

WEBVTT

NOTE duration:"01:06:50.1120000"

NOTE language:en-us

NOTE Confidence: 0.78131855

00:00:00.000 --> 00:00:02.825 Welcome everyone, I'm right here.

NOTE Confidence: 0.78131855

00:00:02.825 --> 00:00:05.650 Still be the moderated today.

NOTE Confidence: 0.78131855

00:00:05.650 --> 00:00:08.236 Just as we started this remind

NOTE Confidence: 0.78131855

00:00:08.236 --> 00:00:10.755 everyone that this Friday from 8:00

NOTE Confidence: 0.78131855

00:00:10.755 --> 00:00:13.975 to 12:30 is our annual review of ASCO.

NOTE Confidence: 0.78131855

00:00:13.975 --> 00:00:16.451 And I'm very excited this is the 10th

NOTE Confidence: 0.78131855

00:00:16.451 --> 00:00:18.706 year I'll be doing it, but we had it

NOTE Confidence: 0.78131855

00:00:18.706 --> 00:00:20.870 in place a number of years before that.

NOTE Confidence: 0.78131855

00:00:20.870 --> 00:00:22.910 Eddie used to run it and it should

NOTE Confidence: 0.78131855

00:00:22.910 --> 00:00:24.617 be very nice of you, Barbara.

NOTE Confidence: 0.78131855

00:00:24.617 --> 00:00:26.999 Already one of you are probably

NOTE Confidence: 0.78131855

00:00:26.999 --> 00:00:29.060 speaking on heading that cancer.

NOTE Confidence: 0.78131855

00:00:29.060 --> 00:00:31.130 So, uh, another chance to hear,

NOTE Confidence: 0.78131855

00:00:31.130 --> 00:00:33.890 hear them, and then it'll be very special.

NOTE Confidence: 0.78131855

00:00:33.890 --> 00:00:35.620 3540 minutes around 11:00 o'clock,

NOTE Confidence: 0.78131855

00:00:35.620 --> 00:00:37.958 where Vince Devita and his daughter Elizabeth

NOTE Confidence: 0.78131855

00:00:37.958 --> 00:00:40.786 and a few questions for myself as well.

NOTE Confidence: 0.78131855

00:00:40.790 --> 00:00:43.454 We'll discuss a little bit about the 50th

NOTE Confidence: 0.78131855

00:00:43.454 --> 00:00:45.617 anniversary of the National Cancer Act,

NOTE Confidence: 0.78131855

00:00:45.620 --> 00:00:47.690 so that should be very excited.

NOTE Confidence: 0.78131855

00:00:47.690 --> 00:00:50.280 So now I'm going to introduce today's

NOTE Confidence: 0.78131855

00:00:50.280 --> 00:00:52.518 speakers on introduce all three of you,

NOTE Confidence: 0.78131855

00:00:52.520 --> 00:00:54.590 and then I'll let Barbara moderate

NOTE Confidence: 0.78131855

00:00:54.590 --> 00:00:55.970 through the the presentations,

NOTE Confidence: 0.78131855

00:00:55.970 --> 00:00:58.890 and then we'll have questions at the end.

NOTE Confidence: 0.78131855

00:00:58.890 --> 00:01:01.123 And one of the things we've been

NOTE Confidence: 0.78131855

00:01:01.123 --> 00:01:02.957 doing is we've been highlighting

NOTE Confidence: 0.78131855

00:01:02.957 --> 00:01:05.764 our darts or disease teams at these

NOTE Confidence: 0.78131855

00:01:05.764 --> 00:01:08.755 grand rounds and it's a great way to

NOTE Confidence: 0.78131855

00:01:08.755 --> 00:01:10.205 develop multi modality discussions.  
NOTE Confidence: 0.78131855

00:01:10.205 --> 00:01:12.395 An interaction between the disease programs  
NOTE Confidence: 0.78131855

00:01:12.395 --> 00:01:14.947 and the research programs with Cancer Center.  
NOTE Confidence: 0.78131855

00:01:14.950 --> 00:01:16.410 So we're very excited.  
NOTE Confidence: 0.78131855

00:01:16.410 --> 00:01:18.235 We have a group today,  
NOTE Confidence: 0.78131855

00:01:18.240 --> 00:01:19.335 a tremendous team.  
NOTE Confidence: 0.78131855

00:01:19.335 --> 00:01:21.160 First speaker will be Doctor  
NOTE Confidence: 0.78131855

00:01:21.160 --> 00:01:21.890 Barbara Burtness,  
NOTE Confidence: 0.78131855

00:01:21.890 --> 00:01:23.885 Barbara Professor of medicine and  
NOTE Confidence: 0.78131855

00:01:23.885 --> 00:01:25.880 medical in country and disease  
NOTE Confidence: 0.78131855

00:01:25.948 --> 00:01:27.818 aligned research team leader for  
NOTE Confidence: 0.78131855

00:01:27.818 --> 00:01:29.314 head and neck cancer.  
NOTE Confidence: 0.78131855

00:01:29.320 --> 00:01:31.456 She was recently named as interim  
NOTE Confidence: 0.78131855

00:01:31.456 --> 00:01:33.510 Associate cancer Director for Diversity,  
NOTE Confidence: 0.78131855

00:01:33.510 --> 00:01:34.968 Equity and Inclusion.  
NOTE Confidence: 0.78131855

00:01:34.968 --> 00:01:36.912 Congratulations Barber Chief Medical

NOTE Confidence: 0.78131855

00:01:36.912 --> 00:01:39.447 degree from SUNY at Stony Brook

NOTE Confidence: 0.78131855

00:01:39.447 --> 00:01:41.806 completed a residency at Yale and our

NOTE Confidence: 0.78131855

00:01:41.872 --> 00:01:44.397 Fellowship at Memorial Sloan Kettering.

NOTE Confidence: 0.78131855

00:01:44.400 --> 00:01:45.828 Is that on faculty?

NOTE Confidence: 0.78131855

00:01:45.828 --> 00:01:47.256 Of course that yeah,

NOTE Confidence: 0.78131855

00:01:47.260 --> 00:01:49.766 she left in and she's come back.

NOTE Confidence: 0.78131855

00:01:49.770 --> 00:01:51.955 Doctor Bernice is an internationally

NOTE Confidence: 0.78131855

00:01:51.955 --> 00:01:54.738 recognized leader in the treatment of head

NOTE Confidence: 0.78131855

00:01:54.738 --> 00:01:57.290 and neck cancer and as chair of the Ikago,

NOTE Confidence: 0.78131855

00:01:57.290 --> 00:01:59.438 Akron and Therapeutics Committee since 2006.

NOTE Confidence: 0.78131855

00:01:59.440 --> 00:02:00.210 Pioneering biomarker,

NOTE Confidence: 0.78131855

00:02:00.210 --> 00:02:02.520 guided treatment and treatment at the

NOTE Confidence: 0.78131855

00:02:02.520 --> 00:02:04.090 intensification studies in this disease.

NOTE Confidence: 0.78131855

00:02:04.090 --> 00:02:05.875 She also leads the Yellowhead

NOTE Confidence: 0.78131855

00:02:05.875 --> 00:02:07.303 and explore recently awarded.

NOTE Confidence: 0.78131855

00:02:07.310 --> 00:02:09.458 Finished just finished the first year,  
NOTE Confidence: 0.78131855

00:02:09.460 --> 00:02:11.300 which addresses critical barriers to  
NOTE Confidence: 0.78131855

00:02:11.300 --> 00:02:13.966 treatment of head and neck squamous cell  
NOTE Confidence: 0.78131855

00:02:13.966 --> 00:02:16.246 carcinoma due to resistance to immune.  
NOTE Confidence: 0.78131855

00:02:16.250 --> 00:02:18.565 DNA damaging and targeted therapy  
NOTE Confidence: 0.78131855

00:02:18.565 --> 00:02:19.954 so welcome Barbara.  
NOTE Confidence: 0.78131855

00:02:19.960 --> 00:02:22.428 And also on the panel this morning  
NOTE Confidence: 0.78131855

00:02:22.428 --> 00:02:24.540 or this afternoon is already Bhatia.  
NOTE Confidence: 0.78131855

00:02:24.540 --> 00:02:26.544 Doctor Bhatia is an assistant professor  
NOTE Confidence: 0.78131855

00:02:26.544 --> 00:02:28.410 of medicine and medical oncology.  
NOTE Confidence: 0.78131855

00:02:28.410 --> 00:02:30.370 She received her medical degree  
NOTE Confidence: 0.78131855

00:02:30.370 --> 00:02:32.330 from Toccoa National Medical College  
NOTE Confidence: 0.78131855

00:02:32.396 --> 00:02:34.124 and her MPH from the University  
NOTE Confidence: 0.78131855

00:02:34.124 --> 00:02:36.149 of Texas School of Public Health.  
NOTE Confidence: 0.78131855

00:02:36.150 --> 00:02:38.400 She played her residency at Johns  
NOTE Confidence: 0.78131855

00:02:38.400 --> 00:02:40.268 Hopkins University Sinai Hospital and

NOTE Confidence: 0.78131855

00:02:40.268 --> 00:02:42.134 I fell asleep at Temple University,

NOTE Confidence: 0.78131855

00:02:42.140 --> 00:02:43.456 Fox Chase Cancer Center.

NOTE Confidence: 0.78131855

00:02:43.456 --> 00:02:45.430 Dr Bhatia treats patients with head

NOTE Confidence: 0.78131855

00:02:45.489 --> 00:02:47.595 and neck cancers and a research

NOTE Confidence: 0.78131855

00:02:47.595 --> 00:02:48.999 interest include exploring novel

NOTE Confidence: 0.78131855

00:02:49.057 --> 00:02:50.320 therapies for patients.

NOTE Confidence: 0.78131855

00:02:50.320 --> 00:02:52.090 She designs and conducts clinical

NOTE Confidence: 0.78131855

00:02:52.090 --> 00:02:54.540 trials and also serves as a site

NOTE Confidence: 0.78131855

00:02:54.540 --> 00:02:56.376 Pi for several multi center studies

NOTE Confidence: 0.78131855

00:02:56.376 --> 00:02:58.899 and then last but not least from

NOTE Confidence: 0.78131855

00:02:58.899 --> 00:02:59.637 radiation oncology.

NOTE Confidence: 0.78131855

00:02:59.640 --> 00:03:01.446 We have Melissa Young and Doctor

NOTE Confidence: 0.78131855

00:03:01.446 --> 00:03:02.650 Young is an assistant

NOTE Confidence: 0.8251946

00:03:02.711 --> 00:03:04.721 professor of therapeutic radiology and chief

NOTE Confidence: 0.8251946

00:03:04.721 --> 00:03:07.570 of the head and neck radiotherapy program.

NOTE Confidence: 0.8251946

00:03:07.570 --> 00:03:09.432 She completed her MD PhD training as  
NOTE Confidence: 0.8251946

00:03:09.432 --> 00:03:11.526 part of the Medical Scientist Training  
NOTE Confidence: 0.8251946

00:03:11.526 --> 00:03:13.992 program at the University of Texas  
NOTE Confidence: 0.8251946

00:03:13.992 --> 00:03:15.849 Southwestern Medical Center in Dallas.  
NOTE Confidence: 0.8251946

00:03:15.850 --> 00:03:17.575 She then continued her training  
NOTE Confidence: 0.8251946

00:03:17.575 --> 00:03:19.007 in radiation oncology, yeah,  
NOTE Confidence: 0.8251946

00:03:19.007 --> 00:03:22.183 and stayed and joined our faculty in 2015.  
NOTE Confidence: 0.8251946

00:03:22.190 --> 00:03:24.338 Doctor Young treats patients as part  
NOTE Confidence: 0.8251946

00:03:24.338 --> 00:03:26.789 of their head in their cancers.  
NOTE Confidence: 0.8251946

00:03:26.790 --> 00:03:28.635 Multi disciplinary clinic at the  
NOTE Confidence: 0.8251946

00:03:28.635 --> 00:03:30.480 Smile Cancer Hospital Care Center  
NOTE Confidence: 0.8251946

00:03:30.536 --> 00:03:32.882 in Trumbull and also specializes in  
NOTE Confidence: 0.8251946

00:03:32.882 --> 00:03:34.446 breast and gynecological agencies.  
NOTE Confidence: 0.8251946

00:03:34.450 --> 00:03:36.736 So finally, just a quick word.  
NOTE Confidence: 0.8251946

00:03:36.740 --> 00:03:39.176 The head and neck cancers dark  
NOTE Confidence: 0.8251946

00:03:39.176 --> 00:03:40.800 provides expert multidisciplinary care

NOTE Confidence: 0.8251946

00:03:40.866 --> 00:03:42.870 for head and neck cancer patients.

NOTE Confidence: 0.8251946

00:03:42.870 --> 00:03:44.837 Names to advance new research and the

NOTE Confidence: 0.8251946

00:03:44.837 --> 00:03:47.556 force of the next generation of hedex

NOTE Confidence: 0.8251946

00:03:47.556 --> 00:03:49.376 cancer translational researchers through

NOTE Confidence: 0.8251946

00:03:49.376 --> 00:03:51.299 a developmental research program.

NOTE Confidence: 0.8251946

00:03:51.300 --> 00:03:52.248 Career enhancement program.

NOTE Confidence: 0.8251946

00:03:52.248 --> 00:03:54.144 An interaction in collaboration with the

NOTE Confidence: 0.8251946

00:03:54.144 --> 00:03:56.199 wider spore and head and neck squamous

NOTE Confidence: 0.8251946

00:03:56.199 --> 00:03:57.327 cell Cancer Research communities.

NOTE Confidence: 0.8251946

00:03:57.330 --> 00:03:58.680 So what an amazing team.

NOTE Confidence: 0.8251946

00:03:58.680 --> 00:04:00.288 I've used up five of your

NOTE Confidence: 0.8251946

00:04:00.288 --> 00:04:01.092 minutes introducing you.

NOTE Confidence: 0.8251946

00:04:01.100 --> 00:04:01.934 You're also qualified.

NOTE Confidence: 0.8251946

00:04:01.934 --> 00:04:04.598 I'm going to stop by to turn over to you.

NOTE Confidence: 0.8251946

00:04:04.600 --> 00:04:04.909 Barbara,

NOTE Confidence: 0.8251946



00:04:04.909 --> 00:04:07.381 one of the best things that ever happened

NOTE Confidence: 0.8251946

00:04:07.381 --> 00:04:09.440 here at yell for me in my 10 years,

NOTE Confidence: 0.8251946

00:04:09.440 --> 00:04:11.376 is when you came and joined us and

NOTE Confidence: 0.8251946

00:04:11.376 --> 00:04:13.301 you know Barbara and I worked together

NOTE Confidence: 0.8251946

00:04:13.301 --> 00:04:15.360 20 years ago in the early ages,

NOTE Confidence: 0.8251946

00:04:15.360 --> 00:04:16.170 so Texas map.

NOTE Confidence: 0.8251946

00:04:16.170 --> 00:04:17.790 So Barbara thank you for all

NOTE Confidence: 0.8251946

00:04:17.790 --> 00:04:19.658 you've done and the floor is yours.

NOTE Confidence: 0.8714161

00:04:26.900 --> 00:04:29.265 OK, well thank you for that

NOTE Confidence: 0.8714161

00:04:29.265 --> 00:04:31.230 very kind introduction and for

NOTE Confidence: 0.8714161

00:04:31.309 --> 00:04:34.011 recruiting me back and I'm also very

NOTE Confidence: 0.8714161

00:04:34.011 --> 00:04:36.423 grateful to have the opportunity to

NOTE Confidence: 0.8714161

00:04:36.423 --> 00:04:39.575 talk about what we've been doing in the

NOTE Confidence: 0.8714161

00:04:39.575 --> 00:04:43.098 in the head neck DART. As you heard,

NOTE Confidence: 0.8714161

00:04:43.098 --> 00:04:47.180 the way we're going to do this is.

NOTE Confidence: 0.8714161

00:04:47.180 --> 00:04:50.548 My team I'm gonna spend about half an

NOTE Confidence: 0.8714161

00:04:50.548 --> 00:04:53.751 hour trying to do a world whirlwind tour

NOTE Confidence: 0.8714161

00:04:53.751 --> 00:04:57.419 of some of what our dart has been up to,

NOTE Confidence: 0.8714161

00:04:57.420 --> 00:04:59.737 then turn it over to Doctor Bhatia

NOTE Confidence: 0.8714161

00:04:59.737 --> 00:05:02.348 to talk about some of the clinical

NOTE Confidence: 0.8714161

00:05:02.348 --> 00:05:04.278 trials she's been developing in

NOTE Confidence: 0.8714161

00:05:04.278 --> 00:05:06.879 her collaboration with the sporlan,

NOTE Confidence: 0.8714161

00:05:06.880 --> 00:05:08.564 then to Doctor Young,

NOTE Confidence: 0.8714161

00:05:08.564 --> 00:05:10.669 who leads our therapeutic radiation

NOTE Confidence: 0.8714161

00:05:10.669 --> 00:05:12.000 efforts in this area.

NOTE Confidence: 0.8714161

00:05:12.000 --> 00:05:14.364 So just a brief introduction to

NOTE Confidence: 0.8714161

00:05:14.364 --> 00:05:15.546 our clinical membership.

NOTE Confidence: 0.8714161

00:05:15.550 --> 00:05:18.469 The nature of of head neck cancer.

NOTE Confidence: 0.8714161

00:05:18.470 --> 00:05:21.010 Given its anatomic complexity,

NOTE Confidence: 0.8714161

00:05:21.010 --> 00:05:24.185 its tendency to treatment resistance.

NOTE Confidence: 0.8714161

00:05:24.190 --> 00:05:27.067 It has been that very clearly outcome

NOTE Confidence: 0.8714161

00:05:27.067 --> 00:05:29.854 is improved when patients get surgery  
NOTE Confidence: 0.8714161

00:05:29.854 --> 00:05:32.800 and radiation at high volume centers,  
NOTE Confidence: 0.8714161

00:05:32.800 --> 00:05:35.495 and so we have a dedicated focus  
NOTE Confidence: 0.8714161

00:05:35.495 --> 00:05:38.347 on trying to have pockets of  
NOTE Confidence: 0.8714161

00:05:38.347 --> 00:05:40.495 excellence around the state.  
NOTE Confidence: 0.8714161

00:05:40.500 --> 00:05:44.126 So in addition to the program, it's Milo.  
NOTE Confidence: 0.8714161

00:05:44.126 --> 00:05:47.750 There are hubs for head and neck cancer,  
NOTE Confidence: 0.8714161

00:05:47.750 --> 00:05:48.654 multidisciplinary care,  
NOTE Confidence: 0.8714161

00:05:48.654 --> 00:05:51.366 including at Trumbull Ann Lawrence Memorial.  
NOTE Confidence: 0.8714161

00:05:51.370 --> 00:05:55.114 I know Emily Collier is going to be.  
NOTE Confidence: 0.8714161

00:05:55.120 --> 00:05:57.170 Joining us at Saint Francis.  
NOTE Confidence: 0.8714161

00:05:57.170 --> 00:06:00.040 So it's a it's a terrific team.  
NOTE Confidence: 0.8714161

00:06:00.040 --> 00:06:03.730 A lot of fun to work with with everybody.  
NOTE Confidence: 0.8714161

00:06:03.730 --> 00:06:05.610 The patients who present with  
NOTE Confidence: 0.8714161

00:06:05.610 --> 00:06:08.028 with head neck cancer often come  
NOTE Confidence: 0.8714161

00:06:08.028 --> 00:06:09.880 with locally advanced disease,

NOTE Confidence: 0.8714161

00:06:09.880 --> 00:06:10.724 so local,

NOTE Confidence: 0.8714161

00:06:10.724 --> 00:06:12.834 regionally invasive and not meta

NOTE Confidence: 0.8714161

00:06:12.834 --> 00:06:15.344 static and may present many times

NOTE Confidence: 0.8714161

00:06:15.344 --> 00:06:17.666 in a curative state or cure,

NOTE Confidence: 0.8714161

00:06:17.670 --> 00:06:18.972 potentially curable stage.

NOTE Confidence: 0.8714161

00:06:18.972 --> 00:06:22.010 But these tumors are located in areas

NOTE Confidence: 0.8714161

00:06:22.079 --> 00:06:24.830 that are very critical for speech and

NOTE Confidence: 0.8714161

00:06:24.830 --> 00:06:27.368 swallowing and taste and appearance and.

NOTE Confidence: 0.8714161

00:06:27.370 --> 00:06:30.282 And many of the things that we do

NOTE Confidence: 0.8714161

00:06:30.282 --> 00:06:32.957 to interact with with other people.

NOTE Confidence: 0.8714161

00:06:32.960 --> 00:06:34.552 So having a conversation,

NOTE Confidence: 0.8714161

00:06:34.552 --> 00:06:35.746 sharing a meal,

NOTE Confidence: 0.8714161

00:06:35.750 --> 00:06:38.102 singing all of these things can

NOTE Confidence: 0.8714161

00:06:38.102 --> 00:06:40.541 be impacted by either the cancer

NOTE Confidence: 0.8714161

00:06:40.541 --> 00:06:42.923 or the treatment for the cancer.

NOTE Confidence: 0.8714161

00:06:42.930 --> 00:06:44.522 Treatments are further constrained  
NOTE Confidence: 0.8714161

00:06:44.522 --> 00:06:46.114 by some anatomic peculiarities,  
NOTE Confidence: 0.8714161

00:06:46.120 --> 00:06:48.514 like the carotid artery in the  
NOTE Confidence: 0.8714161

00:06:48.514 --> 00:06:50.110 base of the skull,  
NOTE Confidence: 0.8714161

00:06:50.110 --> 00:06:51.870 and even patients who are  
NOTE Confidence: 0.8714161

00:06:51.870 --> 00:06:53.630 successfully treated may be left  
NOTE Confidence: 0.8714161

00:06:53.695 --> 00:06:55.699 with very significant impairment,  
NOTE Confidence: 0.8714161

00:06:55.700 --> 00:06:57.220 functional restriction, and actually.  
NOTE Confidence: 0.8714161

00:06:57.220 --> 00:06:59.864 May succumb to the consequences of their  
NOTE Confidence: 0.8714161

00:06:59.864 --> 00:07:01.718 treatment even when they are cured.  
NOTE Confidence: 0.8714161

00:07:01.720 --> 00:07:04.015 So there is a lot of work to do  
NOTE Confidence: 0.8714161

00:07:04.015 --> 00:07:06.370 to improve our standard of care  
NOTE Confidence: 0.8714161

00:07:06.370 --> 00:07:09.070 even when its curative an as well.  
NOTE Confidence: 0.8714161

00:07:09.070 --> 00:07:11.410 There are a lot of of I think areas of  
NOTE Confidence: 0.8714161

00:07:11.479 --> 00:07:13.957 difficulty in the science underlying or  
NOTE Confidence: 0.8714161

00:07:13.957 --> 00:07:16.419 the biology underlying head neck cancer.

NOTE Confidence: 0.8714161

00:07:16.420 --> 00:07:19.332 So Roy mentioned that he and I first

NOTE Confidence: 0.8714161

00:07:19.332 --> 00:07:21.450 worked together in the context of

NOTE Confidence: 0.8714161

00:07:21.450 --> 00:07:24.085 cetuximab and it was a thrill when we

NOTE Confidence: 0.8714161

00:07:24.085 --> 00:07:26.437 saw that lead to responses as a as

NOTE Confidence: 0.8714161

00:07:26.440 --> 00:07:28.904 a single agent in head neck cancer.

NOTE Confidence: 0.8714161

00:07:28.910 --> 00:07:31.874 But it's clear that both constitutive

NOTE Confidence: 0.8714161

00:07:31.874 --> 00:07:33.850 resistance and adaptive resistance

NOTE Confidence: 0.8714161

00:07:33.919 --> 00:07:36.089 greatly limit the utility of

NOTE Confidence: 0.8714161

00:07:36.089 --> 00:07:37.825 EGFR inhibitors and another.

NOTE Confidence: 0.8714161

00:07:37.830 --> 00:07:39.900 Her family inhibitors the genome

NOTE Confidence: 0.8714161

00:07:39.900 --> 00:07:43.110 of head neck cancer is dominated by

NOTE Confidence: 0.8714161

00:07:43.110 --> 00:07:45.750 mutations in tumor suppressor genes,

NOTE Confidence: 0.8714161

00:07:45.750 --> 00:07:48.276 so this has been very difficult

NOTE Confidence: 0.8714161

00:07:48.276 --> 00:07:49.539 to target there.

NOTE Confidence: 0.8714161

00:07:49.540 --> 00:07:52.571 There are not a lot of successes

NOTE Confidence: 0.8714161

00:07:52.571 --> 00:07:54.971 with kinase inhibitors of activated  
NOTE Confidence: 0.8714161

00:07:54.971 --> 00:07:57.015 oncogenes in this disease.  
NOTE Confidence: 0.8009887

00:07:57.020 --> 00:08:00.002 Although we have activity for immune  
NOTE Confidence: 0.8009887

00:08:00.002 --> 00:08:01.990 checkpoint inhibition and I'll  
NOTE Confidence: 0.8009887

00:08:02.068 --> 00:08:04.735 briefly show you some of those data.  
NOTE Confidence: 0.8009887

00:08:04.740 --> 00:08:06.810 The effective immunotherapy is more  
NOTE Confidence: 0.8009887

00:08:06.810 --> 00:08:09.343 modest in head and neck cancer  
NOTE Confidence: 0.8009887

00:08:09.343 --> 00:08:11.689 than in many other solid tumors.  
NOTE Confidence: 0.8009887

00:08:11.690 --> 00:08:13.670 And part of this story certainly  
NOTE Confidence: 0.8009887

00:08:13.670 --> 00:08:16.190 lies in the tumor microenvironment,  
NOTE Confidence: 0.8009887

00:08:16.190 --> 00:08:18.235 which is hostile to immune  
NOTE Confidence: 0.8009887

00:08:18.235 --> 00:08:20.280 effector cells because of hypoxia.  
NOTE Confidence: 0.8009887

00:08:20.280 --> 00:08:22.330 Expression of Ido macrophage polarization.  
NOTE Confidence: 0.8009887

00:08:22.330 --> 00:08:24.370 Very high abundance of Milo  
NOTE Confidence: 0.8009887

00:08:24.370 --> 00:08:25.594 drive suppressor cells,  
NOTE Confidence: 0.8009887

00:08:25.600 --> 00:08:28.016 an lymphocyte excluded phenotypes

NOTE Confidence: 0.8009887  
00:08:28.016 --> 00:08:29.828 of the cancer.  
NOTE Confidence: 0.8009887  
00:08:29.830 --> 00:08:33.430 We have a new kind of head neck cancer.  
NOTE Confidence: 0.8009887  
00:08:33.430 --> 00:08:35.922 Over the past 1520 years which is  
NOTE Confidence: 0.8009887  
00:08:35.922 --> 00:08:38.230 driven by human papilloma virus,  
NOTE Confidence: 0.8009887  
00:08:38.230 --> 00:08:41.790 which gives us both an immune target and  
NOTE Confidence: 0.8009887  
00:08:41.790 --> 00:08:46.028 and and maybe also a way to interfere with.  
NOTE Confidence: 0.8009887  
00:08:46.030 --> 00:08:48.088 The signaling that drives these cancers,  
NOTE Confidence: 0.8009887  
00:08:48.090 --> 00:08:50.592 but there has been pretty low  
NOTE Confidence: 0.8009887  
00:08:50.592 --> 00:08:53.404 success in targeting HPV as a driver  
NOTE Confidence: 0.8009887  
00:08:53.404 --> 00:08:54.816 of head neck cancer.  
NOTE Confidence: 0.8009887  
00:08:54.820 --> 00:08:56.760 We see very grave disparities  
NOTE Confidence: 0.8009887  
00:08:56.760 --> 00:08:58.312 in outcome in HPV.  
NOTE Confidence: 0.8009887  
00:08:58.320 --> 00:08:59.872 Negative cancers between black  
NOTE Confidence: 0.8009887  
00:08:59.872 --> 00:09:01.424 patients and other groups,  
NOTE Confidence: 0.8009887  
00:09:01.430 --> 00:09:04.020 and although much of this is is  
NOTE Confidence: 0.8009887



00:09:04.020 --> 00:09:05.710 explained by socioeconomic factors,  
NOTE Confidence: 0.8009887

00:09:05.710 --> 00:09:07.730 it's becoming clearer that their  
NOTE Confidence: 0.8009887

00:09:07.730 --> 00:09:09.346 ancestry based differences in  
NOTE Confidence: 0.8009887

00:09:09.346 --> 00:09:10.768 treatment response as well,  
NOTE Confidence: 0.8009887

00:09:10.770 --> 00:09:13.842 and these have kind of been lost in  
NOTE Confidence: 0.8009887

00:09:13.842 --> 00:09:17.206 a pool of trials that did not include  
NOTE Confidence: 0.8009887

00:09:17.206 --> 00:09:20.720 a lot of patients of African ancestry.  
NOTE Confidence: 0.8009887

00:09:20.720 --> 00:09:23.212 And then the field as a whole  
NOTE Confidence: 0.8009887

00:09:23.212 --> 00:09:24.740 has historically suffered from  
NOTE Confidence: 0.8009887

00:09:24.740 --> 00:09:26.316 underinvestment in clinical trials  
NOTE Confidence: 0.8009887

00:09:26.316 --> 00:09:28.730 and low access to new patients  
NOTE Confidence: 0.8009887

00:09:28.730 --> 00:09:30.950 to new agents for our patients.  
NOTE Confidence: 0.8009887

00:09:30.950 --> 00:09:32.847 So what I'd like to quickly do  
NOTE Confidence: 0.8009887

00:09:32.847 --> 00:09:35.303 is talk a little bit about  
NOTE Confidence: 0.8009887

00:09:35.303 --> 00:09:37.395 multidisciplinary clinical care here,  
NOTE Confidence: 0.8009887

00:09:37.400 --> 00:09:39.290 how we address problems in

NOTE Confidence: 0.8009887

00:09:39.290 --> 00:09:40.424 our catchment area,

NOTE Confidence: 0.8009887

00:09:40.430 --> 00:09:41.942 a few highlights of our

NOTE Confidence: 0.8009887

00:09:41.942 --> 00:09:43.076 clinical research portfolio,

NOTE Confidence: 0.8009887

00:09:43.080 --> 00:09:45.040 some of the correlative and

NOTE Confidence: 0.8009887

00:09:45.040 --> 00:09:47.250 translational science that is going on.

NOTE Confidence: 0.8009887

00:09:47.250 --> 00:09:50.166 Some of our translation to the

NOTE Confidence: 0.8009887

00:09:50.166 --> 00:09:51.624 cooperative group network.

NOTE Confidence: 0.8009887

00:09:51.630 --> 00:09:53.838 Engagement with policy and then career

NOTE Confidence: 0.8009887

00:09:53.838 --> 00:09:55.946 development and then part of career

NOTE Confidence: 0.8009887

00:09:55.946 --> 00:09:57.955 development will be turning it off to

NOTE Confidence: 0.8009887

00:09:57.955 --> 00:10:00.378 my two very talented junior colleagues.

NOTE Confidence: 0.8009887

00:10:00.380 --> 00:10:02.024 Multidisciplinary care I mentioned

NOTE Confidence: 0.8009887

00:10:02.024 --> 00:10:04.490 that high high case volume is

NOTE Confidence: 0.8009887

00:10:04.561 --> 00:10:06.487 important and so you see here,

NOTE Confidence: 0.8009887

00:10:06.490 --> 00:10:09.185 at least from the pre pandemic numbers

NOTE Confidence: 0.8009887

00:10:09.185 --> 00:10:11.458 are surgical volumes for oral cavity,  
NOTE Confidence: 0.8009887

00:10:11.460 --> 00:10:13.260 pharynx and larynx cancer.  
NOTE Confidence: 0.8009887

00:10:13.260 --> 00:10:15.960 We have a multidisciplinary tumor board.  
NOTE Confidence: 0.8009887

00:10:15.960 --> 00:10:17.920 That brings together surgery,  
NOTE Confidence: 0.8009887

00:10:17.920 --> 00:10:19.626 radiation, medical oncology,  
NOTE Confidence: 0.8009887

00:10:19.626 --> 00:10:20.842 neuro radiology,  
NOTE Confidence: 0.8009887

00:10:20.842 --> 00:10:23.882 pathology and speech language pathology  
NOTE Confidence: 0.8009887

00:10:23.882 --> 00:10:27.037 which helps us to make treatment  
NOTE Confidence: 0.8009887

00:10:27.037 --> 00:10:29.507 recommendations that optimize both our  
NOTE Confidence: 0.8009887

00:10:29.584 --> 00:10:32.376 drive for cure and the need to think  
NOTE Confidence: 0.8009887

00:10:32.376 --> 00:10:34.056 about the functional consequences  
NOTE Confidence: 0.8009887

00:10:34.056 --> 00:10:36.496 of treatment for our patients.  
NOTE Confidence: 0.8009887

00:10:36.500 --> 00:10:38.500 We've rolled out chemoradiation  
NOTE Confidence: 0.8009887

00:10:38.500 --> 00:10:40.500 supportive care order sets  
NOTE Confidence: 0.8009887

00:10:40.500 --> 00:10:42.858 across that the health system.  
NOTE Confidence: 0.8009887

00:10:42.860 --> 00:10:45.440 We work very closely with

NOTE Confidence: 0.8009887

00:10:45.440 --> 00:10:46.988 speech language pathology.

NOTE Confidence: 0.8009887

00:10:46.990 --> 00:10:49.026 And function preservation beginning

NOTE Confidence: 0.8009887

00:10:49.026 --> 00:10:52.625 with pre him before the surgery or

NOTE Confidence: 0.8009887

00:10:52.625 --> 00:10:55.403 or chemoradiation even begins and we

NOTE Confidence: 0.8009887

00:10:55.403 --> 00:10:58.131 have dedicated social work to help

NOTE Confidence: 0.8009887

00:10:58.131 --> 00:11:01.057 with many of the problems with employment.

NOTE Confidence: 0.8009887

00:11:01.060 --> 00:11:04.077 That and and other socio economic problems

NOTE Confidence: 0.8009887

00:11:04.077 --> 00:11:07.159 that this group of patients encounters.

NOTE Confidence: 0.8009887

00:11:07.160 --> 00:11:09.862 Several marijuana var or the leader of

NOTE Confidence: 0.8009887

00:11:09.862 --> 00:11:12.761 our head and neck surgical oncology

NOTE Confidence: 0.8009887

00:11:12.761 --> 00:11:15.526 program introduced to clinic clinical

NOTE Confidence: 0.8009887

00:11:15.526 --> 00:11:17.998 care pathway for reducing ICU.

NOTE Confidence: 0.8009887

00:11:18.000 --> 00:11:20.682 Usage in head neck cancer microvascular

NOTE Confidence: 0.8009887

00:11:20.682 --> 00:11:23.365 reconstruction and you can see here

NOTE Confidence: 0.8009887

00:11:23.365 --> 00:11:25.430 these absolutely stunning data not

NOTE Confidence: 0.8009887

00:11:25.430 --> 00:11:27.816 only lowering the average length of  
NOTE Confidence: 0.8009887

00:11:27.816 --> 00:11:30.329 stay to a week for very complicated  
NOTE Confidence: 0.8516818

00:11:30.330 --> 00:11:31.563 large reconstructive surgeries,  
NOTE Confidence: 0.8516818

00:11:31.563 --> 00:11:34.029 but also bringing ICU stays from  
NOTE Confidence: 0.8516818

00:11:34.029 --> 00:11:37.235 100% to 6% and dramatically reducing  
NOTE Confidence: 0.8516818

00:11:37.235 --> 00:11:40.030 unplanned 30 day re admission.  
NOTE Confidence: 0.8516818

00:11:40.030 --> 00:11:41.722 Within our catchment area,  
NOTE Confidence: 0.8516818

00:11:41.722 --> 00:11:44.260 New Haven County is well documented  
NOTE Confidence: 0.8516818

00:11:44.333 --> 00:11:47.007 to have excess rates of tobacco use  
NOTE Confidence: 0.8516818

00:11:47.007 --> 00:11:49.248 relative to national rates and in  
NOTE Confidence: 0.8516818

00:11:49.248 --> 00:11:51.294 lower income adults in New Haven  
NOTE Confidence: 0.8516818

00:11:51.294 --> 00:11:53.580 uses twice as high oral cavity.  
NOTE Confidence: 0.8516818

00:11:53.580 --> 00:11:55.124 Cancer is increasing dramatically.  
NOTE Confidence: 0.8516818

00:11:55.124 --> 00:11:57.770 In Connecticut, Ann is 50% higher in  
NOTE Confidence: 0.8516818

00:11:57.770 --> 00:12:00.540 the Latin X population in the state,  
NOTE Confidence: 0.8516818

00:12:00.540 --> 00:12:02.916 so we have a very significant focus on

NOTE Confidence: 0.8516818

00:12:02.916 --> 00:12:05.960 the on the tobacco associated malignancies.

NOTE Confidence: 0.8516818

00:12:05.960 --> 00:12:07.960 We have trials and Artie

NOTE Confidence: 0.8516818

00:12:07.960 --> 00:12:09.960 Patio will speak later about.

NOTE Confidence: 0.8516818

00:12:09.960 --> 00:12:11.736 About one of them,

NOTE Confidence: 0.8516818

00:12:11.736 --> 00:12:15.040 but moving forward in the cooperative groups,

NOTE Confidence: 0.8516818

00:12:15.040 --> 00:12:16.426 international trials focused

NOTE Confidence: 0.8516818

00:12:16.426 --> 00:12:18.274 on HPV negative disease.

NOTE Confidence: 0.8516818

00:12:18.280 --> 00:12:21.136 Two of the projects in our

NOTE Confidence: 0.8516818

00:12:21.136 --> 00:12:23.820 head and explore focus on HPV,

NOTE Confidence: 0.8516818

00:12:23.820 --> 00:12:27.404 negative disease and in the E con Akron

NOTE Confidence: 0.8516818

00:12:27.404 --> 00:12:31.209 health Head Neck Committee that that I lead.

NOTE Confidence: 0.8516818

00:12:31.210 --> 00:12:33.425 We are now developing HealthEquity

NOTE Confidence: 0.8516818

00:12:33.425 --> 00:12:35.640 coast studies with many of

NOTE Confidence: 0.8516818

00:12:35.717 --> 00:12:37.677 our larger clinical trials.

NOTE Confidence: 0.8516818

00:12:37.680 --> 00:12:40.530 I mentioned that the outcomes disparities.

NOTE Confidence: 0.8516818

00:12:40.530 --> 00:12:42.756 For HPV negative head neck cancer  
NOTE Confidence: 0.8516818

00:12:42.756 --> 00:12:45.105 are among the most dramatic for  
NOTE Confidence: 0.8516818

00:12:45.105 --> 00:12:47.463 any solid tumor and a collaborator  
NOTE Confidence: 0.8516818

00:12:47.463 --> 00:12:50.175 of mine from my time at Fox Chase.  
NOTE Confidence: 0.8516818

00:12:50.180 --> 00:12:53.519 Camille Reagan, who is now part of our spore,  
NOTE Confidence: 0.8516818

00:12:53.520 --> 00:12:55.550 has demonstrated that African ancestry  
NOTE Confidence: 0.8516818

00:12:55.550 --> 00:12:57.580 informative markers are associated with  
NOTE Confidence: 0.8516818

00:12:57.639 --> 00:12:59.174 overexpression of DNA polymerase beta  
NOTE Confidence: 0.8516818

00:12:59.174 --> 00:13:01.555 and that this in turn is associated  
NOTE Confidence: 0.8516818

00:13:01.555 --> 00:13:03.525 with platinum and radiation resistance.  
NOTE Confidence: 0.8516818

00:13:03.530 --> 00:13:05.868 She's got a large collection of patients  
NOTE Confidence: 0.8516818

00:13:05.868 --> 00:13:08.727 in the temple system that she's sequencing.  
NOTE Confidence: 0.8516818

00:13:08.730 --> 00:13:11.142 It's highly enriched for African American  
NOTE Confidence: 0.8516818

00:13:11.142 --> 00:13:13.300 patients and we're collaborating with her.  
NOTE Confidence: 0.8516818

00:13:13.300 --> 00:13:15.688 To bring forward.  
NOTE Confidence: 0.8516818

00:13:15.690 --> 00:13:18.365 Patient drive tissue resources for

NOTE Confidence: 0.8516818

00:13:18.365 --> 00:13:20.505 studying alternative therapies to

NOTE Confidence: 0.8516818

00:13:20.505 --> 00:13:23.340 platinum and radiation in these patients.

NOTE Confidence: 0.8516818

00:13:23.340 --> 00:13:26.154 We have a large clinical trial portfolio.

NOTE Confidence: 0.8516818

00:13:26.160 --> 00:13:29.787 I don't want to go through it in detail,

NOTE Confidence: 0.8516818

00:13:29.790 --> 00:13:32.576 but I'll just emphasize that we always

NOTE Confidence: 0.8516818

00:13:32.576 --> 00:13:34.220 prioritize investigator initiated trials.

NOTE Confidence: 0.8516818

00:13:34.220 --> 00:13:37.034 Doctor Bhatia will talk about the Phantom,

NOTE Confidence: 0.8516818

00:13:37.040 --> 00:13:39.060 so tuck some AB work.

NOTE Confidence: 0.8516818

00:13:39.060 --> 00:13:42.068 I'll talk a little bit about a trial

NOTE Confidence: 0.8516818

00:13:42.068 --> 00:13:44.057 for pembrolizumab in primary radiation

NOTE Confidence: 0.8516818

00:13:44.057 --> 00:13:47.294 resistance and the five Aza work we have

NOTE Confidence: 0.8516818

00:13:47.294 --> 00:13:50.339 phase one trials particularly focused on HPV,

NOTE Confidence: 0.8516818

00:13:50.340 --> 00:13:52.292 therapeutic vaccines for HPV.

NOTE Confidence: 0.8516818

00:13:52.292 --> 00:13:53.268 Associated cancer.

NOTE Confidence: 0.8516818

00:13:53.270 --> 00:13:55.780 Have participated or LED some

NOTE Confidence: 0.8516818



00:13:55.780 --> 00:13:57.788 practice changing trials including.  
NOTE Confidence: 0.8516818

00:13:57.790 --> 00:13:59.650 Not that we let it,  
NOTE Confidence: 0.8516818

00:13:59.650 --> 00:14:01.500 but contributed to the cabins  
NOTE Confidence: 0.8516818

00:14:01.500 --> 00:14:02.610 antonym in radioiodine.  
NOTE Confidence: 0.8516818

00:14:02.610 --> 00:14:04.695 Refractory thyroid cancer study that  
NOTE Confidence: 0.8516818

00:14:04.695 --> 00:14:07.762 was presented at ASCO this year and I  
NOTE Confidence: 0.8516818

00:14:07.762 --> 00:14:09.890 think is really going to change the  
NOTE Confidence: 0.8516818

00:14:09.964 --> 00:14:12.603 standard of care for Len Bat neighbor  
NOTE Confidence: 0.8516818

00:14:12.603 --> 00:14:15.552 factory disease and on going late phase  
NOTE Confidence: 0.8516818

00:14:15.552 --> 00:14:17.817 trials in the chemoradiation setting.  
NOTE Confidence: 0.8516818

00:14:17.820 --> 00:14:20.476 So let me tell you a little bit  
NOTE Confidence: 0.8516818

00:14:20.476 --> 00:14:22.960 about this radioresistance trial.  
NOTE Confidence: 0.8516818

00:14:22.960 --> 00:14:25.851 This was started by Zen Hussain when  
NOTE Confidence: 0.8516818

00:14:25.851 --> 00:14:29.248 when he was here before he left for  
NOTE Confidence: 0.8516818

00:14:29.248 --> 00:14:32.288 Toronto and the idea was that we  
NOTE Confidence: 0.8516818

00:14:32.288 --> 00:14:34.934 had patients in our practice HPV.

NOTE Confidence: 0.8516818

00:14:34.940 --> 00:14:36.275 Negative cancers predominantly,

NOTE Confidence: 0.8516818

00:14:36.275 --> 00:14:38.945 who had presented with very advanced

NOTE Confidence: 0.8516818

00:14:38.945 --> 00:14:41.008 disease and had primary radio

NOTE Confidence: 0.8516818

00:14:41.008 --> 00:14:41.788 resistant disease.

NOTE Confidence: 0.8516818

00:14:41.790 --> 00:14:44.913 At that time there was no standard of care

NOTE Confidence: 0.8516818

00:14:44.913 --> 00:14:47.780 with immunotherapy for those patients,

NOTE Confidence: 0.8516818

00:14:47.780 --> 00:14:50.420 and so he put together a.

NOTE Confidence: 0.8516818

00:14:50.420 --> 00:14:52.610 Phase two trial for moving them

NOTE Confidence: 0.8516818

00:14:52.610 --> 00:14:55.378 right on to Pember Lizum app with

NOTE Confidence: 0.8516818

00:14:55.378 --> 00:14:57.832 the advantage that we would have

NOTE Confidence: 0.8516818

00:14:57.832 --> 00:15:00.621 baseline tissue tissue from the biopsy

NOTE Confidence: 0.8516818

00:15:00.621 --> 00:15:02.921 that prove persistent disease and

NOTE Confidence: 0.820107

00:15:02.930 --> 00:15:05.348 if the patient had become resectable

NOTE Confidence: 0.820107

00:15:05.348 --> 00:15:08.320 by the end of four cycles of

NOTE Confidence: 0.820107

00:15:08.320 --> 00:15:10.440 Pember lism and they would,

NOTE Confidence: 0.820107

00:15:10.440 --> 00:15:12.936 they would go on to reception.  
NOTE Confidence: 0.820107

00:15:12.940 --> 00:15:15.747 So we are doing immuno profiling on  
NOTE Confidence: 0.820107

00:15:15.747 --> 00:15:18.282 the specimens from this trial and  
NOTE Confidence: 0.820107

00:15:18.282 --> 00:15:20.778 also started sequencing them in the  
NOTE Confidence: 0.820107

00:15:20.778 --> 00:15:23.356 first two cases that we sequenced.  
NOTE Confidence: 0.820107

00:15:23.360 --> 00:15:25.301 Both had this.  
NOTE Confidence: 0.820107

00:15:25.301 --> 00:15:28.536 Very unusual finding of whether  
NOTE Confidence: 0.820107

00:15:28.536 --> 00:15:31.703 new emergence or enrichment for  
NOTE Confidence: 0.820107

00:15:31.703 --> 00:15:35.225 mutation in tenascin R1 of the.  
NOTE Confidence: 0.820107

00:15:35.230 --> 00:15:36.622 Tenascin family proteins that  
NOTE Confidence: 0.820107

00:15:36.622 --> 00:15:39.350 controls EMT and can be involved in  
NOTE Confidence: 0.820107

00:15:39.350 --> 00:15:41.078 an immunosuppressive microenvironment.  
NOTE Confidence: 0.820107

00:15:41.080 --> 00:15:43.968 So we have just gone back and received  
NOTE Confidence: 0.820107

00:15:43.968 --> 00:15:46.099 funding to finish sequencing.  
NOTE Confidence: 0.820107

00:15:46.100 --> 00:15:48.278 All the cases here and think  
NOTE Confidence: 0.820107

00:15:48.278 --> 00:15:50.732 that this is potentially a very

NOTE Confidence: 0.820107

00:15:50.732 --> 00:15:53.062 interesting lead into the biology

NOTE Confidence: 0.820107

00:15:53.062 --> 00:15:54.460 of primary radioresistance.

NOTE Confidence: 0.820107

00:15:54.460 --> 00:15:57.428 The pictures at the bottom just show

NOTE Confidence: 0.820107

00:15:57.428 --> 00:16:01.145 you one of our patients who had a CR.

NOTE Confidence: 0.820107

00:16:01.150 --> 00:16:04.730 He's now four years out.

NOTE Confidence: 0.820107

00:16:04.730 --> 00:16:08.250 Just to switch gears now to some of

NOTE Confidence: 0.820107

00:16:08.250 --> 00:16:10.950 the correlative work along time ago,

NOTE Confidence: 0.820107

00:16:10.950 --> 00:16:12.880 the Kaag committee had demonstrated

NOTE Confidence: 0.820107

00:16:12.880 --> 00:16:15.449 that for patients who had undergone

NOTE Confidence: 0.820107

00:16:15.449 --> 00:16:17.159 margin negative resection,

NOTE Confidence: 0.820107

00:16:17.160 --> 00:16:19.380 but who had disruptive mutation of

NOTE Confidence: 0.820107

00:16:19.380 --> 00:16:22.711 TP 53 that they continued to have a

NOTE Confidence: 0.820107

00:16:22.711 --> 00:16:24.931 pretty poor outcome despite getting

NOTE Confidence: 0.820107

00:16:24.931 --> 00:16:28.409 risk based appropriate postoperative therapy.

NOTE Confidence: 0.820107

00:16:28.410 --> 00:16:31.469 And that was done with older sequencing

NOTE Confidence: 0.820107

00:16:31.469 --> 00:16:34.064 technology as next Gen sequencing came  
NOTE Confidence: 0.820107

00:16:34.064 --> 00:16:36.864 on and a number of new algorithms  
NOTE Confidence: 0.820107

00:16:36.940 --> 00:16:40.108 for calling P53 mutation became available.  
NOTE Confidence: 0.820107

00:16:40.110 --> 00:16:43.323 We undertook a comparison of all of  
NOTE Confidence: 0.820107

00:16:43.323 --> 00:16:45.208 these different classifying schemes  
NOTE Confidence: 0.820107

00:16:45.208 --> 00:16:48.204 in the specimens from that ekonk trial,  
NOTE Confidence: 0.820107

00:16:48.210 --> 00:16:50.460 finding that our original rule,  
NOTE Confidence: 0.820107

00:16:50.460 --> 00:16:52.710 which was DNA binding domain  
NOTE Confidence: 0.820107

00:16:52.710 --> 00:16:54.510 mutations or truncation mutations,  
NOTE Confidence: 0.820107

00:16:54.510 --> 00:16:55.860 somewhat supplemented with  
NOTE Confidence: 0.820107

00:16:55.860 --> 00:16:57.660 information about splice variants,  
NOTE Confidence: 0.820107

00:16:57.660 --> 00:17:01.260 really was the best predictor of bad outcome.  
NOTE Confidence: 0.820107

00:17:01.260 --> 00:17:02.230 And since.  
NOTE Confidence: 0.820107

00:17:02.230 --> 00:17:04.655 P53 mutation is quite prevalent  
NOTE Confidence: 0.820107

00:17:04.655 --> 00:17:06.820 in head neck cancer.  
NOTE Confidence: 0.820107

00:17:06.820 --> 00:17:09.136 And difficult to target this has,

NOTE Confidence: 0.820107  
00:17:09.140 --> 00:17:09.816 I think,  
NOTE Confidence: 0.820107  
00:17:09.816 --> 00:17:11.844 really helped us focus on the  
NOTE Confidence: 0.820107  
00:17:11.844 --> 00:17:13.505 importance of understanding the  
NOTE Confidence: 0.820107  
00:17:13.505 --> 00:17:15.329 biology of these people.  
NOTE Confidence: 0.55447125  
00:17:31.580 --> 00:17:32.270 Barbara  
NOTE Confidence: 0.9002802  
00:17:36.000 --> 00:17:37.200 did we lose Barbara?  
NOTE Confidence: 0.688106935  
00:17:48.180 --> 00:17:52.020 Yeah, look. Her Internet is down.  
NOTE Confidence: 0.7985662  
00:17:55.620 --> 00:17:57.580 OK, well these things happens.  
NOTE Confidence: 0.7985662  
00:17:57.580 --> 00:18:00.349 It's the storms.  
NOTE Confidence: 0.7985662  
00:18:00.350 --> 00:18:02.250 Who's ready to step up?  
NOTE Confidence: 0.7985662  
00:18:02.250 --> 00:18:04.590 Oh, here she is. Barbara  
NOTE Confidence: 0.7560468  
00:18:07.000 --> 00:18:07.820 you're muted.  
NOTE Confidence: 0.7999617  
00:18:22.160 --> 00:18:24.830 Sorry about that. So we sequenced  
NOTE Confidence: 0.7999617  
00:18:24.830 --> 00:18:27.040 these or characid sequenced over  
NOTE Confidence: 0.7999617  
00:18:27.114 --> 00:18:29.030 1000 HPV negative cancers.  
NOTE Confidence: 0.7999617

00:18:29.030 --> 00:18:31.694 We classified the P53 mutation using  
NOTE Confidence: 0.7999617

00:18:31.694 --> 00:18:34.529 a variety of different schemes ever.  
NOTE Confidence: 0.7999617

00:18:34.530 --> 00:18:38.190 You need to share your slides again, sorry.  
NOTE Confidence: 0.8168372

00:18:40.930 --> 00:18:42.440 Will give you 2 extra minutes at  
NOTE Confidence: 0.8168372

00:18:42.440 --> 00:18:44.050 the end of the hour, don't worry.  
NOTE Confidence: 0.8312539

00:18:46.900 --> 00:18:49.546 Alright, am I doing better now?  
NOTE Confidence: 0.8312539

00:18:49.550 --> 00:18:51.790 There's this better perfect looked  
NOTE Confidence: 0.8312539

00:18:51.790 --> 00:18:54.997 at CDK into a mutations and then  
NOTE Confidence: 0.8312539

00:18:54.997 --> 00:18:56.761 calculated tumor mutation burden  
NOTE Confidence: 0.8312539

00:18:56.761 --> 00:18:59.436 and So what was quite interesting  
NOTE Confidence: 0.8312539

00:18:59.436 --> 00:19:02.355 here was that either P53 or CDK  
NOTE Confidence: 0.8312539

00:19:02.355 --> 00:19:04.544 into a mutation was associated  
NOTE Confidence: 0.8312539

00:19:04.544 --> 00:19:06.749 with higher tumor mutation burden,  
NOTE Confidence: 0.8312539

00:19:06.750 --> 00:19:09.697 with the exception of when that P53  
NOTE Confidence: 0.8312539

00:19:09.697 --> 00:19:12.478 mutation was a gain of function,  
NOTE Confidence: 0.8312539

00:19:12.480 --> 00:19:14.680 not loss of function mutation,

NOTE Confidence: 0.8312539  
00:19:14.680 --> 00:19:17.767 but that the Co occurrence of P53,  
NOTE Confidence: 0.8312539  
00:19:17.770 --> 00:19:19.216 CDK and 2A.  
NOTE Confidence: 0.8312539  
00:19:19.216 --> 00:19:22.108 Mutation was associated with the HYEST  
NOTE Confidence: 0.8312539  
00:19:22.108 --> 00:19:25.042 tumor mutation burden and this came  
NOTE Confidence: 0.8312539  
00:19:25.042 --> 00:19:28.789 into the 15 mutations per megabase range,  
NOTE Confidence: 0.8312539  
00:19:28.790 --> 00:19:31.202 which has been informative  
NOTE Confidence: 0.8312539  
00:19:31.202 --> 00:19:33.614 for response to immunotherapy.  
NOTE Confidence: 0.8312539  
00:19:33.620 --> 00:19:36.119 But it's been understood for a long  
NOTE Confidence: 0.8312539  
00:19:36.119 --> 00:19:38.580 time that there's a range of TMB  
NOTE Confidence: 0.8312539  
00:19:38.580 --> 00:19:40.560 across different kinds of both HPV  
NOTE Confidence: 0.8312539  
00:19:40.630 --> 00:19:42.720 positive and HPV negative head,  
NOTE Confidence: 0.8312539  
00:19:42.720 --> 00:19:43.450 neck cancers,  
NOTE Confidence: 0.8312539  
00:19:43.450 --> 00:19:45.275 both smokers and nonsmokers that  
NOTE Confidence: 0.8312539  
00:19:45.275 --> 00:19:47.515 this is associated with response to  
NOTE Confidence: 0.8312539  
00:19:47.515 --> 00:19:49.675 pembrolizumab and more recently in a  
NOTE Confidence: 0.8312539



00:19:49.675 --> 00:19:51.510 randomized trial of development that  
NOTE Confidence: 0.8312539

00:19:51.510 --> 00:19:53.634 was actually negative for all comers.  
NOTE Confidence: 0.8312539

00:19:53.640 --> 00:19:56.184 If you focused on the group with high  
NOTE Confidence: 0.8312539

00:19:56.184 --> 00:19:58.524 TMB there was a survival advantage  
NOTE Confidence: 0.8312539

00:19:58.524 --> 00:20:00.559 for the use of immunotherapy,  
NOTE Confidence: 0.8312539

00:20:00.560 --> 00:20:03.048 so I think one thing this points us  
NOTE Confidence: 0.8312539

00:20:03.048 --> 00:20:06.108 to is the early use of immunotherapy.  
NOTE Confidence: 0.8312539

00:20:06.110 --> 00:20:08.630 In P53 mutated head neck cancer  
NOTE Confidence: 0.8312539

00:20:08.630 --> 00:20:11.672 and I'll maybe take a brief detour  
NOTE Confidence: 0.8312539

00:20:11.672 --> 00:20:13.368 here because this is.  
NOTE Confidence: 0.8312539

00:20:13.370 --> 00:20:15.866 This is work that Yale investigators  
NOTE Confidence: 0.8312539

00:20:15.866 --> 00:20:18.489 participated in before I arrived here.  
NOTE Confidence: 0.8312539

00:20:18.490 --> 00:20:20.980 And then I've been very involved  
NOTE Confidence: 0.8312539

00:20:20.980 --> 00:20:23.190 with the keynote 012 trial,  
NOTE Confidence: 0.8312539

00:20:23.190 --> 00:20:26.032 which was the first large scale study  
NOTE Confidence: 0.8312539

00:20:26.032 --> 00:20:27.761 of immune checkpoint inhibition

NOTE Confidence: 0.8312539

00:20:27.761 --> 00:20:30.848 in head and neck cancer was done

NOTE Confidence: 0.8312539

00:20:30.848 --> 00:20:31.730 with pembrolizumab.

NOTE Confidence: 0.8312539

00:20:31.730 --> 00:20:34.898 We had a big focus on including both

NOTE Confidence: 0.8312539

00:20:34.898 --> 00:20:37.707 HPV negative and HPV positive cancer,

NOTE Confidence: 0.8312539

00:20:37.710 --> 00:20:39.130 and you can see.

NOTE Confidence: 0.8312539

00:20:39.130 --> 00:20:40.905 That durable responses were seen

NOTE Confidence: 0.8312539

00:20:40.905 --> 00:20:43.332 in both types of head neck cancer

NOTE Confidence: 0.8312539

00:20:43.332 --> 00:20:45.559 and looking at the spider plot,

NOTE Confidence: 0.8312539

00:20:45.560 --> 00:20:48.220 I think that you see.

NOTE Confidence: 0.8312539

00:20:48.220 --> 00:20:48.606 Really,

NOTE Confidence: 0.8312539

00:20:48.606 --> 00:20:51.308 what the next five years of research

NOTE Confidence: 0.8312539

00:20:51.308 --> 00:20:53.050 into immunotherapy in head neck

NOTE Confidence: 0.8312539

00:20:53.050 --> 00:20:55.150 cancer has has played out as because

NOTE Confidence: 0.8312539

00:20:55.221 --> 00:20:57.369 there are early and deep responses,

NOTE Confidence: 0.8312539

00:20:57.370 --> 00:20:59.130 there are somewhat slower responses,

NOTE Confidence: 0.8312539

00:20:59.130 --> 00:21:01.594 but that are deep and very durable.

NOTE Confidence: 0.8312539

00:21:01.600 --> 00:21:03.714 But there's a subset of patients who

NOTE Confidence: 0.8312539

00:21:03.714 --> 00:21:06.168 not only don't respond to immunotherapy,

NOTE Confidence: 0.8312539

00:21:06.170 --> 00:21:09.668 but appear to almost have accelerated.

NOTE Confidence: 0.8312539

00:21:09.670 --> 00:21:12.295 Disease growth and so we need to

NOTE Confidence: 0.8312539

00:21:12.295 --> 00:21:14.243 understand what's suppressive in the

NOTE Confidence: 0.8312539

00:21:14.243 --> 00:21:15.767 tumor microenvironment that leads

NOTE Confidence: 0.8312539

00:21:15.767 --> 00:21:18.384 to this resistance and what it might

NOTE Confidence: 0.8312539

00:21:18.384 --> 00:21:20.104 be in the tumor microenvironment

NOTE Confidence: 0.8312539

00:21:20.104 --> 00:21:21.913 that's PDL one expressing that

NOTE Confidence: 0.8312539

00:21:21.913 --> 00:21:24.139 it's actually bad to turn off.

NOTE Confidence: 0.8312539

00:21:24.140 --> 00:21:27.080 So I think there's there's some.

NOTE Confidence: 0.8312539

00:21:27.080 --> 00:21:29.150 Some work to be done there,

NOTE Confidence: 0.8312539

00:21:29.150 --> 00:21:31.565 but given the strong signal with 18%

NOTE Confidence: 0.8312539

00:21:31.570 --> 00:21:33.640 response rate and durable CRS in

NOTE Confidence: 0.8312539

00:21:33.640 --> 00:21:35.020 the treatment refractory setting,

NOTE Confidence: 0.8312539

00:21:35.020 --> 00:21:36.966 we move this forward as a first

NOTE Confidence: 0.8312539

00:21:36.966 --> 00:21:38.577 line trial in metastatic recurrent

NOTE Confidence: 0.8312539

00:21:38.577 --> 00:21:41.048 disease and this had a little bit

NOTE Confidence: 0.8312539

00:21:41.048 --> 00:21:43.416 of a complicated design because we

NOTE Confidence: 0.8312539

00:21:43.416 --> 00:21:45.660 recognized that the standard of care

NOTE Confidence: 0.8312539

00:21:45.660 --> 00:21:47.110 which was chemotherapy with Cytosan

NOTE Confidence: 0.8312539

00:21:47.110 --> 00:21:49.181 Mab actually had a higher response

NOTE Confidence: 0.8312539

00:21:49.181 --> 00:21:50.889 rate than pembrolizumab monotherapy,

NOTE Confidence: 0.8312539

00:21:50.890 --> 00:21:53.291 but it didn't have the same duration

NOTE Confidence: 0.8312539

00:21:53.291 --> 00:21:55.549 of response and it didn't have

NOTE Confidence: 0.8312539

00:21:55.549 --> 00:21:57.484 the same complete response rate.

NOTE Confidence: 0.8312539

00:21:57.490 --> 00:21:59.716 So we had to experimental arms.

NOTE Confidence: 0.8312539

00:21:59.720 --> 00:22:02.352 One was Pember Lism AB alone and one

NOTE Confidence: 0.8312539

00:22:02.352 --> 00:22:04.910 was purple is made with chemotherapy,

NOTE Confidence: 0.8312539

00:22:04.910 --> 00:22:06.645 each of them independently compared

NOTE Confidence: 0.8312539

00:22:06.645 --> 00:22:08.380 to the standard of care  
NOTE Confidence: 0.8051728

00:22:08.443 --> 00:22:10.323 of chemotherapy with cetuximab and  
NOTE Confidence: 0.8051728

00:22:10.323 --> 00:22:12.647 then we undertook a biomarker driven  
NOTE Confidence: 0.8051728

00:22:12.647 --> 00:22:14.527 analysis because the hypothesis was  
NOTE Confidence: 0.8051728

00:22:14.527 --> 00:22:16.730 that those cases that express PD,  
NOTE Confidence: 0.8051728

00:22:16.730 --> 00:22:18.800 L1 the most richly might be  
NOTE Confidence: 0.8051728

00:22:18.800 --> 00:22:20.858 the most likely to respond,  
NOTE Confidence: 0.8051728

00:22:20.860 --> 00:22:23.289 and there the advantage over chemo cetuximab  
NOTE Confidence: 0.8051728

00:22:23.289 --> 00:22:25.690 would would be more readily apparent.  
NOTE Confidence: 0.8051728

00:22:25.690 --> 00:22:27.218 Actually, Pember Lism had  
NOTE Confidence: 0.8051728

00:22:27.218 --> 00:22:28.364 performed better than.  
NOTE Confidence: 0.8051728

00:22:28.370 --> 00:22:29.890 Then we could have imagined,  
NOTE Confidence: 0.8051728

00:22:29.890 --> 00:22:32.306 but so this is the CPS 20 group,  
NOTE Confidence: 0.8051728

00:22:32.310 --> 00:22:34.128 the highest PDL one expressing an  
NOTE Confidence: 0.8051728

00:22:34.128 --> 00:22:36.291 you see here a hazard ratio of  
NOTE Confidence: 0.8051728

00:22:36.291 --> 00:22:38.363 .61 in favor of Pember Lism AB.

NOTE Confidence: 0.8051728

00:22:38.370 --> 00:22:40.978 We now have four year data showing that

NOTE Confidence: 0.8051728

00:22:40.978 --> 00:22:44.548 this group has over a 20% for your survival.

NOTE Confidence: 0.8051728

00:22:44.550 --> 00:22:46.680 This is all PDL one.

NOTE Confidence: 0.8051728

00:22:46.680 --> 00:22:47.416 Expressing cancers,

NOTE Confidence: 0.8051728

00:22:47.416 --> 00:22:49.992 hazard ratios of 0.78 and this was

NOTE Confidence: 0.8051728

00:22:49.992 --> 00:22:51.423 also statistically significant

NOTE Confidence: 0.8051728

00:22:51.423 --> 00:22:53.918 compared with the control arm.

NOTE Confidence: 0.8051728

00:22:53.920 --> 00:22:57.424 And then if you took all comers so

NOTE Confidence: 0.8051728

00:22:57.424 --> 00:23:00.392 that includes the 15% that are PDL,

NOTE Confidence: 0.8051728

00:23:00.392 --> 00:23:03.116 one negative Pember Lizum app was

NOTE Confidence: 0.8051728

00:23:03.116 --> 00:23:05.660 noninferior to chemotherapy cetuximab.

NOTE Confidence: 0.8051728

00:23:05.660 --> 00:23:08.341 Going back and looking at that PDL

NOTE Confidence: 0.8051728

00:23:08.341 --> 00:23:10.604 one subset they do substantially

NOTE Confidence: 0.8051728

00:23:10.604 --> 00:23:13.688 worse with Pember Lizum app then

NOTE Confidence: 0.8051728

00:23:13.688 --> 00:23:15.926 with chemotherapy cytoxan and so

NOTE Confidence: 0.8051728

00:23:15.926 --> 00:23:18.558 they should not get pembrolizumab in  
NOTE Confidence: 0.8051728

00:23:18.560 --> 00:23:20.635 monotherapy and then Pembrolizumab  
NOTE Confidence: 0.8051728

00:23:20.635 --> 00:23:23.219 app plus chemotherapy superior to the  
NOTE Confidence: 0.8051728

00:23:23.219 --> 00:23:25.439 reference regimen across all regimens,  
NOTE Confidence: 0.8051728

00:23:25.440 --> 00:23:27.080 across all biomarker subgroups.  
NOTE Confidence: 0.8051728

00:23:27.080 --> 00:23:30.600 So this study has been very fruitful.  
NOTE Confidence: 0.8051728

00:23:30.600 --> 00:23:32.320 Subsequent publications coming out  
NOTE Confidence: 0.8051728

00:23:32.320 --> 00:23:34.040 about patient reported outcomes.  
NOTE Confidence: 0.8051728

00:23:34.040 --> 00:23:36.304 The PDL one subsets.  
NOTE Confidence: 0.8051728

00:23:36.304 --> 00:23:38.568 In long term survival.  
NOTE Confidence: 0.8051728

00:23:38.570 --> 00:23:42.476 I would like to introduce you to  
NOTE Confidence: 0.8051728

00:23:42.476 --> 00:23:46.478 our head expert team so spores are.  
NOTE Confidence: 0.8051728

00:23:46.480 --> 00:23:48.732 Programs of research excellence  
NOTE Confidence: 0.8051728

00:23:48.732 --> 00:23:52.590 usually centered around a given disease type.  
NOTE Confidence: 0.8051728

00:23:52.590 --> 00:23:55.362 They they need to have at  
NOTE Confidence: 0.8051728

00:23:55.362 --> 00:23:58.070 least three projects and cores

NOTE Confidence: 0.8051728

00:23:58.070 --> 00:24:00.359 and developmental projects,

NOTE Confidence: 0.8051728

00:24:00.360 --> 00:24:04.092 and we received very generous support

NOTE Confidence: 0.8051728

00:24:04.092 --> 00:24:08.554 from the Cancer Center in the medical

NOTE Confidence: 0.8051728

00:24:08.554 --> 00:24:12.286 school to jumpstart these projects and.

NOTE Confidence: 0.8051728

00:24:12.290 --> 00:24:14.534 The first review had some some

NOTE Confidence: 0.8051728

00:24:14.534 --> 00:24:16.909 comments that we had to address,

NOTE Confidence: 0.8051728

00:24:16.910 --> 00:24:19.605 but we were funded late last year,

NOTE Confidence: 0.8051728

00:24:19.610 --> 00:24:21.530 so we have three projects,

NOTE Confidence: 0.8051728

00:24:21.530 --> 00:24:23.840 one on targeting the EGFR family.

NOTE Confidence: 0.8051728

00:24:23.840 --> 00:24:26.066 An artifact will talk about that

NOTE Confidence: 0.8051728

00:24:26.066 --> 00:24:28.459 more in a couple of minutes,

NOTE Confidence: 0.8051728

00:24:28.460 --> 00:24:30.770 one on synthetic lethal therapy for

NOTE Confidence: 0.8051728

00:24:30.770 --> 00:24:32.310 predominantly P53 mutated cancer.

NOTE Confidence: 0.8051728

00:24:32.310 --> 00:24:35.005 I'll speak about that a little bit,

NOTE Confidence: 0.8051728

00:24:35.010 --> 00:24:37.698 and then Karen Anderson and Del Yarbrough,

NOTE Confidence: 0.8051728



00:24:37.700 --> 00:24:38.594 leader project.  
NOTE Confidence: 0.8051728

00:24:38.594 --> 00:24:40.829 Looking at demethylation to trigger  
NOTE Confidence: 0.8051728

00:24:40.829 --> 00:24:43.580 a pevec induced synthetic lethality,  
NOTE Confidence: 0.8051728

00:24:43.580 --> 00:24:47.556 and I'll introduce them briefly as well.  
NOTE Confidence: 0.8051728

00:24:47.560 --> 00:24:50.906 So I've been talking about P53 mutant  
NOTE Confidence: 0.8051728

00:24:50.906 --> 00:24:54.209 cells really being sort of one of  
NOTE Confidence: 0.8051728

00:24:54.209 --> 00:24:56.429 the last bastions of undruggable  
NOTE Confidence: 0.8051728

00:24:56.429 --> 00:24:57.990 head neck cancer,  
NOTE Confidence: 0.8051728

00:24:57.990 --> 00:25:01.294 and we know that these cells exhibit  
NOTE Confidence: 0.8051728

00:25:01.294 --> 00:25:04.149 impaired regulation of G1 S checkpoints,  
NOTE Confidence: 0.8051728

00:25:04.150 --> 00:25:06.706 increasing their dependence on the G2  
NOTE Confidence: 0.8051728

00:25:06.706 --> 00:25:09.839 M transition to repair replication damage,  
NOTE Confidence: 0.8051728

00:25:09.840 --> 00:25:11.736 creating vulnerability to inhibitors  
NOTE Confidence: 0.8051728

00:25:11.736 --> 00:25:14.580 of these processes through DNA damage,  
NOTE Confidence: 0.8051728

00:25:14.580 --> 00:25:15.608 G2 checkpoints,  
NOTE Confidence: 0.8051728

00:25:15.608 --> 00:25:19.206 restrictive mitotic entry and we have had.

NOTE Confidence: 0.8051728

00:25:19.210 --> 00:25:21.498 An interest in in this for a long

NOTE Confidence: 0.8051728

00:25:21.498 --> 00:25:24.089 time going back to work when I was

NOTE Confidence: 0.8051728

00:25:24.089 --> 00:25:25.946 at Fox Chase demonstrating that

NOTE Confidence: 0.8051728

00:25:25.946 --> 00:25:28.386 Aurora kinase overexpression in the

NOTE Confidence: 0.8051728

00:25:28.386 --> 00:25:30.338 nuclear compartment was associated

NOTE Confidence: 0.8051728

00:25:30.340 --> 00:25:31.912 with worse overall survival,

NOTE Confidence: 0.8051728

00:25:31.912 --> 00:25:34.789 we know that Aurora is regulated by P53,

NOTE Confidence: 0.8051728

00:25:34.790 --> 00:25:37.226 and so if you look across these

NOTE Confidence: 0.8051728

00:25:37.226 --> 00:25:39.513 commonly used P53 mutated or null

NOTE Confidence: 0.8051728

00:25:39.513 --> 00:25:41.463 head neck cancer cell lines,

NOTE Confidence: 0.8051728

00:25:41.470 --> 00:25:44.572 they all over expresser or relative

NOTE Confidence: 0.8051728

00:25:44.572 --> 00:25:46.123 to normal tissue.

NOTE Confidence: 0.81956977

00:25:46.130 --> 00:25:48.356 And so we began to look at

NOTE Confidence: 0.81956977

00:25:48.356 --> 00:25:50.370 using Aurora as an inhibitor.

NOTE Confidence: 0.81956977

00:25:50.370 --> 00:25:53.121 Both preclinically and in the clinic and

NOTE Confidence: 0.81956977

00:25:53.121 --> 00:25:55.664 the clinic it hit a 9% response rate,  
NOTE Confidence: 0.81956977

00:25:55.664 --> 00:25:57.776 so that was obviously pretty disappointing.  
NOTE Confidence: 0.81956977

00:25:57.780 --> 00:25:59.950 And what we found when we gave  
NOTE Confidence: 0.81956977

00:25:59.950 --> 00:26:01.874 it clinically and this is with  
NOTE Confidence: 0.81956977

00:26:01.874 --> 00:26:03.734 an agent called ellisor tip is  
NOTE Confidence: 0.81956977

00:26:03.734 --> 00:26:06.328 that it it did actually aggregate  
NOTE Confidence: 0.81956977

00:26:06.328 --> 00:26:07.660 phosphorylation of Aurora.  
NOTE Confidence: 0.81956977

00:26:07.660 --> 00:26:10.124 It did change the function of Aurora,  
NOTE Confidence: 0.81956977

00:26:10.130 --> 00:26:11.542 so we got these.  
NOTE Confidence: 0.81956977

00:26:11.542 --> 00:26:12.954 Try and quadripolar spindles.  
NOTE Confidence: 0.80716515

00:26:16.080 --> 00:26:19.550 And and yet what happened was that the cells,  
NOTE Confidence: 0.80716515

00:26:19.550 --> 00:26:21.838 I'm sorry, but the cells entered  
NOTE Confidence: 0.80716515

00:26:21.838 --> 00:26:24.344 really a cell cycle arrest that was  
NOTE Confidence: 0.80716515

00:26:24.344 --> 00:26:26.499 mediated through phosphorylation of CDK.  
NOTE Confidence: 0.80716515

00:26:26.500 --> 00:26:29.828 One is, you see here that that inhibitory  
NOTE Confidence: 0.80716515

00:26:29.828 --> 00:26:31.907 phosphorylation is placed by we won,

NOTE Confidence: 0.80716515

00:26:31.910 --> 00:26:34.703 and so we combine the Aurora inhibitor

NOTE Confidence: 0.80716515

00:26:34.703 --> 00:26:38.463 with the wee one inhibitor we want is a

NOTE Confidence: 0.80716515

00:26:38.463 --> 00:26:41.188 regulator of mitotic entry and you see

NOTE Confidence: 0.80716515

00:26:41.188 --> 00:26:43.899 here when you give the wee one inhibitor,

NOTE Confidence: 0.80716515

00:26:43.899 --> 00:26:45.535 you accelerate mitotic entry

NOTE Confidence: 0.80716515

00:26:45.535 --> 00:26:47.900 and find these cells that are.

NOTE Confidence: 0.80716515

00:26:47.900 --> 00:26:50.427 Sort of held up in late mitosis,

NOTE Confidence: 0.80716515

00:26:50.430 --> 00:26:53.318 but when you give the two agents together,

NOTE Confidence: 0.80716515

00:26:53.320 --> 00:26:55.528 you precipitate mitotic catastrophe and the

NOTE Confidence: 0.80716515

00:26:55.528 --> 00:26:58.009 cells undergoing a pup tatic cell death.

NOTE Confidence: 0.80716515

00:26:58.010 --> 00:27:00.674 As you can see here with the Nixon

NOTE Confidence: 0.80716515

00:27:00.674 --> 00:27:02.340 5 and Cliff Park,

NOTE Confidence: 0.80716515

00:27:02.340 --> 00:27:04.506 we treated animals with the combination.

NOTE Confidence: 0.80716515

00:27:04.510 --> 00:27:06.610 Their survival was markedly improved compared

NOTE Confidence: 0.80716515

00:27:06.610 --> 00:27:09.198 to either of the amount of therapies,

NOTE Confidence: 0.80716515

00:27:09.200 --> 00:27:11.366 and tumor growth was really controlled.

NOTE Confidence: 0.80716515

00:27:11.370 --> 00:27:13.536 If you looked at these mirroring

NOTE Confidence: 0.80716515

00:27:13.536 --> 00:27:14.980 tumors under the microscope,

NOTE Confidence: 0.80716515

00:27:14.980 --> 00:27:17.314 you saw that the combination increased

NOTE Confidence: 0.80716515

00:27:17.314 --> 00:27:18.870 cleaved caspase reduced proliferation.

NOTE Confidence: 0.80716515

00:27:18.870 --> 00:27:20.610 Looking in the leading edge

NOTE Confidence: 0.80716515

00:27:20.610 --> 00:27:22.350 of these tumors using Aqua,

NOTE Confidence: 0.80716515

00:27:22.350 --> 00:27:24.294 we could count phospho CDK one

NOTE Confidence: 0.80716515

00:27:24.294 --> 00:27:26.180 and it was markedly reduced.

NOTE Confidence: 0.80716515

00:27:26.180 --> 00:27:28.441 We've now moved to a more selective

NOTE Confidence: 0.80716515

00:27:28.441 --> 00:27:30.010 second generation Aurora inhibitor,

NOTE Confidence: 0.80716515

00:27:30.010 --> 00:27:31.942 which we think will be easier

NOTE Confidence: 0.80716515

00:27:31.942 --> 00:27:33.830 to use in the clinic,

NOTE Confidence: 0.80716515

00:27:33.830 --> 00:27:36.194 'cause it's not as myelosuppressive and

NOTE Confidence: 0.80716515

00:27:36.194 --> 00:27:38.412 been able to replicate these findings

NOTE Confidence: 0.80716515

00:27:38.412 --> 00:27:41.469 and so part of our score is to take this

NOTE Confidence: 0.80716515

00:27:41.469 --> 00:27:44.269 combination forward as a window trial in HPV,

NOTE Confidence: 0.80716515

00:27:44.270 --> 00:27:44.966 negative disease,

NOTE Confidence: 0.80716515

00:27:44.966 --> 00:27:47.054 going for resection with those escalation,

NOTE Confidence: 0.80716515

00:27:47.060 --> 00:27:50.160 and then an expansion cohort.

NOTE Confidence: 0.80716515

00:27:50.160 --> 00:27:51.930 Collaborating with the Glamis lab,

NOTE Confidence: 0.80716515

00:27:51.930 --> 00:27:54.078 we've done a high throughput screen

NOTE Confidence: 0.80716515

00:27:54.078 --> 00:27:55.510 to identify additional synergistic

NOTE Confidence: 0.80716515

00:27:55.570 --> 00:27:57.568 pairs or additional partners for agave,

NOTE Confidence: 0.80716515

00:27:57.570 --> 00:27:59.335 assertive and our strongest hit

NOTE Confidence: 0.80716515

00:27:59.335 --> 00:28:00.747 was with the check.

NOTE Confidence: 0.80716515

00:28:00.750 --> 00:28:02.868 One check two inhibitor prex assertive.

NOTE Confidence: 0.80716515

00:28:02.870 --> 00:28:05.686 When I first saw saw that come out,

NOTE Confidence: 0.80716515

00:28:05.690 --> 00:28:07.202 I was pretty discouraged.

NOTE Confidence: 0.80716515

00:28:07.202 --> 00:28:08.714 'cause that's a pretty

NOTE Confidence: 0.80716515

00:28:08.714 --> 00:28:10.280 myelosuppressive agent in the clinic,

NOTE Confidence: 0.80716515

00:28:10.280 --> 00:28:12.562 and I was fearful that we wouldn't  
NOTE Confidence: 0.80716515

00:28:12.562 --> 00:28:15.218 be able to use it in combination.  
NOTE Confidence: 0.80716515

00:28:15.220 --> 00:28:16.990 But if you look here,  
NOTE Confidence: 0.80716515

00:28:16.990 --> 00:28:20.780 you can see that even at 25 nanomolar we get.  
NOTE Confidence: 0.80716515

00:28:20.780 --> 00:28:22.650 Clonogenic survival effects in combination,  
NOTE Confidence: 0.80716515

00:28:22.650 --> 00:28:25.845 so these pairs are going to be tested in  
NOTE Confidence: 0.80716515

00:28:25.845 --> 00:28:29.007 animal models as part of our sport project.  
NOTE Confidence: 0.80716515

00:28:29.010 --> 00:28:31.170 I think in the interest of  
NOTE Confidence: 0.80716515

00:28:31.170 --> 00:28:33.120 time I will skip this.  
NOTE Confidence: 0.80716515

00:28:33.120 --> 00:28:35.374 This sort of side branch story that  
NOTE Confidence: 0.80716515

00:28:35.374 --> 00:28:37.627 we have trying to explore these  
NOTE Confidence: 0.80716515

00:28:37.627 --> 00:28:39.657 therapies for patients with Fanconi  
NOTE Confidence: 0.80716515

00:28:39.657 --> 00:28:42.056 anemia who developed head neck cancer  
NOTE Confidence: 0.80716515

00:28:42.056 --> 00:28:44.336 at very high rates in adulthood.  
NOTE Confidence: 0.80716515

00:28:44.340 --> 00:28:47.028 But let me introduce you to Karen Anderson  
NOTE Confidence: 0.80716515

00:28:47.028 --> 00:28:49.947 and Dell Yarbrough's project in the spore.

NOTE Confidence: 0.80716515

00:28:49.950 --> 00:28:50.832 There's a.

NOTE Confidence: 0.80716515

00:28:50.832 --> 00:28:53.037 Observation from the TSJ that

NOTE Confidence: 0.80716515

00:28:53.037 --> 00:28:54.820 they're striking differences in

NOTE Confidence: 0.80716515

00:28:54.820 --> 00:28:56.380 metalation between HPV negative

NOTE Confidence: 0.80716515

00:28:56.380 --> 00:28:58.910 and HPV positive head neck cancers,

NOTE Confidence: 0.80716515

00:28:58.910 --> 00:29:01.520 and else lamp had done work

NOTE Confidence: 0.80716515

00:29:01.520 --> 00:29:03.260 demonstrating that this metalation

NOTE Confidence: 0.80716515

00:29:03.334 --> 00:29:05.944 induces immune silencing and if you

NOTE Confidence: 0.80716515

00:29:05.944 --> 00:29:08.529 give a demethylating agent like 5 Aza,

NOTE Confidence: 0.80716515

00:29:08.530 --> 00:29:11.026 you downregulate HPV and MMP expression.

NOTE Confidence: 0.80716515

00:29:11.030 --> 00:29:14.198 You stabilize P 53 and you induce a

NOTE Confidence: 0.80716515

00:29:14.198 --> 00:29:17.398 pop ptosis so we ran a window trial

NOTE Confidence: 0.80716515

00:29:17.398 --> 00:29:20.095 of Viveza siding and HPV negative

NOTE Confidence: 0.80716515

00:29:20.095 --> 00:29:22.215 and HPV positive cancer.

NOTE Confidence: 0.80716515

00:29:22.220 --> 00:29:24.649 No effects in the HPV negative cancers,

NOTE Confidence: 0.7707334



00:29:24.650 --> 00:29:29.170 but in the HPV positive cancers. We saw.

NOTE Confidence: 0.8572656

00:29:31.330 --> 00:29:35.240 That there was activation of.

NOTE Confidence: 0.8572656

00:29:35.240 --> 00:29:36.992 Type One interferon signaling.

NOTE Confidence: 0.8572656

00:29:36.992 --> 00:29:39.182 Upregulation of the gene editing

NOTE Confidence: 0.8572656

00:29:39.182 --> 00:29:41.164 protein apobec 3B which increased

NOTE Confidence: 0.8572656

00:29:41.164 --> 00:29:43.384 double strand DNA breaks and there

NOTE Confidence: 0.8572656

00:29:43.449 --> 00:29:45.269 was activated T cell infiltration

NOTE Confidence: 0.8572656

00:29:45.269 --> 00:29:47.501 within tumors and you see here.

NOTE Confidence: 0.8572656

00:29:47.501 --> 00:29:49.145 Photomicrographs before and after

NOTE Confidence: 0.8572656

00:29:49.145 --> 00:29:51.829 that were stained in David Rims Lab,

NOTE Confidence: 0.8572656

00:29:51.830 --> 00:29:54.358 looking for CD4 CD 8 and CD 20

NOTE Confidence: 0.8572656

00:29:54.358 --> 00:29:56.323 cells and I just Representative

NOTE Confidence: 0.8572656

00:29:56.323 --> 00:29:59.249 Lee have shown you the CD eight

NOTE Confidence: 0.8572656

00:29:59.335 --> 00:30:01.939 counts within the tumor mask before

NOTE Confidence: 0.8572656

00:30:01.939 --> 00:30:05.016 and after five days of siding.

NOTE Confidence: 0.8572656

00:30:05.016 --> 00:30:08.356 So we are taking this.

NOTE Confidence: 0.8572656

00:30:08.360 --> 00:30:11.318 Forward now in a store window,

NOTE Confidence: 0.8572656

00:30:11.320 --> 00:30:13.604 trial either 5/8 sided,

NOTE Confidence: 0.8572656

00:30:13.604 --> 00:30:15.888 being alone nivolumab alone

NOTE Confidence: 0.8572656

00:30:15.888 --> 00:30:19.443 or the combination in the new

NOTE Confidence: 0.8572656

00:30:19.443 --> 00:30:21.755 edmont setting and are.

NOTE Confidence: 0.8572656

00:30:21.760 --> 00:30:24.532 Also hoping to add to this 18 F energy

NOTE Confidence: 0.8572656

00:30:24.532 --> 00:30:26.499 pet for noninvasive quantitation

NOTE Confidence: 0.8572656

00:30:26.499 --> 00:30:29.139 of activated T cell infiltration

NOTE Confidence: 0.8572656

00:30:29.139 --> 00:30:32.431 across the course of the new engine

NOTE Confidence: 0.8572656

00:30:32.431 --> 00:30:34.159 therapy and collecting samples

NOTE Confidence: 0.8572656

00:30:34.159 --> 00:30:35.878 for tumor neoantigen expression.

NOTE Confidence: 0.84220314

00:30:38.500 --> 00:30:40.978 The cooperative groups are, I think,

NOTE Confidence: 0.84220314

00:30:40.980 --> 00:30:42.915 an important venue for asking

NOTE Confidence: 0.84220314

00:30:42.915 --> 00:30:45.520 questions that are closer to practice,

NOTE Confidence: 0.84220314

00:30:45.520 --> 00:30:48.404 and I've talked a lot about HPV,

NOTE Confidence: 0.84220314

00:30:48.410 --> 00:30:50.888 negative disease in HPV positive disease.

NOTE Confidence: 0.84220314

00:30:50.890 --> 00:30:52.960 Are questions center more on?

NOTE Confidence: 0.84220314

00:30:52.960 --> 00:30:55.115 How can we enhance function

NOTE Confidence: 0.84220314

00:30:55.115 --> 00:30:57.723 preservation and these are data we

NOTE Confidence: 0.84220314

00:30:57.723 --> 00:30:59.979 just presented at ASCO this year,

NOTE Confidence: 0.84220314

00:30:59.980 --> 00:31:02.566 showing that if you take patients

NOTE Confidence: 0.84220314

00:31:02.566 --> 00:31:04.290 with resectable stage HPV

NOTE Confidence: 0.84220314

00:31:04.364 --> 00:31:06.232 associated cancer to transoral

NOTE Confidence: 0.84220314

00:31:06.232 --> 00:31:09.034 resection and then you have that.

NOTE Confidence: 0.84220314

00:31:09.040 --> 00:31:11.240 Pathologic staging from the surgical

NOTE Confidence: 0.84220314

00:31:11.240 --> 00:31:14.014 material in hand that really permits

NOTE Confidence: 0.84220314

00:31:14.014 --> 00:31:16.018 much more dramatic treatment.

NOTE Confidence: 0.84220314

00:31:16.020 --> 00:31:18.264 The intensification than if

NOTE Confidence: 0.84220314

00:31:18.264 --> 00:31:21.069 you have to rely on.

NOTE Confidence: 0.84220314

00:31:21.070 --> 00:31:23.380 Clinical variables and so here you see

NOTE Confidence: 0.84220314

00:31:23.380 --> 00:31:25.665 that for favorable risk surgical staging

NOTE Confidence: 0.84220314

00:31:25.665 --> 00:31:27.725 without any post operative therapy,

NOTE Confidence: 0.84220314

00:31:27.730 --> 00:31:29.580 we have three year progression

NOTE Confidence: 0.84220314

00:31:29.580 --> 00:31:31.060 free survival approaching 97%

NOTE Confidence: 0.84220314

00:31:31.060 --> 00:31:32.910 for the intermediate risk group.

NOTE Confidence: 0.84220314

00:31:32.910 --> 00:31:35.130 So this is node positive but

NOTE Confidence: 0.84220314

00:31:35.130 --> 00:31:36.240 no extranodal extension.

NOTE Confidence: 0.84220314

00:31:36.240 --> 00:31:38.690 Whether we gave 60 Gy of radiation

NOTE Confidence: 0.84220314

00:31:38.690 --> 00:31:40.679 or 50 grey Anne Frank,

NOTE Confidence: 0.84220314

00:31:40.680 --> 00:31:42.972 the fields we maintain three year

NOTE Confidence: 0.84220314

00:31:42.972 --> 00:31:44.842 progression free survival of about

NOTE Confidence: 0.84220314

00:31:44.842 --> 00:31:47.286 94% and then even the very high

NOTE Confidence: 0.84220314

00:31:47.286 --> 00:31:49.946 risk patients we were able to be

NOTE Confidence: 0.84220314

00:31:49.946 --> 00:31:51.836 intensify therapy by going to.

NOTE Confidence: 0.84220314

00:31:51.840 --> 00:31:53.795 So weekly chemotherapy in the

NOTE Confidence: 0.84220314

00:31:53.795 --> 00:31:54.968 post op setting.

NOTE Confidence: 0.84220314

00:31:54.970 --> 00:31:57.070 You'll see here that about a third  
NOTE Confidence: 0.84220314

00:31:57.070 --> 00:31:59.350 of the patients on the trial ended  
NOTE Confidence: 0.84220314

00:31:59.350 --> 00:32:01.000 up needing Tri modality therapy  
NOTE Confidence: 0.84220314

00:32:01.000 --> 00:32:03.130 that is not the goal of treatment.  
NOTE Confidence: 0.84220314

00:32:03.130 --> 00:32:05.328 The intensification and so one question is,  
NOTE Confidence: 0.84220314

00:32:05.330 --> 00:32:07.256 how can we better identify the  
NOTE Confidence: 0.84220314

00:32:07.256 --> 00:32:09.203 patients who have higher risk of  
NOTE Confidence: 0.84220314

00:32:09.203 --> 00:32:10.991 let's say any or positive margin  
NOTE Confidence: 0.84220314

00:32:10.991 --> 00:32:13.199 from going on to a surgical trial  
NOTE Confidence: 0.84220314

00:32:13.199 --> 00:32:14.749 because they ought to probably  
NOTE Confidence: 0.84220314

00:32:14.750 --> 00:32:17.158 go straight to chemoradiation.  
NOTE Confidence: 0.84220314

00:32:17.160 --> 00:32:17.852 Ben Khan,  
NOTE Confidence: 0.84220314

00:32:17.852 --> 00:32:19.582 who's now a junior faculty  
NOTE Confidence: 0.84220314

00:32:19.582 --> 00:32:22.427 member at the Farber but was a  
NOTE Confidence: 0.84220314

00:32:22.427 --> 00:32:24.159 radiation oncology resident here,  
NOTE Confidence: 0.84220314

00:32:24.160 --> 00:32:25.940 undertook a machine learning project

NOTE Confidence: 0.84220314

00:32:25.940 --> 00:32:28.663 where he developed a deep neural network

NOTE Confidence: 0.84220314

00:32:28.663 --> 00:32:30.431 algorithm for identifying extranodal

NOTE Confidence: 0.84220314

00:32:30.431 --> 00:32:32.720 extension from a baseline CT scan.

NOTE Confidence: 0.84220314

00:32:32.720 --> 00:32:35.006 We've now validated that on the

NOTE Confidence: 0.84220314

00:32:35.006 --> 00:32:37.389 cooperative group trial in 76 patients,

NOTE Confidence: 0.84220314

00:32:37.390 --> 00:32:40.612 and this has moved on to part of the

NOTE Confidence: 0.84220314

00:32:40.612 --> 00:32:43.148 University of Pittsburgh head next door

NOTE Confidence: 0.84220314

00:32:43.148 --> 00:32:46.088 that I'm a Co investigator on where

NOTE Confidence: 0.84220314

00:32:46.088 --> 00:32:48.755 we're going to be linking radio MIC.

NOTE Confidence: 0.84220314

00:32:48.760 --> 00:32:51.315 To genomic signatures so that we hopefully

NOTE Confidence: 0.84220314

00:32:51.315 --> 00:32:54.269 can have a better means of identifying

NOTE Confidence: 0.84220314

00:32:54.269 --> 00:32:56.951 these high risk patients at baseline.

NOTE Confidence: 0.84220314

00:32:56.960 --> 00:32:59.430 In terms of policy there,

NOTE Confidence: 0.84220314

00:32:59.430 --> 00:33:02.830 I think have been.

NOTE Confidence: 0.84220314

00:33:02.830 --> 00:33:03.245 Really,

NOTE Confidence: 0.84220314

00:33:03.245 --> 00:33:05.320 a paucity of FDA approvals

NOTE Confidence: 0.84220314

00:33:05.320 --> 00:33:06.980 in head neck cancer.

NOTE Confidence: 0.84220314

00:33:06.980 --> 00:33:10.238 The approvals of pembrolizumab in Nevala

NOTE Confidence: 0.84220314

00:33:10.238 --> 00:33:15.088 map in 2017 were the first in over a decade.

NOTE Confidence: 0.84220314

00:33:15.090 --> 00:33:17.729 And these trials have become more difficult.

NOTE Confidence: 0.84220314

00:33:17.730 --> 00:33:19.986 Certainly for the HPV associated cancers,

NOTE Confidence: 0.84220314

00:33:19.990 --> 00:33:22.629 where the event rates are quite low,

NOTE Confidence: 0.84220314

00:33:22.630 --> 00:33:24.610 and designing randomized trials where

NOTE Confidence: 0.84220314

00:33:24.610 --> 00:33:26.590 you're looking to have something

NOTE Confidence: 0.84220314

00:33:26.649 --> 00:33:28.654 happen that's better than 94% at

NOTE Confidence: 0.84220314

00:33:28.654 --> 00:33:30.474 three years really becomes prohibitive

NOTE Confidence: 0.84220314

00:33:30.474 --> 00:33:32.810 in terms of size and duration.

NOTE Confidence: 0.84220314

00:33:32.810 --> 00:33:35.519 And although we see many ways that

NOTE Confidence: 0.84220314

00:33:35.519 --> 00:33:37.101 immunotherapy and targeted therapy

NOTE Confidence: 0.84220314

00:33:37.101 --> 00:33:39.600 could allow us to D intensify trials,

NOTE Confidence: 0.84220314

00:33:39.600 --> 00:33:41.970 there is no accepted regulatory strategy

NOTE Confidence: 0.84220314

00:33:41.970 --> 00:33:44.119 for demonstrating that that's the case.

NOTE Confidence: 0.84220314

00:33:44.120 --> 00:33:46.496 So the goals of Project 2025.

NOTE Confidence: 0.84220314

00:33:46.500 --> 00:33:50.490 Are to find harmonized surrogate

NOTE Confidence: 0.84220314

00:33:50.490 --> 00:33:56.220 endpoints that the FDA will accept they.

NOTE Confidence: 0.84220314

00:33:56.220 --> 00:33:58.390 You know want to have public meeting

NOTE Confidence: 0.84220314

00:33:58.390 --> 00:34:00.161 with all the stakeholders present

NOTE Confidence: 0.84220314

00:34:00.161 --> 00:34:02.870 that that will kind of refine PFS?

NOTE Confidence: 0.8097394

00:34:02.870 --> 00:34:03.920 Probably looking better

NOTE Confidence: 0.8097394

00:34:03.920 --> 00:34:05.320 than local regional control.

NOTE Confidence: 0.8097394

00:34:05.320 --> 00:34:07.070 What's the role of following

NOTE Confidence: 0.8097394

00:34:07.070 --> 00:34:08.470 each PV circulating DNA?

NOTE Confidence: 0.8097394

00:34:08.470 --> 00:34:10.285 How do functional endpoints get

NOTE Confidence: 0.8097394

00:34:10.285 --> 00:34:12.837 defined to permit approval in the D

NOTE Confidence: 0.8097394

00:34:12.837 --> 00:34:14.507 intensification trial and then the

NOTE Confidence: 0.8097394

00:34:14.507 --> 00:34:16.929 last thing that I think is really

NOTE Confidence: 0.8097394



00:34:16.929 --> 00:34:18.969 important for us is career development.

NOTE Confidence: 0.8097394

00:34:18.970 --> 00:34:21.770 And before I turn it over to RT,

NOTE Confidence: 0.8097394

00:34:21.770 --> 00:34:23.456 I just want to highlight that

NOTE Confidence: 0.8097394

00:34:23.456 --> 00:34:25.174 the sport does have developmental

NOTE Confidence: 0.8097394

00:34:25.174 --> 00:34:27.290 research and career enhancement.

NOTE Confidence: 0.8097394

00:34:27.290 --> 00:34:32.010 Programs that offer up to 50K pilot funding.

NOTE Confidence: 0.8097394

00:34:32.010 --> 00:34:33.498 Our pay line is pretty good.

NOTE Confidence: 0.8097394

00:34:33.500 --> 00:34:35.250 We give out seven awards a year.

NOTE Confidence: 0.8097394

00:34:35.250 --> 00:34:36.930 We just had a cycle but please

NOTE Confidence: 0.8097394

00:34:36.930 --> 00:34:38.240 think about us next year.

NOTE Confidence: 0.8097394

00:34:38.240 --> 00:34:39.728 So with that I'm going to.

NOTE Confidence: 0.8224244

00:34:42.390 --> 00:34:44.539 I think not introduce my two Co

NOTE Confidence: 0.8224244

00:34:44.539 --> 00:34:46.507 speakers 'cause Roy Herbst did very

NOTE Confidence: 0.8224244

00:34:46.507 --> 00:34:48.463 nice job with that just mentioned

NOTE Confidence: 0.8224244

00:34:48.463 --> 00:34:50.539 that obviously this work was done

NOTE Confidence: 0.8224244

00:34:50.539 --> 00:34:52.590 by many many people besides myself.

NOTE Confidence: 0.8224244

00:34:52.590 --> 00:34:54.390 Thank my funding agencies and

NOTE Confidence: 0.8224244

00:34:54.390 --> 00:34:56.731 stop sharing so that I can turn

NOTE Confidence: 0.8224244

00:34:56.731 --> 00:34:58.126 it over to Doctor Bhatia.

NOTE Confidence: 0.8287728

00:35:15.380 --> 00:35:17.615 Good afternoon everyone. Thank you for

NOTE Confidence: 0.8287728

00:35:17.615 --> 00:35:19.880 the opportunity to present here today.

NOTE Confidence: 0.8287728

00:35:19.880 --> 00:35:22.274 I'll be talking briefly about research

NOTE Confidence: 0.8287728

00:35:22.274 --> 00:35:24.359 strategies that we have undertaken

NOTE Confidence: 0.8287728

00:35:24.359 --> 00:35:26.449 at Yale to overcome cetuximab

NOTE Confidence: 0.8287728

00:35:26.449 --> 00:35:28.710 resistance and head neck cancers.

NOTE Confidence: 0.8287728

00:35:28.710 --> 00:35:31.526 As we all know, so toxic members in

NOTE Confidence: 0.8287728

00:35:31.526 --> 00:35:33.814 monoclonal antibody against EGFR an it's

NOTE Confidence: 0.8287728

00:35:33.814 --> 00:35:36.082 the only approved targeted therapy for

NOTE Confidence: 0.8287728

00:35:36.151 --> 00:35:38.455 patients with head and neck cancers.

NOTE Confidence: 0.8287728

00:35:38.460 --> 00:35:41.028 This approval was based on improved

NOTE Confidence: 0.8287728

00:35:41.028 --> 00:35:42.740 locoregional control and survival

NOTE Confidence: 0.8287728

00:35:42.811 --> 00:35:45.043 when it was given concurrently with  
NOTE Confidence: 0.8287728

00:35:45.043 --> 00:35:47.222 radiation in the locally advanced setting  
NOTE Confidence: 0.8287728

00:35:47.222 --> 00:35:49.702 and do to improve PFS and OS when  
NOTE Confidence: 0.8287728

00:35:49.710 --> 00:35:51.585 administered in combination with chemo  
NOTE Confidence: 0.8287728

00:35:51.585 --> 00:35:53.460 in the recurrent metastatic setting.  
NOTE Confidence: 0.8287728

00:35:53.460 --> 00:35:55.265 However, these effects are modest  
NOTE Confidence: 0.8287728

00:35:55.265 --> 00:35:57.539 and the definitive setting in the  
NOTE Confidence: 0.8287728

00:35:57.539 --> 00:35:59.187 definitive settings attacks map.  
NOTE Confidence: 0.8287728

00:35:59.190 --> 00:36:01.550 In radiation is proven inferior  
NOTE Confidence: 0.8287728

00:36:01.550 --> 00:36:02.494 to chemoradiation.  
NOTE Confidence: 0.8287728

00:36:02.500 --> 00:36:04.695 Its clinical utility is limited  
NOTE Confidence: 0.8287728

00:36:04.695 --> 00:36:06.890 primarily by either inherent or  
NOTE Confidence: 0.8287728

00:36:06.960 --> 00:36:09.120 acquired resistance to therapy,  
NOTE Confidence: 0.8287728

00:36:09.120 --> 00:36:12.431 like and binding of EGFR needs to  
NOTE Confidence: 0.8287728

00:36:12.431 --> 00:36:14.587 \*\*\*\* and Heterodimerization with  
NOTE Confidence: 0.8287728

00:36:14.587 --> 00:36:17.941 other her family receptors or other

NOTE Confidence: 0.8287728

00:36:17.941 --> 00:36:21.388 receptors in kinases such as met and

NOTE Confidence: 0.8287728

00:36:21.388 --> 00:36:23.256 subsequent downstream signaling of

NOTE Confidence: 0.8287728

00:36:23.342 --> 00:36:25.592 MAP kinase K3 kinase mtor pathway

NOTE Confidence: 0.8287728

00:36:25.592 --> 00:36:28.948 rest Ref Mac or Pathway or Jack stat.

NOTE Confidence: 0.8287728

00:36:28.948 --> 00:36:31.258 And resistance can be mediated

NOTE Confidence: 0.8287728

00:36:31.258 --> 00:36:33.918 either by over expression of EGFR,

NOTE Confidence: 0.8287728

00:36:33.920 --> 00:36:37.061 or it's like ends as we see in hidden

NOTE Confidence: 0.8287728

00:36:37.061 --> 00:36:40.094 cancers and in response to smoking it can

NOTE Confidence: 0.8287728

00:36:40.094 --> 00:36:43.620 be mediated by nuclear translocation of EGFR,

NOTE Confidence: 0.8287728

00:36:43.620 --> 00:36:45.822 where it stabilizes P CNA and

NOTE Confidence: 0.8287728

00:36:45.822 --> 00:36:48.060 enhances DNA repair and synthesis,

NOTE Confidence: 0.8287728

00:36:48.060 --> 00:36:49.242 or increase headers.

NOTE Confidence: 0.8287728

00:36:49.242 --> 00:36:50.818 Dimerization with other members

NOTE Confidence: 0.8287728

00:36:50.818 --> 00:36:52.510 of the her family,

NOTE Confidence: 0.8287728

00:36:52.510 --> 00:36:54.530 her two and her three,

NOTE Confidence: 0.8287728

00:36:54.530 --> 00:36:56.972 or with cross talk with other  
NOTE Confidence: 0.8287728

00:36:56.972 --> 00:36:59.490 receptors in kinases such as Seemeth.  
NOTE Confidence: 0.8287728

00:36:59.490 --> 00:37:02.738 In bed rest and identifying effective means  
NOTE Confidence: 0.8287728

00:37:02.738 --> 00:37:05.379 of sensitizing hidden cancers to EGFR  
NOTE Confidence: 0.8287728

00:37:05.379 --> 00:37:08.123 inhibition is an important goal for us.  
NOTE Confidence: 0.8287728

00:37:08.130 --> 00:37:10.806 An important part of our sport  
NOTE Confidence: 0.8287728

00:37:10.806 --> 00:37:13.310 project to prior research at Yale.  
NOTE Confidence: 0.8287728

00:37:13.310 --> 00:37:15.425 Done on tissue microarrays that  
NOTE Confidence: 0.8287728

00:37:15.425 --> 00:37:17.117 were constructed from oropharyngeal  
NOTE Confidence: 0.8287728

00:37:17.117 --> 00:37:19.299 cancer specimens showed a significant  
NOTE Confidence: 0.8287728

00:37:19.299 --> 00:37:21.414 association of nuclear EGFR with  
NOTE Confidence: 0.8287728

00:37:21.414 --> 00:37:22.819 membranous EGFR expression.  
NOTE Confidence: 0.8287728

00:37:22.820 --> 00:37:24.980 An with nuclear P CNA,  
NOTE Confidence: 0.8287728

00:37:24.980 --> 00:37:27.380 and that suggested that EGFR  
NOTE Confidence: 0.8287728

00:37:27.380 --> 00:37:30.286 functions as a tossing pennies in  
NOTE Confidence: 0.8287728

00:37:30.286 --> 00:37:33.205 the nucleus where it stabilizes PC na.

NOTE Confidence: 0.8287728

00:37:33.210 --> 00:37:36.282 The nuclear activity will could therefore

NOTE Confidence: 0.8287728

00:37:36.282 --> 00:37:38.900 constitute a novel therapeutic target.

NOTE Confidence: 0.8287728

00:37:38.900 --> 00:37:40.181 Subsequent to that,

NOTE Confidence: 0.8287728

00:37:40.181 --> 00:37:43.701 we designed a phase two trial using a

NOTE Confidence: 0.8287728

00:37:43.701 --> 00:37:46.401 chemo backbone and dual EGFR blockade

NOTE Confidence: 0.8287728

00:37:46.401 --> 00:37:48.689 with cetuximab and or lachnit.

NOTE Confidence: 0.8287728

00:37:48.690 --> 00:37:51.406 The rationale was that dual EGFR blockade

NOTE Confidence: 0.8287728

00:37:51.406 --> 00:37:53.590 would overcome EGFR overexpression,

NOTE Confidence: 0.8287728

00:37:53.590 --> 00:37:56.104 and it's like an independent downstream

NOTE Confidence: 0.8287728

00:37:56.104 --> 00:37:58.480 signaling an show improved responses.

NOTE Confidence: 0.8287728

00:37:58.480 --> 00:38:00.705 The tumor biopsies were planned

NOTE Confidence: 0.8287728

00:38:00.705 --> 00:38:02.485 at baseline font treatment,

NOTE Confidence: 0.8287728

00:38:02.490 --> 00:38:04.270 an at disease progression.

NOTE Confidence: 0.8287728

00:38:04.270 --> 00:38:06.050 An encore native analysis,

NOTE Confidence: 0.8287728

00:38:06.050 --> 00:38:09.956 we found that nuclear PC na staining.

NOTE Confidence: 0.8287728

00:38:09.960 --> 00:38:12.246 A decrease in the standing actually  
NOTE Confidence: 0.8287728

00:38:12.246 --> 00:38:14.147 correlated with clinical response to  
NOTE Confidence: 0.8287728

00:38:14.147 --> 00:38:16.037 treatment for several patients who had  
NOTE Confidence: 0.8287728

00:38:16.037 --> 00:38:18.102 matched pre and post treatment biopsies  
NOTE Confidence: 0.8287728

00:38:18.102 --> 00:38:20.226 and that suggested that nuclear EGFR  
NOTE Confidence: 0.8287728

00:38:20.226 --> 00:38:23.466 may also be inhibited with this combination.  
NOTE Confidence: 0.8287728

00:38:23.470 --> 00:38:26.207 As a follow up to that study,  
NOTE Confidence: 0.8287728

00:38:26.210 --> 00:38:28.429 we proposed and received an CC and  
NOTE Confidence: 0.8287728

00:38:28.429 --> 00:38:30.979 funding for a phase two trial of  
NOTE Confidence: 0.8287728

00:38:30.979 --> 00:38:32.894 cetuximab and afatinib in patients  
NOTE Confidence: 0.8287728

00:38:32.894 --> 00:38:35.193 with platinum and mostly immune  
NOTE Confidence: 0.8287728

00:38:35.193 --> 00:38:37.041 checkpoint inhibition had neck  
NOTE Confidence: 0.8287728

00:38:37.041 --> 00:38:39.146 cancers were really no effective.  
NOTE Confidence: 0.8287728

00:38:39.146 --> 00:38:40.714 An approved treatments exist.  
NOTE Confidence: 0.8287728

00:38:40.720 --> 00:38:42.856 This trial is ongoing for a  
NOTE Confidence: 0.8287728

00:38:42.856 --> 00:38:45.030 target accrual of 50 patients.

NOTE Confidence: 0.8287728

00:38:45.030 --> 00:38:48.026 We have already approved 38 tissue for

NOTE Confidence: 0.8287728

00:38:48.026 --> 00:38:50.649 correlatives is being obtained both pre

NOTE Confidence: 0.8287728

00:38:50.649 --> 00:38:53.596 pre and post treatment for most patients.

NOTE Confidence: 0.75890964

00:38:53.600 --> 00:38:56.558 An existing funding from NC, CNN,

NOTE Confidence: 0.75890964

00:38:56.558 --> 00:38:59.248 the Patterson Foundation will support

NOTE Confidence: 0.75890964

00:38:59.248 --> 00:39:00.324 quantitative immunohistochemical

NOTE Confidence: 0.75890964

00:39:00.324 --> 00:39:02.688 assessment of the known biomarkers

NOTE Confidence: 0.75890964

00:39:02.688 --> 00:39:04.728 of resistance to EGFR inhibition,

NOTE Confidence: 0.75890964

00:39:04.730 --> 00:39:06.182 namely P-10, Phosphoric,

NOTE Confidence: 0.75890964

00:39:06.182 --> 00:39:08.118 Phospho, AKT and PCN.

NOTE Confidence: 0.75890964

00:39:08.120 --> 00:39:10.952 A tumor biopsies from patients on

NOTE Confidence: 0.75890964

00:39:10.952 --> 00:39:14.188 this trial will also be used in

NOTE Confidence: 0.75890964

00:39:14.188 --> 00:39:17.121 project one of the sport to establish

NOTE Confidence: 0.75890964

00:39:17.217 --> 00:39:21.011 PDX is an immune deficient mice and

NOTE Confidence: 0.75890964

00:39:21.011 --> 00:39:23.680 recent structural insights into TKI

NOTE Confidence: 0.75890964



00:39:23.680 --> 00:39:26.280 binding have shown that stabilization  
NOTE Confidence: 0.75890964

00:39:26.280 --> 00:39:28.450 of receptor activation states.  
NOTE Confidence: 0.75890964

00:39:28.450 --> 00:39:29.454 For instance,  
NOTE Confidence: 0.75890964

00:39:29.454 --> 00:39:31.964 after Heterodimerization with her three  
NOTE Confidence: 0.75890964

00:39:31.964 --> 00:39:34.200 produces EGFR confirmations that do  
NOTE Confidence: 0.75890964

00:39:34.200 --> 00:39:36.204 not bind inhibitors like Patna benefit  
NOTE Confidence: 0.75890964

00:39:36.204 --> 00:39:38.796 net and that could lead to resistance.  
NOTE Confidence: 0.75890964

00:39:38.800 --> 00:39:41.584 So the goal is to identify TK eyes  
NOTE Confidence: 0.75890964

00:39:41.584 --> 00:39:43.821 that bind to EGFR confirmations  
NOTE Confidence: 0.75890964

00:39:43.821 --> 00:39:46.246 that are occurring in head,  
NOTE Confidence: 0.75890964

00:39:46.250 --> 00:39:48.734 neck cancers or those that are  
NOTE Confidence: 0.75890964

00:39:48.734 --> 00:39:50.390 not restricted by confirmation.  
NOTE Confidence: 0.75890964

00:39:50.390 --> 00:39:52.435 State dependent binding and to  
NOTE Confidence: 0.75890964

00:39:52.435 --> 00:39:54.480 test the effectiveness of these  
NOTE Confidence: 0.75890964

00:39:54.552 --> 00:39:56.597 compounds in head neck cancers.  
NOTE Confidence: 0.75890964

00:39:56.600 --> 00:39:58.870 So PDX is derived from.

NOTE Confidence: 0.75890964

00:39:58.870 --> 00:40:01.838 Biopsies from patients on the trial will

NOTE Confidence: 0.75890964

00:40:01.838 --> 00:40:04.860 be treated with EGFR directed TK Eyes,

NOTE Confidence: 0.75890964

00:40:04.860 --> 00:40:08.130 which retain efficacy against her three

NOTE Confidence: 0.75890964

00:40:08.130 --> 00:40:10.964 an EGFR heterodimers We also received

NOTE Confidence: 0.75890964

00:40:10.964 --> 00:40:13.352 a recent Department of Defense funding

NOTE Confidence: 0.75890964

00:40:13.352 --> 00:40:15.955 to a define the relationship between

NOTE Confidence: 0.75890964

00:40:15.955 --> 00:40:18.910 TP 53 genotype Aurora kinase expression,

NOTE Confidence: 0.75890964

00:40:18.910 --> 00:40:21.592 an response to EGFR inhibition using

NOTE Confidence: 0.75890964

00:40:21.592 --> 00:40:24.560 patient samples from the same NSN trial.

NOTE Confidence: 0.75890964

00:40:24.560 --> 00:40:27.170 In the absence of TP 53,

NOTE Confidence: 0.75890964

00:40:27.170 --> 00:40:29.882 or in the presence of TPX 2 Aurora

NOTE Confidence: 0.75890964

00:40:29.882 --> 00:40:32.829 kinase is highly expressed and it

NOTE Confidence: 0.75890964

00:40:32.829 --> 00:40:35.564 provides an alternative mechanism of

NOTE Confidence: 0.75890964

00:40:35.564 --> 00:40:37.984 downstream signaling of EGFR using

NOTE Confidence: 0.75890964

00:40:37.984 --> 00:40:40.666 the tissue samples from the trial.

NOTE Confidence: 0.75890964

00:40:40.670 --> 00:40:43.328 We will be able to determine  
NOTE Confidence: 0.75890964

00:40:43.328 --> 00:40:44.657 if the combination.  
NOTE Confidence: 0.75890964

00:40:44.660 --> 00:40:47.108 I'm sorry whether TP 53 mutation  
NOTE Confidence: 0.75890964

00:40:47.108 --> 00:40:49.327 will predict for baseline or  
NOTE Confidence: 0.75890964

00:40:49.327 --> 00:40:50.857 post treatment resistance,  
NOTE Confidence: 0.75890964

00:40:50.860 --> 00:40:53.075 an weath Aurora kinase and  
NOTE Confidence: 0.75890964

00:40:53.075 --> 00:40:55.290 TPX 2 levels are predicted.  
NOTE Confidence: 0.75890964

00:40:55.290 --> 00:40:57.515 Biomarkers of non response to  
NOTE Confidence: 0.75890964

00:40:57.515 --> 00:40:59.740 dual EGFR inhibition and correlate  
NOTE Confidence: 0.75890964

00:40:59.818 --> 00:41:01.490 with a shorter survival.  
NOTE Confidence: 0.75890964

00:41:01.490 --> 00:41:03.278 Also using posttreatment biopsies,  
NOTE Confidence: 0.75890964

00:41:03.278 --> 00:41:06.510 we can determine whether a rise in  
NOTE Confidence: 0.75890964

00:41:06.510 --> 00:41:08.915 Aurora kinase levels will predict  
NOTE Confidence: 0.75890964

00:41:08.915 --> 00:41:10.839 for disease progression following.  
NOTE Confidence: 0.75890964

00:41:10.840 --> 00:41:11.971 Progression clinical progression  
NOTE Confidence: 0.75890964

00:41:11.971 --> 00:41:14.100 on treatment.

NOTE Confidence: 0.75890964

00:41:14.100 --> 00:41:16.752 Yale is also participated in a multi

NOTE Confidence: 0.75890964

00:41:16.752 --> 00:41:18.769 institutional IIT of an hepatocyte

NOTE Confidence: 0.75890964

00:41:18.769 --> 00:41:21.069 growth factor cement pathway inhibitor

NOTE Confidence: 0.75890964

00:41:21.069 --> 00:41:23.829 similar to the map in combination

NOTE Confidence: 0.75890964

00:41:23.829 --> 00:41:26.811 with Cytosan map in patients who have

NOTE Confidence: 0.75890964

00:41:26.811 --> 00:41:28.437 previously progressed onset eczema.

NOTE Confidence: 0.75890964

00:41:28.437 --> 00:41:31.230 There is cross talk between EGFR and

NOTE Confidence: 0.75890964

00:41:31.302 --> 00:41:34.186 the cement pathways and it's a known

NOTE Confidence: 0.75890964

00:41:34.186 --> 00:41:36.150 tumor intrinsic resistance mechanism,

NOTE Confidence: 0.75890964

00:41:36.150 --> 00:41:39.314 a phase one trial of this combination

NOTE Confidence: 0.75890964

00:41:39.314 --> 00:41:42.150 showed a response rate of 17% in

NOTE Confidence: 0.75890964

00:41:42.150 --> 00:41:44.110 syntax map resistant patients.

NOTE Confidence: 0.75890964

00:41:44.110 --> 00:41:46.095 And the subsequent randomized phase

NOTE Confidence: 0.75890964

00:41:46.095 --> 00:41:48.374 two trials showed a response rate

NOTE Confidence: 0.75890964

00:41:48.374 --> 00:41:50.322 of 38% in HPV negative patients,

NOTE Confidence: 0.75890964

00:41:50.322 --> 00:41:52.187 and these results were presented  
NOTE Confidence: 0.75890964

00:41:52.187 --> 00:41:53.549 at ASCO this year.  
NOTE Confidence: 0.8379239

00:41:55.690 --> 00:41:57.755 So while keynote over 8 has established  
NOTE Confidence: 0.8379239

00:41:57.755 --> 00:41:59.476 the role of immune checkpoint  
NOTE Confidence: 0.8379239

00:41:59.476 --> 00:42:01.416 inhibition in the first line,  
NOTE Confidence: 0.8379239

00:42:01.420 --> 00:42:03.100 treatment of head neck cancers,  
NOTE Confidence: 0.8379239

00:42:03.100 --> 00:42:04.962 so toxic map continues to hold a  
NOTE Confidence: 0.8379239

00:42:04.962 --> 00:42:06.633 place in the treatment of this  
NOTE Confidence: 0.8379239

00:42:06.633 --> 00:42:09.059 disease and it is one of the most  
NOTE Confidence: 0.8379239

00:42:09.059 --> 00:42:11.364 frequently chosen second line treatment  
NOTE Confidence: 0.8379239

00:42:11.364 --> 00:42:13.208 in combination with chemotherapy.  
NOTE Confidence: 0.8379239

00:42:13.210 --> 00:42:15.450 For patients who came off keynote over  
NOTE Confidence: 0.8379239

00:42:15.450 --> 00:42:18.189 8 on the Pembroke monotherapy arm.  
NOTE Confidence: 0.8379239

00:42:18.190 --> 00:42:21.262 We now seek to explore the best second  
NOTE Confidence: 0.8379239

00:42:21.262 --> 00:42:23.695 line treatment options for head and  
NOTE Confidence: 0.8379239

00:42:23.695 --> 00:42:26.083 neck cancers and multiple lines of

NOTE Confidence: 0.8379239

00:42:26.162 --> 00:42:28.622 evidence has suggested that head

NOTE Confidence: 0.8379239

00:42:28.622 --> 00:42:31.082 neck tumors are frequently hypoxic.

NOTE Confidence: 0.8379239

00:42:31.090 --> 00:42:33.240 An have elevated VEGF signaling,

NOTE Confidence: 0.8379239

00:42:33.240 --> 00:42:35.390 which is associated with immunosuppression.

NOTE Confidence: 0.8379239

00:42:35.390 --> 00:42:37.502 The object via the stat three

NOTE Confidence: 0.8379239

00:42:37.502 --> 00:42:39.490 signaling pathway or impairment of

NOTE Confidence: 0.8379239

00:42:39.490 --> 00:42:41.566 dendritic cell maturation induction

NOTE Confidence: 0.8379239

00:42:41.566 --> 00:42:43.123 of immunosuppressive populations,

NOTE Confidence: 0.8379239

00:42:43.130 --> 00:42:45.710 such as MDF, season T regs,

NOTE Confidence: 0.8379239

00:42:45.710 --> 00:42:47.610 and reduce recruitment of

NOTE Confidence: 0.8379239

00:42:47.610 --> 00:42:48.560 cytotoxic effectors.

NOTE Confidence: 0.8379239

00:42:48.560 --> 00:42:50.012 Including CD 8 cells,

NOTE Confidence: 0.8379239

00:42:50.012 --> 00:42:52.808 CD 8 positive T cells and natural

NOTE Confidence: 0.8379239

00:42:52.808 --> 00:42:53.888 killer cells.

NOTE Confidence: 0.8379239

00:42:53.890 --> 00:42:56.200 So we postulate that VEGF blockade

NOTE Confidence: 0.8379239

00:42:56.200 --> 00:42:58.243 with bevacizumab will reverse these  
NOTE Confidence: 0.8379239

00:42:58.243 --> 00:42:59.979 suppressive mechanisms and lead  
NOTE Confidence: 0.8379239

00:42:59.979 --> 00:43:02.149 to improved antitumor immunity and  
NOTE Confidence: 0.8379239

00:43:02.211 --> 00:43:03.799 clinical responses in patients  
NOTE Confidence: 0.8379239

00:43:03.799 --> 00:43:05.784 who were previously treated with  
NOTE Confidence: 0.8379239

00:43:05.784 --> 00:43:07.426 in the checkpoint inhibition.  
NOTE Confidence: 0.8379239

00:43:07.426 --> 00:43:09.074 The combination of immunotherapy  
NOTE Confidence: 0.8379239

00:43:09.074 --> 00:43:11.995 and veg F inhibition has also shown  
NOTE Confidence: 0.8379239

00:43:11.995 --> 00:43:14.025 excellent clinical efficacy in other  
NOTE Confidence: 0.8379239

00:43:14.025 --> 00:43:16.030 solid tumor types, including renal,  
NOTE Confidence: 0.8379239

00:43:16.030 --> 00:43:17.670 cell, lung, and hepatocellular,  
NOTE Confidence: 0.8379239

00:43:17.670 --> 00:43:19.955 and was recently approved as  
NOTE Confidence: 0.8379239

00:43:19.955 --> 00:43:22.240 first line treatment for HCC.  
NOTE Confidence: 0.8379239

00:43:22.240 --> 00:43:23.348 Anne in head neck.  
NOTE Confidence: 0.8379239

00:43:23.348 --> 00:43:25.467 We had a Phase 1B trial looking  
NOTE Confidence: 0.8379239

00:43:25.467 --> 00:43:27.801 at the combination of Pedro and

NOTE Confidence: 0.8379239

00:43:27.801 --> 00:43:29.908 botnet which showed a response rate

NOTE Confidence: 0.8379239

00:43:29.908 --> 00:43:33.190 of 36% and the PFS of 8.2 months.

NOTE Confidence: 0.8379239

00:43:33.190 --> 00:43:35.430 So we designed a Phase 2 slash

NOTE Confidence: 0.8379239

00:43:35.430 --> 00:43:36.880 3 trial through ekach.

NOTE Confidence: 0.8379239

00:43:36.880 --> 00:43:39.886 There will be 3 arms in the initial phase.

NOTE Confidence: 0.8379239

00:43:39.890 --> 00:43:41.570 Two portion of this study.

NOTE Confidence: 0.8379239

00:43:41.570 --> 00:43:43.943 We chose chemo and cetuximab as a

NOTE Confidence: 0.8379239

00:43:43.943 --> 00:43:46.101 control arm because that was the

NOTE Confidence: 0.8379239

00:43:46.101 --> 00:43:47.891 regimen most patients coming off

NOTE Confidence: 0.8379239

00:43:47.891 --> 00:43:50.439 of keynote over 8 went on to an

NOTE Confidence: 0.8379239

00:43:50.439 --> 00:43:52.242 the two experimental arms are chemo

NOTE Confidence: 0.8379239

00:43:52.242 --> 00:43:54.419 and Beves is a map anitys alisme

NOTE Confidence: 0.8379239

00:43:54.419 --> 00:43:56.926 AB Inbev's is a map 216 patients

NOTE Confidence: 0.8379239

00:43:56.926 --> 00:43:59.062 will be randomized in the initial

NOTE Confidence: 0.8379239

00:43:59.062 --> 00:44:01.337 phase two part of the trial and

NOTE Confidence: 0.8379239



00:44:01.337 --> 00:44:03.390 the winner of the phase two.  
NOTE Confidence: 0.8379239

00:44:03.390 --> 00:44:05.514 Portion will then move to phase  
NOTE Confidence: 0.8379239

00:44:05.514 --> 00:44:07.377 three against the standard chemo's  
NOTE Confidence: 0.8379239

00:44:07.377 --> 00:44:09.681 attacks ARM and another 214 patients  
NOTE Confidence: 0.8379239

00:44:09.681 --> 00:44:11.741 will be randomized in phase three  
NOTE Confidence: 0.8379239

00:44:11.741 --> 00:44:13.701 for a total sample size of 430.  
NOTE Confidence: 0.8379239

00:44:13.710 --> 00:44:15.430 Expected study duration is about  
NOTE Confidence: 0.8379239

00:44:15.430 --> 00:44:17.150 four and a half years.  
NOTE Confidence: 0.8379239

00:44:17.150 --> 00:44:19.214 We expect this study to actually  
NOTE Confidence: 0.8379239

00:44:19.214 --> 00:44:20.246 be activated soon.  
NOTE Confidence: 0.8379239

00:44:20.250 --> 00:44:22.818 We are collaborating with Jeff Ishizuka  
NOTE Confidence: 0.8379239

00:44:22.818 --> 00:44:25.157 on that issue Correlatives an at  
NOTE Confidence: 0.8379239

00:44:25.157 --> 00:44:27.110 the end of the phase three portion  
NOTE Confidence: 0.8379239

00:44:27.110 --> 00:44:29.632 we hope to have a clear answer for  
NOTE Confidence: 0.8379239

00:44:29.632 --> 00:44:31.869 best second line treatment moving forward.  
NOTE Confidence: 0.8379239

00:44:31.869 --> 00:44:32.302 Uhm,

NOTE Confidence: 0.8379239

00:44:32.302 --> 00:44:36.317 that's all I have for my work here so far.

NOTE Confidence: 0.8379239

00:44:36.320 --> 00:44:39.896 I'll pass it on to Melissa.

NOTE Confidence: 0.8379239

00:44:39.900 --> 00:44:41.170 Screen sharing.

NOTE Confidence: 0.89253813

00:44:48.760 --> 00:44:50.322 Alright now and thank you.

NOTE Confidence: 0.89253813

00:44:50.322 --> 00:44:54.510 I'll try to get my screen up. Next

NOTE Confidence: 0.8404386

00:45:02.550 --> 00:45:04.532 and I am again I want to

NOTE Confidence: 0.8404386

00:45:04.532 --> 00:45:05.640 thank everyone here for

NOTE Confidence: 0.8404386

00:45:05.707 --> 00:45:07.407 the opportunity to discuss.

NOTE Confidence: 0.8404386

00:45:07.410 --> 00:45:09.346 It's such an honor to be able to

NOTE Confidence: 0.8404386

00:45:09.346 --> 00:45:11.191 speak in combination with Doctor

NOTE Confidence: 0.8404386

00:45:11.191 --> 00:45:12.915 Burtness and Doctor Bhatia,

NOTE Confidence: 0.8404386

00:45:12.920 --> 00:45:15.368 and I look forward to the years that we

NOTE Confidence: 0.8404386

00:45:15.368 --> 00:45:17.756 have in the future to continue these

NOTE Confidence: 0.8404386

00:45:17.756 --> 00:45:20.050 projects that we're all excited about.

NOTE Confidence: 0.8404386

00:45:20.050 --> 00:45:23.040 Part of what I wanted to do today in terms

NOTE Confidence: 0.8404386

00:45:23.119 --> 00:45:26.255 of my brief presentation was to really also.

NOTE Confidence: 0.8404386

00:45:26.260 --> 00:45:27.845 While we're focusing a lot

NOTE Confidence: 0.8404386

00:45:27.845 --> 00:45:29.840 on the head and neck dart,

NOTE Confidence: 0.8404386

00:45:29.840 --> 00:45:32.440 Anan the spore that we have funding for,

NOTE Confidence: 0.8404386

00:45:32.440 --> 00:45:34.150 and how we're incorporating that

NOTE Confidence: 0.8404386

00:45:34.150 --> 00:45:35.860 to the clinical trial progression

NOTE Confidence: 0.8404386

00:45:35.913 --> 00:45:37.683 at Yale didn't want to discount

NOTE Confidence: 0.8404386

00:45:37.683 --> 00:45:39.248 the the contribution that the

NOTE Confidence: 0.8404386

00:45:39.248 --> 00:45:40.888 radiation oncology Dart also does.

NOTE Confidence: 0.8404386

00:45:40.890 --> 00:45:42.615 And we work very collaboratively

NOTE Confidence: 0.8404386

00:45:42.615 --> 00:45:43.650 collaboratively between the

NOTE Confidence: 0.8404386

00:45:43.650 --> 00:45:44.789 two organizations and arts,

NOTE Confidence: 0.8404386

00:45:44.790 --> 00:45:47.294 so I wanted to kind of highlight some

NOTE Confidence: 0.8404386

00:45:47.294 --> 00:45:49.987 of the trials that we do have open,

NOTE Confidence: 0.8404386

00:45:49.990 --> 00:45:52.006 and some of the hope that that

NOTE Confidence: 0.8404386

00:45:52.006 --> 00:45:54.209 will be able to help contribute,

NOTE Confidence: 0.8404386

00:45:54.210 --> 00:45:56.866 both with supporting the head and neck dart.

NOTE Confidence: 0.8404386

00:45:56.870 --> 00:45:59.374 But also with the head and neck score,

NOTE Confidence: 0.8404386

00:45:59.380 --> 00:46:01.592 I have no disclosures and I am

NOTE Confidence: 0.8404386

00:46:01.592 --> 00:46:04.088 not going to spend a lot of time.

NOTE Confidence: 0.8404386

00:46:04.090 --> 00:46:06.916 I know we're running a little short on time,

NOTE Confidence: 0.8404386

00:46:06.920 --> 00:46:08.873 but as everyone here knows that you

NOTE Confidence: 0.8404386

00:46:08.873 --> 00:46:10.750 know head and neck squamous cell

NOTE Confidence: 0.8404386

00:46:10.750 --> 00:46:13.025 carcinoma is very common with at least

NOTE Confidence: 0.8404386

00:46:13.086 --> 00:46:15.036 64,000 cases in the United States

NOTE Confidence: 0.8404386

00:46:15.036 --> 00:46:17.402 and this is reiterating some of what

NOTE Confidence: 0.8404386

00:46:17.402 --> 00:46:19.172 Doctor Burtness had previously already

NOTE Confidence: 0.8404386

00:46:19.172 --> 00:46:21.297 mentioned is that the head and neck

NOTE Confidence: 0.8404386

00:46:21.297 --> 00:46:23.016 location of cancer is very sensitive

NOTE Confidence: 0.8404386

00:46:23.016 --> 00:46:25.144 part of the body and it's very

NOTE Confidence: 0.8404386

00:46:25.144 --> 00:46:27.330 important with how we interact with society.

NOTE Confidence: 0.8404386

00:46:27.330 --> 00:46:28.548 Maintain nutrition, communicate.  
NOTE Confidence: 0.8404386

00:46:28.548 --> 00:46:29.766 Anan, it's what,  
NOTE Confidence: 0.8404386

00:46:29.770 --> 00:46:31.366 especially in a pandemic.  
NOTE Confidence: 0.8404386

00:46:31.366 --> 00:46:34.329 How we visualize each other to how we,  
NOTE Confidence: 0.8404386

00:46:34.330 --> 00:46:37.370 how we see each other and communicate orally.  
NOTE Confidence: 0.8404386

00:46:37.370 --> 00:46:39.519 So currently as we know that in  
NOTE Confidence: 0.8404386

00:46:39.519 --> 00:46:41.454 order to provide curative treatment  
NOTE Confidence: 0.8404386

00:46:41.454 --> 00:46:43.829 for people who are nonmetastatic,  
NOTE Confidence: 0.8404386

00:46:43.830 --> 00:46:46.702 that is usually some form of local therapy  
NOTE Confidence: 0.8404386

00:46:46.702 --> 00:46:49.148 which may be surgery or radiation,  
NOTE Confidence: 0.8404386

00:46:49.150 --> 00:46:51.430 or sometimes a combination of both,  
NOTE Confidence: 0.8404386

00:46:51.430 --> 00:46:53.710 which carries a lot of potential  
NOTE Confidence: 0.8404386

00:46:53.710 --> 00:46:55.230 risk for functional impairment.  
NOTE Confidence: 0.8404386

00:46:55.230 --> 00:46:57.510 Whether it's related to surgical changes,  
NOTE Confidence: 0.8404386

00:46:57.510 --> 00:46:59.988 scar tissue from both, surgery radiation.  
NOTE Confidence: 0.8404386

00:46:59.990 --> 00:47:01.868 I'm swallowing dysfunction pain dry mouth.

NOTE Confidence: 0.8404386

00:47:01.870 --> 00:47:02.532 You know,

NOTE Confidence: 0.8404386

00:47:02.532 --> 00:47:04.187 complications that can arise from

NOTE Confidence: 0.8404386

00:47:04.187 --> 00:47:06.102 dental health and other things that

NOTE Confidence: 0.8404386

00:47:06.102 --> 00:47:07.836 that come down the line after.

NOTE Confidence: 0.8404386

00:47:07.840 --> 00:47:09.718 As a consequence of the curative

NOTE Confidence: 0.8404386

00:47:09.718 --> 00:47:10.344 intent treatment.

NOTE Confidence: 0.8404386

00:47:10.350 --> 00:47:12.240 So while patients may be cured,

NOTE Confidence: 0.8404386

00:47:12.240 --> 00:47:14.556 they could be left with lifelong

NOTE Confidence: 0.8404386

00:47:14.556 --> 00:47:16.418 implications of their treatment and

NOTE Confidence: 0.8404386

00:47:16.418 --> 00:47:18.695 some of the goals that we have both at

NOTE Confidence: 0.8404386

00:47:18.762 --> 00:47:20.785 Yale but also across the country in

NOTE Confidence: 0.8404386

00:47:20.785 --> 00:47:23.005 the world or to understand how we can

NOTE Confidence: 0.8404386

00:47:23.005 --> 00:47:25.141 try to reduce the morbidity of that

NOTE Confidence: 0.8404386

00:47:25.141 --> 00:47:26.986 treatment without compromising cure rates.

NOTE Confidence: 0.8404386

00:47:26.990 --> 00:47:27.884 But also importantly,

NOTE Confidence: 0.8404386

00:47:27.884 --> 00:47:29.970 we still have a long ways to  
NOTE Confidence: 0.8404386

00:47:30.031 --> 00:47:31.696 go in certain disease sites.  
NOTE Confidence: 0.8404386

00:47:31.700 --> 00:47:33.692 We've already heard a lot about  
NOTE Confidence: 0.8404386

00:47:33.692 --> 00:47:35.020 the P-16 negative population.  
NOTE Confidence: 0.8404386

00:47:35.020 --> 00:47:36.812 And and disease resistance.  
NOTE Confidence: 0.8404386

00:47:36.812 --> 00:47:39.500 And how can we overcome treatment  
NOTE Confidence: 0.8404386

00:47:39.580 --> 00:47:42.040 resistance but also prevent further  
NOTE Confidence: 0.8404386

00:47:42.040 --> 00:47:45.389 morbidity of the treatment that we provide?  
NOTE Confidence: 0.8404386

00:47:45.390 --> 00:47:47.959 Some of what's been touched on already,  
NOTE Confidence: 0.8404386

00:47:47.960 --> 00:47:50.162 as is the importance in recognition  
NOTE Confidence: 0.8404386

00:47:50.162 --> 00:47:51.630 of immune checkpoint inhibitors.  
NOTE Confidence: 0.8404386

00:47:51.630 --> 00:47:53.682 Certainly other disease sites and FDA  
NOTE Confidence: 0.8404386

00:47:53.682 --> 00:47:56.029 approvals have come along showing activity.  
NOTE Confidence: 0.8404386

00:47:56.030 --> 00:47:57.878 An other disease sites and we  
NOTE Confidence: 0.8404386

00:47:57.878 --> 00:47:59.110 now see data showing  
NOTE Confidence: 0.8281421

00:47:59.180 --> 00:48:01.305 the efficacy that immune checkpoint

NOTE Confidence: 0.8281421

00:48:01.305 --> 00:48:03.005 inhibitors appear to have,

NOTE Confidence: 0.8281421

00:48:03.010 --> 00:48:05.206 both also in head and neck

NOTE Confidence: 0.8281421

00:48:05.206 --> 00:48:06.978 cancer as well, and therefore,

NOTE Confidence: 0.8281421

00:48:06.978 --> 00:48:09.650 while a lot of initial data has indicated

NOTE Confidence: 0.8281421

00:48:09.718 --> 00:48:11.808 efficacy in the metastatic setting,

NOTE Confidence: 0.8281421

00:48:11.810 --> 00:48:13.784 we're also now looking to see

NOTE Confidence: 0.8281421

00:48:13.784 --> 00:48:16.090 how this might be incorporated.

NOTE Confidence: 0.8281421

00:48:16.090 --> 00:48:18.250 In the upfront definitive setting

NOTE Confidence: 0.8281421

00:48:18.250 --> 00:48:20.956 and whether or not that might

NOTE Confidence: 0.8281421

00:48:20.956 --> 00:48:23.306 also provide some opportunity for

NOTE Confidence: 0.8281421

00:48:23.306 --> 00:48:26.020 either reduced dose of radiation,

NOTE Confidence: 0.8281421

00:48:26.020 --> 00:48:28.390 reduced need for cytotoxic chemotherapy,

NOTE Confidence: 0.8281421

00:48:28.390 --> 00:48:31.609 but still maintaining.

NOTE Confidence: 0.8281421

00:48:31.610 --> 00:48:33.310 Equivalent cure rates as to

NOTE Confidence: 0.8281421

00:48:33.310 --> 00:48:34.670 what we already have,

NOTE Confidence: 0.8281421



00:48:34.670 --> 00:48:36.958 so a lot of these trials are now  
NOTE Confidence: 0.8281421

00:48:36.958 --> 00:48:39.089 moving into the definitive setting,  
NOTE Confidence: 0.8281421

00:48:39.090 --> 00:48:40.470 looking at multiple different  
NOTE Confidence: 0.8281421

00:48:40.470 --> 00:48:41.505 immune checkpoint inhibitors  
NOTE Confidence: 0.8281421

00:48:41.505 --> 00:48:43.170 that I've got listed here.  
NOTE Confidence: 0.8281421

00:48:43.170 --> 00:48:44.910 Some of the former trials that  
NOTE Confidence: 0.8281421

00:48:44.910 --> 00:48:47.267 we are now in in either actively  
NOTE Confidence: 0.8281421

00:48:47.267 --> 00:48:49.523 enrolling on through the head and  
NOTE Confidence: 0.8281421

00:48:49.523 --> 00:48:52.005 neck through the head and neck DART,  
NOTE Confidence: 0.8281421

00:48:52.010 --> 00:48:54.050 but also previously open trials that  
NOTE Confidence: 0.8281421

00:48:54.050 --> 00:48:56.090 are now in their follow-up phase,  
NOTE Confidence: 0.8281421

00:48:56.090 --> 00:48:57.946 have used immune checkpoint inhibitors  
NOTE Confidence: 0.8281421

00:48:57.946 --> 00:48:59.841 in the upfront setting whether  
NOTE Confidence: 0.8281421

00:48:59.841 --> 00:49:02.020 it was in keynote for 12, where.  
NOTE Confidence: 0.8281421

00:49:02.020 --> 00:49:04.470 Checkpoint inhibitor Kimbrough was added  
NOTE Confidence: 0.8281421

00:49:04.470 --> 00:49:06.430 in conjunction with CHEMORADIATION

NOTE Confidence: 0.8281421

00:49:06.496 --> 00:49:08.530 but also in the maintenance phase.

NOTE Confidence: 0.8281421

00:49:08.530 --> 00:49:10.828 We are currently enrolling on the

NOTE Confidence: 0.8281421

00:49:10.828 --> 00:49:13.183 ikago Akron 3161 that is looking

NOTE Confidence: 0.8281421

00:49:13.183 --> 00:49:15.815 at addition of at atrovent you know

NOTE Confidence: 0.8281421

00:49:15.815 --> 00:49:18.663 therapy after an initial phase of

NOTE Confidence: 0.8281421

00:49:18.663 --> 00:49:20.103 definitive chemoradiotherapy and

NOTE Confidence: 0.8281421

00:49:20.103 --> 00:49:22.634 there have been some phase one

NOTE Confidence: 0.8281421

00:49:22.634 --> 00:49:24.980 trials including H NO3 that have

NOTE Confidence: 0.8281421

00:49:25.060 --> 00:49:27.130 looked at how immunotherapy may

NOTE Confidence: 0.8281421

00:49:27.130 --> 00:49:30.265 play some role and also safety and

NOTE Confidence: 0.8281421

00:49:30.265 --> 00:49:32.735 the adjuvant setting after surgery.

NOTE Confidence: 0.8281421

00:49:32.740 --> 00:49:35.309 One of the trials that we currently

NOTE Confidence: 0.8281421

00:49:35.309 --> 00:49:37.362 have open through the radiation

NOTE Confidence: 0.8281421

00:49:37.362 --> 00:49:39.984 oncology DART is looking at how

NOTE Confidence: 0.8281421

00:49:39.984 --> 00:49:41.814 immunotherapy may perhaps improve

NOTE Confidence: 0.8281421

00:49:41.814 --> 00:49:44.466 efficacy in a high risk population.

NOTE Confidence: 0.8281421

00:49:44.470 --> 00:49:45.242 So specifically,

NOTE Confidence: 0.8281421

00:49:45.242 --> 00:49:47.944 this is looking at patients who have

NOTE Confidence: 0.8281421

00:49:47.944 --> 00:49:50.244 positive margin or extranodal extension

NOTE Confidence: 0.8281421

00:49:50.244 --> 00:49:52.549 after initial surgical resection of

NOTE Confidence: 0.8281421

00:49:52.549 --> 00:49:54.949 locally advanced head and neck cancer,

NOTE Confidence: 0.8281421

00:49:54.950 --> 00:49:57.045 and patients are currently standard

NOTE Confidence: 0.8281421

00:49:57.045 --> 00:49:59.140 of care is radiation cisplatin,

NOTE Confidence: 0.8281421

00:49:59.140 --> 00:50:01.840 but this is now heading into

NOTE Confidence: 0.8281421

00:50:01.840 --> 00:50:03.640 the phase three design.

NOTE Confidence: 0.8281421

00:50:03.640 --> 00:50:05.873 An activation and this is now exploring

NOTE Confidence: 0.8281421

00:50:05.873 --> 00:50:07.705 the combination of Docetaxel subtaxa

NOTE Confidence: 0.8281421

00:50:07.705 --> 00:50:09.740 map with radiotherapy versus cisplatin

NOTE Confidence: 0.8281421

00:50:09.740 --> 00:50:11.959 with the addition of immunotherapy,

NOTE Confidence: 0.8281421

00:50:11.960 --> 00:50:13.850 this one being a tease.

NOTE Confidence: 0.8281421

00:50:13.850 --> 00:50:15.740 Oh, and this has been.

NOTE Confidence: 0.8281421

00:50:15.740 --> 00:50:17.248 Unfortunately, I must admit,

NOTE Confidence: 0.8281421

00:50:17.248 --> 00:50:20.272 a high accruing trial. In part, I think.

NOTE Confidence: 0.8281421

00:50:20.272 --> 00:50:23.824 Again, we're seeing this.

NOTE Confidence: 0.8281421

00:50:23.824 --> 00:50:28.056 A phenomenon of increased.

NOTE Confidence: 0.8281421

00:50:28.060 --> 00:50:28.873 Higher stage disease,

NOTE Confidence: 0.8281421

00:50:28.873 --> 00:50:29.957 more locally advanced disease,

NOTE Confidence: 0.8281421

00:50:29.960 --> 00:50:31.857 especially as patients have have had maybe

NOTE Confidence: 0.8281421

00:50:31.857 --> 00:50:33.770 some delays in their care from COVID.

NOTE Confidence: 0.8281421

00:50:33.770 --> 00:50:34.874 And so we have.

NOTE Confidence: 0.8281421

00:50:34.874 --> 00:50:36.254 We have actually been accruing

NOTE Confidence: 0.8281421

00:50:36.254 --> 00:50:38.119 to this at a rather high rate,

NOTE Confidence: 0.8281421

00:50:38.120 --> 00:50:41.540 and we look forward to the results to come.

NOTE Confidence: 0.8281421

00:50:41.540 --> 00:50:45.769 We are also, as I alluded to, looking at how.

NOTE Confidence: 0.8281421

00:50:45.770 --> 00:50:47.798 We might be able to improve

NOTE Confidence: 0.8281421

00:50:47.798 --> 00:50:48.812 our definitive intent,

NOTE Confidence: 0.8281421

00:50:48.820 --> 00:50:50.108 and there's certain populations  
NOTE Confidence: 0.8281421

00:50:50.108 --> 00:50:52.550 where we have some room to improve,  
NOTE Confidence: 0.8281421

00:50:52.550 --> 00:50:54.572 and one of that population is  
NOTE Confidence: 0.8281421

00:50:54.572 --> 00:50:56.315 a cisplatin ineligible group of  
NOTE Confidence: 0.8281421

00:50:56.315 --> 00:50:58.307 patients has already been alluded to,  
NOTE Confidence: 0.8281421

00:50:58.310 --> 00:51:01.700 so I won't get into the details of the data.  
NOTE Confidence: 0.8281421

00:51:01.700 --> 00:51:03.400 But as was previously mentioned,  
NOTE Confidence: 0.8281421

00:51:03.400 --> 00:51:06.104 so tuck some AB does have some improvement.  
NOTE Confidence: 0.8281421

00:51:06.110 --> 00:51:08.144 The Bonner Trials had indicated some  
NOTE Confidence: 0.8281421

00:51:08.144 --> 00:51:09.500 improvement over radiotherapy alone,  
NOTE Confidence: 0.8281421

00:51:09.500 --> 00:51:11.200 but when compared to cisplatin,  
NOTE Confidence: 0.8281421

00:51:11.200 --> 00:51:12.028 it is inferior,  
NOTE Confidence: 0.8281421

00:51:12.028 --> 00:51:13.960 although we do have that group of  
NOTE Confidence: 0.8304057

00:51:14.024 --> 00:51:15.660 patients that are ineligible  
NOTE Confidence: 0.8304057

00:51:15.660 --> 00:51:17.296 for cisplatin instaed eczema,  
NOTE Confidence: 0.8304057

00:51:17.300 --> 00:51:20.037 maybe that that therapy that we have.

NOTE Confidence: 0.8304057

00:51:20.040 --> 00:51:22.504 And so H&O four is now looking at

NOTE Confidence: 0.8304057

00:51:22.504 --> 00:51:25.051 whether or not we can take those

NOTE Confidence: 0.8304057

00:51:25.051 --> 00:51:26.906 patients who are ineligible for

NOTE Confidence: 0.8304057

00:51:26.984 --> 00:51:29.784 cisplatin and compare how they might do.

NOTE Confidence: 0.8304057

00:51:29.790 --> 00:51:31.590 And compared to Subtaxa ma'am.

NOTE Confidence: 0.8304057

00:51:31.590 --> 00:51:34.839 So this is using a derbe as an immunotherapy,

NOTE Confidence: 0.8304057

00:51:34.840 --> 00:51:37.017 and whether or not this might also

NOTE Confidence: 0.8304057

00:51:37.017 --> 00:51:38.362 provide meaningful outcomes help

NOTE Confidence: 0.8304057

00:51:38.362 --> 00:51:39.430 radiosensitizing those patients

NOTE Confidence: 0.8304057

00:51:39.430 --> 00:51:41.210 who are not otherwise eligible

NOTE Confidence: 0.8304057

00:51:41.210 --> 00:51:42.780 for cytotoxic chemotherapy.

NOTE Confidence: 0.8304057

00:51:42.780 --> 00:51:45.307 This is open to more advanced P.

NOTE Confidence: 0.8304057

00:51:45.310 --> 00:51:48.198 16 and higher risk P 16 positive population,

NOTE Confidence: 0.8304057

00:51:48.200 --> 00:51:50.360 but also the P-16 negative population.

NOTE Confidence: 0.8304057

00:51:50.360 --> 00:51:53.370 Both stage three and stage four cancers.

NOTE Confidence: 0.8304057

00:51:53.370 --> 00:51:55.674 I mean and also a trial that we  
NOTE Confidence: 0.8304057

00:51:55.674 --> 00:51:57.895 have been enrolling on with at  
NOTE Confidence: 0.8304057

00:51:57.895 --> 00:51:59.860 least about 7 patients currently  
NOTE Confidence: 0.8304057

00:51:59.860 --> 00:52:02.508 on study and in its current state.  
NOTE Confidence: 0.8304057

00:52:02.510 --> 00:52:03.530 And then lastly,  
NOTE Confidence: 0.8304057

00:52:03.530 --> 00:52:05.230 in terms of the intensification,  
NOTE Confidence: 0.8304057

00:52:05.230 --> 00:52:07.012 it is certainly one of our  
NOTE Confidence: 0.8304057

00:52:07.012 --> 00:52:09.309 goals as is also been mentioned,  
NOTE Confidence: 0.8304057

00:52:09.310 --> 00:52:10.462 the HPV population.  
NOTE Confidence: 0.8304057

00:52:10.462 --> 00:52:13.150 Has been recognized as having a better  
NOTE Confidence: 0.8304057

00:52:13.218 --> 00:52:15.480 prognosis than that of the P-16  
NOTE Confidence: 0.8304057

00:52:15.480 --> 00:52:17.590 population and across the country.  
NOTE Confidence: 0.8304057

00:52:17.590 --> 00:52:20.117 We're now trying to tease out how.  
NOTE Confidence: 0.8304057

00:52:20.120 --> 00:52:22.752 How might we be able to safely D  
NOTE Confidence: 0.8304057

00:52:22.752 --> 00:52:25.528 intensify in therapy and the ikago Akron,  
NOTE Confidence: 0.8304057

00:52:25.530 --> 00:52:27.696 3311, or this I should say,

NOTE Confidence: 0.8304057

00:52:27.700 --> 00:52:30.451 the COGS 3311 is kind of one

NOTE Confidence: 0.8304057

00:52:30.451 --> 00:52:33.292 example of where there might be

NOTE Confidence: 0.8304057

00:52:33.292 --> 00:52:35.388 some opportunity to reduce.

NOTE Confidence: 0.8304057

00:52:35.390 --> 00:52:35.704 Treatment,

NOTE Confidence: 0.8304057

00:52:35.704 --> 00:52:37.902 but the outcomes and the number of

NOTE Confidence: 0.8304057

00:52:37.902 --> 00:52:40.365 failures are low because this is a

NOTE Confidence: 0.8304057

00:52:40.365 --> 00:52:41.785 relatively good prognosis population,

NOTE Confidence: 0.8304057

00:52:41.790 --> 00:52:44.051 so we have to think about this

NOTE Confidence: 0.8304057

00:52:44.051 --> 00:52:45.811 meaningfully and carefully and whether

NOTE Confidence: 0.8304057

00:52:45.811 --> 00:52:47.995 or not that's some combination of

NOTE Confidence: 0.8304057

00:52:47.995 --> 00:52:49.716 reducing radiation dose whether or

NOTE Confidence: 0.8304057

00:52:49.716 --> 00:52:51.588 not it's a combination of surgery

NOTE Confidence: 0.8304057

00:52:51.588 --> 00:52:52.908 with reduced radiation dose.

NOTE Confidence: 0.8304057

00:52:52.908 --> 00:52:55.260 I'm not going to be talking about

NOTE Confidence: 0.8304057

00:52:55.322 --> 00:52:57.252 any kind of induction, you know,

NOTE Confidence: 0.8304057



00:52:57.252 --> 00:52:59.148 systemic therapy followed by your dose

NOTE Confidence: 0.8304057

00:52:59.148 --> 00:53:01.338 reduced or risk adjusted local therapy,

NOTE Confidence: 0.8304057

00:53:01.340 --> 00:53:03.446 but certainly a lot of different

NOTE Confidence: 0.8304057

00:53:03.446 --> 00:53:06.160 ways in which this could be explored.

NOTE Confidence: 0.8304057

00:53:06.160 --> 00:53:09.985 And we are going to be looking to move.

NOTE Confidence: 0.8304057

00:53:09.990 --> 00:53:12.979 We're moving to open H and O5,

NOTE Confidence: 0.8304057

00:53:12.980 --> 00:53:15.955 which is looking at our low risk.

NOTE Confidence: 0.8304057

00:53:15.960 --> 00:53:17.238 P-16 population today.

NOTE Confidence: 0.8304057

00:53:17.238 --> 00:53:18.090 Intensified protocol,

NOTE Confidence: 0.8304057

00:53:18.090 --> 00:53:21.261 kind of as a jumping point from

NOTE Confidence: 0.8304057

00:53:21.261 --> 00:53:23.379 previously published results of H

NOTE Confidence: 0.8304057

00:53:23.379 --> 00:53:25.419 and O2 that had shown reasonably

NOTE Confidence: 0.8304057

00:53:25.419 --> 00:53:27.459 good to your progression.

NOTE Confidence: 0.8304057

00:53:27.460 --> 00:53:30.470 Free survival of 90% with the instead

NOTE Confidence: 0.8304057

00:53:30.470 --> 00:53:33.419 of our typical 70 Gy of radiation.

NOTE Confidence: 0.8304057

00:53:33.420 --> 00:53:35.720 Instead 60 Gy radiation with

NOTE Confidence: 0.8304057

00:53:35.720 --> 00:53:37.560 cisplatin omitting the cisplatin

NOTE Confidence: 0.8304057

00:53:37.560 --> 00:53:40.121 did did cross to lower progression

NOTE Confidence: 0.8304057

00:53:40.121 --> 00:53:41.339 free survival so.

NOTE Confidence: 0.8304057

00:53:41.340 --> 00:53:41.623 Hi,

NOTE Confidence: 0.8304057

00:53:41.623 --> 00:53:43.887 no five is looking to keep the 60

NOTE Confidence: 0.8304057

00:53:43.887 --> 00:53:46.064 Gray with cisplatin arm but also

NOTE Confidence: 0.8304057

00:53:46.064 --> 00:53:48.399 then looking at a somewhat escalated

NOTE Confidence: 0.8304057

00:53:48.399 --> 00:53:50.155 or hyper accelerated radiation

NOTE Confidence: 0.8304057

00:53:50.155 --> 00:53:53.102 delivery of 60 Gray over 5 weeks

NOTE Confidence: 0.8304057

00:53:53.102 --> 00:53:54.982 with the addition of immunotherapy

NOTE Confidence: 0.8304057

00:53:54.982 --> 00:53:57.394 to compare how that may may relate

NOTE Confidence: 0.8304057

00:53:57.394 --> 00:53:59.711 to the standard of care 70 grain

NOTE Confidence: 0.8304057

00:53:59.711 --> 00:54:02.255 cisplatin versus 60 Gray and cisplatin.

NOTE Confidence: 0.8304057

00:54:02.260 --> 00:54:04.885 So we do look forward to opening

NOTE Confidence: 0.8304057

00:54:04.885 --> 00:54:06.711 this specific population that we

NOTE Confidence: 0.8304057

00:54:06.711 --> 00:54:08.923 don't have a lot of trial opportunity

NOTE Confidence: 0.8304057

00:54:08.923 --> 00:54:11.073 in clinical trial opportunity and

NOTE Confidence: 0.8304057

00:54:11.073 --> 00:54:12.399 look forward to.

NOTE Confidence: 0.8304057

00:54:12.400 --> 00:54:14.935 To providing more options and

NOTE Confidence: 0.8304057

00:54:14.935 --> 00:54:16.963 contributing to important questions

NOTE Confidence: 0.8304057

00:54:16.963 --> 00:54:18.880 nationally and internationally.

NOTE Confidence: 0.8304057

00:54:18.880 --> 00:54:19.396 And then,

NOTE Confidence: 0.8304057

00:54:19.396 --> 00:54:21.460 in terms of the future goals for our

NOTE Confidence: 0.8304057

00:54:21.522 --> 00:54:23.138 therapeutic radiation oncology dart

NOTE Confidence: 0.8304057

00:54:23.138 --> 00:54:25.562 in combination with how we interface

NOTE Confidence: 0.8559582

00:54:25.625 --> 00:54:26.915 with all of the other

NOTE Confidence: 0.8559582

00:54:26.915 --> 00:54:28.205 darts that we work with.

NOTE Confidence: 0.8559582

00:54:28.210 --> 00:54:29.740 But today specifically the head

NOTE Confidence: 0.8559582

00:54:29.740 --> 00:54:31.630 in our head and neck dart,

NOTE Confidence: 0.8559582

00:54:31.630 --> 00:54:33.639 you know our goal is to continue

NOTE Confidence: 0.8559582

00:54:33.639 --> 00:54:35.442 to collaborate with this for a

NOTE Confidence: 0.8559582

00:54:35.442 --> 00:54:37.200 lot of the physicians that doctor

NOTE Confidence: 0.8559582

00:54:37.200 --> 00:54:38.583 Burtness had previously indicated

NOTE Confidence: 0.8559582

00:54:38.583 --> 00:54:40.647 at the beginning of her slides,

NOTE Confidence: 0.8559582

00:54:40.650 --> 00:54:42.911 there were at least six physicians just

NOTE Confidence: 0.8559582

00:54:42.911 --> 00:54:44.521 from radiation oncology faculty alone

NOTE Confidence: 0.8559582

00:54:44.521 --> 00:54:46.558 who are part of this combined effort.

NOTE Confidence: 0.8559582

00:54:46.560 --> 00:54:48.772 We have a lot of clinician scientists

NOTE Confidence: 0.8559582

00:54:48.772 --> 00:54:50.660 who are actively engaged in DNA.

NOTE Confidence: 0.8559582

00:54:50.660 --> 00:54:53.332 Repair and how we might be able to

NOTE Confidence: 0.8559582

00:54:53.332 --> 00:54:55.640 improve outcomes in this fits nicely with

NOTE Confidence: 0.8559582

00:54:55.640 --> 00:54:58.069 the purpose and an goal of the head.

NOTE Confidence: 0.8559582

00:54:58.070 --> 00:54:59.036 And next four,

NOTE Confidence: 0.8559582

00:54:59.036 --> 00:55:00.968 and will also be continuing toward

NOTE Confidence: 0.8559582

00:55:00.968 --> 00:55:03.253 to support the head and neck dart

NOTE Confidence: 0.8559582

00:55:03.253 --> 00:55:05.150 with the trials that were able

NOTE Confidence: 0.8559582

00:55:05.150 --> 00:55:07.078 to open our resources as well.

NOTE Confidence: 0.8559582

00:55:07.078 --> 00:55:09.332 Also, we want to continue to open

NOTE Confidence: 0.8559582

00:55:09.332 --> 00:55:10.992 cooperative group trials that will

NOTE Confidence: 0.8559582

00:55:10.992 --> 00:55:13.204 align with the needs of our patient

NOTE Confidence: 0.8559582

00:55:13.204 --> 00:55:14.844 population here in Connecticut and

NOTE Confidence: 0.8559582

00:55:14.844 --> 00:55:17.056 continue to assess that and make sure

NOTE Confidence: 0.8559582

00:55:17.060 --> 00:55:18.926 that we're opening trials that are

NOTE Confidence: 0.8559582

00:55:18.926 --> 00:55:20.610 appropriate for our Community efforts.

NOTE Confidence: 0.8559582

00:55:20.610 --> 00:55:21.879 And then lastly,

NOTE Confidence: 0.8559582

00:55:21.879 --> 00:55:23.994 is was also alluded to.

NOTE Confidence: 0.8559582

00:55:24.000 --> 00:55:26.520 Outcomes are better at high volume centers,

NOTE Confidence: 0.8559582

00:55:26.520 --> 00:55:28.935 so as we continue to expand an

NOTE Confidence: 0.8559582

00:55:28.935 --> 00:55:30.839 need to serve a greater,

NOTE Confidence: 0.8559582

00:55:30.840 --> 00:55:32.515 expensive community across the entire

NOTE Confidence: 0.8559582

00:55:32.515 --> 00:55:34.800 state of Connecticut and our department,

NOTE Confidence: 0.8559582

00:55:34.800 --> 00:55:37.159 we are working very vigorously of maintaining

NOTE Confidence: 0.8559582

00:55:37.159 --> 00:55:39.838 high quality at our care center specifically.

NOTE Confidence: 0.8559582

00:55:39.840 --> 00:55:41.640 Really water for Dan Trumbull.

NOTE Confidence: 0.8559582

00:55:41.640 --> 00:55:43.800 In addition to our main campus

NOTE Confidence: 0.8559582

00:55:43.800 --> 00:55:45.240 here in New Haven.

NOTE Confidence: 0.8559582

00:55:45.240 --> 00:55:47.655 So we have extensive efforts in standardizing

NOTE Confidence: 0.8559582

00:55:47.655 --> 00:55:49.200 our radiation treatment planning,

NOTE Confidence: 0.8559582

00:55:49.200 --> 00:55:51.720 ensuring we have quality across the system.

NOTE Confidence: 0.8559582

00:55:51.720 --> 00:55:54.240 How we do that is multi factorial,

NOTE Confidence: 0.8559582

00:55:54.240 --> 00:55:55.960 but certainly we have peer

NOTE Confidence: 0.8559582

00:55:55.960 --> 00:55:58.200 review of all of our cases.

NOTE Confidence: 0.8559582

00:55:58.200 --> 00:55:58.532 We've.

NOTE Confidence: 0.8559582

00:55:58.532 --> 00:56:00.524 Do them regularly whether patients are

NOTE Confidence: 0.8559582

00:56:00.524 --> 00:56:03.188 on or off clinical trial to make sure

NOTE Confidence: 0.8559582

00:56:03.188 --> 00:56:05.340 that we have and maintain quality.

NOTE Confidence: 0.8559582

00:56:05.340 --> 00:56:06.705 All the physicians that participate

NOTE Confidence: 0.8559582

00:56:06.705 --> 00:56:08.955 in any head and neck treatment under  
NOTE Confidence: 0.8559582

00:56:08.955 --> 00:56:10.615 satellite through also attending  
NOTE Confidence: 0.8559582

00:56:10.615 --> 00:56:12.275 these multidisciplinary tumor boards  
NOTE Confidence: 0.8559582

00:56:12.327 --> 00:56:14.343 and and many of us also attend  
NOTE Confidence: 0.8559582

00:56:14.343 --> 00:56:15.533 multidisciplinary clinics as well.  
NOTE Confidence: 0.8559582

00:56:15.533 --> 00:56:17.471 So we're very engaged with with  
NOTE Confidence: 0.8559582

00:56:17.471 --> 00:56:19.160 the head and neck team.  
NOTE Confidence: 0.8674745

00:56:23.950 --> 00:56:26.100 Like any of the cooperative groups  
NOTE Confidence: 0.8674745

00:56:26.100 --> 00:56:27.900 that have external review required  
NOTE Confidence: 0.8674745

00:56:27.957 --> 00:56:29.865 as part of our radiation planning,  
NOTE Confidence: 0.8674745

00:56:29.870 --> 00:56:31.605 have have identified no concerns  
NOTE Confidence: 0.8674745

00:56:31.605 --> 00:56:32.993 with our radiation planning.  
NOTE Confidence: 0.8674745

00:56:33.000 --> 00:56:33.975 And then lastly,  
NOTE Confidence: 0.8674745

00:56:33.975 --> 00:56:36.637 I think one of the things that is  
NOTE Confidence: 0.8674745

00:56:36.637 --> 00:56:38.863 important is that we work very hard  
NOTE Confidence: 0.8674745

00:56:38.863 --> 00:56:41.890 to make sure that we have the clinical

NOTE Confidence: 0.8674745

00:56:41.890 --> 00:56:43.788 support services that are key.

NOTE Confidence: 0.8674745

00:56:43.788 --> 00:56:45.527 So the speech, language, pathology,

NOTE Confidence: 0.8674745

00:56:45.527 --> 00:56:47.609 the social work that was mentioned,

NOTE Confidence: 0.8674745

00:56:47.610 --> 00:56:49.595 the surgical resources and expert

NOTE Confidence: 0.8674745

00:56:49.595 --> 00:56:52.447 experts on site so that we can

NOTE Confidence: 0.8674745

00:56:52.447 --> 00:56:54.027 make sure to appropriately.

NOTE Confidence: 0.8674745

00:56:54.030 --> 00:56:55.650 I'm triage our patience is as

NOTE Confidence: 0.8674745

00:56:55.650 --> 00:56:57.320 they go through their treatment,

NOTE Confidence: 0.8674745

00:56:57.320 --> 00:56:59.060 but also have the same high

NOTE Confidence: 0.8674745

00:56:59.060 --> 00:57:00.220 quality surveillance and and

NOTE Confidence: 0.8674745

00:57:00.273 --> 00:57:02.373 also support as they are in their

NOTE Confidence: 0.8674745

00:57:02.373 --> 00:57:03.900 survivorship from heaven and cancer.

NOTE Confidence: 0.8674745

00:57:03.900 --> 00:57:04.713 And I'll combine.

NOTE Confidence: 0.8674745

00:57:04.713 --> 00:57:06.994 I think this will help continue to improve

NOTE Confidence: 0.8674745

00:57:06.994 --> 00:57:09.276 access as well as improved clinical trial,

NOTE Confidence: 0.8674745



00:57:09.280 --> 00:57:10.174 trial, enrollment everywhere.

NOTE Confidence: 0.8674745

00:57:10.174 --> 00:57:11.962 And with that I want to.

NOTE Confidence: 0.8674745

00:57:11.970 --> 00:57:12.864 I'll stop here.

NOTE Confidence: 0.8674745

00:57:12.864 --> 00:57:14.652 I want to thank everybody again,

NOTE Confidence: 0.8674745

00:57:14.660 --> 00:57:16.746 I I don't have an acknowledgement slide,

NOTE Confidence: 0.8674745

00:57:16.750 --> 00:57:17.950 but certainly everyone that

NOTE Confidence: 0.8674745

00:57:17.950 --> 00:57:19.150 Doctor Burtness had mentioned,

NOTE Confidence: 0.8674745

00:57:19.150 --> 00:57:21.579 plus or clinical trials team has been

NOTE Confidence: 0.8674745

00:57:21.579 --> 00:57:23.819 very critical in our ability to do

NOTE Confidence: 0.8674745

00:57:23.819 --> 00:57:26.159 what we've been able to do in serve.

NOTE Confidence: 0.8674745

00:57:26.160 --> 00:57:27.440 Our patients here in Connecticut.

NOTE Confidence: 0.78651327

00:57:31.300 --> 00:57:32.272 OK, thanks Melissa.

NOTE Confidence: 0.78651327

00:57:32.272 --> 00:57:34.540 We have time for a couple questions.

NOTE Confidence: 0.78651327

00:57:34.540 --> 00:57:37.133 Please put them into the chat or if

NOTE Confidence: 0.78651327

00:57:37.133 --> 00:57:39.724 you want will unmute you so you can

NOTE Confidence: 0.78651327

00:57:39.724 --> 00:57:41.989 speak while I'm waiting for you. I'll

NOTE Confidence: 0.78651327

00:57:41.990 --> 00:57:44.041 just say Melissa, I was very impressed

NOTE Confidence: 0.78651327

00:57:44.041 --> 00:57:46.271 by the multi modality nature of care

NOTE Confidence: 0.78651327

00:57:46.271 --> 00:57:48.618 and the fact that you're writing these

NOTE Confidence: 0.78651327

00:57:48.618 --> 00:57:50.736 trials and all the different centers.

NOTE Confidence: 0.78651327

00:57:50.740 --> 00:57:52.684 So what's the secret we need

NOTE Confidence: 0.78651327

00:57:52.684 --> 00:57:53.980 more trials like that?

NOTE Confidence: 0.78651327

00:57:53.980 --> 00:57:55.276 You know higher crewing.

NOTE Confidence: 0.78651327

00:57:55.276 --> 00:57:57.222 You know where you can can.

NOTE Confidence: 0.78651327

00:57:57.222 --> 00:57:58.892 It's a very prevalent type

NOTE Confidence: 0.78651327

00:57:58.892 --> 00:58:00.998 of disease with a trial that.

NOTE Confidence: 0.78651327

00:58:01.000 --> 00:58:02.455 I guess the eligibility criteria

NOTE Confidence: 0.78651327

00:58:02.455 --> 00:58:03.910 are quite broad to allow

NOTE Confidence: 0.78651327

00:58:03.964 --> 00:58:05.188 most patients to enroll.

NOTE Confidence: 0.8262875

00:58:06.280 --> 00:58:08.790 Yeah, I think that's part of it is as we as

NOTE Confidence: 0.8262875

00:58:08.854 --> 00:58:10.429 our darts and doctor Burtness

NOTE Confidence: 0.8262875

00:58:10.429 --> 00:58:12.310 can can attest to this too.

NOTE Confidence: 0.8262875

00:58:12.310 --> 00:58:13.565 We really try to understand

NOTE Confidence: 0.8262875

00:58:13.565 --> 00:58:15.182 what's going to likely accrue for

NOTE Confidence: 0.8262875

00:58:15.182 --> 00:58:16.418 our current patient population,

NOTE Confidence: 0.8262875

00:58:16.420 --> 00:58:18.338 and I think that that's been key.

NOTE Confidence: 0.8262875

00:58:18.340 --> 00:58:20.244 But also making sure to advertise it.

NOTE Confidence: 0.8262875

00:58:20.250 --> 00:58:21.942 And I think because our physicians

NOTE Confidence: 0.8262875

00:58:21.942 --> 00:58:23.891 have been so engaged at the other

NOTE Confidence: 0.8262875

00:58:23.891 --> 00:58:25.683 centers were able to get these opened

NOTE Confidence: 0.8262875

00:58:25.739 --> 00:58:27.377 in enrolled at the care centers.

NOTE Confidence: 0.8262875

00:58:27.380 --> 00:58:28.745 Sometimes we're able to meet

NOTE Confidence: 0.8262875

00:58:28.745 --> 00:58:29.564 these patients locally.

NOTE Confidence: 0.8262875

00:58:29.570 --> 00:58:31.214 I think that's been a huge

NOTE Confidence: 0.8262875

00:58:31.214 --> 00:58:32.310 part of our success.

NOTE Confidence: 0.8262875

00:58:32.310 --> 00:58:34.228 Is is making sure those patients who,

NOTE Confidence: 0.8262875

00:58:34.230 --> 00:58:36.148 specially if they're seeing a New Haven,

NOTE Confidence: 0.8262875

00:58:36.150 --> 00:58:38.390 are seeing all of us and and have.

NOTE Confidence: 0.8262875

00:58:38.390 --> 00:58:40.405 Have full venue and access

NOTE Confidence: 0.8262875

00:58:40.405 --> 00:58:42.017 to understanding every every

NOTE Confidence: 0.8262875

00:58:42.017 --> 00:58:43.999 clinical trial available to them.

NOTE Confidence: 0.8262875

00:58:44.000 --> 00:58:44.310 Great

NOTE Confidence: 0.76599836

00:58:44.310 --> 00:58:46.678 thanks. We have a we have a question

NOTE Confidence: 0.76599836

00:58:46.678 --> 00:58:48.761 from Tommy Tommy you want to unmute

NOTE Confidence: 0.76599836

00:58:48.761 --> 00:58:51.130 and will let you ask your question.

NOTE Confidence: 0.9110757

00:58:51.870 --> 00:58:55.210 Yes, first of all.

NOTE Confidence: 0.9110757

00:58:55.210 --> 00:58:58.538 Barbara and I you have and also others.

NOTE Confidence: 0.9110757

00:58:58.540 --> 00:59:03.428 I think that progress in this area is.

NOTE Confidence: 0.9110757

00:59:03.430 --> 00:59:06.550 Very impressed my sections to you.

NOTE Confidence: 0.9110757

00:59:06.550 --> 00:59:10.730 Is all of your services go up to

NOTE Confidence: 0.9110757

00:59:10.730 --> 00:59:13.880 the what is happening after those

NOTE Confidence: 0.9110757

00:59:13.984 --> 00:59:17.998 combination in terms of adverse effect.

NOTE Confidence: 0.9110757

00:59:18.000 --> 00:59:21.563 Is it getting worse for the same  
NOTE Confidence: 0.9110757

00:59:21.563 --> 00:59:24.566 Orpik or less? And you know this.  
NOTE Confidence: 0.9110757

00:59:24.566 --> 00:59:26.780 So putting index is the most  
NOTE Confidence: 0.9110757

00:59:26.864 --> 00:59:29.379 important part of the treatment.  
NOTE Confidence: 0.9110757

00:59:29.380 --> 00:59:30.463 One of motion.  
NOTE Confidence: 0.9110757

00:59:30.463 --> 00:59:33.614 So could you come in anger and the  
NOTE Confidence: 0.9110757

00:59:33.614 --> 00:59:37.031 particular you several, or you'll be  
NOTE Confidence: 0.9110757

00:59:37.031 --> 00:59:40.016 involving using antibody email check.  
NOTE Confidence: 0.9110757

00:59:40.020 --> 00:59:42.213 What's the impact?  
NOTE Confidence: 0.9110757

00:59:42.213 --> 00:59:48.560 On the enterprise, the combination on the 88.  
NOTE Confidence: 0.9110757

00:59:48.560 --> 00:59:51.360 In other words, anybody you want her?  
NOTE Confidence: 0.9110757

00:59:51.360 --> 00:59:53.760 You go stand by the response.  
NOTE Confidence: 0.9110757

00:59:53.760 --> 00:59:58.500 Is that like getting more or less or or what?  
NOTE Confidence: 0.9110757

00:59:58.500 --> 01:00:01.630 So could you sort of comment on this so so  
NOTE Confidence: 0.85662603

01:00:01.630 --> 01:00:03.996 maybe I'll start and then I'll pass  
NOTE Confidence: 0.85662603

01:00:03.996 --> 01:00:06.927 it to to Melissa because I think.

NOTE Confidence: 0.85662603

01:00:06.930 --> 01:00:10.242 Radiation has its its whole own story with

NOTE Confidence: 0.85662603

01:00:10.242 --> 01:00:13.038 the toxicity in terms of the combination

NOTE Confidence: 0.85662603

01:00:13.038 --> 01:00:15.980 of Pember Lism AB with chemotherapy,

NOTE Confidence: 0.85662603

01:00:15.980 --> 01:00:18.605 it did not lead to more toxicity

NOTE Confidence: 0.85662603

01:00:18.605 --> 01:00:21.537 than people is made with the taxman

NOTE Confidence: 0.85662603

01:00:21.537 --> 01:00:24.123 and pembrolizumab alone was a lot

NOTE Confidence: 0.85662603

01:00:24.205 --> 01:00:26.760 less toxic than the combination.

NOTE Confidence: 0.85662603

01:00:26.760 --> 01:00:29.245 The there is a suggestion that there

NOTE Confidence: 0.85662603

01:00:29.245 --> 01:00:32.028 is a little bit of intensification

NOTE Confidence: 0.85662603

01:00:32.028 --> 01:00:35.310 of the myelosuppression when you give

NOTE Confidence: 0.85662603

01:00:35.310 --> 01:00:38.159 pembrolizumab chemo relative to the tax man.

NOTE Confidence: 0.85662603

01:00:38.160 --> 01:00:41.488 Chemo and although it didn't lead to a

NOTE Confidence: 0.85662603

01:00:41.488 --> 01:00:44.086 significant increase in the number of deaths,

NOTE Confidence: 0.85662603

01:00:44.090 --> 01:00:47.422 we did see more tumor bleeding when

NOTE Confidence: 0.85662603

01:00:47.422 --> 01:00:51.180 we used pen bro or Pembroke chemo.

NOTE Confidence: 0.85662603

01:00:51.180 --> 01:00:56.220 And that I think may have to do with.  
NOTE Confidence: 0.85662603

01:00:56.220 --> 01:00:59.545 Loss of immune checkpoint at as regards  
NOTE Confidence: 0.85662603

01:00:59.545 --> 01:01:02.333 the interaction of the activated T  
NOTE Confidence: 0.85662603

01:01:02.333 --> 01:01:05.315 cells with the wall of these damaged  
NOTE Confidence: 0.85662603

01:01:05.398 --> 01:01:08.018 blood vessels within the tumors,  
NOTE Confidence: 0.85662603

01:01:08.020 --> 01:01:11.110 these are these antibodies are  
NOTE Confidence: 0.85662603

01:01:11.110 --> 01:01:15.269 not inducing a a high rate of.  
NOTE Confidence: 0.85662603

01:01:15.270 --> 01:01:16.730 Anti humanized antibody antibodies.  
NOTE Confidence: 0.85662603

01:01:16.730 --> 01:01:19.337 So overall I would say our experience  
NOTE Confidence: 0.85662603

01:01:19.337 --> 01:01:21.491 with toxicity is this the subgroup  
NOTE Confidence: 0.85662603

01:01:21.491 --> 01:01:23.687 of patients who have high grade  
NOTE Confidence: 0.85662603

01:01:23.687 --> 01:01:25.452 immune related adverse events and  
NOTE Confidence: 0.85662603

01:01:25.452 --> 01:01:27.556 other than that not really worse  
NOTE Confidence: 0.85662603

01:01:27.556 --> 01:01:30.878 than it used to be in the prior era.  
NOTE Confidence: 0.85662603

01:01:30.880 --> 01:01:31.750 And then Melissa,  
NOTE Confidence: 0.85662603

01:01:31.750 --> 01:01:34.244 I don't know if you want to talk

NOTE Confidence: 0.85662603

01:01:34.244 --> 01:01:36.602 about is we've added the immune

NOTE Confidence: 0.85662603

01:01:36.602 --> 01:01:38.500 checkpoint inhibitors to radiation.

NOTE Confidence: 0.8164279

01:01:40.640 --> 01:01:41.639 So certainly some

NOTE Confidence: 0.8164279

01:01:41.640 --> 01:01:43.978 of the initial patients that we've followed.

NOTE Confidence: 0.8164279

01:01:43.980 --> 01:01:45.649 I think there's the immune,

NOTE Confidence: 0.8164279

01:01:45.650 --> 01:01:47.648 so we talk about potentially using.

NOTE Confidence: 0.8164279

01:01:47.650 --> 01:01:49.325 I mean therapies is something

NOTE Confidence: 0.8164279

01:01:49.325 --> 01:01:50.330 to avoid cytotoxic,

NOTE Confidence: 0.8164279

01:01:50.330 --> 01:01:51.820 but certainly there's the immune

NOTE Confidence: 0.8164279

01:01:51.820 --> 01:01:53.750 concern and we certainly are seeing

NOTE Confidence: 0.8164279

01:01:53.750 --> 01:01:55.665 activation of psoriasis skin conditions.

NOTE Confidence: 0.8164279

01:01:55.670 --> 01:01:57.250 You know anything underlying those

NOTE Confidence: 0.8164279

01:01:57.250 --> 01:01:59.531 are the things that I think we're

NOTE Confidence: 0.8164279

01:01:59.531 --> 01:02:01.778 still learning to manage in terms of

NOTE Confidence: 0.8164279

01:02:01.778 --> 01:02:03.683 toxicity during radiation have not

NOTE Confidence: 0.8164279



01:02:03.683 --> 01:02:05.313 necessarily seen any worse toxicity  
NOTE Confidence: 0.8164279

01:02:05.313 --> 01:02:07.239 during the actual course of radiation  
NOTE Confidence: 0.8164279

01:02:07.239 --> 01:02:09.363 and these initial patients that have  
NOTE Confidence: 0.8164279

01:02:09.363 --> 01:02:11.103 been on these combined modality.  
NOTE Confidence: 0.8164279

01:02:11.110 --> 01:02:12.772 Therapy, but there are different things  
NOTE Confidence: 0.8164279

01:02:12.772 --> 01:02:14.480 that we're having to think about.  
NOTE Confidence: 0.8164279

01:02:14.480 --> 01:02:15.884 You know when do we,  
NOTE Confidence: 0.8164279

01:02:15.884 --> 01:02:17.585 you know we're having to determine  
NOTE Confidence: 0.8164279

01:02:17.585 --> 01:02:19.580 whether or not we're needing to add  
NOTE Confidence: 0.8164279

01:02:19.640 --> 01:02:21.509 steroids at any point along the way.  
NOTE Confidence: 0.8164279

01:02:21.510 --> 01:02:22.810 Different toxicities that we didn't  
NOTE Confidence: 0.8164279

01:02:22.810 --> 01:02:24.110 necessarily have to think about  
NOTE Confidence: 0.8164279

01:02:24.157 --> 01:02:25.361 checking for during radiation  
NOTE Confidence: 0.8164279

01:02:25.361 --> 01:02:26.565 for definitive intent treatment,  
NOTE Confidence: 0.8164279

01:02:26.570 --> 01:02:28.439 but I think that is what we  
NOTE Confidence: 0.8164279

01:02:28.439 --> 01:02:29.660 are continuing to learn.

NOTE Confidence: 0.8164279

01:02:29.660 --> 01:02:30.640 And for these trials,

NOTE Confidence: 0.8164279

01:02:30.640 --> 01:02:32.110 the information we get from these

NOTE Confidence: 0.8164279

01:02:32.158 --> 01:02:33.718 trials and toxicity assessments will

NOTE Confidence: 0.8164279

01:02:33.718 --> 01:02:35.278 be very important in determining.

NOTE Confidence: 0.8164279

01:02:35.280 --> 01:02:37.240 Is this a way of the intensifying?

NOTE Confidence: 0.7297384

01:02:39.060 --> 01:02:42.109 That's the way we're going to.

NOTE Confidence: 0.7297384

01:02:42.110 --> 01:02:42.978 So I'll go ahead

NOTE Confidence: 0.84002036

01:02:42.980 --> 01:02:44.492 with just about overtime, but I know

NOTE Confidence: 0.84002036

01:02:44.492 --> 01:02:46.020 my car, which has a question too,

NOTE Confidence: 0.84002036

01:02:46.020 --> 01:02:47.964 but you can do a quick follow up time.

NOTE Confidence: 0.80312536

01:02:48.750 --> 01:02:53.160 OK. In terms of skin, \*\*\*\* city.

NOTE Confidence: 0.80312536

01:02:53.160 --> 01:02:55.545 Your EGFR inhibitor,

NOTE Confidence: 0.80312536

01:02:55.545 --> 01:02:58.725 but it caused skin.

NOTE Confidence: 0.80312536

01:02:58.730 --> 01:03:00.440 And also the other antibody,

NOTE Confidence: 0.80312536

01:03:00.440 --> 01:03:01.826 also called skin.

NOTE Confidence: 0.80312536

01:03:01.826 --> 01:03:05.400 So what happens if you use combination as?

NOTE Confidence: 0.80312536

01:03:05.400 --> 01:03:08.088 I think it was mentioned it's getting

NOTE Confidence: 0.80312536

01:03:08.088 --> 01:03:11.387 worse as that is a quite a very

NOTE Confidence: 0.80312536

01:03:11.387 --> 01:03:13.457 unpleasant this toxicity patient app.

NOTE Confidence: 0.80312536

01:03:13.460 --> 01:03:15.878 If you have a skin issues.

NOTE Confidence: 0.7891823

01:03:19.270 --> 01:03:20.850 So I don't know if if

NOTE Confidence: 0.7891823

01:03:20.850 --> 01:03:22.150 Artie wants to address The

NOTE Confidence: 0.7891823

01:03:22.215 --> 01:03:23.199 Phantoms to talk.

NOTE Confidence: 0.7891823

01:03:23.200 --> 01:03:24.344 Samantha has been associated

NOTE Confidence: 0.7891823

01:03:24.344 --> 01:03:26.506 with a fair bit of skin toxicity

NOTE Confidence: 0.7891823

01:03:26.506 --> 01:03:28.046 that responds to steroids.

NOTE Confidence: 0.7891823

01:03:28.050 --> 01:03:29.880 So talk some ampem Bros.

NOTE Confidence: 0.7891823

01:03:29.880 --> 01:03:31.920 Been reported now in head neck

NOTE Confidence: 0.7891823

01:03:31.920 --> 01:03:34.134 cancer to be quite active without

NOTE Confidence: 0.7891823

01:03:34.134 --> 01:03:36.468 really much of a difference in

NOTE Confidence: 0.7891823

01:03:36.468 --> 01:03:38.639 the safety signal so you know,

NOTE Confidence: 0.7891823

01:03:38.640 --> 01:03:40.608 I think there's there's obviously still

NOTE Confidence: 0.7891823

01:03:40.608 --> 01:03:43.195 a lot to learn with these regiments

NOTE Confidence: 0.7891823

01:03:43.195 --> 01:03:45.210 that are reported with patients,

NOTE Confidence: 0.7891823

01:03:45.210 --> 01:03:47.388 but I think we're all quite

NOTE Confidence: 0.7891823

01:03:47.388 --> 01:03:49.265 intrigued by the possibility of

NOTE Confidence: 0.7891823

01:03:49.265 --> 01:03:51.045 the IO anti EGFR combinations.

NOTE Confidence: 0.76544744

01:03:54.750 --> 01:03:56.335 OK, and then the final question

NOTE Confidence: 0.76544744

01:03:56.335 --> 01:03:57.660 Micro it's you've had your

NOTE Confidence: 0.76544744

01:03:57.715 --> 01:03:58.647 hand up along time.

NOTE Confidence: 0.70547545

01:04:02.390 --> 01:04:06.250 No, not always. Mark Horowitz,

NOTE Confidence: 0.65168154

01:04:06.250 --> 01:04:09.764 yes, so fresh ham it number one.

NOTE Confidence: 0.65168154

01:04:09.770 --> 01:04:13.856 I had an HPV positive tumors that I was

NOTE Confidence: 0.65168154

01:04:13.856 --> 01:04:17.797 she at yeah portion is actually bad.

NOTE Confidence: 0.65168154

01:04:17.800 --> 01:04:21.816 Yeah I was my holiday since actually yeah,

NOTE Confidence: 0.65168154

01:04:21.820 --> 01:04:24.640 'cause my radiation allergist and

NOTE Confidence: 0.65168154

01:04:24.640 --> 01:04:27.460 Schumer was eventually recessive as  
NOTE Confidence: 0.65168154

01:04:27.549 --> 01:04:29.879 absolute treasure and who oppose  
NOTE Confidence: 0.65168154

01:04:29.879 --> 01:04:33.004 them by Sasha Mirror and tell you  
NOTE Confidence: 0.65168154

01:04:33.004 --> 01:04:35.384 that I received superior hair?  
NOTE Confidence: 0.65168154

01:04:35.384 --> 01:04:38.468 I just change and your experience  
NOTE Confidence: 0.65168154

01:04:38.468 --> 01:04:40.010 is just fantastic.  
NOTE Confidence: 0.65168154

01:04:40.010 --> 01:04:46.370 So I'm a year and a half out tumor free.  
NOTE Confidence: 0.65168154

01:04:46.370 --> 01:04:47.792 Couldn't be happier.  
NOTE Confidence: 0.65168154

01:04:47.792 --> 01:04:52.450 I'm back in my lab in the Department of  
NOTE Confidence: 0.65168154

01:04:52.450 --> 01:04:56.776 Voice appears looking away so thank you.  
NOTE Confidence: 0.65168154

01:04:56.780 --> 01:04:58.888 I work with pleasure.  
NOTE Confidence: 0.68799436

01:05:00.980 --> 01:05:04.136 They have voted, but you see,  
NOTE Confidence: 0.68799436

01:05:04.140 --> 01:05:07.745 an influx of mafic ages fo a  
NOTE Confidence: 0.68799436

01:05:07.745 --> 01:05:10.968 positive cells in or around HPV.  
NOTE Confidence: 0.68799436

01:05:10.970 --> 01:05:14.882 Positive tumors in the presence of  
NOTE Confidence: 0.68799436

01:05:14.882 --> 01:05:18.599 patients who are treated with the.

NOTE Confidence: 0.68799436

01:05:18.600 --> 01:05:21.568 Checkpoint inhibitors versus intros.

NOTE Confidence: 0.8499375

01:05:25.580 --> 01:05:28.821 So I think less so than the

NOTE Confidence: 0.8499375

01:05:28.821 --> 01:05:30.930 infiltration of T cells.

NOTE Confidence: 0.8499375

01:05:30.930 --> 01:05:33.360 It is well understood that,

NOTE Confidence: 0.8499375

01:05:33.360 --> 01:05:35.775 particularly in the more hypoxic

NOTE Confidence: 0.8499375

01:05:35.775 --> 01:05:38.190 and HPV negative head neck

NOTE Confidence: 0.8499375

01:05:38.275 --> 01:05:40.650 cancers there is at baseline.

NOTE Confidence: 0.8499375

01:05:40.650 --> 01:05:42.590 Quite a lot of.

NOTE Confidence: 0.84170383

01:05:45.820 --> 01:05:47.356 Extensive macrophage population and

NOTE Confidence: 0.84170383

01:05:47.356 --> 01:05:50.473 that it's sort of M2 polarized and make

NOTE Confidence: 0.84170383

01:05:50.473 --> 01:05:52.338 correspond to the macrophage populations

NOTE Confidence: 0.84170383

01:05:52.338 --> 01:05:54.894 that have been defined in preclinical

NOTE Confidence: 0.84170383

01:05:54.894 --> 01:05:57.189 models for predicting hyper progression.

NOTE Confidence: 0.84170383

01:05:57.190 --> 01:06:00.438 For example in non small cell lung cancer.

NOTE Confidence: 0.84170383

01:06:00.440 --> 01:06:02.995 So I think still a lot of

NOTE Confidence: 0.84170383

01:06:02.995 --> 01:06:05.310 work to be done there,  
NOTE Confidence: 0.84170383

01:06:05.310 --> 01:06:07.896 but the the response when someone  
NOTE Confidence: 0.84170383

01:06:07.896 --> 01:06:10.441 is responding seems to be that  
NOTE Confidence: 0.84170383

01:06:10.441 --> 01:06:13.017 we're seeing in ingress of T cells.  
NOTE Confidence: 0.8907175

01:06:15.220 --> 01:06:17.164 Well, thank you. Thank you for  
NOTE Confidence: 0.8907175

01:06:17.164 --> 01:06:18.844 your wonderful comment and for  
NOTE Confidence: 0.8907175

01:06:18.844 --> 01:06:20.506 telling the whole world what how  
NOTE Confidence: 0.8907175

01:06:20.506 --> 01:06:22.720 lucky I am to work with these two.  
NOTE Confidence: 0.6882981

01:06:24.100 --> 01:06:25.369 It's just issue,  
NOTE Confidence: 0.77037885

01:06:25.370 --> 01:06:27.810 yes issues. Well, well, you  
NOTE Confidence: 0.82509935

01:06:27.810 --> 01:06:29.581 know that's a great way to end  
NOTE Confidence: 0.82509935

01:06:29.581 --> 01:06:31.409 and you know with the patient,  
NOTE Confidence: 0.82509935

01:06:31.410 --> 01:06:33.060 care comes first and the the  
NOTE Confidence: 0.82509935

01:06:33.060 --> 01:06:34.740 amazing work that you're all doing.  
NOTE Confidence: 0.82509935

01:06:34.740 --> 01:06:36.679 And we have an example right here.  
NOTE Confidence: 0.82509935

01:06:36.680 --> 01:06:37.784 So keep it up.

NOTE Confidence: 0.82509935

01:06:37.784 --> 01:06:39.164 Lab to clinic clinical lab.

NOTE Confidence: 0.82509935

01:06:39.170 --> 01:06:40.550 You know multi modality care.

NOTE Confidence: 0.82509935

01:06:40.550 --> 01:06:42.489 It's exactly what we all aspire to.

NOTE Confidence: 0.82509935

01:06:42.490 --> 01:06:44.714 So thank you all for coming to grand

NOTE Confidence: 0.82509935

01:06:44.714 --> 01:06:46.920 Rounds today and we'll see you next week.