
NOTE Confidence: 0.8938304
00:22:05.275 --> 00:22:06.895 just for both for doctor
NOTE Confidence: 0.8938304
00:22:07.035 --> 00:22:08.895 Swozier and for doctor Roche.
NOTE Confidence: 0.8938304
00:22:09.195 --> 00:22:10.494 When you're determining
NOTE Confidence: 0.9890137
00:22:10.955 --> 00:22:12.315 kind of the margins for
NOTE Confidence: 0.9890137
00:22:12.315 --> 00:22:14.395 for those, either patients with
NOTE Confidence: 0.9890137
00:22:14.395 --> 00:22:16.190 us today or providers,
NOTE Confidence: 0.96952057
00:22:16.649 --> 00:22:18.169 at the community. How are
NOTE Confidence: 0.96952057
00:22:18.169 --> 00:22:20.510 you determining what you're considering
NOTE Confidence: 0.96952057
00:22:20.809 --> 00:22:22.889 to be clinically viable disease
NOTE Confidence: 0.96952057
00:22:22.889 --> 00:22:23.389 besides,
NOTE Confidence: 0.99574786

00:22:24.090 --> 00:22:24.970 you know, the wealth of
NOTE Confidence: 0.99574786

00:22:24.970 --> 00:22:26.889 experience that you've accumulated over
NOTE Confidence: 0.99574786

00:22:26.889 --> 00:22:27.549 the years
NOTE Confidence: 0.9616699

00:22:28.035 --> 00:22:29.795 about ensuring then that you're
NOTE Confidence: 0.9616699

00:22:29.795 --> 00:22:31.975 you're getting an adequate resection
NOTE Confidence: 0.95336914

00:22:32.515 --> 00:22:33.635 and again and how you
NOTE Confidence: 0.95336914

00:22:33.635 --> 00:22:35.475 think that these responses are
NOTE Confidence: 0.95336914

00:22:35.475 --> 00:22:37.315 different than sometimes patients who
NOTE Confidence: 0.95336914

00:22:37.315 --> 00:22:39.015 may have historically been treated
NOTE Confidence: 0.9836426

00:22:39.315 --> 00:22:40.994 with other modalities that are
NOTE Confidence: 0.9836426

00:22:40.994 --> 00:22:42.455 not immune therapy.
NOTE Confidence: 0.9680873

00:22:46.210 --> 00:22:47.570 Kathleen, you wanna take that
NOTE Confidence: 0.9680873

00:22:47.570 --> 00:22:48.310 one first?
NOTE Confidence: 0.9929199

00:22:49.250 --> 00:22:50.690 Sure. I would say that
NOTE Confidence: 0.9929199

00:22:50.690 --> 00:22:51.170 in the,
NOTE Confidence: 0.99076337

00:22:52.609 --> 00:22:53.430 in the neoadjuvant

NOTE Confidence: 0.9586995
00:22:53.890 --> 00:22:56.165 setting so using it upfront
NOTE Confidence: 0.9586995
00:22:56.225 --> 00:22:56.665 in,
NOTE Confidence: 0.9873183
00:22:57.105 --> 00:22:58.945 high risk cutaneous SCC, this
NOTE Confidence: 0.9873183
00:22:58.945 --> 00:23:00.025 is pretty novel for us.
NOTE Confidence: 0.9873183
00:23:00.025 --> 00:23:00.645 So in
NOTE Confidence: 0.9760298
00:23:01.025 --> 00:23:02.145 most of in most of
NOTE Confidence: 0.9760298
00:23:02.145 --> 00:23:03.525 those cases, then the patients
NOTE Confidence: 0.9760298
00:23:03.744 --> 00:23:05.105 have already been sort of
NOTE Confidence: 0.9760298
00:23:05.105 --> 00:23:06.225 referred to our head and
NOTE Confidence: 0.9760298
00:23:06.225 --> 00:23:06.885 neck surgery
NOTE Confidence: 0.95505667
00:23:07.345 --> 00:23:09.105 colleagues for potential wide local
NOTE Confidence: 0.95505667
00:23:09.105 --> 00:23:11.700 excision afterwards. Right? For for
NOTE Confidence: 0.95505667
00:23:11.700 --> 00:23:13.220 most micrographic surgery, right, in
NOTE Confidence: 0.95505667
00:23:13.220 --> 00:23:14.760 that tissue sparing sense,
NOTE Confidence: 0.9995117
00:23:15.220 --> 00:23:17.160 once we're no longer
NOTE Confidence: 0.95243835

00:23:17.859 --> 00:23:19.619 in those low risk SCC
NOTE Confidence: 0.95243835

00:23:19.619 --> 00:23:20.820 types there, you know, we're
NOTE Confidence: 0.95243835

00:23:20.820 --> 00:23:22.420 thinking more wide local margin
NOTE Confidence: 0.95243835

00:23:22.420 --> 00:23:22.920 where,
NOTE Confidence: 0.9468784

00:23:23.675 --> 00:23:25.275 I'm I'm not necessarily gonna
NOTE Confidence: 0.9468784

00:23:25.275 --> 00:23:26.715 need that MOSE to be
NOTE Confidence: 0.9468784

00:23:26.715 --> 00:23:28.475 really particular about our margin
NOTE Confidence: 0.9468784

00:23:28.475 --> 00:23:29.755 or marginal control where we
NOTE Confidence: 0.9468784

00:23:29.755 --> 00:23:30.635 wanna more take, like, a
NOTE Confidence: 0.9468784

00:23:30.635 --> 00:23:32.255 wider two, three centimeter
NOTE Confidence: 0.9971147

00:23:32.715 --> 00:23:34.155 margin around the area when
NOTE Confidence: 0.9971147

00:23:34.155 --> 00:23:35.355 we're worried about those in
NOTE Confidence: 0.9971147

00:23:35.355 --> 00:23:35.855 transit
NOTE Confidence: 0.97318524

00:23:37.000 --> 00:23:38.600 in transit meds. But I
NOTE Confidence: 0.97318524

00:23:38.600 --> 00:23:40.200 think, you know, I didn't
NOTE Confidence: 0.97318524

00:23:40.200 --> 00:23:41.400 show an after picture of

NOTE Confidence: 0.97318524
00:23:41.400 --> 00:23:42.539 my patient, but,
NOTE Confidence: 0.9752752
00:23:42.919 --> 00:23:44.299 in that case, that patient
NOTE Confidence: 0.9752752
00:23:44.359 --> 00:23:45.960 did not have had a
NOTE Confidence: 0.9752752
00:23:45.960 --> 00:23:46.460 complete,
NOTE Confidence: 0.9995117
00:23:47.320 --> 00:23:48.380 clinical response
NOTE Confidence: 0.85809326
00:23:49.000 --> 00:23:50.299 to, samiplimab
NOTE Confidence: 0.9526367
00:23:50.679 --> 00:23:51.179 and
NOTE Confidence: 0.9718262
00:23:51.845 --> 00:23:53.945 did not have, further surgery
NOTE Confidence: 0.9934082
00:23:54.325 --> 00:23:56.325 after, similar to doctor Roche's
NOTE Confidence: 0.9934082
00:23:56.325 --> 00:23:56.825 patient.
NOTE Confidence: 0.99269104
00:23:57.445 --> 00:23:58.965 But there aren't clear guidelines
NOTE Confidence: 0.99269104
00:23:58.965 --> 00:24:00.005 of, like, for example, how
NOTE Confidence: 0.99269104
00:24:00.005 --> 00:24:01.685 many centimeters outside of their
NOTE Confidence: 0.99269104
00:24:01.685 --> 00:24:02.185 scar,
NOTE Confidence: 0.99641925
00:24:02.725 --> 00:24:03.765 you would go at this
NOTE Confidence: 0.99641925

00:24:03.765 --> 00:24:04.265 point.
NOTE Confidence: 0.989858

00:24:05.670 --> 00:24:06.950 Right. I mean, the standard,
NOTE Confidence: 0.989858

00:24:06.950 --> 00:24:08.710 you know, for surgery being
NOTE Confidence: 0.989858

00:24:08.710 --> 00:24:10.310 the first modality of treatment
NOTE Confidence: 0.989858

00:24:10.310 --> 00:24:11.830 for these patients, it's generally
NOTE Confidence: 0.989858

00:24:11.830 --> 00:24:13.050 a a good centimeter,
NOTE Confidence: 0.98583984

00:24:13.670 --> 00:24:14.890 kind of in the cutaneous
NOTE Confidence: 0.98597

00:24:15.430 --> 00:24:17.210 direction for wide local excisions.
NOTE Confidence: 0.99466646

00:24:18.825 --> 00:24:20.105 We you know, for deeper
NOTE Confidence: 0.99466646

00:24:20.105 --> 00:24:21.465 structures, we try to maintain
NOTE Confidence: 0.99466646

00:24:21.465 --> 00:24:22.365 that as well.
NOTE Confidence: 0.9698794

00:24:24.105 --> 00:24:25.804 It's often a a conversation
NOTE Confidence: 0.9698794

00:24:25.945 --> 00:24:28.505 intraoperative conversation about, well, here's
NOTE Confidence: 0.9698794

00:24:28.505 --> 00:24:30.105 a palpable tumor that's, like,
NOTE Confidence: 0.9698794

00:24:30.105 --> 00:24:31.225 right up against the facial
NOTE Confidence: 0.9698794

00:24:31.225 --> 00:24:32.664 nerve. It's not invading the

NOTE Confidence: 0.9698794
00:24:32.664 --> 00:24:34.109 facial nerve. And so in
NOTE Confidence: 0.9698794
00:24:34.109 --> 00:24:35.470 those cases, we do try
NOTE Confidence: 0.9698794
00:24:35.470 --> 00:24:36.910 to spare, you know, preserve
NOTE Confidence: 0.9698794
00:24:36.910 --> 00:24:38.670 function and spare. You know,
NOTE Confidence: 0.9698794
00:24:38.670 --> 00:24:39.730 we we kind of
NOTE Confidence: 0.9893799
00:24:40.109 --> 00:24:42.130 overlook our ideal one centimeter
NOTE Confidence: 0.9893799
00:24:42.190 --> 00:24:43.470 margin in all directions for
NOTE Confidence: 0.9893799
00:24:43.470 --> 00:24:44.130 these cases.
NOTE Confidence: 0.9933008
00:24:45.470 --> 00:24:46.690 And then for the neoadjuvant,
NOTE Confidence: 0.98372394
00:24:47.070 --> 00:24:48.575 you know, as kind of
NOTE Confidence: 0.98372394
00:24:48.575 --> 00:24:49.955 what's described in this,
NOTE Confidence: 0.967041
00:24:50.575 --> 00:24:51.555 study schema,
NOTE Confidence: 0.93747556
00:24:53.295 --> 00:24:54.915 I think just the appearance,
NOTE Confidence: 0.9922714
00:24:55.295 --> 00:24:56.255 we start with just the
NOTE Confidence: 0.9922714
00:24:56.255 --> 00:24:57.375 appearance. Like, if it looks
NOTE Confidence: 0.9922714

00:24:57.375 --> 00:24:58.575 like scar, if it's not
NOTE Confidence: 0.9922714

00:24:58.575 --> 00:25:00.430 friable, if it's not kind
NOTE Confidence: 0.9922714

00:25:00.430 --> 00:25:01.869 of angry looking, then then
NOTE Confidence: 0.9922714

00:25:01.869 --> 00:25:02.750 we kind of treat that
NOTE Confidence: 0.9922714

00:25:02.750 --> 00:25:03.490 as scar.
NOTE Confidence: 0.9853335

00:25:04.830 --> 00:25:06.750 But I would typically go
NOTE Confidence: 0.9853335

00:25:06.750 --> 00:25:08.030 about a centimeter outside of
NOTE Confidence: 0.9853335

00:25:08.030 --> 00:25:09.950 the scar and then, you
NOTE Confidence: 0.9853335

00:25:09.950 --> 00:25:10.750 know, send that to the
NOTE Confidence: 0.9853335

00:25:10.750 --> 00:25:12.350 pathologist for real time frozen
NOTE Confidence: 0.9853335

00:25:12.350 --> 00:25:13.170 section analysis.
NOTE Confidence: 0.97483885

00:25:14.615 --> 00:25:16.135 All the more, interest and
NOTE Confidence: 0.97483885

00:25:16.135 --> 00:25:17.575 excitement about the the trial
NOTE Confidence: 0.97483885

00:25:17.575 --> 00:25:19.115 besides some of these magnificent
NOTE Confidence: 0.97483885

00:25:19.335 --> 00:25:21.255 responses that we see. So
NOTE Confidence: 0.97483885

00:25:21.255 --> 00:25:22.715 on that note, doctor Bhatia.

NOTE Confidence: 0.99902344

00:25:25.175 --> 00:25:25.975 Thank you.

NOTE Confidence: 0.9850464

00:25:26.455 --> 00:25:27.975 Good evening, everyone, and thank

NOTE Confidence: 0.9850464

00:25:27.975 --> 00:25:29.335 you for attending this very

NOTE Confidence: 0.9850464

00:25:29.335 --> 00:25:30.234 timely discourse.

NOTE Confidence: 0.9609375

00:25:31.150 --> 00:25:32.530 I am a medical oncologist

NOTE Confidence: 0.9609375

00:25:32.670 --> 00:25:33.869 at Yale, and I treat

NOTE Confidence: 0.9609375

00:25:34.430 --> 00:25:35.710 my focus is on head,

NOTE Confidence: 0.9609375

00:25:35.710 --> 00:25:37.150 neck, and skin squamous cell

NOTE Confidence: 0.9609375

00:25:37.150 --> 00:25:37.650 cancers.

NOTE Confidence: 0.99296063

00:25:38.670 --> 00:25:40.109 And I will be reviewing

NOTE Confidence: 0.99296063

00:25:40.109 --> 00:25:42.130 the literature around immune checkpoint

NOTE Confidence: 0.99296063

00:25:42.190 --> 00:25:43.810 therapy to date in cutaneous

NOTE Confidence: 0.99296063

00:25:43.869 --> 00:25:45.090 squamous cell cancers.

NOTE Confidence: 0.99216306

00:25:48.125 --> 00:25:48.353 So I'm just gonna go

NOTE Confidence: 0.99216306

00:25:48.353 --> 00:25:49.505 ahead and share my slides.

NOTE Confidence: 0.58203125

00:25:50.045 --> 00:25:50.545 You
NOTE Confidence: 0.98876953

00:25:51.085 --> 00:25:52.145 can see my screen.
NOTE Confidence: 0.99902344

00:25:57.244 --> 00:25:57.744 Okay.
NOTE Confidence: 0.8186035

00:25:58.205 --> 00:25:58.705 So,
NOTE Confidence: 0.9864502

00:26:00.450 --> 00:26:02.450 oops. Yep. As doctors,
NOTE Confidence: 0.9830548

00:26:02.929 --> 00:26:04.690 Susie and Roach have already
NOTE Confidence: 0.9830548

00:26:04.690 --> 00:26:07.010 outlined before me, surgery followed
NOTE Confidence: 0.9830548

00:26:07.010 --> 00:26:08.450 by radiation for high risk
NOTE Confidence: 0.9830548

00:26:08.450 --> 00:26:10.130 disease is the mainstay for
NOTE Confidence: 0.9830548

00:26:10.130 --> 00:26:12.049 treating these locally advanced high
NOTE Confidence: 0.9830548

00:26:12.049 --> 00:26:12.789 risk tumors.
NOTE Confidence: 0.9816137

00:26:13.835 --> 00:26:15.855 But despite intensive local therapy,
NOTE Confidence: 0.9816137

00:26:15.915 --> 00:26:17.275 about thirteen to forty one
NOTE Confidence: 0.9816137

00:26:17.275 --> 00:26:19.035 percent of these patients can
NOTE Confidence: 0.9816137

00:26:19.035 --> 00:26:20.555 still go on to develop
NOTE Confidence: 0.9816137

00:26:20.555 --> 00:26:22.395 either local regional recurrence or

NOTE Confidence: 0.9816137

00:26:22.395 --> 00:26:23.695 distance spread of disease.

NOTE Confidence: 0.97734916

00:26:24.955 --> 00:26:26.955 And, additionally, surgery and radiation

NOTE Confidence: 0.97734916

00:26:26.955 --> 00:26:28.440 can be physically deforming.

NOTE Confidence: 0.99563265

00:26:28.760 --> 00:26:29.880 It can lead to facial

NOTE Confidence: 0.99563265

00:26:29.880 --> 00:26:31.240 droop. It can involve loss

NOTE Confidence: 0.99563265

00:26:31.240 --> 00:26:31.899 of digits.

NOTE Confidence: 0.9928448

00:26:32.679 --> 00:26:33.799 It can affect speech and

NOTE Confidence: 0.9928448

00:26:33.799 --> 00:26:35.080 swallow, especially in the head

NOTE Confidence: 0.9928448

00:26:35.080 --> 00:26:35.980 and neck region.

NOTE Confidence: 0.95043945

00:26:36.359 --> 00:26:37.640 Many of these tumors occur

NOTE Confidence: 0.95043945

00:26:37.640 --> 00:26:39.240 in elderly patients as doctor

NOTE Confidence: 0.95043945

00:26:39.240 --> 00:26:40.760 Roach pointed out, and surgery

NOTE Confidence: 0.95043945

00:26:40.760 --> 00:26:42.200 can be demanding, if not

NOTE Confidence: 0.95043945

00:26:42.200 --> 00:26:42.700 impossible

NOTE Confidence: 0.7883301

00:26:43.000 --> 00:26:43.659 for them.

NOTE Confidence: 0.9878337

00:26:44.145 --> 00:26:46.065 So, there is or was
NOTE Confidence: 0.9878337

00:26:46.065 --> 00:26:47.665 a critical unmet need for
NOTE Confidence: 0.9878337

00:26:47.665 --> 00:26:49.345 effective systemic therapy in this
NOTE Confidence: 0.9878337

00:26:49.345 --> 00:26:51.185 disease, and there were, actually
NOTE Confidence: 0.9878337

00:26:51.185 --> 00:26:52.805 no FDA approved treatments,
NOTE Confidence: 0.9995117

00:26:53.185 --> 00:26:54.865 as recently as until twenty
NOTE Confidence: 0.9995117

00:26:54.865 --> 00:26:55.365 eighteen.
NOTE Confidence: 0.8758545

00:26:56.830 --> 00:26:57.649 So simiplamab,
NOTE Confidence: 0.9854361

00:26:58.109 --> 00:26:59.309 which is something we've been
NOTE Confidence: 0.9854361

00:26:59.309 --> 00:27:01.070 talking about this evening, is
NOTE Confidence: 0.9854361

00:27:01.070 --> 00:27:02.429 an anti PD one agent,
NOTE Confidence: 0.9854361

00:27:02.429 --> 00:27:03.630 and it was approved for
NOTE Confidence: 0.9854361

00:27:03.630 --> 00:27:05.490 the treatment of locally advanced
NOTE Confidence: 0.9854361

00:27:05.549 --> 00:27:06.049 unresectable
NOTE Confidence: 0.98605955

00:27:06.350 --> 00:27:08.510 and distant metastatic cutaneous squamous
NOTE Confidence: 0.98605955

00:27:08.510 --> 00:27:10.289 cell cancers in twenty eighteen.

NOTE Confidence: 0.9955798

00:27:11.045 --> 00:27:12.565 And that approval came on

NOTE Confidence: 0.9955798

00:27:12.565 --> 00:27:13.765 the basis of an early

NOTE Confidence: 0.9955798

00:27:13.765 --> 00:27:14.804 phase trial. It was a

NOTE Confidence: 0.9955798

00:27:14.804 --> 00:27:16.265 phase one, two trial,

NOTE Confidence: 0.9594948

00:27:16.885 --> 00:27:18.424 in about a hundred patients

NOTE Confidence: 0.9594948

00:27:18.484 --> 00:27:20.184 with locally advanced and metastatic

NOTE Confidence: 0.9594948

00:27:20.325 --> 00:27:20.825 cohorts.

NOTE Confidence: 0.99278843

00:27:21.605 --> 00:27:23.385 About fifty percent of patients

NOTE Confidence: 0.99278843

00:27:23.445 --> 00:27:25.045 had response to treatment in

NOTE Confidence: 0.99278843

00:27:25.045 --> 00:27:26.105 both these cohorts,

NOTE Confidence: 0.99975586

00:27:27.600 --> 00:27:28.720 and many of them had

NOTE Confidence: 0.99975586

00:27:28.720 --> 00:27:30.020 very durable responses.

NOTE Confidence: 0.99208575

00:27:30.320 --> 00:27:31.940 There was another paper published

NOTE Confidence: 0.99208575

00:27:32.080 --> 00:27:33.280 subsequent to this one in

NOTE Confidence: 0.99208575

00:27:33.280 --> 00:27:33.940 the NEJM

NOTE Confidence: 0.98515624

00:27:34.560 --> 00:27:36.340 with a longer follow-up time,
NOTE Confidence: 0.9826416

00:27:36.640 --> 00:27:37.680 and in a bigger in
NOTE Confidence: 0.9826416

00:27:37.680 --> 00:27:39.380 a slightly bigger patient cohort.
NOTE Confidence: 0.99556476

00:27:39.775 --> 00:27:41.135 And the median duration of
NOTE Confidence: 0.99556476

00:27:41.135 --> 00:27:41.635 response,
NOTE Confidence: 0.96713257

00:27:42.095 --> 00:27:43.295 for that cohort for the
NOTE Confidence: 0.96713257

00:27:43.295 --> 00:27:45.215 entire patient cohort was determined
NOTE Confidence: 0.96713257

00:27:45.215 --> 00:27:46.494 to be about forty one
NOTE Confidence: 0.96713257

00:27:46.494 --> 00:27:46.994 months.
NOTE Confidence: 0.9586872

00:27:47.375 --> 00:27:48.494 So, you know, that kinda
NOTE Confidence: 0.9586872

00:27:48.494 --> 00:27:49.855 correlates with what we're seeing
NOTE Confidence: 0.9586872

00:27:49.855 --> 00:27:51.455 clinically with these patients who've
NOTE Confidence: 0.9586872

00:27:51.455 --> 00:27:52.734 received one year, two years
NOTE Confidence: 0.9586872

00:27:52.734 --> 00:27:53.875 of systemic treatment,
NOTE Confidence: 0.9479709

00:27:54.230 --> 00:27:55.270 and many of who were
NOTE Confidence: 0.9479709

00:27:55.270 --> 00:27:56.490 just following in surveillance

NOTE Confidence: 0.9212821

00:27:56.790 --> 00:27:58.150 either with or without scar

NOTE Confidence: 0.9212821

00:27:58.150 --> 00:27:59.130 excision surgery,

NOTE Confidence: 0.9994673

00:28:00.070 --> 00:28:01.109 and many of them do

NOTE Confidence: 0.9994673

00:28:01.109 --> 00:28:02.630 stay cancer free for years

NOTE Confidence: 0.9994673

00:28:02.630 --> 00:28:03.130 afterwards.

NOTE Confidence: 0.95650053

00:28:04.230 --> 00:28:05.750 Around the same time as,

NOTE Confidence: 0.95650053

00:28:06.070 --> 00:28:07.670 the simiclumab paper about a

NOTE Confidence: 0.95650053

00:28:07.670 --> 00:28:09.285 couple years later, keynote six

NOTE Confidence: 0.95650053

00:28:09.365 --> 00:28:11.125 two nine, which evaluated the

NOTE Confidence: 0.95650053

00:28:11.125 --> 00:28:12.345 efficacy of pembrolizumab,

NOTE Confidence: 0.9435425

00:28:13.605 --> 00:28:15.205 another anti PD one agent

NOTE Confidence: 0.9435425

00:28:15.205 --> 00:28:16.325 in a hundred and five

NOTE Confidence: 0.9435425

00:28:16.325 --> 00:28:17.145 patient cohort,

NOTE Confidence: 0.9837472

00:28:17.525 --> 00:28:19.685 also with advanced cutaneous squamous

NOTE Confidence: 0.9837472

00:28:19.685 --> 00:28:20.345 cell cancers,

NOTE Confidence: 0.98916584

00:28:21.205 --> 00:28:22.325 showed a response rate of
NOTE Confidence: 0.98916584

00:28:22.325 --> 00:28:24.040 about thirty five percent, and
NOTE Confidence: 0.98916584

00:28:24.040 --> 00:28:25.720 that led to, the approval
NOTE Confidence: 0.98916584

00:28:25.720 --> 00:28:27.240 of pembro in twenty twenty
NOTE Confidence: 0.98916584

00:28:27.240 --> 00:28:28.220 for this disease.
NOTE Confidence: 0.94047856

00:28:28.760 --> 00:28:30.680 And more recently in, I
NOTE Confidence: 0.94047856

00:28:30.680 --> 00:28:31.800 think, about four or five
NOTE Confidence: 0.94047856

00:28:31.800 --> 00:28:33.340 months ago, casibelumab,
NOTE Confidence: 0.9387207

00:28:33.800 --> 00:28:35.000 which is a PDL one
NOTE Confidence: 0.9387207

00:28:35.000 --> 00:28:35.500 inhibitor,
NOTE Confidence: 0.97358197

00:28:36.135 --> 00:28:37.575 was also approved. So that's
NOTE Confidence: 0.97358197

00:28:37.575 --> 00:28:39.335 the third agent now, for
NOTE Confidence: 0.97358197

00:28:39.335 --> 00:28:41.255 people with advanced cutaneous squamous
NOTE Confidence: 0.97358197

00:28:41.255 --> 00:28:43.015 cell cancers and based on
NOTE Confidence: 0.97358197

00:28:43.015 --> 00:28:44.795 very similar efficacy data.
NOTE Confidence: 0.96151453

00:28:46.135 --> 00:28:47.735 So the success of immune

NOTE Confidence: 0.96151453
00:28:47.735 --> 00:28:49.350 check point agents and advanced
NOTE Confidence: 0.96151453
00:28:49.350 --> 00:28:49.830 disease,
NOTE Confidence: 0.97542316
00:28:50.150 --> 00:28:51.750 led to trials being conducted
NOTE Confidence: 0.97542316
00:28:51.750 --> 00:28:52.870 with these agents in the
NOTE Confidence: 0.97542316
00:28:52.870 --> 00:28:53.850 curative setting.
NOTE Confidence: 0.95192873
00:28:54.230 --> 00:28:56.170 And, actually, two key adjuvant,
NOTE Confidence: 0.8781128
00:28:57.110 --> 00:28:58.410 anti PD one trials,
NOTE Confidence: 0.9984741
00:28:59.270 --> 00:29:00.710 are gonna be presented at
NOTE Confidence: 0.9984741
00:29:00.710 --> 00:29:02.010 ASCO next month.
NOTE Confidence: 0.9463795
00:29:02.390 --> 00:29:03.670 One of them is keynote
NOTE Confidence: 0.9463795
00:29:03.670 --> 00:29:05.554 six six thirty, which enrolled
NOTE Confidence: 0.9463795
00:29:05.615 --> 00:29:07.294 five hundred and seventy patients
NOTE Confidence: 0.9463795
00:29:07.294 --> 00:29:09.235 with high risk locally advanced
NOTE Confidence: 0.9463795
00:29:09.375 --> 00:29:11.375 cutaneous squamous who first underwent
NOTE Confidence: 0.9463795
00:29:11.375 --> 00:29:12.275 upfront surgery,
NOTE Confidence: 0.9969727

00:29:13.215 --> 00:29:15.075 then followed by adjuvant radiation

NOTE Confidence: 0.969348

00:29:15.375 --> 00:29:17.054 and were randomized to receive

NOTE Confidence: 0.969348

00:29:17.054 --> 00:29:18.850 either pembro or placebo for

NOTE Confidence: 0.969348

00:29:18.850 --> 00:29:20.392 a total of one year.

NOTE Confidence: 0.969348

00:29:20.392 --> 00:29:22.210 And the primary endpoint was

NOTE Confidence: 0.969348

00:29:22.210 --> 00:29:23.429 recurrence free survival.

NOTE Confidence: 0.9065186

00:29:24.210 --> 00:29:25.509 On the other hand, enrolling

NOTE Confidence: 1

00:29:26.210 --> 00:29:26.710 simultaneously

NOTE Confidence: 0.9495117

00:29:27.169 --> 00:29:28.549 was the c post trial,

NOTE Confidence: 0.96865237

00:29:28.850 --> 00:29:30.850 which enrolled patients also with

NOTE Confidence: 0.96865237

00:29:30.850 --> 00:29:32.789 high risk locally advanced disease

NOTE Confidence: 0.97250026

00:29:33.154 --> 00:29:34.835 who underwent surgery followed by

NOTE Confidence: 0.97250026

00:29:34.835 --> 00:29:36.595 radiation and were then randomized

NOTE Confidence: 0.97250026

00:29:36.595 --> 00:29:38.534 to receive simoplumab or placebo

NOTE Confidence: 0.97250026

00:29:38.595 --> 00:29:39.575 for one year.

NOTE Confidence: 0.9849355

00:29:39.875 --> 00:29:41.635 And their primary endpoint was,

NOTE Confidence: 0.9849355
00:29:42.034 --> 00:29:43.654 DFS, disease free survival.
NOTE Confidence: 0.984096
00:29:45.394 --> 00:29:46.995 And we don't have the,
NOTE Confidence: 0.984096
00:29:47.235 --> 00:29:48.294 official presentations
NOTE Confidence: 0.984847
00:29:48.740 --> 00:29:50.180 from these trials. They're gonna
NOTE Confidence: 0.984847
00:29:50.180 --> 00:29:51.540 be at ASCO next month,
NOTE Confidence: 0.984847
00:29:51.540 --> 00:29:53.000 but there were press releases,
NOTE Confidence: 0.9988281
00:29:53.540 --> 00:29:55.320 recently for both these studies.
NOTE Confidence: 0.95564467
00:29:56.580 --> 00:29:58.420 The the keynote six thirty
NOTE Confidence: 0.95564467
00:29:58.420 --> 00:29:59.940 trial was reported to be
NOTE Confidence: 0.95564467
00:29:59.940 --> 00:30:02.020 a negative study, by by
NOTE Confidence: 0.95564467
00:30:02.020 --> 00:30:03.515 Merck, And while the c
NOTE Confidence: 0.95564467
00:30:03.515 --> 00:30:04.635 post trial, which was by
NOTE Confidence: 0.95564467
00:30:04.635 --> 00:30:05.135 Regeneron,
NOTE Confidence: 0.9866265
00:30:05.674 --> 00:30:07.115 was a positive study and
NOTE Confidence: 0.9866265
00:30:07.115 --> 00:30:08.875 actually demonstrated a sixty eight
NOTE Confidence: 0.9866265

00:30:08.875 --> 00:30:10.155 percent reduction in the risk
NOTE Confidence: 0.9866265

00:30:10.155 --> 00:30:11.215 of disease recurrence.
NOTE Confidence: 0.8821818

00:30:11.835 --> 00:30:13.115 So it will be interesting
NOTE Confidence: 0.8821818

00:30:13.115 --> 00:30:14.490 next month, to contrast the
NOTE Confidence: 0.8821818

00:30:14.970 --> 00:30:15.870 patient characteristics,
NOTE Confidence: 0.9890408

00:30:16.410 --> 00:30:18.270 median time from RT completion
NOTE Confidence: 0.9890408

00:30:18.490 --> 00:30:20.030 to immune checkpoint therapy,
NOTE Confidence: 0.9731038

00:30:20.809 --> 00:30:22.670 maybe other clinical and pathologic
NOTE Confidence: 0.9731038

00:30:22.809 --> 00:30:24.410 factors that may have accounted
NOTE Confidence: 0.9731038

00:30:24.410 --> 00:30:25.929 for the differences, the stark
NOTE Confidence: 0.9731038

00:30:25.929 --> 00:30:27.150 differences in outcomes,
NOTE Confidence: 0.979716

00:30:27.935 --> 00:30:29.695 using very similar agents and
NOTE Confidence: 0.979716

00:30:29.695 --> 00:30:30.895 what seems like a similar
NOTE Confidence: 0.979716

00:30:30.895 --> 00:30:31.795 patient population.
NOTE Confidence: 0.9745872

00:30:33.535 --> 00:30:34.815 And then in twenty twenty
NOTE Confidence: 0.9745872

00:30:34.815 --> 00:30:36.175 two, as doctor Roach pointed

NOTE Confidence: 0.9745872
00:30:36.175 --> 00:30:37.615 out, came this paper from,
NOTE Confidence: 0.9745872
00:30:37.855 --> 00:30:39.375 doctor Neil Gross's group at
NOTE Confidence: 0.9745872
00:30:39.375 --> 00:30:40.195 MD Anderson.
NOTE Confidence: 0.97046405
00:30:40.519 --> 00:30:41.559 This was a phase two
NOTE Confidence: 0.97046405
00:30:41.559 --> 00:30:43.799 trial that explored, samiplimab in
NOTE Confidence: 0.97046405
00:30:43.799 --> 00:30:44.460 the neoadjuvant
NOTE Confidence: 0.8652344
00:30:44.840 --> 00:30:46.120 or pre op space,
NOTE Confidence: 0.92654854
00:30:46.440 --> 00:30:48.220 for patients with locally advanced
NOTE Confidence: 0.92654854
00:30:48.360 --> 00:30:49.580 receptacle disease.
NOTE Confidence: 0.9660309
00:30:50.440 --> 00:30:52.200 Seventy nine patients were enrolled,
NOTE Confidence: 0.9660309
00:30:52.200 --> 00:30:54.015 and they all received, four
NOTE Confidence: 0.9660309
00:30:54.015 --> 00:30:55.535 doses or twelve weeks of
NOTE Confidence: 0.9660309
00:30:55.535 --> 00:30:56.035 samiplimab,
NOTE Confidence: 0.9992676
00:30:56.735 --> 00:30:58.415 and seventy of them underwent
NOTE Confidence: 0.9992676
00:30:58.415 --> 00:30:58.915 surgery.
NOTE Confidence: 0.9651367

00:30:59.935 --> 00:31:01.455 About fifty one percent of
NOTE Confidence: 0.9651367

00:31:01.455 --> 00:31:03.055 the samples, so forty patients,
NOTE Confidence: 0.9651367

00:31:03.055 --> 00:31:04.995 had a pathologic complete response
NOTE Confidence: 0.95262045

00:31:05.535 --> 00:31:07.215 and ten additional patients, so
NOTE Confidence: 0.95262045

00:31:07.215 --> 00:31:08.655 another thirteen percent of the
NOTE Confidence: 0.95262045

00:31:08.655 --> 00:31:11.169 cohort, had major pathologic response,
NOTE Confidence: 0.95262045

00:31:11.169 --> 00:31:12.789 which was defined as residual
NOTE Confidence: 0.95262045

00:31:12.850 --> 00:31:13.970 tumor in less than ten
NOTE Confidence: 0.95262045

00:31:13.970 --> 00:31:15.750 percent of the surgical specimen.
NOTE Confidence: 0.91657364

00:31:16.929 --> 00:31:18.370 Post op treatment was at
NOTE Confidence: 0.91657364

00:31:18.370 --> 00:31:19.350 physician discretion,
NOTE Confidence: 0.98567706

00:31:19.809 --> 00:31:21.090 and at the eighteen month
NOTE Confidence: 0.98567706

00:31:21.090 --> 00:31:21.590 follow-up,
NOTE Confidence: 0.86572266

00:31:22.049 --> 00:31:22.549 paper,
NOTE Confidence: 0.99658203

00:31:23.265 --> 00:31:24.305 that was published a year
NOTE Confidence: 0.99658203

00:31:24.305 --> 00:31:25.925 later in twenty twenty three,

NOTE Confidence: 0.99658203

00:31:26.065 --> 00:31:27.765 half the patients had chosen

NOTE Confidence: 0.99658203

00:31:27.905 --> 00:31:28.565 or were

NOTE Confidence: 0.9923096

00:31:29.105 --> 00:31:30.485 recommended by their physician,

NOTE Confidence: 0.9439926

00:31:31.345 --> 00:31:33.345 observation post op. About a

NOTE Confidence: 0.9439926

00:31:33.345 --> 00:31:35.285 quarter continued to receive adjuvant

NOTE Confidence: 0.9439926

00:31:35.345 --> 00:31:35.845 samiplimab,

NOTE Confidence: 0.99731445

00:31:36.545 --> 00:31:37.685 and only a quarter

NOTE Confidence: 0.9992947

00:31:38.309 --> 00:31:39.769 received adjuvant radiation.

NOTE Confidence: 0.99934894

00:31:40.549 --> 00:31:41.049 Importantly,

NOTE Confidence: 0.8975941

00:31:41.350 --> 00:31:42.630 none of the forty patients

NOTE Confidence: 0.8975941

00:31:42.630 --> 00:31:43.669 who had a PAT c

NOTE Confidence: 0.8975941

00:31:43.669 --> 00:31:44.169 r,

NOTE Confidence: 0.9890834

00:31:44.549 --> 00:31:45.590 and only one of the

NOTE Confidence: 0.9890834

00:31:45.590 --> 00:31:46.710 ten patients who had a

NOTE Confidence: 0.9890834

00:31:46.710 --> 00:31:49.210 major pathologic response had recurrence

NOTE Confidence: 0.9890834

00:31:49.350 --> 00:31:50.630 at that eighteen month time
NOTE Confidence: 0.9890834

00:31:50.630 --> 00:31:51.130 point,
NOTE Confidence: 0.9881481

00:31:51.785 --> 00:31:53.065 or by that eighteen month
NOTE Confidence: 0.9881481

00:31:53.065 --> 00:31:54.345 time point. And the twelve
NOTE Confidence: 0.9881481

00:31:54.345 --> 00:31:55.945 month disease free survival for
NOTE Confidence: 0.9881481

00:31:55.945 --> 00:31:57.385 the entire cohort was ninety
NOTE Confidence: 0.9881481

00:31:57.385 --> 00:31:58.044 two percent.
NOTE Confidence: 0.9964355

00:31:58.505 --> 00:32:00.365 So very, very encouraging data.
NOTE Confidence: 0.9393136

00:32:01.625 --> 00:32:03.750 And given our experience with
NOTE Confidence: 0.9393136

00:32:03.910 --> 00:32:05.110 anti p d one agents
NOTE Confidence: 0.9393136

00:32:05.110 --> 00:32:06.470 in this disease, perhaps,
NOTE Confidence: 0.99856085

00:32:06.790 --> 00:32:08.230 the best way to harness
NOTE Confidence: 0.99856085

00:32:08.230 --> 00:32:09.910 the full potential of these
NOTE Confidence: 0.99856085

00:32:09.910 --> 00:32:11.430 agents is to administer it
NOTE Confidence: 0.99856085

00:32:11.430 --> 00:32:12.970 in the neoadjuvant space.
NOTE Confidence: 0.9993286

00:32:13.590 --> 00:32:15.030 That's the direction the field

NOTE Confidence: 0.9993286

00:32:15.030 --> 00:32:15.990 is moving in.

NOTE Confidence: 0.9871493

00:32:16.310 --> 00:32:17.190 The hope is that it

NOTE Confidence: 0.9871493

00:32:17.190 --> 00:32:19.030 would decrease the recurrence risk,

NOTE Confidence: 0.9871493

00:32:19.030 --> 00:32:19.530 which,

NOTE Confidence: 0.981656

00:32:20.485 --> 00:32:21.525 you know, seems likely with

NOTE Confidence: 0.981656

00:32:21.525 --> 00:32:22.885 these agents being effective in

NOTE Confidence: 0.981656

00:32:22.885 --> 00:32:24.184 the adjuvant and in the

NOTE Confidence: 0.981656

00:32:24.405 --> 00:32:25.304 advanced space,

NOTE Confidence: 0.95649415

00:32:25.845 --> 00:32:27.445 but more importantly, might actually

NOTE Confidence: 0.95649415

00:32:27.445 --> 00:32:29.225 decrease the morbidity of surgery,

NOTE Confidence: 0.9991537

00:32:30.165 --> 00:32:31.285 at least for the majority

NOTE Confidence: 0.9991537

00:32:31.285 --> 00:32:32.325 of patients who do end

NOTE Confidence: 0.9991537

00:32:32.325 --> 00:32:33.865 up having a treatment response.

NOTE Confidence: 0.99798584

00:32:34.325 --> 00:32:35.820 So with that intent, we're

NOTE Confidence: 0.99798584

00:32:35.820 --> 00:32:36.779 excited to support,

NOTE Confidence: 0.9723598

00:32:37.100 --> 00:32:38.539 NRG h n zero one
NOTE Confidence: 0.9723598

00:32:38.539 --> 00:32:40.220 four, which is, very soon
NOTE Confidence: 0.9723598

00:32:40.220 --> 00:32:41.440 gonna open at Yale.
NOTE Confidence: 0.9823557

00:32:42.059 --> 00:32:42.940 It will be led by
NOTE Confidence: 0.9823557

00:32:42.940 --> 00:32:44.460 doctor Roach, and this is
NOTE Confidence: 0.9823557

00:32:44.460 --> 00:32:46.140 a randomized cooperative group trial
NOTE Confidence: 0.9823557

00:32:46.140 --> 00:32:47.659 as she pointed out. It
NOTE Confidence: 0.9823557

00:32:47.659 --> 00:32:48.940 will be offered to patients
NOTE Confidence: 0.9823557

00:32:48.940 --> 00:32:51.105 with locally advanced cutaneous squamous
NOTE Confidence: 0.9823557

00:32:51.105 --> 00:32:53.265 at any body site. Patients
NOTE Confidence: 0.9823557

00:32:53.265 --> 00:32:54.705 will be randomized to receive
NOTE Confidence: 0.9823557

00:32:54.705 --> 00:32:55.925 either upfront surgery,
NOTE Confidence: 0.98053133

00:32:56.705 --> 00:32:58.545 followed by adjuvant radiation, which
NOTE Confidence: 0.98053133

00:32:58.545 --> 00:32:59.745 is the current standard of
NOTE Confidence: 0.98053133

00:32:59.745 --> 00:33:00.885 care, or neoadjuvant
NOTE Confidence: 0.8004883

00:33:01.265 --> 00:33:01.765 simiplumab.

NOTE Confidence: 0.9745861

00:33:02.800 --> 00:33:03.920 It's gonna be similar to

NOTE Confidence: 0.9745861

00:33:03.920 --> 00:33:05.440 the phase two study design.

NOTE Confidence: 0.9745861

00:33:05.440 --> 00:33:06.960 So patients will receive four

NOTE Confidence: 0.9745861

00:33:06.960 --> 00:33:09.300 doses followed by response adaptive

NOTE Confidence: 0.9745861

00:33:09.360 --> 00:33:09.860 surgery,

NOTE Confidence: 0.9123792

00:33:10.720 --> 00:33:12.960 adjuvant radiation if indicated, which

NOTE Confidence: 0.9123792

00:33:12.960 --> 00:33:14.080 at our site we offer

NOTE Confidence: 0.9123792

00:33:14.080 --> 00:33:15.760 to people with residual disease,

NOTE Confidence: 0.9123792

00:33:15.760 --> 00:33:17.460 but not necessarily otherwise,

NOTE Confidence: 0.9193685

00:33:18.545 --> 00:33:19.765 and adjuvant simiplimab,

NOTE Confidence: 0.9848739

00:33:20.145 --> 00:33:21.345 again, only if there is

NOTE Confidence: 0.9848739

00:33:21.345 --> 00:33:23.105 residual disease for twenty four

NOTE Confidence: 0.9848739

00:33:23.105 --> 00:33:25.184 additional weeks. And four hundred

NOTE Confidence: 0.9848739

00:33:25.184 --> 00:33:26.785 and twenty patients are expected

NOTE Confidence: 0.9848739

00:33:26.785 --> 00:33:27.684 to be enrolled.

NOTE Confidence: 0.99491376

00:33:29.025 --> 00:33:30.405 These are the key eligibility
NOTE Confidence: 0.99491376
00:33:30.625 --> 00:33:31.125 criteria.
NOTE Confidence: 0.9632324
00:33:31.759 --> 00:33:33.539 So patients should have resectable,
NOTE Confidence: 0.9749892
00:33:34.000 --> 00:33:35.539 stage three or four cutaneous
NOTE Confidence: 0.9749892
00:33:35.759 --> 00:33:36.240 squam,
NOTE Confidence: 0.9950358
00:33:36.559 --> 00:33:37.840 or they could have regional
NOTE Confidence: 0.9950358
00:33:37.840 --> 00:33:38.340 lymphadenopathy
NOTE Confidence: 0.98800224
00:33:39.039 --> 00:33:40.240 suspected to be from a
NOTE Confidence: 0.98800224
00:33:40.240 --> 00:33:41.299 cutaneous primary,
NOTE Confidence: 0.9071452
00:33:42.159 --> 00:33:43.539 or in transit METs.
NOTE Confidence: 0.9646403
00:33:43.840 --> 00:33:45.519 Disease should be measurable by
NOTE Confidence: 0.9646403
00:33:45.519 --> 00:33:46.019 resist.
NOTE Confidence: 0.95353884
00:33:46.505 --> 00:33:48.605 And importantly, patients with CLL,
NOTE Confidence: 0.95353884
00:33:48.665 --> 00:33:49.325 so immunosuppressed,
NOTE Confidence: 0.99560547
00:33:50.665 --> 00:33:51.785 who are not on active
NOTE Confidence: 0.99560547
00:33:51.785 --> 00:33:52.285 treatment

NOTE Confidence: 0.9572797

00:33:52.745 --> 00:33:54.425 and with HIV, who are

NOTE Confidence: 0.9572797

00:33:54.425 --> 00:33:56.905 on, entry retroviral therapy and

NOTE Confidence: 0.9572797

00:33:56.905 --> 00:33:58.745 with controlled viral loads will

NOTE Confidence: 0.9572797

00:33:58.745 --> 00:34:00.205 be eligible to enroll.

NOTE Confidence: 0.96547854

00:34:01.380 --> 00:34:02.840 And that's all I have,

NOTE Confidence: 0.9469105

00:34:03.140 --> 00:34:05.480 from the Medanquin immunotherapy perspective.

NOTE Confidence: 0.9469105

00:34:05.700 --> 00:34:06.900 I'm happy to take any

NOTE Confidence: 0.9469105

00:34:06.900 --> 00:34:07.400 questions.

NOTE Confidence: 0.99658203

00:34:07.860 --> 00:34:08.600 Thank you.

NOTE Confidence: 0.9980469

00:34:12.420 --> 00:34:12.920 Doctor

NOTE Confidence: 0.93204755

00:34:13.715 --> 00:34:15.555 could you comment on how

NOTE Confidence: 0.93204755

00:34:15.555 --> 00:34:17.015 we think about the use

NOTE Confidence: 0.93204755

00:34:17.315 --> 00:34:19.235 of checkpoint inhibitors and solid

NOTE Confidence: 0.93204755

00:34:19.235 --> 00:34:20.455 or organ transplant

NOTE Confidence: 0.95007324

00:34:20.835 --> 00:34:22.055 recipients? Because,

NOTE Confidence: 0.9737752

00:34:22.355 --> 00:34:23.795 you know, traditionally, that's been

NOTE Confidence: 0.9737752

00:34:23.795 --> 00:34:25.075 a was a hard no,

NOTE Confidence: 0.9737752

00:34:25.075 --> 00:34:25.815 but now,

NOTE Confidence: 0.9683756

00:34:26.275 --> 00:34:27.719 you know, that's being relooked

NOTE Confidence: 0.9683756

00:34:27.719 --> 00:34:28.760 at. So I'd be curious

NOTE Confidence: 0.9683756

00:34:28.760 --> 00:34:30.380 on your perspective of that.

NOTE Confidence: 1

00:34:30.840 --> 00:34:31.340 Yeah.

NOTE Confidence: 0.9944661

00:34:32.200 --> 00:34:33.180 So we're obviously

NOTE Confidence: 0.9596166

00:34:33.560 --> 00:34:35.640 wary about using immune checkpoint

NOTE Confidence: 0.9596166

00:34:35.640 --> 00:34:37.739 therapy in solid organ transplant

NOTE Confidence: 0.9596166

00:34:37.800 --> 00:34:39.099 as well as in allogeneic

NOTE Confidence: 0.9596166

00:34:39.320 --> 00:34:41.000 stem cell transplant patients because

NOTE Confidence: 0.9596166

00:34:41.000 --> 00:34:42.119 the risk is of graft

NOTE Confidence: 0.9596166

00:34:42.119 --> 00:34:42.619 rejection.

NOTE Confidence: 0.9423191

00:34:43.775 --> 00:34:46.094 There have been retrospective series

NOTE Confidence: 0.9423191

00:34:46.094 --> 00:34:47.935 that have, tried to assess,

NOTE Confidence: 0.9423191
00:34:48.175 --> 00:34:49.614 a a risk sort of
NOTE Confidence: 0.9423191
00:34:49.614 --> 00:34:50.975 like a risk assessment for
NOTE Confidence: 0.9423191
00:34:50.975 --> 00:34:52.035 these patients, and,
NOTE Confidence: 0.97528946
00:34:53.215 --> 00:34:54.515 there has been a reported
NOTE Confidence: 0.97528946
00:34:54.655 --> 00:34:56.255 forty to forty five percent
NOTE Confidence: 0.97528946
00:34:56.255 --> 00:34:57.182 risk of graft rejection,
NOTE Confidence: 0.9976671
00:34:57.950 --> 00:34:59.170 with using immunotherapy,
NOTE Confidence: 0.9649414
00:35:00.269 --> 00:35:02.289 in solid organ transplant recipients.
NOTE Confidence: 0.9851074
00:35:03.309 --> 00:35:04.670 Having said that, there was
NOTE Confidence: 0.9851074
00:35:04.670 --> 00:35:06.130 recently a small,
NOTE Confidence: 0.991092
00:35:06.430 --> 00:35:07.950 prospective trial. I think it
NOTE Confidence: 0.991092
00:35:07.950 --> 00:35:09.710 enrolled eleven or twelve patients
NOTE Confidence: 0.991092
00:35:09.710 --> 00:35:10.690 at Dana Farber.
NOTE Confidence: 0.89603096
00:35:11.535 --> 00:35:13.135 One of the cohorts was
NOTE Confidence: 0.89603096
00:35:13.135 --> 00:35:13.714 in cutaneous
NOTE Confidence: 0.95983064

00:35:14.015 --> 00:35:15.454 squam, and it was in
NOTE Confidence: 0.95983064

00:35:15.454 --> 00:35:17.635 patients who've had renal transplants.
NOTE Confidence: 0.97165644

00:35:19.214 --> 00:35:20.575 And along and they were
NOTE Confidence: 0.97165644

00:35:20.575 --> 00:35:21.555 given immunotherapy.
NOTE Confidence: 0.93350583

00:35:22.734 --> 00:35:23.875 I think it was simiplimab,
NOTE Confidence: 0.8918457

00:35:24.780 --> 00:35:26.640 along with pulse dose steroids
NOTE Confidence: 0.8918457

00:35:26.700 --> 00:35:28.000 and an mTOR inhibitor.
NOTE Confidence: 0.99189454

00:35:28.460 --> 00:35:30.380 And, they did demonstrate a
NOTE Confidence: 0.99189454

00:35:30.380 --> 00:35:31.980 forty to forty five percent
NOTE Confidence: 0.99189454

00:35:31.980 --> 00:35:33.739 response rate, so very similar
NOTE Confidence: 0.99189454

00:35:33.739 --> 00:35:34.940 to what we see in
NOTE Confidence: 0.99189454

00:35:34.940 --> 00:35:35.840 non immunosuppressed,
NOTE Confidence: 0.7940267

00:35:36.460 --> 00:35:38.080 non transplanted patients.
NOTE Confidence: 0.9990932

00:35:38.775 --> 00:35:40.775 And, you know, interestingly, none
NOTE Confidence: 0.9990932

00:35:40.775 --> 00:35:42.055 of those patients had a
NOTE Confidence: 0.9990932

00:35:42.055 --> 00:35:43.755 rejection of their graft.

NOTE Confidence: 0.99452716
00:35:44.855 --> 00:35:46.214 Now are we ready to
NOTE Confidence: 0.99452716
00:35:46.214 --> 00:35:48.135 translate this into other organ
NOTE Confidence: 0.99452716
00:35:48.135 --> 00:35:49.194 transplant recipients?
NOTE Confidence: 0.98444474
00:35:49.734 --> 00:35:51.494 Probably not ready for prime
NOTE Confidence: 0.98444474
00:35:51.494 --> 00:35:52.110 time yet.
NOTE Confidence: 0.98694664
00:35:52.510 --> 00:35:54.110 The risks are obviously lower
NOTE Confidence: 0.98694664
00:35:54.110 --> 00:35:55.790 for renal transplant patients who
NOTE Confidence: 0.98694664
00:35:55.790 --> 00:35:57.410 have dialysis as a backup,
NOTE Confidence: 0.9981166
00:35:58.270 --> 00:36:00.030 but not necessarily for other
NOTE Confidence: 0.9981166
00:36:00.030 --> 00:36:01.070 transplants. So,
NOTE Confidence: 0.9989624
00:36:02.190 --> 00:36:03.810 you know, we have considered
NOTE Confidence: 0.9989624
00:36:03.950 --> 00:36:05.330 cautiously using immunotherapy
NOTE Confidence: 0.9790039
00:36:05.630 --> 00:36:07.170 in renal transplant patients,
NOTE Confidence: 0.97467595
00:36:08.165 --> 00:36:10.025 but haven't yet, you know,
NOTE Confidence: 0.97467595
00:36:10.244 --> 00:36:11.864 made that switch to liver,
NOTE Confidence: 0.97467595

00:36:11.925 --> 00:36:14.085 you know, cardiac lung transplant.
NOTE Confidence: 0.97467595

00:36:14.085 --> 00:36:14.965 That would just be too
NOTE Confidence: 0.97467595

00:36:14.965 --> 00:36:15.625 high risk.
NOTE Confidence: 0.9810791

00:36:16.725 --> 00:36:17.685 Yeah. And then that was
NOTE Confidence: 0.9810791

00:36:17.685 --> 00:36:18.085 the,
NOTE Confidence: 0.97314453

00:36:18.645 --> 00:36:19.765 recent study that I was
NOTE Confidence: 0.97314453

00:36:19.765 --> 00:36:20.910 alluding to, and I think
NOTE Confidence: 0.97314453

00:36:20.910 --> 00:36:22.030 that, like you said, of
NOTE Confidence: 0.97314453

00:36:22.030 --> 00:36:23.250 course, the organ matters.
NOTE Confidence: 0.92247176

00:36:23.790 --> 00:36:25.630 But also the patients who
NOTE Confidence: 0.92247176

00:36:25.630 --> 00:36:27.489 have that catastrophic carcinomatosis
NOTE Confidence: 0.9832031

00:36:27.950 --> 00:36:29.069 tend to be those patients
NOTE Confidence: 0.9832031

00:36:29.069 --> 00:36:31.150 who have cardiac transplant or
NOTE Confidence: 0.9832031

00:36:31.150 --> 00:36:33.170 higher immune suppression. So Mhmm.
NOTE Confidence: 0.9942278

00:36:33.815 --> 00:36:34.935 But I think being able
NOTE Confidence: 0.9942278

00:36:34.935 --> 00:36:36.535 to consider it for patients

NOTE Confidence: 0.9942278

00:36:36.535 --> 00:36:37.995 who have renal transplant,

NOTE Confidence: 0.9822998

00:36:38.375 --> 00:36:39.735 is where we're moving, it

NOTE Confidence: 0.9822998

00:36:39.735 --> 00:36:40.235 seems.

NOTE Confidence: 0.9992676

00:36:40.535 --> 00:36:41.435 Yes. Exactly.

NOTE Confidence: 0.95022404

00:36:44.055 --> 00:36:45.175 I think to add along

NOTE Confidence: 0.95022404

00:36:45.175 --> 00:36:46.469 those points, too, we always

NOTE Confidence: 0.95022404

00:36:46.469 --> 00:36:47.590 just try to work with

NOTE Confidence: 0.95022404

00:36:47.590 --> 00:36:48.489 the transplant

NOTE Confidence: 0.9333984

00:36:49.510 --> 00:36:51.850 physician about minimizing their immunosuppression

NOTE Confidence: 0.95144314

00:36:52.230 --> 00:36:53.270 as well because that in

NOTE Confidence: 0.95144314

00:36:53.270 --> 00:36:54.570 and of itself sometimes

NOTE Confidence: 0.9716797

00:36:55.030 --> 00:36:56.010 can help reactivate,

NOTE Confidence: 0.97596574

00:36:56.310 --> 00:36:58.070 reinvigorate the immune system to

NOTE Confidence: 0.97596574

00:36:58.070 --> 00:36:59.805 provide a clinical response

NOTE Confidence: 0.9336548

00:37:00.505 --> 00:37:02.425 particularly in these earlier stage

NOTE Confidence: 0.9336548
00:37:02.425 --> 00:37:03.565 squamous cell carcinomas
NOTE Confidence: 0.98324585
00:37:04.344 --> 00:37:05.545 to try to avoid all
NOTE Confidence: 0.98324585
00:37:05.545 --> 00:37:07.085 systemic therapy altogether.
NOTE Confidence: 0.91012573
00:37:09.705 --> 00:37:10.844 That's a great point.
NOTE Confidence: 0.91557616
00:37:11.219 --> 00:37:12.260 Again, our our q and
NOTE Confidence: 0.91557616
00:37:12.260 --> 00:37:13.540 a is open if if
NOTE Confidence: 0.91557616
00:37:13.540 --> 00:37:14.980 anyone in the audience wants
NOTE Confidence: 0.91557616
00:37:14.980 --> 00:37:16.840 to, send us any chats.
NOTE Confidence: 0.9318719
00:37:17.619 --> 00:37:18.900 We keep asking each other
NOTE Confidence: 0.9318719
00:37:18.900 --> 00:37:20.340 very hard questions so someone
NOTE Confidence: 0.9318719
00:37:20.340 --> 00:37:21.460 someone needs to help us
NOTE Confidence: 0.9318719
00:37:21.460 --> 00:37:22.520 save us from ourselves.
NOTE Confidence: 0.9830322
00:37:23.700 --> 00:37:24.920 On on that note,
NOTE Confidence: 0.8737793
00:37:26.075 --> 00:37:28.255 doctor doctor Tran will begin,
NOTE Confidence: 0.97172624
00:37:28.714 --> 00:37:30.635 our, segue into the world
NOTE Confidence: 0.97172624

00:37:30.635 --> 00:37:31.535 of melanoma.
NOTE Confidence: 0.97038317

00:37:32.875 --> 00:37:34.714 Alright. So just building upon
NOTE Confidence: 0.97038317

00:37:34.714 --> 00:37:35.994 already kind of the excellent
NOTE Confidence: 0.97038317

00:37:35.994 --> 00:37:37.594 response data that we've already
NOTE Confidence: 0.97038317

00:37:37.594 --> 00:37:38.954 seen from our colleagues here
NOTE Confidence: 0.97038317

00:37:38.954 --> 00:37:40.174 in cutaneous gramisocarcinomas.
NOTE Confidence: 0.98024267

00:37:41.434 --> 00:37:42.130 I I think the next
NOTE Confidence: 0.98024267

00:37:42.130 --> 00:37:43.489 set of questions that Doctor.
NOTE Confidence: 0.98024267

00:37:43.489 --> 00:37:44.850 Alina and I will discuss
NOTE Confidence: 0.98024267

00:37:44.850 --> 00:37:46.530 are basically how to select
NOTE Confidence: 0.98024267

00:37:46.530 --> 00:37:48.290 the populations that would benefit
NOTE Confidence: 0.98024267

00:37:48.290 --> 00:37:48.950 the most
NOTE Confidence: 0.8972168

00:37:49.410 --> 00:37:50.150 while minimizing
NOTE Confidence: 0.9406738

00:37:50.450 --> 00:37:50.950 overtreatment
NOTE Confidence: 0.99902344

00:37:51.570 --> 00:37:52.310 and toxicity
NOTE Confidence: 0.92470706

00:37:52.610 --> 00:37:54.310 from the systemic immunotherapies.

NOTE Confidence: 0.9227387

00:37:55.275 --> 00:37:56.555 And while our colleagues have

NOTE Confidence: 0.9227387

00:37:56.555 --> 00:37:58.474 eloquently reviewed kind of cutaneous

NOTE Confidence: 0.9227387

00:37:58.474 --> 00:38:00.154 gramian cell carcinomas, Doctor. Lina

NOTE Confidence: 0.9227387

00:38:00.154 --> 00:38:00.875 and I will kind of

NOTE Confidence: 0.9227387

00:38:00.875 --> 00:38:01.775 focus now

NOTE Confidence: 0.97319883

00:38:02.154 --> 00:38:03.375 specifically on melanomas.

NOTE Confidence: 0.99487305

00:38:04.395 --> 00:38:05.674 And so whenever we think

NOTE Confidence: 0.99487305

00:38:05.674 --> 00:38:06.174 about

NOTE Confidence: 0.9637146

00:38:06.635 --> 00:38:08.954 utilizing systemic therapy for a

NOTE Confidence: 0.9637146

00:38:08.954 --> 00:38:10.260 disease that's surgically

NOTE Confidence: 0.8382433

00:38:10.560 --> 00:38:12.480 technically curative, although may be

NOTE Confidence: 0.8382433

00:38:12.480 --> 00:38:12.980 morbid,

NOTE Confidence: 0.99515474

00:38:13.440 --> 00:38:14.640 we have to stop and

NOTE Confidence: 0.99515474

00:38:14.640 --> 00:38:16.400 ask the question about risk

NOTE Confidence: 0.99515474

00:38:16.400 --> 00:38:17.460 and benefit ratio

NOTE Confidence: 0.93228585

00:38:17.920 --> 00:38:19.360 per the patient. You know,
NOTE Confidence: 0.93228585

00:38:19.360 --> 00:38:20.500 what is in the patient's
NOTE Confidence: 0.93228585

00:38:20.560 --> 00:38:22.000 best interest, the individual in
NOTE Confidence: 0.93228585

00:38:22.000 --> 00:38:24.055 front of us? So as
NOTE Confidence: 0.93228585

00:38:24.055 --> 00:38:25.175 with their a lot of
NOTE Confidence: 0.93228585

00:38:25.175 --> 00:38:26.395 other main therapies,
NOTE Confidence: 0.98055017

00:38:27.175 --> 00:38:28.395 irreversible toxicities,
NOTE Confidence: 0.9956462

00:38:28.775 --> 00:38:29.815 as you all know, can
NOTE Confidence: 0.9956462

00:38:29.815 --> 00:38:30.315 occur,
NOTE Confidence: 0.99437803

00:38:31.415 --> 00:38:32.795 which can be life altering.
NOTE Confidence: 0.99437803

00:38:33.015 --> 00:38:34.695 So to give someone a
NOTE Confidence: 0.99437803

00:38:34.695 --> 00:38:35.755 permanent endocrinopathy
NOTE Confidence: 0.9549713

00:38:36.730 --> 00:38:38.570 or even more severe toxicity
NOTE Confidence: 0.9549713

00:38:38.570 --> 00:38:39.550 such as myocarditis,
NOTE Confidence: 0.98876953

00:38:41.450 --> 00:38:42.969 in something that is potentially
NOTE Confidence: 0.98876953

00:38:42.969 --> 00:38:45.370 just curative with surgery alone,

NOTE Confidence: 0.98876953
00:38:45.370 --> 00:38:47.230 that can be particularly devastating.
NOTE Confidence: 0.98875844
00:38:48.785 --> 00:38:50.225 So generally, we're able to
NOTE Confidence: 0.98875844
00:38:50.225 --> 00:38:51.505 accept more of a risk
NOTE Confidence: 0.98875844
00:38:51.505 --> 00:38:53.025 profile when we think about
NOTE Confidence: 0.98875844
00:38:53.025 --> 00:38:54.705 treating more aggressive cancers or
NOTE Confidence: 0.98875844
00:38:54.705 --> 00:38:56.065 recurrent cancers in the hopes
NOTE Confidence: 0.98875844
00:38:56.065 --> 00:38:57.265 that we can kind of
NOTE Confidence: 0.98875844
00:38:57.265 --> 00:38:58.725 balance out the side effect
NOTE Confidence: 0.98875844
00:38:58.785 --> 00:39:00.625 ratios to avoid impacting an
NOTE Confidence: 0.98875844
00:39:00.625 --> 00:39:02.325 individual's quality of life.
NOTE Confidence: 0.9644968
00:39:03.850 --> 00:39:04.730 And so there are a
NOTE Confidence: 0.9644968
00:39:04.730 --> 00:39:05.930 lot of factors that get
NOTE Confidence: 0.9644968
00:39:05.930 --> 00:39:07.450 integrated into how we approach
NOTE Confidence: 0.9644968
00:39:07.450 --> 00:39:08.910 and treat skin cancers.
NOTE Confidence: 0.95157874
00:39:09.609 --> 00:39:11.369 Even for melanoma, certain types
NOTE Confidence: 0.95157874

00:39:11.369 --> 00:39:12.890 are much more responsive to
NOTE Confidence: 0.95157874

00:39:12.890 --> 00:39:13.390 immunotherapy
NOTE Confidence: 0.9942627

00:39:13.850 --> 00:39:14.590 than others.
NOTE Confidence: 0.9887251

00:39:15.234 --> 00:39:16.355 For example, kind of one
NOTE Confidence: 0.9887251

00:39:16.355 --> 00:39:17.875 of our classic scenarios is
NOTE Confidence: 0.9887251

00:39:17.875 --> 00:39:18.375 desmoplastic
NOTE Confidence: 0.9513594

00:39:18.755 --> 00:39:20.114 melanomas of the head and
NOTE Confidence: 0.9513594

00:39:20.114 --> 00:39:22.275 neck. Those are particularly even
NOTE Confidence: 0.9513594

00:39:22.275 --> 00:39:24.035 more responsive to single agent
NOTE Confidence: 0.9513594

00:39:24.035 --> 00:39:26.114 immune therapeutics, and sometimes that's
NOTE Confidence: 0.9513594

00:39:26.114 --> 00:39:27.415 all patients need,
NOTE Confidence: 0.97340494

00:39:27.960 --> 00:39:29.239 versus things that are more
NOTE Confidence: 0.97340494

00:39:29.239 --> 00:39:30.760 refractory that don't carry the
NOTE Confidence: 0.97340494

00:39:30.760 --> 00:39:33.100 typical UV induced mutational signature.
NOTE Confidence: 0.8918728

00:39:33.480 --> 00:39:35.160 So things like mucosal April
NOTE Confidence: 0.8918728

00:39:35.160 --> 00:39:35.660 melanomas.

NOTE Confidence: 0.92306083

00:39:36.840 --> 00:39:38.200 Additionally, there is other risk

NOTE Confidence: 0.92306083

00:39:38.200 --> 00:39:39.260 factors, including

NOTE Confidence: 0.9793565

00:39:40.075 --> 00:39:41.355 where the mass is, you

NOTE Confidence: 0.9793565

00:39:41.355 --> 00:39:42.395 know, is it a large

NOTE Confidence: 0.9793565

00:39:42.395 --> 00:39:43.915 axillary mass that's pressing on

NOTE Confidence: 0.9793565

00:39:43.915 --> 00:39:45.055 the brachial plexus

NOTE Confidence: 0.9443185

00:39:45.594 --> 00:39:47.035 that could potentially lead to

NOTE Confidence: 0.9443185

00:39:47.035 --> 00:39:48.235 loss of function and over

NOTE Confidence: 0.9443185

00:39:48.235 --> 00:39:49.375 the next few months,

NOTE Confidence: 0.9361003

00:39:50.235 --> 00:39:51.935 where we need rapid cytoreduction

NOTE Confidence: 0.8294678

00:40:05.154 --> 00:40:06.555 the lytic virus therapy is

NOTE Confidence: 0.8294678

00:40:06.555 --> 00:40:08.015 already approved. I mean, checkpoint

NOTE Confidence: 0.8294678

00:40:08.075 --> 00:40:09.695 inhibitors, we all know about.

NOTE Confidence: 0.96442205

00:40:10.395 --> 00:40:12.655 Adoptive T cell transfer therapies

NOTE Confidence: 0.96442205

00:40:12.715 --> 00:40:14.155 have also now been FDA

NOTE Confidence: 0.96442205

00:40:14.155 --> 00:40:14.655 approved.
NOTE Confidence: 0.97216797

00:40:15.114 --> 00:40:16.415 And under investigation
NOTE Confidence: 0.8259006

00:40:16.875 --> 00:40:18.975 currently are cancer vaccine therapies,
NOTE Confidence: 0.8259006

00:40:19.114 --> 00:40:19.950 in which we'll discuss
NOTE Confidence: 0.9278642

00:40:28.670 --> 00:40:30.430 classically high dose IL-two is
NOTE Confidence: 0.9278642

00:40:30.430 --> 00:40:32.210 fairly toxic. How can we
NOTE Confidence: 0.9278642

00:40:32.270 --> 00:40:33.969 kind of redesign these cytokine
NOTE Confidence: 0.9278642

00:40:34.030 --> 00:40:35.150 drugs to make them more
NOTE Confidence: 0.9278642

00:40:35.150 --> 00:40:35.650 tolerable,
NOTE Confidence: 0.9852702

00:40:36.405 --> 00:40:37.864 while maintaining efficacy.
NOTE Confidence: 0.97914165

00:40:39.525 --> 00:40:41.705 And so because these treatments
NOTE Confidence: 0.97914165

00:40:41.765 --> 00:40:43.285 can be quite effective in
NOTE Confidence: 0.97914165

00:40:43.285 --> 00:40:45.045 melanoma, the next question is
NOTE Confidence: 0.97914165

00:40:45.045 --> 00:40:46.325 how can we optimize sort
NOTE Confidence: 0.97914165

00:40:46.325 --> 00:40:47.605 of the sequencing of these
NOTE Confidence: 0.97914165

00:40:47.605 --> 00:40:48.105 therapies

NOTE Confidence: 0.9995117
00:40:48.670 --> 00:40:49.489 to maximize
NOTE Confidence: 0.9519043
00:40:49.950 --> 00:40:51.790 response and also durability of
NOTE Confidence: 0.9519043
00:40:51.790 --> 00:40:52.290 response?
NOTE Confidence: 0.96489793
00:40:53.230 --> 00:40:54.590 So when we think about
NOTE Confidence: 0.96489793
00:40:54.590 --> 00:40:55.950 melanoma, we like to talk
NOTE Confidence: 0.96489793
00:40:55.950 --> 00:40:57.170 about melanoma
NOTE Confidence: 0.9970703
00:40:57.550 --> 00:40:58.050 specific
NOTE Confidence: 0.9519043
00:40:58.350 --> 00:40:58.850 survival.
NOTE Confidence: 0.9869963
00:40:59.790 --> 00:41:00.910 And then over on the
NOTE Confidence: 0.9869963
00:41:00.910 --> 00:41:02.270 right here is the table
NOTE Confidence: 0.9869963
00:41:02.270 --> 00:41:03.844 by stage of the five
NOTE Confidence: 0.9869963
00:41:03.844 --> 00:41:04.984 year and ten year
NOTE Confidence: 0.97960484
00:41:05.285 --> 00:41:07.444 melanoma specific survival. And as
NOTE Confidence: 0.97960484
00:41:07.444 --> 00:41:08.405 you can see, most of
NOTE Confidence: 0.97960484
00:41:08.405 --> 00:41:09.704 this data correlates.
NOTE Confidence: 0.9888509

00:41:10.244 --> 00:41:11.765 You know, individuals with lower

NOTE Confidence: 0.9888509

00:41:11.765 --> 00:41:13.224 risk, lower stage melanomas

NOTE Confidence: 0.9802246

00:41:13.525 --> 00:41:15.464 have improved survival overall.

NOTE Confidence: 0.9437256

00:41:16.020 --> 00:41:17.300 And generally, in the higher

NOTE Confidence: 0.9437256

00:41:17.300 --> 00:41:17.780 risk,

NOTE Confidence: 0.91956466

00:41:18.260 --> 00:41:19.620 melanomas, so those that are

NOTE Confidence: 0.91956466

00:41:19.620 --> 00:41:21.320 stage IIBs and beyond,

NOTE Confidence: 0.97802734

00:41:21.940 --> 00:41:22.980 the five and ten year

NOTE Confidence: 0.97802734

00:41:22.980 --> 00:41:23.480 overall

NOTE Confidence: 0.99279785

00:41:24.020 --> 00:41:25.239 melanoma survival

NOTE Confidence: 0.95011395

00:41:25.780 --> 00:41:26.680 can be between,

NOTE Confidence: 0.9930943

00:41:27.219 --> 00:41:28.820 the low 80s to twenty

NOTE Confidence: 0.9930943

00:41:28.820 --> 00:41:29.640 four percent.

NOTE Confidence: 0.9618014

00:41:30.305 --> 00:41:31.345 This is also kind of

NOTE Confidence: 0.9618014

00:41:31.345 --> 00:41:33.105 with exception of the stage

NOTE Confidence: 0.9618014

00:41:33.105 --> 00:41:34.485 three a population,

NOTE Confidence: 0.9975586

00:41:34.785 --> 00:41:35.685 which actually

NOTE Confidence: 0.98222655

00:41:36.385 --> 00:41:38.165 performs better than a standard

NOTE Confidence: 0.98222655

00:41:38.225 --> 00:41:39.685 two b or two c.

NOTE Confidence: 0.9814182

00:41:41.505 --> 00:41:42.785 So what we wanna do

NOTE Confidence: 0.9814182

00:41:42.785 --> 00:41:43.985 is now that we have

NOTE Confidence: 0.9814182

00:41:43.985 --> 00:41:46.440 these adjuvant therapies approved for

NOTE Confidence: 0.9814182

00:41:46.440 --> 00:41:47.660 high risk melanomas,

NOTE Confidence: 0.9944735

00:41:48.520 --> 00:41:49.960 now we're trying to kind

NOTE Confidence: 0.9944735

00:41:49.960 --> 00:41:51.239 of hone in on the

NOTE Confidence: 0.9944735

00:41:51.239 --> 00:41:51.739 subpopulation

NOTE Confidence: 0.93111163

00:41:52.520 --> 00:41:54.359 that would potentially benefit for

NOTE Confidence: 0.93111163

00:41:54.359 --> 00:41:55.820 new adjuvant consideration.

NOTE Confidence: 0.99358577

00:41:56.680 --> 00:41:58.540 And the rationale is that,

NOTE Confidence: 0.99358577

00:41:58.704 --> 00:41:59.825 you know, for a long

NOTE Confidence: 0.99358577

00:41:59.825 --> 00:42:01.665 time, there was very little

NOTE Confidence: 0.99358577

00:42:01.665 --> 00:42:03.424 to offer for individuals with
NOTE Confidence: 0.99358577

00:42:03.424 --> 00:42:04.565 metastatic melanoma.
NOTE Confidence: 0.9950506

00:42:06.224 --> 00:42:07.585 It's really been over the
NOTE Confidence: 0.9950506

00:42:07.585 --> 00:42:09.265 past twenty years that we've
NOTE Confidence: 0.9950506

00:42:09.265 --> 00:42:09.765 seen
NOTE Confidence: 0.99641925

00:42:10.464 --> 00:42:11.525 a vast proliferation
NOTE Confidence: 0.99853516

00:42:11.825 --> 00:42:12.724 of available
NOTE Confidence: 0.829834

00:42:13.025 --> 00:42:13.525 therapeutics,
NOTE Confidence: 0.9276123

00:42:13.825 --> 00:42:15.810 both immune checkpoint inhibitors,
NOTE Confidence: 0.98669434

00:42:16.190 --> 00:42:17.810 but also targeted therapy,
NOTE Confidence: 0.9890747

00:42:19.230 --> 00:42:20.750 and T cell therapies that
NOTE Confidence: 0.9890747

00:42:20.750 --> 00:42:21.650 have been approved.
NOTE Confidence: 0.98732215

00:42:22.109 --> 00:42:23.550 And it's kind of like
NOTE Confidence: 0.98732215

00:42:23.550 --> 00:42:24.829 a trickle down effect. If
NOTE Confidence: 0.98732215

00:42:24.829 --> 00:42:25.730 you have a medication
NOTE Confidence: 0.9295247

00:42:26.270 --> 00:42:27.230 that works so well in

NOTE Confidence: 0.9295247
00:42:27.230 --> 00:42:29.250 individuals with metastatic disease,
NOTE Confidence: 0.99482423
00:42:29.625 --> 00:42:30.585 how can we move and
NOTE Confidence: 0.99482423
00:42:30.585 --> 00:42:32.585 make these therapies available for
NOTE Confidence: 0.99482423
00:42:32.585 --> 00:42:34.105 individuals at higher risk for
NOTE Confidence: 0.99482423
00:42:34.105 --> 00:42:35.725 recurrence to try to prevent
NOTE Confidence: 0.9609375
00:42:36.185 --> 00:42:37.405 relapse in the future?
NOTE Confidence: 0.9513075
00:42:38.025 --> 00:42:39.565 And so, as a consequence
NOTE Confidence: 0.9513075
00:42:39.785 --> 00:42:40.905 to that, a lot of
NOTE Confidence: 0.9513075
00:42:40.905 --> 00:42:42.585 these same medications have then
NOTE Confidence: 0.9513075
00:42:42.585 --> 00:42:44.285 since been approved for adjuvant
NOTE Confidence: 0.9513075
00:42:44.344 --> 00:42:44.844 therapy.
NOTE Confidence: 0.95555204
00:42:45.369 --> 00:42:46.410 And so now the real
NOTE Confidence: 0.95555204
00:42:46.410 --> 00:42:47.690 question is, you know, how
NOTE Confidence: 0.95555204
00:42:47.690 --> 00:42:49.450 can we further optimize on
NOTE Confidence: 0.95555204
00:42:49.450 --> 00:42:50.190 this? Because
NOTE Confidence: 0.99960935

00:42:50.489 --> 00:42:52.190 there are still real limitations
NOTE Confidence: 0.99902344

00:42:52.650 --> 00:42:54.109 of adjuvant treatment.
NOTE Confidence: 0.9469075

00:42:55.050 --> 00:42:57.230 So, for stage two melanoma,
NOTE Confidence: 0.940486

00:42:57.530 --> 00:42:58.969 so high risk stage twos,
NOTE Confidence: 0.940486

00:42:58.969 --> 00:42:59.930 these are the two Bs
NOTE Confidence: 0.940486

00:42:59.930 --> 00:43:00.830 and two Cs,
NOTE Confidence: 0.97265625

00:43:01.235 --> 00:43:03.575 There's two separate clinical trials,
NOTE Confidence: 0.83542013

00:43:04.035 --> 00:43:05.715 phase three studies, the CheckMate
NOTE Confidence: 0.83542013

00:43:05.715 --> 00:43:06.855 seven sixty,
NOTE Confidence: 0.8524577

00:43:08.355 --> 00:43:09.335 I'm sorry, seven,
NOTE Confidence: 0.8879743

00:43:10.275 --> 00:43:11.795 seventy six ks and keynote
NOTE Confidence: 0.8879743

00:43:11.795 --> 00:43:12.614 seven sixteen
NOTE Confidence: 0.82046956

00:43:13.235 --> 00:43:14.114 that had led to the
NOTE Confidence: 0.82046956

00:43:14.114 --> 00:43:14.361 approval of nivolumab and pembrolizumab
NOTE Confidence: 0.82046956

00:43:14.361 --> 00:43:14.607 respectively. And as you can
NOTE Confidence: 0.82046956

00:43:14.607 --> 00:43:15.505 see, based on these early

NOTE Confidence: 0.9946289
00:43:17.090 --> 00:43:17.590 respectively.
NOTE Confidence: 0.9605713
00:43:18.290 --> 00:43:19.410 As you can see, based
NOTE Confidence: 0.9605713
00:43:19.410 --> 00:43:21.650 on these early readouts from
NOTE Confidence: 0.9605713
00:43:21.650 --> 00:43:22.390 these studies,
NOTE Confidence: 0.9856179
00:43:22.850 --> 00:43:24.210 there is a slight improvement
NOTE Confidence: 0.9856179
00:43:24.210 --> 00:43:26.469 in recurrence free survival and
NOTE Confidence: 0.9856179
00:43:26.530 --> 00:43:27.030 metastatic
NOTE Confidence: 0.97387695
00:43:27.330 --> 00:43:27.830 distant,
NOTE Confidence: 0.8330078
00:43:28.290 --> 00:43:30.230 free disease for survival,
NOTE Confidence: 0.99799263
00:43:30.665 --> 00:43:31.705 but there really is no
NOTE Confidence: 0.99799263
00:43:31.705 --> 00:43:33.565 data on overall survival.
NOTE Confidence: 0.9833008
00:43:35.945 --> 00:43:37.484 When we think about stage,
NOTE Confidence: 0.92529297
00:43:38.105 --> 00:43:39.005 three melanomas,
NOTE Confidence: 0.9348958
00:43:39.305 --> 00:43:40.505 so these are kind of
NOTE Confidence: 0.9348958
00:43:40.505 --> 00:43:41.005 three
NOTE Confidence: 0.9211989

00:43:41.545 --> 00:43:43.805 a's in some studies, primarily
NOTE Confidence: 0.9211989

00:43:43.945 --> 00:43:45.224 three b's and beyond in
NOTE Confidence: 0.9211989

00:43:45.224 --> 00:43:46.364 most other studies,
NOTE Confidence: 0.9980469

00:43:47.430 --> 00:43:48.250 looking at
NOTE Confidence: 0.8620361

00:43:48.550 --> 00:43:50.489 first initially like does ipilimumab
NOTE Confidence: 0.92756534

00:43:50.950 --> 00:43:52.469 work? Yes. The answer is
NOTE Confidence: 0.92756534

00:43:52.469 --> 00:43:54.410 yes. But with significant toxicity
NOTE Confidence: 0.92756534

00:43:54.469 --> 00:43:55.530 in some studies,
NOTE Confidence: 0.95929784

00:43:56.150 --> 00:43:57.910 forty one percent depending on
NOTE Confidence: 0.95929784

00:43:57.910 --> 00:43:59.030 the dose. If you give
NOTE Confidence: 0.95929784

00:43:59.030 --> 00:44:00.465 ten of epi, then it
NOTE Confidence: 0.95929784

00:44:00.465 --> 00:44:01.505 can be as high as
NOTE Confidence: 0.95929784

00:44:01.505 --> 00:44:02.864 fifty eight percent with grade
NOTE Confidence: 0.95929784

00:44:02.864 --> 00:44:03.685 three toxicities.
NOTE Confidence: 0.95647323

00:44:04.465 --> 00:44:05.985 And really also, you're still
NOTE Confidence: 0.95647323

00:44:05.985 --> 00:44:07.765 not seeing a terrible significant

NOTE Confidence: 0.95647323

00:44:07.985 --> 00:44:09.925 improvement in overall survival.

NOTE Confidence: 0.94672304

00:44:11.105 --> 00:44:12.645 With CheckMate twothirty

NOTE Confidence: 0.9616699

00:44:13.025 --> 00:44:13.525 eight,

NOTE Confidence: 0.9787133

00:44:13.905 --> 00:44:16.085 which compared ipi versus nivo,

NOTE Confidence: 0.9787133

00:44:16.219 --> 00:44:18.400 Clearly, ipi was less toxic,

NOTE Confidence: 0.9787133

00:44:18.460 --> 00:44:20.299 fourteen point four percent compared

NOTE Confidence: 0.9787133

00:44:20.299 --> 00:44:21.660 to forty five point nine

NOTE Confidence: 0.9787133

00:44:21.660 --> 00:44:22.160 percent.

NOTE Confidence: 0.9758676

00:44:22.940 --> 00:44:24.859 But, again, really no clear

NOTE Confidence: 0.9758676

00:44:24.859 --> 00:44:27.019 difference in overall survival between

NOTE Confidence: 0.9758676

00:44:27.019 --> 00:44:27.920 these two groups.

NOTE Confidence: 0.9923096

00:44:28.380 --> 00:44:29.475 And then with the

NOTE Confidence: 0.9951443

00:44:29.955 --> 00:44:31.335 approval of pembrolizumab

NOTE Confidence: 0.703125

00:44:31.875 --> 00:44:32.375 two

NOTE Confidence: 0.50897217

00:44:32.755 --> 00:44:33.575 and candidate

NOTE Confidence: 0.9358724

00:44:34.114 --> 00:44:35.255 zero fifty four,
NOTE Confidence: 0.9924665

00:44:36.114 --> 00:44:38.695 again, really no reported overall
NOTE Confidence: 0.9924665

00:44:38.755 --> 00:44:39.715 survival difference,
NOTE Confidence: 0.7763672

00:44:40.515 --> 00:44:41.015 but,
NOTE Confidence: 0.8691628

00:44:41.475 --> 00:44:43.075 slight, you know, increase in
NOTE Confidence: 0.8691628

00:44:43.075 --> 00:44:44.950 toxicity with even single agent
NOTE Confidence: 0.8691628

00:44:44.950 --> 00:44:45.450 pembrolizumab.
NOTE Confidence: 0.9625244

00:44:47.910 --> 00:44:49.670 Combi AD, I just included
NOTE Confidence: 0.9625244

00:44:49.670 --> 00:44:50.950 here, but it's actually a
NOTE Confidence: 0.9625244

00:44:50.950 --> 00:44:52.090 targeted therapy,
NOTE Confidence: 0.8616769

00:44:52.630 --> 00:44:53.989 for individuals who have a
NOTE Confidence: 0.8616769

00:44:53.989 --> 00:44:55.590 BRAF e six hundred e,
NOTE Confidence: 0.8616769

00:44:55.830 --> 00:44:56.970 E or K mutation.
NOTE Confidence: 0.99938965

00:44:57.725 --> 00:44:59.085 This was really the only
NOTE Confidence: 0.99938965

00:44:59.085 --> 00:45:00.305 study that demonstrated
NOTE Confidence: 0.969583

00:45:01.085 --> 00:45:02.765 a trend towards an improvement

NOTE Confidence: 0.969583
00:45:02.765 --> 00:45:04.525 in overall survival. And this
NOTE Confidence: 0.969583
00:45:04.525 --> 00:45:05.725 is the latest eight year
NOTE Confidence: 0.969583
00:45:05.725 --> 00:45:06.785 updated data,
NOTE Confidence: 0.95247394
00:45:08.285 --> 00:45:09.905 whereby with all the preexisting
NOTE Confidence: 0.84002686
00:45:10.205 --> 00:45:11.730 adjuvant immune therapy options,
NOTE Confidence: 0.78125
00:45:13.170 --> 00:45:13.670 improvement.
NOTE Confidence: 0.8565674
00:45:15.010 --> 00:45:16.390 And then also just
NOTE Confidence: 0.88238937
00:45:16.770 --> 00:45:18.950 as a side here, ongoing
NOTE Confidence: 0.88238937
00:45:19.010 --> 00:45:20.869 clinical trial of an adjuvant
NOTE Confidence: 0.8671875
00:45:21.410 --> 00:45:21.910 mRNA
NOTE Confidence: 0.92918396
00:45:22.210 --> 00:45:23.410 vaccine. So this is a
NOTE Confidence: 0.92918396
00:45:23.410 --> 00:45:25.810 personalized mRNA vaccine that encodes
NOTE Confidence: 0.92918396
00:45:25.810 --> 00:45:27.275 up to thirty four different
NOTE Confidence: 0.92918396
00:45:27.275 --> 00:45:27.775 neoantigens
NOTE Confidence: 0.99746096
00:45:28.475 --> 00:45:30.415 associated with an individual's tumor
NOTE Confidence: 0.98052305

00:45:30.715 --> 00:45:32.395 that's given in combination with

NOTE Confidence: 0.98052305

00:45:32.395 --> 00:45:32.895 pembrolizumab

NOTE Confidence: 0.99837244

00:45:33.355 --> 00:45:34.655 versus pembrolizumab

NOTE Confidence: 0.99902344

00:45:35.035 --> 00:45:35.535 alone.

NOTE Confidence: 0.98721313

00:45:36.635 --> 00:45:38.955 Again, there's some improvement in

NOTE Confidence: 0.98721313

00:45:38.955 --> 00:45:40.095 relapse free survival

NOTE Confidence: 0.98982745

00:45:40.610 --> 00:45:41.670 and distant metastasis

NOTE Confidence: 0.94421387

00:45:42.050 --> 00:45:42.790 free survival.

NOTE Confidence: 0.97147626

00:45:43.170 --> 00:45:44.770 There's still no clear OS

NOTE Confidence: 0.97147626

00:45:44.770 --> 00:45:46.210 data that has yet to

NOTE Confidence: 0.97147626

00:45:46.210 --> 00:45:46.950 be reported,

NOTE Confidence: 0.88216144

00:45:47.890 --> 00:45:49.330 and hopefully updates will be

NOTE Confidence: 0.88216144

00:45:49.330 --> 00:45:49.830 forthcoming.

NOTE Confidence: 0.9744991

00:45:51.330 --> 00:45:53.010 And so all of these

NOTE Confidence: 0.9744991

00:45:53.010 --> 00:45:54.770 prior therapies have really focused

NOTE Confidence: 0.9744991

00:45:54.770 --> 00:45:56.135 on, you know, this paradigm

NOTE Confidence: 0.9744991
00:45:56.275 --> 00:45:57.875 of, okay, let's get this
NOTE Confidence: 0.9744991
00:45:57.875 --> 00:45:59.955 tumor out and then let's
NOTE Confidence: 0.9744991
00:45:59.955 --> 00:46:01.155 determine whether or not this
NOTE Confidence: 0.9744991
00:46:01.155 --> 00:46:01.655 patient
NOTE Confidence: 0.97171456
00:46:02.114 --> 00:46:04.295 can get additional immune therapy
NOTE Confidence: 0.97171456
00:46:04.435 --> 00:46:06.035 versus targeted therapy if they
NOTE Confidence: 0.97171456
00:46:06.035 --> 00:46:07.255 have a BRAF mutation.
NOTE Confidence: 0.9854612
00:46:07.830 --> 00:46:08.950 And again, a lot of
NOTE Confidence: 0.9854612
00:46:08.950 --> 00:46:10.950 these studies with adjuvant immune
NOTE Confidence: 0.9854612
00:46:10.950 --> 00:46:13.050 therapies have demonstrated no improvement
NOTE Confidence: 0.9854612
00:46:13.110 --> 00:46:14.550 in overall survival, which is
NOTE Confidence: 0.9854612
00:46:14.550 --> 00:46:15.690 our gold standard
NOTE Confidence: 0.9996745
00:46:16.230 --> 00:46:17.430 for how we want to
NOTE Confidence: 0.9996745
00:46:17.430 --> 00:46:17.930 measure
NOTE Confidence: 0.9088658
00:46:18.630 --> 00:46:20.790 significant improvements in patients' outcome
NOTE Confidence: 0.9088658

00:46:20.790 --> 00:46:21.610 over time.
NOTE Confidence: 0.97650504

00:46:22.385 --> 00:46:24.145 So the new shift is
NOTE Confidence: 0.97650504

00:46:24.145 --> 00:46:25.505 trying to evaluate whether we
NOTE Confidence: 0.97650504

00:46:25.505 --> 00:46:26.785 can utilize some of these
NOTE Confidence: 0.97650504

00:46:26.785 --> 00:46:27.844 therapies upfront,
NOTE Confidence: 0.9400635

00:46:28.385 --> 00:46:30.325 sort of like that mRNA
NOTE Confidence: 0.9400635

00:46:30.464 --> 00:46:32.085 vaccine study whereby
NOTE Confidence: 0.9914551

00:46:32.464 --> 00:46:33.984 instead of a very costly
NOTE Confidence: 0.9914551

00:46:33.984 --> 00:46:35.605 and expensive way to reintroduce
NOTE Confidence: 0.9914551

00:46:35.825 --> 00:46:36.724 tumor antigens
NOTE Confidence: 0.96623886

00:46:37.460 --> 00:46:38.900 in the context of concurrent
NOTE Confidence: 0.96623886

00:46:38.900 --> 00:46:39.719 immune therapy,
NOTE Confidence: 0.9226074

00:46:40.099 --> 00:46:41.779 basically to use the patient's
NOTE Confidence: 0.9226074

00:46:41.779 --> 00:46:42.920 in situ tumor
NOTE Confidence: 0.9941406

00:46:43.380 --> 00:46:44.119 to reinvigorate
NOTE Confidence: 0.9803245

00:46:44.420 --> 00:46:46.339 and restimulate the immune system

NOTE Confidence: 0.9803245

00:46:46.339 --> 00:46:48.420 with the added neoadjuvant immune

NOTE Confidence: 0.9803245

00:46:48.420 --> 00:46:48.920 therapy,

NOTE Confidence: 0.9998047

00:46:49.940 --> 00:46:52.039 and determine whether that improves

NOTE Confidence: 0.9875488

00:46:52.339 --> 00:46:52.839 response.

NOTE Confidence: 0.8232422

00:46:53.744 --> 00:46:55.984 So basically giving patients treatment

NOTE Confidence: 0.8232422

00:46:55.984 --> 00:46:57.525 upfront followed by surgery

NOTE Confidence: 0.9582171

00:46:57.984 --> 00:46:59.025 and then kind of a

NOTE Confidence: 0.9582171

00:46:59.025 --> 00:46:59.844 risk stratification

NOTE Confidence: 0.94033206

00:47:00.305 --> 00:47:01.744 whether that patient needs any

NOTE Confidence: 0.94033206

00:47:01.744 --> 00:47:03.924 additional therapy based on pathologic

NOTE Confidence: 0.99658203

00:47:04.224 --> 00:47:04.724 response.

NOTE Confidence: 0.96375227

00:47:06.930 --> 00:47:08.210 And so I'll hand it

NOTE Confidence: 0.96375227

00:47:08.210 --> 00:47:09.730 over to Doctor. Alino to

NOTE Confidence: 0.96375227

00:47:09.730 --> 00:47:10.850 lead the next section of

NOTE Confidence: 0.96375227

00:47:10.850 --> 00:47:11.510 the discussion.

NOTE Confidence: 0.9795329

00:47:12.530 --> 00:47:14.089 Again, just to reiterate some
NOTE Confidence: 0.9795329

00:47:14.089 --> 00:47:15.090 of the points brought up
NOTE Confidence: 0.9795329

00:47:15.090 --> 00:47:16.070 earlier. So
NOTE Confidence: 0.9985817

00:47:16.770 --> 00:47:18.265 why would we shift from
NOTE Confidence: 0.9985817

00:47:18.265 --> 00:47:18.925 the adjuvant
NOTE Confidence: 0.9415364

00:47:19.225 --> 00:47:20.744 paradigm that served us so
NOTE Confidence: 0.9415364

00:47:20.744 --> 00:47:22.605 well to this neo adjuvant
NOTE Confidence: 0.99731445

00:47:23.145 --> 00:47:24.285 paradigm? So
NOTE Confidence: 0.9857443

00:47:24.585 --> 00:47:26.605 one is we can actually
NOTE Confidence: 0.9857443

00:47:26.744 --> 00:47:28.985 now determine responses to therapy.
NOTE Confidence: 0.9857443

00:47:28.985 --> 00:47:29.864 So if we're going to
NOTE Confidence: 0.9857443

00:47:29.864 --> 00:47:31.385 do something different, some of
NOTE Confidence: 0.9857443

00:47:31.385 --> 00:47:32.844 these conditional trials,
NOTE Confidence: 0.99890137

00:47:33.430 --> 00:47:35.290 it's really valuable information.
NOTE Confidence: 0.9533534

00:47:36.070 --> 00:47:37.350 What began with kind of,
NOTE Confidence: 0.9533534

00:47:37.350 --> 00:47:38.890 I think, you know, biomarker

NOTE Confidence: 0.9533534
00:47:38.950 --> 00:47:40.390 driven studies, I think, was
NOTE Confidence: 0.9533534
00:47:40.390 --> 00:47:42.469 really surprising what people found
NOTE Confidence: 0.9533534
00:47:42.469 --> 00:47:43.590 even during some of our
NOTE Confidence: 0.9533534
00:47:43.590 --> 00:47:45.110 early new adjuvant studies in
NOTE Confidence: 0.9533534
00:47:45.110 --> 00:47:45.610 melanoma.
NOTE Confidence: 0.9797058
00:47:46.614 --> 00:47:47.895 In some cases, it can
NOTE Confidence: 0.9797058
00:47:47.895 --> 00:47:49.655 actually markedly reduce the size
NOTE Confidence: 0.9797058
00:47:49.655 --> 00:47:50.935 of a tumor before surgery,
NOTE Confidence: 0.9797058
00:47:50.935 --> 00:47:52.215 although we don't begin with
NOTE Confidence: 0.9797058
00:47:52.215 --> 00:47:53.355 that as our expectation.
NOTE Confidence: 0.9750213
00:47:54.535 --> 00:47:55.655 And if you look kind
NOTE Confidence: 0.9750213
00:47:55.655 --> 00:47:57.275 of at the tumor immunology
NOTE Confidence: 0.9750213
00:47:57.495 --> 00:47:59.435 or true immune system level,
NOTE Confidence: 0.9750213
00:47:59.655 --> 00:48:00.695 there's a lot of thought
NOTE Confidence: 0.9750213
00:48:00.695 --> 00:48:02.090 that if you have a
NOTE Confidence: 0.9750213

00:48:02.090 --> 00:48:03.690 tumor in place, you're gonna
NOTE Confidence: 0.9750213

00:48:03.690 --> 00:48:05.290 have a greater chance to
NOTE Confidence: 0.9750213

00:48:05.290 --> 00:48:07.290 be encountering different types of
NOTE Confidence: 0.9750213

00:48:07.290 --> 00:48:08.410 parts of that tumor. We
NOTE Confidence: 0.9750213

00:48:08.410 --> 00:48:09.790 call those tumor antigens
NOTE Confidence: 0.94259983

00:48:10.250 --> 00:48:11.530 that then may be useful
NOTE Confidence: 0.94259983

00:48:11.530 --> 00:48:13.310 to prevent recurrence later.
NOTE Confidence: 1

00:48:13.610 --> 00:48:14.430 It's also
NOTE Confidence: 0.9637451

00:48:15.025 --> 00:48:16.385 thought that we may have
NOTE Confidence: 0.9637451

00:48:16.385 --> 00:48:17.445 those T cells
NOTE Confidence: 0.9600195

00:48:17.905 --> 00:48:19.744 better activated and actually having
NOTE Confidence: 0.9600195

00:48:19.744 --> 00:48:22.065 them lasting longer and leading
NOTE Confidence: 0.9600195

00:48:22.065 --> 00:48:23.505 to better memory response is
NOTE Confidence: 0.9600195

00:48:23.505 --> 00:48:25.025 the same reason why when
NOTE Confidence: 0.9600195

00:48:25.025 --> 00:48:26.645 you get your measles vaccine
NOTE Confidence: 0.96981007

00:48:26.945 --> 00:48:27.905 that you're, you know, you

NOTE Confidence: 0.96981007
00:48:27.905 --> 00:48:29.739 get a booster, but you
NOTE Confidence: 0.96981007
00:48:29.739 --> 00:48:31.260 won't get measles. Right. So
NOTE Confidence: 0.96981007
00:48:31.260 --> 00:48:32.540 having that memory in your
NOTE Confidence: 0.96981007
00:48:32.540 --> 00:48:34.060 immune system is really key
NOTE Confidence: 0.96981007
00:48:34.060 --> 00:48:35.900 and really the holy grail
NOTE Confidence: 0.96981007
00:48:35.900 --> 00:48:36.780 for a lot of us
NOTE Confidence: 0.96981007
00:48:36.780 --> 00:48:38.080 in cancer treatments.
NOTE Confidence: 0.9952567
00:48:38.700 --> 00:48:40.060 And the thing that becomes
NOTE Confidence: 0.9952567
00:48:40.060 --> 00:48:41.040 really incredibly
NOTE Confidence: 0.999783
00:48:41.500 --> 00:48:43.205 unique is much of what
NOTE Confidence: 0.999783
00:48:43.205 --> 00:48:44.585 we study in oncology
NOTE Confidence: 0.99833983
00:48:45.205 --> 00:48:46.665 is based upon our failures.
NOTE Confidence: 0.9922228
00:48:47.525 --> 00:48:49.605 When we actually combine these
NOTE Confidence: 0.9922228
00:48:49.605 --> 00:48:51.605 neoadjuvant approaches and then combine
NOTE Confidence: 0.9922228
00:48:51.605 --> 00:48:53.385 them actually with surgical resection,
NOTE Confidence: 0.982387

00:48:53.685 --> 00:48:54.965 we can actually learn from
NOTE Confidence: 0.982387

00:48:54.965 --> 00:48:55.705 our successes.
NOTE Confidence: 0.96658456

00:48:56.550 --> 00:48:58.310 What happens in this circumstance
NOTE Confidence: 0.96658456

00:48:58.310 --> 00:48:59.590 that this patient actually had
NOTE Confidence: 0.96658456

00:48:59.590 --> 00:49:01.130 a great response? We have
NOTE Confidence: 0.96658456

00:49:01.350 --> 00:49:03.190 tumor tissue available for that.
NOTE Confidence: 0.96658456

00:49:03.190 --> 00:49:04.170 So it actually
NOTE Confidence: 0.93081665

00:49:04.630 --> 00:49:06.630 globally also helps us advance
NOTE Confidence: 0.93081665

00:49:06.630 --> 00:49:07.770 the field. Next.
NOTE Confidence: 0.9755592

00:49:09.665 --> 00:49:10.965 And this is a cartoon
NOTE Confidence: 0.9755592

00:49:11.185 --> 00:49:12.545 rendition of some of those
NOTE Confidence: 0.9755592

00:49:12.545 --> 00:49:13.825 principles. In the upper left,
NOTE Confidence: 0.9755592

00:49:13.825 --> 00:49:14.705 you can see kind of
NOTE Confidence: 0.9755592

00:49:14.705 --> 00:49:16.325 what our old paradigm was.
NOTE Confidence: 0.9755592

00:49:16.385 --> 00:49:17.905 You send the person to
NOTE Confidence: 0.9755592

00:49:17.905 --> 00:49:19.905 to myself, doctor Swozi, doctor

NOTE Confidence: 0.9755592
00:49:19.905 --> 00:49:21.519 Roche, and, you know, a
NOTE Confidence: 0.9755592
00:49:21.519 --> 00:49:23.839 surgeon removes the tumor lesion,
NOTE Confidence: 0.9755592
00:49:23.839 --> 00:49:25.119 but what's left behind is
NOTE Confidence: 0.9755592
00:49:25.119 --> 00:49:26.559 quite minimal. So the thought
NOTE Confidence: 0.9755592
00:49:26.559 --> 00:49:27.519 is, what are we mounting
NOTE Confidence: 0.9755592
00:49:27.519 --> 00:49:28.259 that immune
NOTE Confidence: 0.95051455
00:49:28.559 --> 00:49:30.160 response against? Where is the
NOTE Confidence: 0.95051455
00:49:30.160 --> 00:49:31.440 tumor that we're supposed to
NOTE Confidence: 0.95051455
00:49:31.519 --> 00:49:32.500 where's the antigen?
NOTE Confidence: 0.98173827
00:49:32.880 --> 00:49:34.000 What is the immune system
NOTE Confidence: 0.98173827
00:49:34.000 --> 00:49:35.619 there to recognize and attack?
NOTE Confidence: 0.9742296
00:49:36.075 --> 00:49:37.355 However, if we leave that
NOTE Confidence: 0.9742296
00:49:37.355 --> 00:49:38.494 in the bottom panel,
NOTE Confidence: 0.99032825
00:49:39.035 --> 00:49:40.635 maybe we'll activate more t
NOTE Confidence: 0.99032825
00:49:40.635 --> 00:49:41.994 cells. Maybe we'll give ourselves
NOTE Confidence: 0.99032825

00:49:41.994 --> 00:49:43.055 a better opportunity.
NOTE Confidence: 0.9920726

00:49:43.675 --> 00:49:45.035 Then the surgeon goes in,
NOTE Confidence: 0.9920726

00:49:45.035 --> 00:49:46.795 removes the tumor, and what's
NOTE Confidence: 0.9920726

00:49:46.795 --> 00:49:48.955 left behind, we're hoping, is
NOTE Confidence: 0.9920726

00:49:48.955 --> 00:49:49.695 a greater
NOTE Confidence: 0.90625

00:49:50.075 --> 00:49:51.135 diverse pool.
NOTE Confidence: 0.9844709

00:49:51.440 --> 00:49:52.880 And, again, when the immune
NOTE Confidence: 0.9844709

00:49:52.880 --> 00:49:54.960 system at these earlier nodal
NOTE Confidence: 0.9844709

00:49:54.960 --> 00:49:56.640 stages before the body is
NOTE Confidence: 0.9844709

00:49:56.640 --> 00:49:58.720 ravaged by multiple metastatic sites
NOTE Confidence: 0.9844709

00:49:58.720 --> 00:50:00.080 that we usually are studying
NOTE Confidence: 0.9844709

00:50:00.080 --> 00:50:01.060 our patients in,
NOTE Confidence: 0.98046875

00:50:01.520 --> 00:50:02.960 you know, we'll have less
NOTE Confidence: 0.98046875

00:50:02.960 --> 00:50:03.460 dysfunctional
NOTE Confidence: 0.99135745

00:50:04.000 --> 00:50:06.180 cells around. So maybe, again,
NOTE Confidence: 0.8915202

00:50:06.515 --> 00:50:07.895 we can have that investment

NOTE Confidence: 0.8915202
00:50:08.114 --> 00:50:08.614 upfront
NOTE Confidence: 0.9934489
00:50:08.915 --> 00:50:10.755 and actually have durable, curative
NOTE Confidence: 0.9934489
00:50:10.755 --> 00:50:11.255 responses
NOTE Confidence: 0.98301476
00:50:11.635 --> 00:50:13.715 that may actually truly have
NOTE Confidence: 0.98301476
00:50:13.715 --> 00:50:15.235 a long term survival benefit.
NOTE Confidence: 0.98301476
00:50:15.235 --> 00:50:16.435 We're not there, but that's
NOTE Confidence: 0.98301476
00:50:16.435 --> 00:50:17.655 the hope and the rationale.
NOTE Confidence: 0.98301476
00:50:17.875 --> 00:50:18.375 Next.
NOTE Confidence: 0.96429443
00:50:20.640 --> 00:50:21.520 So why did we think
NOTE Confidence: 0.96429443
00:50:21.520 --> 00:50:22.820 that? Well, historically,
NOTE Confidence: 0.99104816
00:50:23.440 --> 00:50:24.560 you know, if you flip
NOTE Confidence: 0.99104816
00:50:24.560 --> 00:50:26.000 things around, when you have
NOTE Confidence: 0.99104816
00:50:26.000 --> 00:50:27.060 effective treatments
NOTE Confidence: 0.98339844
00:50:27.520 --> 00:50:28.480 and then you give a
NOTE Confidence: 0.98339844
00:50:28.480 --> 00:50:28.980 patient
NOTE Confidence: 0.9745343

00:50:29.440 --> 00:50:30.480 to a surgeon and you
NOTE Confidence: 0.9745343

00:50:30.480 --> 00:50:32.015 say, take out this area
NOTE Confidence: 0.9745343

00:50:32.015 --> 00:50:33.235 that's not responding.
NOTE Confidence: 0.88626534

00:50:34.175 --> 00:50:35.295 Those patients you can see
NOTE Confidence: 0.88626534

00:50:35.295 --> 00:50:36.675 here with the with the
NOTE Confidence: 0.88626534

00:50:36.735 --> 00:50:38.355 use of adjuvant surgery
NOTE Confidence: 0.92366534

00:50:38.895 --> 00:50:40.035 and doing a metastaticomy
NOTE Confidence: 0.9569452

00:50:40.415 --> 00:50:42.175 following systemic immunotherapy. This is
NOTE Confidence: 0.9569452

00:50:42.175 --> 00:50:43.855 some data from Danielle Bella,
NOTE Confidence: 0.9569452

00:50:43.855 --> 00:50:45.315 who's a Yale graduate, unfortunately
NOTE Confidence: 0.9569452

00:50:45.375 --> 00:50:46.850 went to Memorial, but She's
NOTE Confidence: 0.9569452

00:50:46.850 --> 00:50:48.130 wonderful. You know, our data
NOTE Confidence: 0.9569452

00:50:48.130 --> 00:50:48.850 at Yale, if you look
NOTE Confidence: 0.9569452

00:50:48.850 --> 00:50:49.969 at the data from Duke,
NOTE Confidence: 0.9569452

00:50:49.969 --> 00:50:50.690 if you look at all
NOTE Confidence: 0.9569452

00:50:50.690 --> 00:50:52.210 of our institutions, we're seeing

NOTE Confidence: 0.9569452
00:50:52.210 --> 00:50:53.570 the same thing. So if
NOTE Confidence: 0.9569452
00:50:53.570 --> 00:50:54.550 we're consolidating
NOTE Confidence: 0.9936148
00:50:55.010 --> 00:50:57.030 patients with systemic immune therapy
NOTE Confidence: 0.9936148
00:50:57.170 --> 00:50:58.130 and then going out and
NOTE Confidence: 0.9936148
00:50:58.130 --> 00:50:59.270 removing the tumor
NOTE Confidence: 0.9382975
00:50:59.594 --> 00:51:00.715 in those folks that are
NOTE Confidence: 0.9382975
00:51:00.715 --> 00:51:01.915 responding that we can get
NOTE Confidence: 0.9382975
00:51:01.915 --> 00:51:03.535 them to very limited disease.
NOTE Confidence: 0.98619497
00:51:03.915 --> 00:51:05.275 These patients are doing quite
NOTE Confidence: 0.98619497
00:51:05.275 --> 00:51:06.955 well, and we're separating that
NOTE Confidence: 0.98619497
00:51:06.955 --> 00:51:07.455 biology
NOTE Confidence: 0.96623886
00:51:07.835 --> 00:51:09.275 actually from those folks that
NOTE Confidence: 0.96623886
00:51:09.275 --> 00:51:09.935 are having
NOTE Confidence: 0.97942096
00:51:10.395 --> 00:51:12.255 multiple areas of progression where
NOTE Confidence: 0.97942096
00:51:12.395 --> 00:51:14.250 maybe surgery is not the
NOTE Confidence: 0.97942096

00:51:14.250 --> 00:51:15.829 the ideal, but we've identified
NOTE Confidence: 0.97942096

00:51:15.890 --> 00:51:17.410 those patients and perhaps spared
NOTE Confidence: 0.97942096

00:51:17.410 --> 00:51:18.469 them from an operation.
NOTE Confidence: 0.99902344

00:51:18.849 --> 00:51:19.349 Next.
NOTE Confidence: 0.93896484

00:51:20.609 --> 00:51:21.349 So, again,
NOTE Confidence: 0.95076907

00:51:21.650 --> 00:51:23.569 I'd like to people to
NOTE Confidence: 0.95076907

00:51:23.569 --> 00:51:24.770 think about there's a big
NOTE Confidence: 0.95076907

00:51:24.770 --> 00:51:27.010 difference in when we're comparing
NOTE Confidence: 0.95076907

00:51:27.010 --> 00:51:28.665 with who these patients are.
NOTE Confidence: 0.9765292

00:51:29.145 --> 00:51:30.265 So if you look at
NOTE Confidence: 0.9765292

00:51:30.265 --> 00:51:31.465 people if we look at
NOTE Confidence: 0.9765292

00:51:31.465 --> 00:51:33.305 our historical outcomes in patients
NOTE Confidence: 0.9765292

00:51:33.305 --> 00:51:35.565 who present with clinically apparent
NOTE Confidence: 0.9765292

00:51:35.705 --> 00:51:36.605 nodal disease,
NOTE Confidence: 0.9838958

00:51:36.905 --> 00:51:38.105 still stage three, but these
NOTE Confidence: 0.9838958

00:51:38.105 --> 00:51:39.225 are not the patients that

NOTE Confidence: 0.9838958
00:51:39.225 --> 00:51:40.585 were doing a central node
NOTE Confidence: 0.9838958
00:51:40.585 --> 00:51:43.079 biopsy and detecting microscopic disease.
NOTE Confidence: 0.9838958
00:51:43.079 --> 00:51:44.520 This is a much different
NOTE Confidence: 0.9838958
00:51:44.520 --> 00:51:45.579 patient population.
NOTE Confidence: 0.9524219
00:51:46.119 --> 00:51:47.079 Right? So this is, again,
NOTE Confidence: 0.9524219
00:51:47.079 --> 00:51:49.079 historical before our advent of
NOTE Confidence: 0.9524219
00:51:49.079 --> 00:51:51.180 immune therapy. But even having
NOTE Confidence: 0.9524219
00:51:51.319 --> 00:51:53.575 one clinically enlarged nose, when
NOTE Confidence: 0.9524219
00:51:53.575 --> 00:51:55.114 you're looking at that survival,
NOTE Confidence: 0.99316406
00:51:55.415 --> 00:51:55.915 right,
NOTE Confidence: 0.9555176
00:51:56.455 --> 00:51:58.155 forty percent is not ideal.
NOTE Confidence: 0.96260405
00:51:58.535 --> 00:52:00.055 Four lots of nodes in
NOTE Confidence: 0.96260405
00:52:00.055 --> 00:52:01.335 that basin, right, that is
NOTE Confidence: 0.96260405
00:52:01.335 --> 00:52:02.635 almost that is the equivalent
NOTE Confidence: 0.96260405
00:52:02.695 --> 00:52:03.895 of what we see many
NOTE Confidence: 0.96260405

00:52:03.895 --> 00:52:04.875 times from metastatic
NOTE Confidence: 0.92297363

00:52:05.255 --> 00:52:06.614 disease. And the same thing
NOTE Confidence: 0.92297363

00:52:06.614 --> 00:52:07.755 for some of our thicker
NOTE Confidence: 0.9770648

00:52:08.079 --> 00:52:09.280 tumors. So, again, we have
NOTE Confidence: 0.9770648

00:52:09.280 --> 00:52:09.920 to make sure when we're
NOTE Confidence: 0.9770648

00:52:09.920 --> 00:52:11.440 looking at these patients that
NOTE Confidence: 0.9770648

00:52:11.440 --> 00:52:12.640 we're looking at the correct
NOTE Confidence: 0.9770648

00:52:12.640 --> 00:52:14.480 patient population. These are not
NOTE Confidence: 0.9770648

00:52:14.480 --> 00:52:15.940 the same stage threes,
NOTE Confidence: 0.99956596

00:52:16.400 --> 00:52:17.680 even though they may fall
NOTE Confidence: 0.99956596

00:52:17.680 --> 00:52:18.900 into the same category
NOTE Confidence: 0.98377824

00:52:19.280 --> 00:52:20.319 on our card there on
NOTE Confidence: 0.98377824

00:52:20.319 --> 00:52:22.020 the right when they're presenting
NOTE Confidence: 0.98377824

00:52:22.319 --> 00:52:23.280 that way to us in
NOTE Confidence: 0.98377824

00:52:23.280 --> 00:52:24.395 our clinics. Next.
NOTE Confidence: 0.9811379

00:52:26.135 --> 00:52:27.255 So a lot of those

NOTE Confidence: 0.9811379

00:52:27.255 --> 00:52:28.695 initial works were done with

NOTE Confidence: 0.9811379

00:52:28.695 --> 00:52:30.255 small trials, and we've kind

NOTE Confidence: 0.9811379

00:52:30.255 --> 00:52:31.655 of I've divided this table

NOTE Confidence: 0.9811379

00:52:31.655 --> 00:52:33.094 into some different sections. So

NOTE Confidence: 0.9811379

00:52:33.094 --> 00:52:33.895 if we look at the

NOTE Confidence: 0.9811379

00:52:33.895 --> 00:52:36.055 anti PD-one monotherapy, again, some

NOTE Confidence: 0.9811379

00:52:36.055 --> 00:52:37.094 early trials that were done

NOTE Confidence: 0.9811379

00:52:37.094 --> 00:52:38.135 just to get a semblance

NOTE Confidence: 0.9811379

00:52:38.135 --> 00:52:39.700 of safety And, actually, as

NOTE Confidence: 0.9811379

00:52:39.700 --> 00:52:41.000 I said, really biomarker

NOTE Confidence: 0.99572754

00:52:41.300 --> 00:52:43.060 driven. The biggest one was

NOTE Confidence: 0.99572754

00:52:43.060 --> 00:52:43.380 the,

NOTE Confidence: 0.97413725

00:52:44.100 --> 00:52:45.460 the the phase two trial

NOTE Confidence: 0.97413725

00:52:45.460 --> 00:52:46.820 done, the swag eighteen o

NOTE Confidence: 0.97413725

00:52:46.820 --> 00:52:48.020 one. I'll highlight that in

NOTE Confidence: 0.97413725

00:52:48.020 --> 00:52:49.140 a little bit. But that
NOTE Confidence: 0.97413725

00:52:49.140 --> 00:52:50.739 was giving patients, you know,
NOTE Confidence: 0.97413725

00:52:50.739 --> 00:52:52.180 a sandwich approach. You get
NOTE Confidence: 0.97413725

00:52:52.180 --> 00:52:53.480 three cycles of neoadjuvant
NOTE Confidence: 0.8083496

00:52:54.135 --> 00:52:54.635 therapy,
NOTE Confidence: 0.959727

00:52:55.015 --> 00:52:56.395 and then you have surgery,
NOTE Confidence: 0.959727

00:52:56.614 --> 00:52:57.655 and then you're still gonna
NOTE Confidence: 0.959727

00:52:57.655 --> 00:52:58.935 continue to get adjuvant therapy.
NOTE Confidence: 0.959727

00:52:58.935 --> 00:52:59.975 And they compared that to
NOTE Confidence: 0.959727

00:52:59.975 --> 00:53:01.655 our typical paradigm, which was
NOTE Confidence: 0.959727

00:53:01.655 --> 00:53:03.435 upfront surgery for these patients
NOTE Confidence: 0.959727

00:53:03.655 --> 00:53:05.575 with clinically apparent nodal disease
NOTE Confidence: 0.959727

00:53:05.575 --> 00:53:07.515 or resectable stage four disease,
NOTE Confidence: 0.9838867

00:53:08.140 --> 00:53:10.380 enrolled, you know, over three
NOTE Confidence: 0.9838867

00:53:10.380 --> 00:53:11.280 hundred patients.
NOTE Confidence: 0.9980469

00:53:11.580 --> 00:53:12.080 Again,

NOTE Confidence: 0.93875825
00:53:12.460 --> 00:53:14.000 things to highlight the pathologic
NOTE Confidence: 0.93875825
00:53:14.219 --> 00:53:15.420 response in those patients who
NOTE Confidence: 0.93875825
00:53:15.420 --> 00:53:16.320 got the neoadjuvant
NOTE Confidence: 0.97216797
00:53:17.020 --> 00:53:18.619 therapy was only about twenty
NOTE Confidence: 0.97216797
00:53:18.619 --> 00:53:19.119 percent,
NOTE Confidence: 0.9423828
00:53:20.915 --> 00:53:22.775 but they only had about
NOTE Confidence: 0.9423828
00:53:22.835 --> 00:53:24.355 a twelve to fourteen percent
NOTE Confidence: 0.9423828
00:53:24.355 --> 00:53:25.815 toxicity. So that neoadjuvant
NOTE Confidence: 0.98464197
00:53:26.114 --> 00:53:27.715 group really wasn't harmed any
NOTE Confidence: 0.98464197
00:53:27.715 --> 00:53:28.594 more than they would have,
NOTE Confidence: 0.98464197
00:53:28.594 --> 00:53:29.555 and that's kind of our
NOTE Confidence: 0.98464197
00:53:29.555 --> 00:53:31.234 typical acceptable rates of what
NOTE Confidence: 0.98464197
00:53:31.234 --> 00:53:32.455 we would see with monotherapy.
NOTE Confidence: 0.920166
00:53:34.020 --> 00:53:34.180 Again,
NOTE Confidence: 0.8660656
00:53:34.980 --> 00:53:36.660 OPDUALAG, that's the anti PD
NOTE Confidence: 0.8660656

00:53:36.660 --> 00:53:38.180 one, LAG three dual therapy,
NOTE Confidence: 0.8660656

00:53:38.180 --> 00:53:39.239 a very small trial.
NOTE Confidence: 0.949338

00:53:39.860 --> 00:53:41.380 Regeneron has a bigger trial
NOTE Confidence: 0.949338

00:53:41.380 --> 00:53:42.580 that we're we're working towards
NOTE Confidence: 0.949338

00:53:42.580 --> 00:53:44.420 opening here at Yale. Again,
NOTE Confidence: 0.949338

00:53:44.420 --> 00:53:46.100 looking to see, again, a
NOTE Confidence: 0.949338

00:53:46.100 --> 00:53:47.640 doublet therapy in the neoadjuvant
NOTE Confidence: 0.949338

00:53:47.780 --> 00:53:50.025 setting. Again, a small setting.
NOTE Confidence: 0.949338

00:53:50.025 --> 00:53:52.025 Again, seeing overall response rates,
NOTE Confidence: 0.949338

00:53:52.025 --> 00:53:53.705 much higher path response rates
NOTE Confidence: 0.949338

00:53:53.705 --> 00:53:55.165 that over fifty percent,
NOTE Confidence: 0.98909503

00:53:56.105 --> 00:53:57.165 but with the
NOTE Confidence: 0.9278343

00:53:57.785 --> 00:53:59.724 almost twice the the toxicity
NOTE Confidence: 0.9278343

00:53:59.864 --> 00:54:01.080 about twenty six percent when
NOTE Confidence: 0.9278343

00:54:01.080 --> 00:54:02.460 we look at grade three
NOTE Confidence: 0.9278343

00:54:02.520 --> 00:54:04.040 and four. And again, those

NOTE Confidence: 0.9278343
00:54:04.040 --> 00:54:05.020 patients got,
NOTE Confidence: 0.9022042
00:54:05.400 --> 00:54:06.760 a couple of months upfront
NOTE Confidence: 0.9022042
00:54:06.760 --> 00:54:07.500 of treatment.
NOTE Confidence: 0.90600586
00:54:08.200 --> 00:54:08.700 Next.
NOTE Confidence: 0.9348863
00:54:09.239 --> 00:54:10.440 Now a lot of the
NOTE Confidence: 0.9348863
00:54:10.440 --> 00:54:12.614 initial work and ongoing work
NOTE Confidence: 0.9348863
00:54:12.935 --> 00:54:14.135 has been really done with
NOTE Confidence: 0.9348863
00:54:14.135 --> 00:54:14.795 the combination
NOTE Confidence: 0.89920044
00:54:15.175 --> 00:54:16.614 of anti PD one with
NOTE Confidence: 0.89920044
00:54:16.614 --> 00:54:18.075 anti CTLA four.
NOTE Confidence: 0.92606884
00:54:18.375 --> 00:54:19.735 Most of that beginning and
NOTE Confidence: 0.92606884
00:54:19.735 --> 00:54:21.175 building upon the APOCEN and
NOTE Confidence: 0.92606884
00:54:21.175 --> 00:54:23.035 then the APOCEN NEO trial,
NOTE Confidence: 0.9825684
00:54:23.575 --> 00:54:25.195 which began with small numbers.
NOTE Confidence: 0.9308715
00:54:25.560 --> 00:54:27.160 The APISEN NEO trial highlight
NOTE Confidence: 0.9308715

00:54:27.160 --> 00:54:28.360 in a moment really tried
NOTE Confidence: 0.9308715

00:54:28.360 --> 00:54:29.400 to say, well, where is
NOTE Confidence: 0.9308715

00:54:29.400 --> 00:54:31.340 where does our Goldilocks dose?
NOTE Confidence: 0.9994141

00:54:31.640 --> 00:54:32.680 Where do we get the
NOTE Confidence: 0.9994141

00:54:32.680 --> 00:54:34.760 most amount of response with
NOTE Confidence: 0.9994141

00:54:34.760 --> 00:54:36.219 the least amount of toxicity?
NOTE Confidence: 0.97434646

00:54:36.920 --> 00:54:38.520 We'll also highlight the PRADA
NOTE Confidence: 0.97434646

00:54:38.520 --> 00:54:39.714 trial that tries to look
NOTE Confidence: 0.97434646

00:54:39.714 --> 00:54:41.075 at things similarly to what
NOTE Confidence: 0.97434646

00:54:41.075 --> 00:54:42.594 many may be accustomed to
NOTE Confidence: 0.97434646

00:54:42.594 --> 00:54:44.114 with breast cancer surgery, where
NOTE Confidence: 0.97434646

00:54:44.114 --> 00:54:46.195 we're giving neoadjuvant treatment. We're
NOTE Confidence: 0.97434646

00:54:46.195 --> 00:54:47.875 testing the nodes and then
NOTE Confidence: 0.97434646

00:54:47.875 --> 00:54:48.835 saying, do we have to
NOTE Confidence: 0.97434646

00:54:48.835 --> 00:54:50.355 do more node surgery? That's
NOTE Confidence: 0.97434646

00:54:50.355 --> 00:54:51.474 not quite ready for prime

NOTE Confidence: 0.97434646

00:54:51.474 --> 00:54:52.515 time, but that's something people

NOTE Confidence: 0.97434646

00:54:52.515 --> 00:54:53.474 are gonna be hearing more

NOTE Confidence: 0.97434646

00:54:53.474 --> 00:54:54.960 and more about. And then

NOTE Confidence: 0.97434646

00:54:54.960 --> 00:54:56.400 the other study to highlight

NOTE Confidence: 0.97434646

00:54:56.400 --> 00:54:57.680 is the Nadina trial, which

NOTE Confidence: 0.97434646

00:54:57.680 --> 00:54:59.280 is our largest trial done

NOTE Confidence: 0.97434646

00:54:59.280 --> 00:55:01.040 in the neoadjuvant setting using

NOTE Confidence: 0.97434646

00:55:01.040 --> 00:55:03.200 doublet therapy that for many

NOTE Confidence: 0.97434646

00:55:03.200 --> 00:55:03.700 people,

NOTE Confidence: 0.99975586

00:55:04.239 --> 00:55:05.780 has led to practice

NOTE Confidence: 0.99886066

00:55:06.080 --> 00:55:07.700 changing patterns worldwide.

NOTE Confidence: 0.9654508

00:55:10.945 --> 00:55:12.325 So for PD one monotherapy,

NOTE Confidence: 0.9654508

00:55:12.385 --> 00:55:13.744 again, the swag eighteen o

NOTE Confidence: 0.9654508

00:55:13.744 --> 00:55:15.665 one, the sandwich approach, either

NOTE Confidence: 0.9654508

00:55:15.665 --> 00:55:16.785 you're gonna have your surgery

NOTE Confidence: 0.9654508

00:55:16.785 --> 00:55:18.065 up front followed by your
NOTE Confidence: 0.9654508

00:55:18.065 --> 00:55:19.585 adjuvant standard of care, or
NOTE Confidence: 0.9654508

00:55:19.585 --> 00:55:20.864 you're gonna get three cycles
NOTE Confidence: 0.9654508

00:55:20.864 --> 00:55:22.450 of PD one, and then
NOTE Confidence: 0.9654508

00:55:22.450 --> 00:55:23.410 you're gonna have your surgery.
NOTE Confidence: 0.9654508

00:55:23.410 --> 00:55:24.370 And again, this trial was
NOTE Confidence: 0.9654508

00:55:24.370 --> 00:55:25.570 designed that no matter what
NOTE Confidence: 0.9654508

00:55:25.570 --> 00:55:27.090 your response was, you were
NOTE Confidence: 0.9654508

00:55:27.090 --> 00:55:28.450 going to then continue to
NOTE Confidence: 0.9654508

00:55:28.450 --> 00:55:30.130 get adjuvant therapy. Now a
NOTE Confidence: 0.9654508

00:55:30.130 --> 00:55:31.250 couple of things for this
NOTE Confidence: 0.9654508

00:55:31.250 --> 00:55:32.950 trial, again, in the neoadjuvant
NOTE Confidence: 0.9654508

00:55:33.090 --> 00:55:35.025 setting, sometimes your endpoints have
NOTE Confidence: 0.9654508

00:55:35.025 --> 00:55:35.825 to be a little bit
NOTE Confidence: 0.9654508

00:55:35.825 --> 00:55:36.704 different because you have to
NOTE Confidence: 0.9654508

00:55:36.704 --> 00:55:38.165 take into account if someone

NOTE Confidence: 0.9654508
00:55:38.224 --> 00:55:39.844 gets a toxicity, the preclusion
NOTE Confidence: 0.9654508
00:55:39.905 --> 00:55:41.344 from surgery, do they progress
NOTE Confidence: 0.9654508
00:55:41.344 --> 00:55:42.625 in the time period before
NOTE Confidence: 0.9654508
00:55:42.625 --> 00:55:43.505 surgery? So they had to
NOTE Confidence: 0.9654508
00:55:43.505 --> 00:55:44.484 create a composite
NOTE Confidence: 0.97833806
00:55:44.945 --> 00:55:47.204 called an event free survival.
NOTE Confidence: 0.97833806
00:55:47.265 --> 00:55:48.785 So not a recurrence free
NOTE Confidence: 0.97833806
00:55:48.785 --> 00:55:49.285 survival,
NOTE Confidence: 0.95184326
00:55:49.800 --> 00:55:51.580 not overall survival, not melanoma
NOTE Confidence: 0.95184326
00:55:51.719 --> 00:55:53.480 specific survival. But again, if
NOTE Confidence: 0.95184326
00:55:53.480 --> 00:55:54.200 you look at this at
NOTE Confidence: 0.95184326
00:55:54.200 --> 00:55:55.320 least superficially, you could see
NOTE Confidence: 0.95184326
00:55:55.320 --> 00:55:56.440 those those are curves that
NOTE Confidence: 0.95184326
00:55:56.440 --> 00:55:57.800 are quite far apart from
NOTE Confidence: 0.95184326
00:55:57.800 --> 00:55:58.460 each other.
NOTE Confidence: 0.95092773

00:55:58.760 --> 00:56:00.120 And in follow-up, they've actually
NOTE Confidence: 0.95092773

00:56:00.120 --> 00:56:01.420 maintained that separation.
NOTE Confidence: 0.97403973

00:56:01.960 --> 00:56:03.000 But again, if you look
NOTE Confidence: 0.97403973

00:56:03.000 --> 00:56:04.605 at the patients themselves,
NOTE Confidence: 0.9628752

00:56:05.145 --> 00:56:06.745 for patients who potentially had
NOTE Confidence: 0.9628752

00:56:06.745 --> 00:56:09.145 curable, resectable disease, you knew
NOTE Confidence: 0.9628752

00:56:09.145 --> 00:56:10.265 about twelve out of a
NOTE Confidence: 0.9628752

00:56:10.265 --> 00:56:11.465 hundred and fifty four of
NOTE Confidence: 0.9628752

00:56:11.465 --> 00:56:12.745 those patients, you had to
NOTE Confidence: 0.9628752

00:56:12.745 --> 00:56:14.525 have a very difficult conversation
NOTE Confidence: 0.9628752

00:56:14.585 --> 00:56:15.625 that none of us love
NOTE Confidence: 0.9628752

00:56:15.625 --> 00:56:17.150 to have, which is with
NOTE Confidence: 0.9628752

00:56:17.150 --> 00:56:17.970 this therapy,
NOTE Confidence: 0.9878695

00:56:18.430 --> 00:56:19.870 you're no longer a surgical
NOTE Confidence: 0.9878695

00:56:19.870 --> 00:56:21.310 candidate. And most of that
NOTE Confidence: 0.9878695

00:56:21.310 --> 00:56:22.590 was actually due to local

NOTE Confidence: 0.9878695
00:56:22.590 --> 00:56:24.610 and not actually distant metastatic
NOTE Confidence: 0.9878695
00:56:24.670 --> 00:56:25.870 progression. But that's, you know,
NOTE Confidence: 0.9878695
00:56:25.870 --> 00:56:26.750 one of the things that
NOTE Confidence: 0.9878695
00:56:26.750 --> 00:56:28.125 becomes important and maybe
NOTE Confidence: 0.94748265
00:56:28.605 --> 00:56:29.805 better judged and said, you
NOTE Confidence: 0.94748265
00:56:29.805 --> 00:56:31.105 know, maybe that person
NOTE Confidence: 0.98031956
00:56:31.485 --> 00:56:33.325 didn't need that operation anyway.
NOTE Confidence: 0.98031956
00:56:33.325 --> 00:56:34.364 So, again, you can look
NOTE Confidence: 0.98031956
00:56:34.364 --> 00:56:35.325 at it both sides of
NOTE Confidence: 0.98031956
00:56:35.325 --> 00:56:36.465 the coin. Next.
NOTE Confidence: 0.8789681
00:56:38.525 --> 00:56:39.885 Now, again, the office in
NOTE Confidence: 0.8789681
00:56:39.885 --> 00:56:40.685 the trial was one of
NOTE Confidence: 0.8789681
00:56:40.685 --> 00:56:42.125 the first doublet treatments that
NOTE Confidence: 0.8789681
00:56:42.125 --> 00:56:43.245 had come out. And, again,
NOTE Confidence: 0.8789681
00:56:43.245 --> 00:56:44.880 this was the Goldilocks trial.
NOTE Confidence: 0.99975586

00:56:45.180 --> 00:56:46.400 How do you determine
NOTE Confidence: 0.9736351

00:56:47.500 --> 00:56:48.700 in a group of patients
NOTE Confidence: 0.9736351

00:56:48.700 --> 00:56:50.300 who, again, could be cured
NOTE Confidence: 0.9736351

00:56:50.300 --> 00:56:52.460 with surgery, only experience about
NOTE Confidence: 0.9736351

00:56:52.460 --> 00:56:53.980 fifteen percent toxicity in the
NOTE Confidence: 0.9736351

00:56:53.980 --> 00:56:55.660 adjuvant setting, how do we
NOTE Confidence: 0.9736351

00:56:55.660 --> 00:56:56.940 pick the right dose to
NOTE Confidence: 0.9736351

00:56:56.940 --> 00:56:57.980 get the most amount of
NOTE Confidence: 0.9736351

00:56:57.980 --> 00:56:58.640 a response
NOTE Confidence: 1

00:56:59.344 --> 00:57:00.964 and then use that information
NOTE Confidence: 0.9951172

00:57:01.825 --> 00:57:02.325 for
NOTE Confidence: 0.9499512

00:57:03.664 --> 00:57:04.644 decision making?
NOTE Confidence: 0.8985021

00:57:05.025 --> 00:57:06.144 So in this case, if
NOTE Confidence: 0.8985021

00:57:06.144 --> 00:57:07.344 you look at the treatment
NOTE Confidence: 0.8985021

00:57:07.344 --> 00:57:08.785 r and b, that became
NOTE Confidence: 0.8985021

00:57:08.785 --> 00:57:10.545 kind of our Goldilocks dose.

NOTE Confidence: 0.8985021
00:57:10.545 --> 00:57:12.144 That was Nivo three ipi
NOTE Confidence: 0.8985021
00:57:12.144 --> 00:57:14.270 one, which again first for
NOTE Confidence: 0.8985021
00:57:14.270 --> 00:57:16.030 systemic treatment is for many
NOTE Confidence: 0.8985021
00:57:16.030 --> 00:57:17.390 people, the preferred option of
NOTE Confidence: 0.8985021
00:57:17.390 --> 00:57:18.910 doing doublet where you have
NOTE Confidence: 0.8985021
00:57:18.910 --> 00:57:20.190 the benefit of having the
NOTE Confidence: 0.8985021
00:57:20.190 --> 00:57:20.690 ipilimumab,
NOTE Confidence: 0.9994141
00:57:21.070 --> 00:57:22.450 but at the lower dose
NOTE Confidence: 0.9908203
00:57:22.830 --> 00:57:24.690 where we have less toxicity
NOTE Confidence: 0.83186847
00:57:25.150 --> 00:57:26.910 and those the opposite neo
NOTE Confidence: 0.83186847
00:57:26.910 --> 00:57:28.130 when that's been updated,
NOTE Confidence: 1
00:57:28.464 --> 00:57:29.825 those responses have been quite
NOTE Confidence: 1
00:57:29.825 --> 00:57:30.325 durable.
NOTE Confidence: 0.95654297
00:57:33.184 --> 00:57:34.944 Next. Now, again, an an
NOTE Confidence: 0.95654297
00:57:34.944 --> 00:57:36.385 idea of, you know, how
NOTE Confidence: 0.95654297

00:57:36.385 --> 00:57:37.045 do we
NOTE Confidence: 0.9767253

00:57:37.425 --> 00:57:37.925 deescalate
NOTE Confidence: 0.9556779

00:57:38.464 --> 00:57:40.704 surgery? So, again, following a
NOTE Confidence: 0.9556779

00:57:40.704 --> 00:57:42.145 paradigm similar to what was
NOTE Confidence: 0.9556779

00:57:42.145 --> 00:57:43.670 seen in breast cancer, again,
NOTE Confidence: 0.9556779

00:57:43.670 --> 00:57:44.790 you had patients these are
NOTE Confidence: 0.9556779

00:57:44.790 --> 00:57:45.910 just three b and c,
NOTE Confidence: 0.9556779

00:57:45.910 --> 00:57:47.670 so not heavy nodal burden
NOTE Confidence: 0.9556779

00:57:47.670 --> 00:57:49.030 disease. Three d's were not
NOTE Confidence: 0.9556779

00:57:49.030 --> 00:57:50.630 included in here. And, again,
NOTE Confidence: 0.9556779

00:57:50.630 --> 00:57:52.070 the patients got the best
NOTE Confidence: 0.9556779

00:57:52.070 --> 00:57:53.910 dose, the Goldilocks dose of
NOTE Confidence: 0.9556779

00:57:53.910 --> 00:57:55.395 ipi one nivo three
NOTE Confidence: 0.90137345

00:57:55.955 --> 00:57:57.155 and got their cycles. And
NOTE Confidence: 0.90137345

00:57:57.155 --> 00:57:58.915 then instead of doing as
NOTE Confidence: 0.90137345

00:57:58.915 --> 00:58:00.195 an opposite NEO and when

NOTE Confidence: 0.90137345
00:58:00.195 --> 00:58:01.395 we talk about the NEDENA
NOTE Confidence: 0.90137345
00:58:01.395 --> 00:58:03.315 trial, a full completion nodal
NOTE Confidence: 0.90137345
00:58:03.315 --> 00:58:03.815 dissection,
NOTE Confidence: 0.8282516
00:58:04.195 --> 00:58:05.875 a fiducial was placed and
NOTE Confidence: 0.8282516
00:58:05.875 --> 00:58:07.575 just that fiducial marked
NOTE Confidence: 0.96606445
00:58:08.380 --> 00:58:09.440 lymph node removed,
NOTE Confidence: 0.97403973
00:58:09.740 --> 00:58:10.940 leaving everything in the rest
NOTE Confidence: 0.97403973
00:58:10.940 --> 00:58:12.380 of the nodal basin. And
NOTE Confidence: 0.97403973
00:58:12.380 --> 00:58:13.260 in this study, then they
NOTE Confidence: 0.97403973
00:58:13.260 --> 00:58:14.940 said, okay. Based upon that
NOTE Confidence: 0.97403973
00:58:14.940 --> 00:58:16.700 one lymph node, we're going
NOTE Confidence: 0.97403973
00:58:16.700 --> 00:58:18.240 to commit to making treatment
NOTE Confidence: 0.97403973
00:58:18.300 --> 00:58:19.820 decisions. So if you had
NOTE Confidence: 0.97403973
00:58:19.820 --> 00:58:21.645 a complete or near
NOTE Confidence: 0.9904785
00:58:22.365 --> 00:58:23.585 pathologic response,
NOTE Confidence: 0.9319092

00:58:23.885 --> 00:58:25.245 you did not then undergo
NOTE Confidence: 0.9319092

00:58:25.245 --> 00:58:27.165 a therapeutic node dissection again
NOTE Confidence: 0.9319092

00:58:27.165 --> 00:58:28.285 similar to the paradigm that
NOTE Confidence: 0.9319092

00:58:28.285 --> 00:58:29.585 we have in breast cancer.
NOTE Confidence: 0.92578125

00:58:29.885 --> 00:58:31.005 And also you didn't get
NOTE Confidence: 0.92578125

00:58:31.005 --> 00:58:32.445 additional systemic treatment.
NOTE Confidence: 0.9653946

00:58:33.660 --> 00:58:35.260 For the pathologic response, you've
NOTE Confidence: 0.9653946

00:58:35.260 --> 00:58:36.940 got a therapeutic node dissection.
NOTE Confidence: 0.9653946

00:58:36.940 --> 00:58:38.079 Those patients then,
NOTE Confidence: 0.9184148

00:58:38.859 --> 00:58:39.980 if they had no distant
NOTE Confidence: 0.9184148

00:58:39.980 --> 00:58:41.260 disease were observed, if there
NOTE Confidence: 0.9184148

00:58:41.260 --> 00:58:43.020 was greater than fifty percent
NOTE Confidence: 0.9184148

00:58:43.020 --> 00:58:44.460 of those non responders, they
NOTE Confidence: 0.9184148

00:58:44.460 --> 00:58:46.059 then got a therapeutic node
NOTE Confidence: 0.9184148

00:58:46.059 --> 00:58:46.559 dissection
NOTE Confidence: 0.9346517

00:58:46.940 --> 00:58:48.140 and then went on to

NOTE Confidence: 0.9346517

00:58:48.140 --> 00:58:48.640 have,

NOTE Confidence: 0.9770741

00:58:49.075 --> 00:58:50.595 the investigator have a choice

NOTE Confidence: 0.9770741

00:58:50.595 --> 00:58:52.515 about what adjuvant treatment then

NOTE Confidence: 0.9770741

00:58:52.515 --> 00:58:53.575 they wanted to give.

NOTE Confidence: 0.94677734

00:58:54.515 --> 00:58:55.015 Next.

NOTE Confidence: 0.95581055

00:58:56.755 --> 00:58:58.115 So, again, if if one

NOTE Confidence: 0.95581055

00:58:58.115 --> 00:58:58.915 looks and this is some

NOTE Confidence: 0.95581055

00:58:58.915 --> 00:59:00.355 of the earlier information, the

NOTE Confidence: 0.95581055

00:59:00.355 --> 00:59:01.715 updates have not come out

NOTE Confidence: 0.95581055

00:59:01.715 --> 00:59:02.100 yet,

NOTE Confidence: 0.9310547

00:59:02.820 --> 00:59:04.600 but there were about sixty

NOTE Confidence: 0.9782715

00:59:05.220 --> 00:59:06.420 patients out of the ninety

NOTE Confidence: 0.9782715

00:59:06.420 --> 00:59:07.560 that did have a complete

NOTE Confidence: 0.9782715

00:59:07.620 --> 00:59:08.980 response, and they had a

NOTE Confidence: 0.9782715

00:59:08.980 --> 00:59:10.760 ninety eight percent distant metastasis

NOTE Confidence: 0.9596545

00:59:11.060 --> 00:59:12.660 free survival. Again, none of
NOTE Confidence: 0.9596545

00:59:12.660 --> 00:59:14.580 them had adjuvant treatment. Less
NOTE Confidence: 0.9596545

00:59:14.580 --> 00:59:15.940 of a number had just
NOTE Confidence: 0.9596545

00:59:15.940 --> 00:59:17.000 partial responses,
NOTE Confidence: 0.9339061

00:59:18.125 --> 00:59:19.885 but their recurrence free survival
NOTE Confidence: 0.9339061

00:59:19.885 --> 00:59:20.845 was less as well as
NOTE Confidence: 0.9339061

00:59:20.845 --> 00:59:22.365 their distant metastasis free survival.
NOTE Confidence: 0.9339061

00:59:22.365 --> 00:59:23.964 So, again, identified a different
NOTE Confidence: 0.9339061

00:59:23.964 --> 00:59:25.964 patient population here. And the
NOTE Confidence: 0.9339061

00:59:25.964 --> 00:59:27.005 same thing with those patients
NOTE Confidence: 0.9339061

00:59:27.005 --> 00:59:28.625 who were non responders.
NOTE Confidence: 0.9797363

00:59:29.165 --> 00:59:29.665 Next.
NOTE Confidence: 1

00:59:31.140 --> 00:59:31.640 So
NOTE Confidence: 0.9443834

00:59:31.940 --> 00:59:33.380 the largest trial by far
NOTE Confidence: 0.9443834

00:59:33.380 --> 00:59:34.579 that's been done and again,
NOTE Confidence: 0.9443834

00:59:34.579 --> 00:59:35.700 the one that many of

NOTE Confidence: 0.9443834
00:59:35.700 --> 00:59:37.079 us feel has been paradigm
NOTE Confidence: 0.9443834
00:59:37.140 --> 00:59:38.819 shifting is the NEDENA trial.
NOTE Confidence: 0.9443834
00:59:38.819 --> 00:59:40.020 So this was a phase
NOTE Confidence: 0.9443834
00:59:40.020 --> 00:59:41.540 three trial again using the
NOTE Confidence: 0.9443834
00:59:41.540 --> 00:59:42.040 same
NOTE Confidence: 0.96118164
00:59:42.865 --> 00:59:43.365 ipilimumab
NOTE Confidence: 0.918861
00:59:43.665 --> 00:59:44.785 one mg per kg with
NOTE Confidence: 0.918861
00:59:44.785 --> 00:59:46.705 enivolumab three mg per kg
NOTE Confidence: 0.918861
00:59:46.705 --> 00:59:47.205 dose.
NOTE Confidence: 0.9873047
00:59:47.665 --> 00:59:48.165 And
NOTE Confidence: 1
00:59:48.705 --> 00:59:49.525 this was
NOTE Confidence: 0.99316406
00:59:50.785 --> 00:59:51.285 randomized
NOTE Confidence: 0.97998047
00:59:51.745 --> 00:59:52.245 where
NOTE Confidence: 0.9775686
00:59:53.105 --> 00:59:55.105 patients either got upfront nodal
NOTE Confidence: 0.9775686
00:59:55.105 --> 00:59:57.025 dissection and then got adjuvant
NOTE Confidence: 0.9775686

00:59:57.025 --> 00:59:57.525 therapy
NOTE Confidence: 0.98828125

00:59:57.990 --> 00:59:59.370 Oregon had a conditional
NOTE Confidence: 0.9996745

00:59:59.910 --> 01:00:01.450 treatment based upon
NOTE Confidence: 0.9942627

01:00:01.990 --> 01:00:02.810 their pathologic
NOTE Confidence: 1

01:00:03.350 --> 01:00:03.850 response
NOTE Confidence: 0.97314453

01:00:04.230 --> 01:00:04.730 following
NOTE Confidence: 0.9875488

01:00:05.110 --> 01:00:05.610 surgery.
NOTE Confidence: 0.9462057

01:00:11.865 --> 01:00:13.705 The primary endpoint was event
NOTE Confidence: 0.9462057

01:00:13.705 --> 01:00:15.565 free survival. Again, a composite
NOTE Confidence: 0.9462057

01:00:15.705 --> 01:00:17.965 score and secondary endpoints included
NOTE Confidence: 0.9462057

01:00:18.025 --> 01:00:20.025 overall recurrence free survival, distant
NOTE Confidence: 0.9462057

01:00:20.025 --> 01:00:22.045 metastasis free survival, the pathologic
NOTE Confidence: 0.9462057

01:00:22.185 --> 01:00:23.865 response, adverse events and quality
NOTE Confidence: 0.9462057

01:00:23.865 --> 01:00:24.905 of life, which was also
NOTE Confidence: 0.9462057

01:00:24.905 --> 01:00:26.570 important for this patient cohort.
NOTE Confidence: 0.9462057

01:00:26.630 --> 01:00:27.130 Next.

NOTE Confidence: 0.97332764
01:00:28.790 --> 01:00:29.590 So you can see in
NOTE Confidence: 0.97332764
01:00:29.590 --> 01:00:30.630 the upper left, if we
NOTE Confidence: 0.97332764
01:00:30.630 --> 01:00:31.770 look at
NOTE Confidence: 0.8734334
01:00:33.670 --> 01:00:35.450 our neoadjuvant versus adjuvant
NOTE Confidence: 0.9890137
01:00:35.910 --> 01:00:36.410 curves,
NOTE Confidence: 0.99902344
01:00:37.350 --> 01:00:38.250 you know, for
NOTE Confidence: 0.9229329
01:00:38.694 --> 01:00:39.994 recurrence free survival.
NOTE Confidence: 0.9594618
01:00:40.775 --> 01:00:42.535 Again, those event I'm sorry,
NOTE Confidence: 0.9594618
01:00:42.535 --> 01:00:43.895 event free survival. Again, you
NOTE Confidence: 0.9594618
01:00:43.895 --> 01:00:45.255 see a similar separation of
NOTE Confidence: 0.9594618
01:00:45.255 --> 01:00:46.295 curves that you did see
NOTE Confidence: 0.9594618
01:00:46.295 --> 01:00:47.494 for the swag eighteen o
NOTE Confidence: 0.9594618
01:00:47.494 --> 01:00:48.375 one trial. If you look
NOTE Confidence: 0.9594618
01:00:48.375 --> 01:00:50.075 at the the left lower
NOTE Confidence: 0.9594618
01:00:50.214 --> 01:00:51.655 area again, if you actually
NOTE Confidence: 0.9594618

01:00:51.655 --> 01:00:53.755 stratify them by pathologic response,
NOTE Confidence: 0.9518599

01:00:54.300 --> 01:00:56.000 those patients with major pathologic
NOTE Confidence: 0.9518599

01:00:56.140 --> 01:00:57.420 response who are then just
NOTE Confidence: 0.9518599

01:00:57.420 --> 01:00:57.920 observed,
NOTE Confidence: 0.9995117

01:00:58.940 --> 01:01:00.140 you know, those are
NOTE Confidence: 0.94959855

01:01:00.940 --> 01:01:01.920 it's, you know,
NOTE Confidence: 0.79589844

01:01:02.380 --> 01:01:02.880 spectacular,
NOTE Confidence: 0.9878817

01:01:03.500 --> 01:01:05.340 you know, greater than ninety
NOTE Confidence: 0.9878817

01:01:05.340 --> 01:01:06.860 percent of those patients having
NOTE Confidence: 0.9878817

01:01:06.860 --> 01:01:07.360 durable,
NOTE Confidence: 0.88322264

01:01:08.220 --> 01:01:10.605 recurrence free survival benefit, not
NOTE Confidence: 0.88322264

01:01:10.605 --> 01:01:12.285 recurring. And those curves actually
NOTE Confidence: 0.88322264

01:01:12.285 --> 01:01:13.805 draw them out now a
NOTE Confidence: 0.88322264

01:01:13.805 --> 01:01:14.765 couple of years out and
NOTE Confidence: 0.88322264

01:01:14.765 --> 01:01:16.945 those curves has maintained themselves.
NOTE Confidence: 0.9844157

01:01:17.405 --> 01:01:19.245 The partial pathologic response patient,

NOTE Confidence: 0.9844157
01:01:19.245 --> 01:01:21.165 again, we're seeing seventy, seventy
NOTE Confidence: 0.9844157
01:01:21.165 --> 01:01:21.900 six percent
NOTE Confidence: 0.9576823
01:01:22.539 --> 01:01:23.760 recurrence free survival.
NOTE Confidence: 0.94588214
01:01:24.380 --> 01:01:25.660 But again, those patients who
NOTE Confidence: 0.94588214
01:01:25.660 --> 01:01:27.200 are not pathologic responders,
NOTE Confidence: 0.99071205
01:01:27.900 --> 01:01:29.260 these are a different patient
NOTE Confidence: 0.99071205
01:01:29.260 --> 01:01:30.539 population. We have to think
NOTE Confidence: 0.99071205
01:01:30.539 --> 01:01:31.980 of them differently. Those are
NOTE Confidence: 0.99071205
01:01:31.980 --> 01:01:33.500 patients you're gonna highlight for
NOTE Confidence: 0.99071205
01:01:33.500 --> 01:01:34.799 maybe early clinical
NOTE Confidence: 0.9939575
01:01:35.145 --> 01:01:36.585 trials. Those are not your
NOTE Confidence: 0.9939575
01:01:36.585 --> 01:01:38.125 immune therapy responders.
NOTE Confidence: 0.97190857
01:01:38.505 --> 01:01:39.465 And again, just the two
NOTE Confidence: 0.97190857
01:01:39.465 --> 01:01:40.905 panels on the right shows
NOTE Confidence: 0.97190857
01:01:40.905 --> 01:01:41.945 that, you know, we saw
NOTE Confidence: 0.97190857

01:01:41.945 --> 01:01:42.445 similar,
NOTE Confidence: 1

01:01:43.385 --> 01:01:43.885 responses
NOTE Confidence: 0.97685105

01:01:44.265 --> 01:01:45.625 to the new adjuvant treatment
NOTE Confidence: 0.97685105

01:01:45.625 --> 01:01:47.405 regardless of your BRAF mutation
NOTE Confidence: 0.97685105

01:01:47.545 --> 01:01:48.045 status.
NOTE Confidence: 0.95874023

01:01:48.665 --> 01:01:49.165 Next.
NOTE Confidence: 0.9763997

01:01:50.280 --> 01:01:51.180 This is just,
NOTE Confidence: 0.9462036

01:01:51.960 --> 01:01:53.240 a smaller trial too that
NOTE Confidence: 0.9462036

01:01:53.240 --> 01:01:54.520 really then pushed the limits
NOTE Confidence: 0.9462036

01:01:54.520 --> 01:01:55.320 a little bit more and
NOTE Confidence: 0.9462036

01:01:55.320 --> 01:01:56.540 said, what if we combine,
NOTE Confidence: 0.99104816

01:01:57.800 --> 01:01:59.420 targeted therapy with,
NOTE Confidence: 0.94189453

01:01:59.880 --> 01:02:00.380 neoadjuvant
NOTE Confidence: 0.97961426

01:02:00.680 --> 01:02:02.760 immune therapy? Again, a smaller
NOTE Confidence: 0.97961426

01:02:02.760 --> 01:02:03.960 study, just a total of
NOTE Confidence: 0.97961426

01:02:03.960 --> 01:02:04.780 thirty patients.

NOTE Confidence: 0.99450684
01:02:05.255 --> 01:02:06.455 And what you can see
NOTE Confidence: 0.99450684
01:02:06.455 --> 01:02:08.235 is, you know, not surprisingly,
NOTE Confidence: 0.97749835
01:02:08.535 --> 01:02:10.055 if you combine patients who
NOTE Confidence: 0.97749835
01:02:10.055 --> 01:02:10.555 have,
NOTE Confidence: 0.9324544
01:02:11.255 --> 01:02:13.335 BRAF mutations, so v six
NOTE Confidence: 0.9324544
01:02:13.335 --> 01:02:15.175 hundred e mutant folks, if
NOTE Confidence: 0.9324544
01:02:15.175 --> 01:02:16.935 you combine immune therapy along
NOTE Confidence: 0.9324544
01:02:16.935 --> 01:02:18.455 with targeted therapy, you're going
NOTE Confidence: 0.9324544
01:02:18.455 --> 01:02:19.515 to have more pathologic
NOTE Confidence: 0.873291
01:02:20.120 --> 01:02:20.620 responses,
NOTE Confidence: 0.9938965
01:02:21.400 --> 01:02:22.360 that did come at the
NOTE Confidence: 0.9938965
01:02:22.360 --> 01:02:23.340 cost of toxicity
NOTE Confidence: 0.9860433
01:02:23.800 --> 01:02:25.160 compared to your BRAF mutant
NOTE Confidence: 0.9860433
01:02:25.160 --> 01:02:26.280 patients, where you really didn't
NOTE Confidence: 0.9860433
01:02:26.280 --> 01:02:28.040 see, in my mind, any
NOTE Confidence: 0.9860433

01:02:28.040 --> 01:02:29.800 additional benefit of adding one
NOTE Confidence: 0.9860433

01:02:29.800 --> 01:02:31.180 of your targeted therapies
NOTE Confidence: 0.90063477

01:02:31.640 --> 01:02:32.520 to your,
NOTE Confidence: 0.9968262

01:02:33.515 --> 01:02:35.775 your monotherapy with immune
NOTE Confidence: 0.8823649

01:02:36.555 --> 01:02:38.235 treatment. So, again, only seeing
NOTE Confidence: 0.8823649

01:02:38.235 --> 01:02:38.735 about
NOTE Confidence: 0.96967375

01:02:41.755 --> 01:02:43.195 thirteen percent of your patients
NOTE Confidence: 0.96967375

01:02:43.195 --> 01:02:44.875 having a pathologic response rate.
NOTE Confidence: 0.96967375

01:02:44.875 --> 01:02:45.995 So I think you could
NOTE Confidence: 0.96967375

01:02:45.995 --> 01:02:47.435 probably, on the basis, even
NOTE Confidence: 0.96967375

01:02:47.435 --> 01:02:48.655 though it's a small trial
NOTE Confidence: 0.96967375

01:02:48.810 --> 01:02:50.330 for your BRAF wild type
NOTE Confidence: 0.96967375

01:02:50.330 --> 01:02:52.330 patients, really not add that
NOTE Confidence: 0.96967375

01:02:52.330 --> 01:02:53.310 selection in,
NOTE Confidence: 0.98835754

01:02:54.170 --> 01:02:55.290 as a choice. But again,
NOTE Confidence: 0.98835754

01:02:55.290 --> 01:02:56.730 if you really needed to

NOTE Confidence: 0.98835754
01:02:56.730 --> 01:02:58.010 have a patient with super
NOTE Confidence: 0.98835754
01:02:58.010 --> 01:02:58.510 bulky
NOTE Confidence: 0.9875488
01:02:58.890 --> 01:02:59.390 disease,
NOTE Confidence: 0.9892578
01:02:59.850 --> 01:03:00.350 you
NOTE Confidence: 0.94895715
01:03:00.650 --> 01:03:02.090 did see really some really
NOTE Confidence: 0.94895715
01:03:02.090 --> 01:03:03.930 impressive early responses in this
NOTE Confidence: 0.94895715
01:03:03.930 --> 01:03:06.185 trial for patients. Next.
NOTE Confidence: 0.912657
01:03:08.325 --> 01:03:09.525 All right. So thank you,
NOTE Confidence: 0.912657
01:03:09.525 --> 01:03:11.285 Doctor. Alina. So we're just
NOTE Confidence: 0.912657
01:03:11.285 --> 01:03:12.725 going to highlight a few
NOTE Confidence: 0.912657
01:03:12.725 --> 01:03:14.805 examples of where new adjuvant
NOTE Confidence: 0.912657
01:03:14.805 --> 01:03:16.325 therapy has led to, you
NOTE Confidence: 0.912657
01:03:16.325 --> 01:03:18.405 know, good responses, but maybe
NOTE Confidence: 0.912657
01:03:18.405 --> 01:03:20.040 also kind of mitigated by
NOTE Confidence: 0.912657
01:03:20.200 --> 01:03:20.940 toxicity. So
NOTE Confidence: 0.9796753

01:03:21.240 --> 01:03:22.920 the first example I wanted
NOTE Confidence: 0.9796753

01:03:22.920 --> 01:03:23.900 to highlight was
NOTE Confidence: 0.9622667

01:03:24.440 --> 01:03:25.800 a lady with a right
NOTE Confidence: 0.9622667

01:03:25.800 --> 01:03:28.140 abdominal melanoma that arose from
NOTE Confidence: 0.9622667

01:03:28.440 --> 01:03:30.440 a congenital mole. So she
NOTE Confidence: 0.9622667

01:03:30.440 --> 01:03:32.140 presented to see Doctor. Alino
NOTE Confidence: 0.9622667

01:03:32.200 --> 01:03:33.820 and myself with a bulky
NOTE Confidence: 0.9622667

01:03:33.960 --> 01:03:34.860 right axillary
NOTE Confidence: 0.89904785

01:03:35.160 --> 01:03:35.985 lymph node,
NOTE Confidence: 0.92089844

01:03:37.425 --> 01:03:38.865 which we which was a
NOTE Confidence: 0.92089844

01:03:38.865 --> 01:03:40.085 stage three b.
NOTE Confidence: 0.9489339

01:03:40.625 --> 01:03:42.865 No other distant metastatic disease,
NOTE Confidence: 0.9489339

01:03:42.865 --> 01:03:43.365 fortunately.
NOTE Confidence: 0.9765896

01:03:43.825 --> 01:03:44.945 She did have a BRAF
NOTE Confidence: 0.9765896

01:03:44.945 --> 01:03:45.445 B600E
NOTE Confidence: 0.9030762

01:03:46.065 --> 01:03:46.565 mutation.

NOTE Confidence: 0.9574382
01:03:47.105 --> 01:03:48.145 And so what we did
NOTE Confidence: 0.9574382
01:03:48.145 --> 01:03:50.065 was given the size of
NOTE Confidence: 0.9574382
01:03:50.065 --> 01:03:51.960 that lymph node and also
NOTE Confidence: 0.9574382
01:03:51.960 --> 01:03:54.220 additional concurrent medical core morbidity
NOTE Confidence: 0.9574382
01:03:54.360 --> 01:03:55.880 such as just optimizing her
NOTE Confidence: 0.9574382
01:03:55.880 --> 01:03:57.800 cardiac performance status, given a
NOTE Confidence: 0.9574382
01:03:57.800 --> 01:03:58.860 history of CHF
NOTE Confidence: 0.94142437
01:03:59.400 --> 01:04:01.240 and a concurrent diagnosis of
NOTE Confidence: 0.94142437
01:04:01.240 --> 01:04:02.700 an early stage endometrial
NOTE Confidence: 0.8814872
01:04:03.080 --> 01:04:03.580 adenocarcinoma,
NOTE Confidence: 0.876244
01:04:05.555 --> 01:04:07.075 We offer her new adjuvant
NOTE Confidence: 0.876244
01:04:07.075 --> 01:04:07.575 nimvolumab.
NOTE Confidence: 0.9456543
01:04:08.515 --> 01:04:09.974 So she got two doses,
NOTE Confidence: 0.92600095
01:04:10.434 --> 01:04:12.515 had a fantastic clinical response
NOTE Confidence: 0.92600095
01:04:12.515 --> 01:04:14.035 in that right axillary lymph
NOTE Confidence: 0.92600095

01:04:14.035 --> 01:04:15.654 node but then developed myocarditis,
NOTE Confidence: 0.9816284

01:04:15.954 --> 01:04:17.654 was hospitalized for that.
NOTE Confidence: 0.87338257

01:04:18.275 --> 01:04:19.894 Troponin's in the hundreds.
NOTE Confidence: 0.89272636

01:04:20.870 --> 01:04:23.110 She was given large doses
NOTE Confidence: 0.89272636

01:04:23.110 --> 01:04:23.850 of Solumedrol
NOTE Confidence: 0.9082031

01:04:24.870 --> 01:04:26.490 followed by cardiac oncology,
NOTE Confidence: 0.9813843

01:04:27.110 --> 01:04:28.470 eventually had to be,
NOTE Confidence: 0.8569743

01:04:29.270 --> 01:04:31.190 you know, given Cellcept and
NOTE Confidence: 0.8569743

01:04:31.190 --> 01:04:31.690 tofacitinib
NOTE Confidence: 0.99365234

01:04:32.230 --> 01:04:32.890 as well.
NOTE Confidence: 0.998291

01:04:34.455 --> 01:04:35.595 However, given
NOTE Confidence: 0.9310303

01:04:35.975 --> 01:04:37.435 improvement in her myocarditis
NOTE Confidence: 0.98837

01:04:38.135 --> 01:04:39.575 and stability of that right
NOTE Confidence: 0.98837

01:04:39.575 --> 01:04:41.735 axillary lymph node, she eventually
NOTE Confidence: 0.98837

01:04:41.735 --> 01:04:42.775 was able to make it
NOTE Confidence: 0.98837

01:04:42.775 --> 01:04:44.135 to surgery. And so these

NOTE Confidence: 0.98837
01:04:44.135 --> 01:04:44.695 are just,
NOTE Confidence: 0.9926758
01:04:45.175 --> 01:04:46.155 CT scans
NOTE Confidence: 0.98976827
01:04:46.480 --> 01:04:48.000 at baseline showing that large
NOTE Confidence: 0.98976827
01:04:48.000 --> 01:04:50.640 right axillary lymph node, probably
NOTE Confidence: 0.98976827
01:04:50.640 --> 01:04:51.140 representing
NOTE Confidence: 0.96972656
01:04:51.520 --> 01:04:52.800 a group of matted lymph
NOTE Confidence: 0.96972656
01:04:52.800 --> 01:04:54.320 nodes in that area. And
NOTE Confidence: 0.96972656
01:04:54.320 --> 01:04:55.700 after just two doses,
NOTE Confidence: 0.9688721
01:04:56.560 --> 01:04:58.400 about a greater than fifty
NOTE Confidence: 0.9688721
01:04:58.400 --> 01:05:00.180 percent reduction in the mass
NOTE Confidence: 0.9688721
01:05:00.320 --> 01:05:01.860 of that lymph node.
NOTE Confidence: 0.96103287
01:05:03.245 --> 01:05:04.685 You know, ideally, we would
NOTE Confidence: 0.96103287
01:05:04.685 --> 01:05:06.045 have taken to her to
NOTE Confidence: 0.96103287
01:05:06.045 --> 01:05:07.405 surgery, you know, if we
NOTE Confidence: 0.96103287
01:05:07.405 --> 01:05:08.685 were going by the swag
NOTE Confidence: 0.96103287

01:05:08.685 --> 01:05:09.965 eighteen o one trial after
NOTE Confidence: 0.96103287

01:05:09.965 --> 01:05:11.405 that third dose of anti
NOTE Confidence: 0.96103287

01:05:11.405 --> 01:05:12.225 PD one.
NOTE Confidence: 0.99576825

01:05:13.085 --> 01:05:14.625 However, given her myocarditis
NOTE Confidence: 0.88728213

01:05:15.005 --> 01:05:16.290 and the fact that that
NOTE Confidence: 0.88728213

01:05:16.450 --> 01:05:17.890 left right axillary lymph node
NOTE Confidence: 0.88728213

01:05:17.890 --> 01:05:18.950 had been stable
NOTE Confidence: 0.9145996

01:05:19.490 --> 01:05:21.030 while despite all the immunosuppression
NOTE Confidence: 0.9920247

01:05:21.330 --> 01:05:22.450 she got for treating her
NOTE Confidence: 0.9920247

01:05:22.450 --> 01:05:22.950 myocarditis,
NOTE Confidence: 0.9563759

01:05:23.810 --> 01:05:25.010 we kind of held study,
NOTE Confidence: 0.9563759

01:05:25.010 --> 01:05:26.610 you know, and made a
NOTE Confidence: 0.9563759

01:05:26.610 --> 01:05:28.130 judgment call to do this
NOTE Confidence: 0.9563759

01:05:28.130 --> 01:05:29.510 as safely as possible.
NOTE Confidence: 0.9980469

01:05:30.285 --> 01:05:30.785 So
NOTE Confidence: 0.9522182

01:05:31.405 --> 01:05:32.605 eventually, she was able to

NOTE Confidence: 0.9522182
01:05:32.605 --> 01:05:33.505 get surgery,
NOTE Confidence: 0.99609375
01:05:34.285 --> 01:05:34.785 about
NOTE Confidence: 0.99316406
01:05:35.244 --> 01:05:37.265 six, seven months after
NOTE Confidence: 0.925136
01:05:37.565 --> 01:05:39.244 her last dose of anti
NOTE Confidence: 0.925136
01:05:39.244 --> 01:05:39.984 PD one.
NOTE Confidence: 0.97349966
01:05:40.684 --> 01:05:42.365 And throughout this entire time,
NOTE Confidence: 0.97349966
01:05:42.365 --> 01:05:43.964 her CT scans had been
NOTE Confidence: 0.97349966
01:05:43.964 --> 01:05:44.464 stable,
NOTE Confidence: 0.9664714
01:05:44.970 --> 01:05:45.869 and her immunosuppression
NOTE Confidence: 0.8276367
01:05:46.330 --> 01:05:46.730 was,
NOTE Confidence: 0.97843426
01:05:47.210 --> 01:05:48.590 weaned down significantly.
NOTE Confidence: 0.97138906
01:05:49.369 --> 01:05:50.730 But when Doctor. Alina went
NOTE Confidence: 0.97138906
01:05:50.730 --> 01:05:52.330 in to remove that lymph
NOTE Confidence: 0.97138906
01:05:52.330 --> 01:05:54.350 node, what she found was
NOTE Confidence: 0.97138906
01:05:54.570 --> 01:05:56.890 mainly necrotic tissue, lots of
NOTE Confidence: 0.97138906

01:05:56.890 --> 01:05:57.390 lymphocytes,
NOTE Confidence: 0.9953788

01:05:58.570 --> 01:06:00.835 that were holding any viable
NOTE Confidence: 0.9953788

01:06:00.835 --> 01:06:02.835 melanoma towards the center of
NOTE Confidence: 0.9953788

01:06:02.835 --> 01:06:04.615 that lymph node. Unfortunately,
NOTE Confidence: 0.99217004

01:06:04.995 --> 01:06:06.115 she did not have a
NOTE Confidence: 0.99217004

01:06:06.115 --> 01:06:08.115 major pathologic response. There was
NOTE Confidence: 0.99217004

01:06:08.115 --> 01:06:09.655 still some viable melanoma
NOTE Confidence: 0.94767255

01:06:10.035 --> 01:06:10.855 at the core.
NOTE Confidence: 0.9366319

01:06:12.270 --> 01:06:14.030 And so subsequently given her
NOTE Confidence: 0.9366319

01:06:14.030 --> 01:06:15.970 BRAF mutation, we kind
NOTE Confidence: 0.9219971

01:06:16.270 --> 01:06:16.930 of then,
NOTE Confidence: 0.98760766

01:06:17.710 --> 01:06:19.470 determined, you know, it was
NOTE Confidence: 0.98760766

01:06:19.470 --> 01:06:21.390 gonna be probably best to
NOTE Confidence: 0.98760766

01:06:21.390 --> 01:06:22.830 treat her with an additional
NOTE Confidence: 0.98760766

01:06:22.830 --> 01:06:23.810 year of adjuvant
NOTE Confidence: 0.87141925

01:06:24.430 --> 01:06:25.490 BRAF MEK inhibitors,

NOTE Confidence: 0.9998779
01:06:26.195 --> 01:06:27.395 given the fact that she
NOTE Confidence: 0.9998779
01:06:27.395 --> 01:06:28.375 would be ineligible
NOTE Confidence: 0.9721492
01:06:28.675 --> 01:06:30.355 to receive any further immune
NOTE Confidence: 0.9721492
01:06:30.355 --> 01:06:31.795 checkpoint therapy in the future
NOTE Confidence: 0.9721492
01:06:31.795 --> 01:06:32.855 given her myocarditis.
NOTE Confidence: 0.97998047
01:06:33.875 --> 01:06:34.375 So
NOTE Confidence: 0.90581936
01:06:34.755 --> 01:06:36.275 despite she completed a year
NOTE Confidence: 0.90581936
01:06:36.275 --> 01:06:38.055 of adjuvant, arafniv, trametinib.
NOTE Confidence: 0.98377824
01:06:38.780 --> 01:06:40.380 And despite this, after two
NOTE Confidence: 0.98377824
01:06:40.380 --> 01:06:41.920 years, her scans remain
NOTE Confidence: 0.99902344
01:06:42.220 --> 01:06:42.720 negative.
NOTE Confidence: 0.9221802
01:06:44.060 --> 01:06:45.760 So, again, great response,
NOTE Confidence: 0.98123604
01:06:46.060 --> 01:06:47.260 but we paid a price
NOTE Confidence: 0.98123604
01:06:47.260 --> 01:06:48.080 for that.
NOTE Confidence: 0.9697876
01:06:48.780 --> 01:06:50.220 The second case example I
NOTE Confidence: 0.9697876

01:06:50.220 --> 01:06:51.119 wanted to highlight,
NOTE Confidence: 0.93272567

01:06:52.095 --> 01:06:53.955 follows more closely the NEDENA
NOTE Confidence: 0.93272567

01:06:54.015 --> 01:06:54.515 trial.
NOTE Confidence: 0.93730026

01:06:54.975 --> 01:06:56.655 So here and we tried
NOTE Confidence: 0.93730026

01:06:56.655 --> 01:06:58.175 ipi one and nivo three
NOTE Confidence: 0.93730026

01:06:58.175 --> 01:06:58.675 instead.
NOTE Confidence: 0.99637276

01:06:59.295 --> 01:07:00.494 So this is a gentleman
NOTE Confidence: 0.99637276

01:07:00.494 --> 01:07:01.234 with cutaneous
NOTE Confidence: 0.9486491

01:07:01.535 --> 01:07:02.975 melanoma of the scalp, and
NOTE Confidence: 0.9486491

01:07:02.975 --> 01:07:04.255 you can see his picture
NOTE Confidence: 0.9486491

01:07:04.255 --> 01:07:04.835 at baseline
NOTE Confidence: 0.98177075

01:07:05.270 --> 01:07:06.869 with those multiple in transit
NOTE Confidence: 0.98177075

01:07:06.869 --> 01:07:09.030 lesions adjacent to that. He
NOTE Confidence: 0.98177075

01:07:09.030 --> 01:07:10.150 actually had a third one
NOTE Confidence: 0.98177075

01:07:10.150 --> 01:07:12.089 that was biopsied to demonstrate
NOTE Confidence: 0.98177075

01:07:12.150 --> 01:07:14.250 and verify in transit metastases.

NOTE Confidence: 0.96989745
01:07:14.869 --> 01:07:15.990 He also did have a
NOTE Confidence: 0.96989745
01:07:15.990 --> 01:07:16.490 BRAFV600E
NOTE Confidence: 0.9880371
01:07:17.430 --> 01:07:17.930 mutation.
NOTE Confidence: 0.9029948
01:07:18.984 --> 01:07:19.885 So he received
NOTE Confidence: 0.8953334
01:07:20.425 --> 01:07:22.105 two cycles of ipi one
NOTE Confidence: 0.8953334
01:07:22.105 --> 01:07:23.085 nivo three,
NOTE Confidence: 0.9347826
01:07:24.105 --> 01:07:26.045 and then given his fantastic
NOTE Confidence: 0.9347826
01:07:26.265 --> 01:07:27.865 clinical response, and as you
NOTE Confidence: 0.9347826
01:07:27.865 --> 01:07:29.145 can see, after two cycles,
NOTE Confidence: 0.9347826
01:07:29.145 --> 01:07:30.984 that lesion really flattened out.
NOTE Confidence: 0.9347826
01:07:30.984 --> 01:07:32.125 It was not
NOTE Confidence: 0.88256836
01:07:32.665 --> 01:07:33.165 nodular
NOTE Confidence: 0.9916992
01:07:33.840 --> 01:07:34.580 any longer.
NOTE Confidence: 0.99820966
01:07:35.440 --> 01:07:37.360 He actually opted to delay
NOTE Confidence: 0.99820966
01:07:37.360 --> 01:07:37.860 surgery
NOTE Confidence: 0.9487793

01:07:38.160 --> 01:07:39.380 a little bit. And so
NOTE Confidence: 0.9879557

01:07:39.680 --> 01:07:41.920 we gave him additional doses
NOTE Confidence: 0.9879557

01:07:41.920 --> 01:07:42.660 of nivolumab.
NOTE Confidence: 0.96132815

01:07:43.040 --> 01:07:44.800 And eventually, when he decided
NOTE Confidence: 0.96132815

01:07:44.800 --> 01:07:46.260 he was ready for surgery,
NOTE Confidence: 0.94077146

01:07:46.935 --> 01:07:48.135 because he didn't want any
NOTE Confidence: 0.94077146

01:07:48.135 --> 01:07:49.815 downtime from any post lock
NOTE Confidence: 0.94077146

01:07:49.815 --> 01:07:51.595 healing given his work schedule,
NOTE Confidence: 0.97210693

01:07:52.215 --> 01:07:53.435 it showed a pathologic
NOTE Confidence: 0.9433594

01:07:53.735 --> 01:07:55.515 complete response. And so,
NOTE Confidence: 0.9980469

01:07:56.295 --> 01:07:57.275 further immunotherapy
NOTE Confidence: 0.92976886

01:07:57.655 --> 01:07:59.255 was stopped and he's been
NOTE Confidence: 0.92976886

01:07:59.255 --> 01:08:01.035 monitored with just surveillance,
NOTE Confidence: 0.9871826

01:08:02.230 --> 01:08:03.770 continues to be NAD
NOTE Confidence: 0.8958217

01:08:04.150 --> 01:08:05.830 on on clinical examine and
NOTE Confidence: 0.8958217

01:08:05.830 --> 01:08:07.050 restaging scans.

NOTE Confidence: 0.81852216
01:08:09.510 --> 01:08:10.490 So in conclusion,
NOTE Confidence: 0.87567824
01:08:10.790 --> 01:08:12.470 you know, neo adjuvant immune
NOTE Confidence: 0.87567824
01:08:12.470 --> 01:08:12.970 therapy,
NOTE Confidence: 0.9995117
01:08:13.590 --> 01:08:14.490 has really
NOTE Confidence: 0.934173
01:08:15.085 --> 01:08:16.765 shifted the paradigm for care,
NOTE Confidence: 0.934173
01:08:16.765 --> 01:08:18.445 particularly with the NEDENA trial,
NOTE Confidence: 0.934173
01:08:18.445 --> 01:08:19.485 which was a large phase
NOTE Confidence: 0.934173
01:08:19.485 --> 01:08:20.305 three study,
NOTE Confidence: 0.9515537
01:08:20.765 --> 01:08:22.604 kind of advocating for improved
NOTE Confidence: 0.9515537
01:08:22.604 --> 01:08:24.365 responses with doublet therapy for
NOTE Confidence: 0.9515537
01:08:24.365 --> 01:08:25.665 individuals with macroscopic
NOTE Confidence: 0.85791016
01:08:26.045 --> 01:08:26.545 stage,
NOTE Confidence: 0.9656372
01:08:27.165 --> 01:08:28.785 3b and above disease.
NOTE Confidence: 0.951709
01:08:30.270 --> 01:08:32.430 There's ongoing clinical interest in
NOTE Confidence: 0.951709
01:08:32.430 --> 01:08:33.790 trying to improve this treatment
NOTE Confidence: 0.951709

01:08:33.790 --> 01:08:35.650 paradigm, maybe make it less
NOTE Confidence: 0.951709

01:08:35.710 --> 01:08:37.150 toxic. And as Doctor. Alluded
NOTE Confidence: 0.951709

01:08:37.150 --> 01:08:38.450 to kind of that Goldilocks
NOTE Confidence: 0.951709

01:08:38.590 --> 01:08:39.710 approach, trying to find the
NOTE Confidence: 0.951709

01:08:39.710 --> 01:08:41.250 right regimen, the right dose
NOTE Confidence: 0.96393377

01:08:41.965 --> 01:08:43.725 with the while trying to
NOTE Confidence: 0.96393377

01:08:43.725 --> 01:08:45.325 all the time minimize any
NOTE Confidence: 0.96393377

01:08:45.325 --> 01:08:45.825 toxicity.
NOTE Confidence: 0.9484619

01:08:47.564 --> 01:08:48.845 You know, a lot of
NOTE Confidence: 0.9484619

01:08:48.845 --> 01:08:50.465 times when we have individuals
NOTE Confidence: 0.9793091

01:08:51.005 --> 01:08:52.545 presenting with bulky disease,
NOTE Confidence: 0.9977214

01:08:52.925 --> 01:08:54.385 disease that could
NOTE Confidence: 0.94331056

01:08:54.860 --> 01:08:57.280 present as functionally limiting disease.
NOTE Confidence: 0.94904613

01:08:57.820 --> 01:08:59.500 We oftentimes, you know, will
NOTE Confidence: 0.94904613

01:08:59.500 --> 01:09:01.340 try an adena style approach,
NOTE Confidence: 0.94904613

01:09:01.340 --> 01:09:03.500 but then it's very good

NOTE Confidence: 0.94904613
01:09:03.500 --> 01:09:04.860 to have our surgeons on
NOTE Confidence: 0.94904613
01:09:04.860 --> 01:09:06.140 hand as well because if
NOTE Confidence: 0.94904613
01:09:06.140 --> 01:09:07.900 things do not clinically shrink,
NOTE Confidence: 0.94904613
01:09:07.900 --> 01:09:08.880 we can always
NOTE Confidence: 0.9538199
01:09:09.454 --> 01:09:11.295 abort and proceed to surgery
NOTE Confidence: 0.9538199
01:09:11.295 --> 01:09:12.814 sooner before there is any
NOTE Confidence: 0.9538199
01:09:12.814 --> 01:09:14.114 compromise of function,
NOTE Confidence: 0.949149
01:09:15.375 --> 01:09:16.974 or any further growth in
NOTE Confidence: 0.949149
01:09:16.974 --> 01:09:17.635 the disease.
NOTE Confidence: 0.94724345
01:09:18.735 --> 01:09:20.014 And it'll be interesting with
NOTE Confidence: 0.94724345
01:09:20.014 --> 01:09:22.175 our ongoing vaccine trials too
NOTE Confidence: 0.94724345
01:09:22.175 --> 01:09:22.675 whether
NOTE Confidence: 0.80566406
01:09:23.190 --> 01:09:23.630 any,
NOTE Confidence: 0.9649949
01:09:24.070 --> 01:09:26.070 adjuvant vaccine is gonna be
NOTE Confidence: 0.9649949
01:09:26.070 --> 01:09:27.350 better than kind of leaving
NOTE Confidence: 0.9649949

01:09:27.350 --> 01:09:29.030 the tumor in situ for,
NOTE Confidence: 0.9649949

01:09:29.030 --> 01:09:30.790 again, trying to immunize and
NOTE Confidence: 0.9649949

01:09:30.790 --> 01:09:31.290 promote,
NOTE Confidence: 0.9594866

01:09:32.070 --> 01:09:33.910 T cell responses to those
NOTE Confidence: 0.9594866

01:09:33.910 --> 01:09:34.890 tumor neoantigens.
NOTE Confidence: 0.8256836

01:09:37.375 --> 01:09:37.875 So
NOTE Confidence: 0.918099

01:09:38.495 --> 01:09:39.455 on go there's a lot
NOTE Confidence: 0.918099

01:09:39.455 --> 01:09:40.895 of ongoing research, a lot
NOTE Confidence: 0.918099

01:09:40.895 --> 01:09:42.435 of development of new targets,
NOTE Confidence: 0.9588216

01:09:42.895 --> 01:09:44.435 and therapeutic strategies,
NOTE Confidence: 0.98430175

01:09:45.215 --> 01:09:46.335 in addition to kind of
NOTE Confidence: 0.98430175

01:09:46.335 --> 01:09:47.695 playing with the sequencing of
NOTE Confidence: 0.98430175

01:09:47.695 --> 01:09:49.375 all these effective immune therapies
NOTE Confidence: 0.98430175

01:09:49.375 --> 01:09:50.755 to try to improve responses.
NOTE Confidence: 0.97314453

01:09:51.280 --> 01:09:52.020 And ultimately
NOTE Confidence: 0.89353025

01:09:52.560 --> 01:09:54.560 our endgame that improvement in

NOTE Confidence: 0.89353025

01:09:54.560 --> 01:09:56.420 overall survival for our patients.

NOTE Confidence: 0.95925

01:09:57.280 --> 01:09:59.200 So that being said, I

NOTE Confidence: 0.95925

01:09:59.200 --> 01:10:01.120 think, any closing remarks, Doctor.

NOTE Confidence: 0.95925

01:10:01.120 --> 01:10:02.720 Alino? Otherwise, we'll open it

NOTE Confidence: 0.95925

01:10:02.720 --> 01:10:03.860 up for further questions.

NOTE Confidence: 0.9576367

01:10:07.915 --> 01:10:09.354 And thank you, everyone. That

NOTE Confidence: 0.9576367

01:10:09.354 --> 01:10:10.395 was kind of a tour

NOTE Confidence: 0.9576367

01:10:10.395 --> 01:10:11.854 de force of the evolution

NOTE Confidence: 0.9576367

01:10:11.915 --> 01:10:13.195 of the last twenty five

NOTE Confidence: 0.9576367

01:10:13.195 --> 01:10:15.135 years in cancer treatment across

NOTE Confidence: 0.9845378

01:10:15.435 --> 01:10:16.735 the spectrum. So

NOTE Confidence: 0.7742513

01:10:17.435 --> 01:10:18.495 and in only

NOTE Confidence: 0.97509766

01:10:19.060 --> 01:10:20.439 sixty minutes. So,

NOTE Confidence: 0.9984131

01:10:20.820 --> 01:10:21.939 thank you to to all

NOTE Confidence: 0.9984131

01:10:21.939 --> 01:10:22.760 of the panelists.

NOTE Confidence: 0.9859968

01:10:23.540 --> 01:10:24.820 I don't see any other
NOTE Confidence: 0.9859968

01:10:24.820 --> 01:10:26.500 additional questions in in the
NOTE Confidence: 0.9859968

01:10:26.500 --> 01:10:28.260 q and a. So,
NOTE Confidence: 0.9691989

01:10:28.820 --> 01:10:30.900 I thank everyone who tuned
NOTE Confidence: 0.9691989

01:10:30.900 --> 01:10:32.020 in and everyone who will
NOTE Confidence: 0.9691989

01:10:32.020 --> 01:10:33.320 watch this in the future.
NOTE Confidence: 0.9691989

01:10:33.535 --> 01:10:34.895 We are all available as
NOTE Confidence: 0.9691989

01:10:34.895 --> 01:10:36.095 well as our teams for
NOTE Confidence: 0.9691989

01:10:36.095 --> 01:10:37.295 some of these really tough
NOTE Confidence: 0.9691989

01:10:37.295 --> 01:10:37.795 cases,
NOTE Confidence: 0.9991862

01:10:38.975 --> 01:10:40.735 and for the clinical trials
NOTE Confidence: 0.9991862

01:10:40.735 --> 01:10:42.035 that we do have open
NOTE Confidence: 0.9991862

01:10:42.175 --> 01:10:44.195 for this unique patient population.
NOTE Confidence: 0.9995117

01:10:44.495 --> 01:10:45.775 So thank you so much
NOTE Confidence: 0.9995117

01:10:45.775 --> 01:10:46.435 to everybody.