WEBVTT

NOTE duration:"01:37:44"

NOTE recognizability:0.838

NOTE language:en-us

NOTE Confidence: 0.791430941428571

00:00:00.000 --> 00:00:04.389 Our group tonight for this CME event.

NOTE Confidence: 0.791430941428571

00:00:04.390 --> 00:00:06.595 Sponsored by our Center for

NOTE Confidence: 0.791430941428571

00:00:06.595 --> 00:00:08.359 Gastrointestinal cancers here at

NOTE Confidence: 0.791430941428571

00:00:08.359 --> 00:00:10.780 Smilow Cancer Hospital in Neoma Haven

NOTE Confidence: 0.791430941428571

00:00:10.780 --> 00:00:13.350 Hospital and Yale School of Medicine,

NOTE Confidence: 0.791430941428571

00:00:13.350 --> 00:00:15.500 so we're delighted that you

NOTE Confidence: 0.791430941428571

00:00:15.500 --> 00:00:17.650 took some time out from.

NOTE Confidence: 0.791430941428571

00:00:17.650 --> 00:00:19.418 I know it is a busy time of

NOTE Confidence: 0.791430941428571

00:00:19.418 --> 00:00:20.910 year for many to join us.

NOTE Confidence: 0.791430941428571

00:00:20.910 --> 00:00:25.348 This evening we're going to be focusing

NOTE Confidence: 0.791430941428571

00:00:25.348 --> 00:00:28.170 in on gastroesophageal cancers.

NOTE Confidence: 0.791430941428571

00:00:28.170 --> 00:00:31.010 We have three talks tonight.

NOTE Confidence: 0.791430941428571

00:00:31.010 --> 00:00:32.954 It will give about 30 minutes

NOTE Confidence: 0.791430941428571

00:00:32.954 --> 00:00:35.508 to each with some time in each

NOTE Confidence: 0.791430941428571

00:00:35.508 --> 00:00:37.084 session for some questions,

NOTE Confidence: 0.791430941428571

00:00:37.090 --> 00:00:39.522 and we'll try to leave some time at

NOTE Confidence: 0.791430941428571

00:00:39.522 --> 00:00:42.060 the end for questions as well in

NOTE Confidence: 0.791430941428571

00:00:42.060 --> 00:00:44.650 terms of the order of the talks,

NOTE Confidence: 0.791430941428571

00:00:44.650 --> 00:00:46.386 we're going to start with Doctor Baffa,

NOTE Confidence: 0.791430941428571

00:00:46.390 --> 00:00:48.496 then move on to Doctor Robert

NOTE Confidence: 0.791430941428571

00:00:48.496 --> 00:00:49.549 and then myself.

NOTE Confidence: 0.791430941428571

00:00:49.550 --> 00:00:52.412 I am doctor Lacey by way of introduction and

NOTE Confidence: 0.791430941428571

00:00:52.412 --> 00:00:55.509 I will introduce myself again at the end.

NOTE Confidence: 0.791430941428571

00:00:55.510 --> 00:00:56.926 So we're going to,

NOTE Confidence: 0.791430941428571

00:00:56.926 --> 00:00:57.988 without further ado,

NOTE Confidence: 0.791430941428571

00:00:57.990 --> 00:01:01.422 get started and Doctor Baffa is

NOTE Confidence: 0.791430941428571

00:01:01.422 --> 00:01:05.769 going to kick this off this evening.

NOTE Confidence: 0.791430941428571

00:01:05.770 --> 00:01:08.008 Doctor Baffa is a colleague that

NOTE Confidence: 0.791430941428571

00:01:08.008 --> 00:01:10.190 I work with very closely.

NOTE Confidence: 0.791430941428571

00:01:10.190 --> 00:01:13.025 He is professor and chief of the

NOTE Confidence: 0.791430941428571

00:01:13.025 --> 00:01:15.150 Division of Thoracic Surgery here

NOTE Confidence: 0.791430941428571

00:01:15.150 --> 00:01:17.628 at the Yale School of Medicine

NOTE Confidence: 0.791430941428571

00:01:17.628 --> 00:01:19.070 and Cancer Center,

NOTE Confidence: 0.791430941428571

00:01:19.070 --> 00:01:22.499 and he is going to be speaking to us

NOTE Confidence: 0.791430941428571

00:01:22.499 --> 00:01:25.310 tonight about the impact of recent.

NOTE Confidence: 0.791430941428571

00:01:25.310 --> 00:01:28.195 Trials on systemic therapy before

NOTE Confidence: 0.791430941428571

00:01:28.195 --> 00:01:29.926 and after esophagectomy.

NOTE Confidence: 0.874224721666667

00:01:31.600 --> 00:01:34.198 Thank you very much and again,

NOTE Confidence: 0.874224721666667

00:01:34.200 --> 00:01:37.686 thank you to everybody who is joining

NOTE Confidence: 0.874224721666667

00:01:37.686 --> 00:01:40.930 either live or after the fact and

NOTE Confidence: 0.874224721666667

00:01:40.930 --> 00:01:44.437 I will tell you that I'm a fast

NOTE Confidence: 0.874224721666667

00:01:44.437 --> 00:01:47.713 talker and I always give short talks.

NOTE Confidence: 0.874224721666667

00:01:47.720 --> 00:01:49.638 So if you feel like you did

NOTE Confidence: 0.874224721666667

00:01:49.638 --> 00:01:51.419 not get your moneys worth,

NOTE Confidence: 0.874224721666667

00:01:51.420 --> 00:01:52.715 I don't know what to tell you,

NOTE Confidence: 0.874224721666667

00:01:52.720 --> 00:01:56.549 but I I will. My e-mail is

NOTE Confidence: 0.9312649275

00:01:59.140 --> 00:02:00.091 daniel.boffa@yale.edu and if

NOTE Confidence: 0.9312649275

00:02:00.091 --> 00:02:01.676 there's anything I say that.

NOTE Confidence: 0.9312649275

00:02:01.680 --> 00:02:04.299 Is unclear or you want to talk more about,

NOTE Confidence: 0.9312649275

00:02:04.300 --> 00:02:07.284 please don't hesitate to reach out to me.

NOTE Confidence: 0.9312649275

00:02:07.290 --> 00:02:11.634 So I have a couple of disclosures, so the.

NOTE Confidence: 0.9312649275

00:02:11.634 --> 00:02:14.868 I'm going to talk 1st about preoperative

NOTE Confidence: 0.9312649275

00:02:14.868 --> 00:02:18.422 therapy and then I will talk about post

NOTE Confidence: 0.9312649275

00:02:18.422 --> 00:02:21.283 operative therapy in patients that have

NOTE Confidence: 0.9312649275

00:02:21.283 --> 00:02:24.253 what is perceived to be resectable,

NOTE Confidence: 0.9312649275

00:02:24.260 --> 00:02:26.276 esophago gastric cancer.

NOTE Confidence: 0.9312649275

00:02:26.276 --> 00:02:29.636 So there was a study,

NOTE Confidence: 0.9312649275

00:02:29.640 --> 00:02:34.870 the CLG B8 O eight O 3 trial that was

NOTE Confidence: 0.9312649275

00:02:35.016 --> 00:02:38.300 pet guided therapy in the preoperative

NOTE Confidence: 0.9312649275

00:02:38.300 --> 00:02:42.085 setting in terms of which chemoradiation

NOTE Confidence: 0.9312649275

00:02:42.085 --> 00:02:45.369 cocktail to be administered.

NOTE Confidence: 0.9312649275

00:02:45.370 --> 00:02:48.044 So this is this is a really

NOTE Confidence: 0.9312649275

00:02:48.044 --> 00:02:50.150 interesting study in my opinion.

NOTE Confidence: 0.9312649275

00:02:50.150 --> 00:02:52.575 I was fortunate enough to

NOTE Confidence: 0.9312649275

00:02:52.575 --> 00:02:54.515 be involved in this.

NOTE Confidence: 0.9312649275

00:02:54.520 --> 00:02:55.995 And I think it's understanding

NOTE Confidence: 0.9312649275

00:02:55.995 --> 00:02:58.180 a little bit of the background.

NOTE Confidence: 0.9312649275

00:02:58.180 --> 00:03:00.236 I think it was a cleverly designed study.

NOTE Confidence: 0.9312649275

00:03:00.240 --> 00:03:02.216 I don't know that it was a huge,

NOTE Confidence: 0.9312649275

00:03:02.220 --> 00:03:03.252 really impactful study,

NOTE Confidence: 0.9312649275

00:03:03.252 --> 00:03:05.316 but I think the study design

NOTE Confidence: 0.9312649275

00:03:05.316 --> 00:03:06.630 was pretty interesting.

NOTE Confidence: 0.9312649275

00:03:06.630 --> 00:03:10.025 So the the fundamental principle that this

NOTE Confidence: 0.9312649275

00:03:10.025 --> 00:03:13.454 was based on is that if you give induction,

NOTE Confidence: 0.9312649275

00:03:13.460 --> 00:03:14.308 chemotherapy,

NOTE Confidence: 0.9312649275

00:03:14.308 --> 00:03:16.004 and radiation,

NOTE Confidence: 0.9312649275

00:03:16.004 --> 00:03:20.736 about 25% of people will sterilize the cancer

NOTE Confidence: 0.9312649275

00:03:20.736 --> 00:03:23.540 within the surgically removed specimen.

NOTE Confidence: 0.9312649275

00:03:23.540 --> 00:03:25.428 But that means that three out of four.

NOTE Confidence: 0.9312649275

00:03:25.430 --> 00:03:28.226 Patients actually have some form of

NOTE Confidence: 0.9312649275

00:03:28.226 --> 00:03:30.870 resistance to that neoadjuvant treatment.

NOTE Confidence: 0.9312649275

00:03:30.870 --> 00:03:32.640 And we know that the best

NOTE Confidence: 0.9312649275

00:03:32.640 --> 00:03:34.673 prognosis is in patients who have

NOTE Confidence: 0.9312649275

00:03:34.673 --> 00:03:36.249 a pathologic complete response,

NOTE Confidence: 0.9312649275

00:03:36.250 --> 00:03:38.546 and so it doesn't take much to connect

NOTE Confidence: 0.9312649275

00:03:38.546 --> 00:03:40.769 those dots that if we can increase the

NOTE Confidence: 0.9312649275

00:03:40.769 --> 00:03:42.905 path CR rate that there's a potential

NOTE Confidence: 0.9312649275

00:03:42.905 --> 00:03:45.285 that we could make people live longer.

NOTE Confidence: 0.9312649275

00:03:45.290 --> 00:03:47.040 And.

NOTE Confidence: 0.9312649275

00:03:47.040 --> 00:03:49.675 Different chemotherapies have been used

NOTE Confidence: 0.9312649275

00:03:49.675 --> 00:03:52.310 for esophageal and gastric carcinoma

NOTE Confidence: 0.9312649275

00:03:52.383 --> 00:03:55.047 and there is potentially a different

NOTE Confidence: 0.9312649275

00:03:55.047 --> 00:03:57.670 mechanism of resistance and so just

NOTE Confidence: 0.9312649275

00:03:57.670 --> 00:03:59.610 because somebody's resistant to one

NOTE Confidence: 0.9312649275

00:03:59.610 --> 00:04:01.936 may not mean they're resistant to both.

NOTE Confidence: 0.9312649275

00:04:01.936 --> 00:04:03.670 So the question is what if

NOTE Confidence: 0.9312649275

00:04:03.733 --> 00:04:05.098 you changed chemotherapy?

NOTE Confidence: 0.9312649275

00:04:05.100 --> 00:04:07.790 If there was a way to know it wasn't working,

NOTE Confidence: 0.9312649275

00:04:07.790 --> 00:04:10.051 could you change it during the neoadjuvant

NOTE Confidence: 0.9312649275

00:04:10.051 --> 00:04:12.219 course to something that's more effective?

NOTE Confidence: 0.9312649275

00:04:12.220 --> 00:04:15.340 So these are the two common

NOTE Confidence: 0.9312649275

00:04:15.340 --> 00:04:16.380 regimens carboplatinum,

NOTE Confidence: 0.9312649275

00:04:16.380 --> 00:04:18.624 paclitaxel and oxaliplatin.

NOTE Confidence: 0.9312649275

00:04:18.624 --> 00:04:20.868 And five FU,

NOTE Confidence: 0.9312649275

00:04:20.870 --> 00:04:25.052 and so they actually do both

NOTE Confidence: 0.9312649275

00:04:25.052 --> 00:04:27.167 have platinum backbones,

NOTE Confidence: 0.9312649275

00:04:27.167 --> 00:04:31.469 but they're they do have different

NOTE Confidence: 0.9312649275

00:04:31.469 --> 00:04:34.450 mechanisms of resistance and so.

NOTE Confidence: 0.9312649275

00:04:34.450 --> 00:04:36.872 This is sort of the founding principle

NOTE Confidence: 0.9312649275

00:04:36.872 --> 00:04:39.928 that if you give a chemotherapy regimen,

NOTE Confidence: 0.9312649275

00:04:39.930 --> 00:04:42.716 we're just going to call regimen a.

NOTE Confidence: 0.9312649275

00:04:42.720 --> 00:04:46.979 And you assess mid treatment pet and if

NOTE Confidence: 0.9312649275

00:04:46.979 --> 00:04:51.148 they don't reduce the Max SUV's by 35%.

NOTE Confidence: 0.9312649275

00:04:51.148 --> 00:04:55.286 So go from 5:50 and a half if they

NOTE Confidence: 0.9312649275

00:04:55.286 --> 00:04:57.703 don't have at least that much

NOTE Confidence: 0.9312649275

00:04:57.703 --> 00:05:00.580 of a response and you keep going

NOTE Confidence: 0.9312649275

00:05:00.580 --> 00:05:02.570 with the same regimen,

NOTE Confidence: 0.9312649275

00:05:02.570 --> 00:05:06.572 then the chance of you having

NOTE Confidence: 0.9312649275

00:05:06.572 --> 00:05:09.240 a pathologic complete response.

NOTE Confidence: 0.9312649275

00:05:09.240 --> 00:05:12.840 Is quite low.

NOTE Confidence: 0.9312649275

00:05:12.840 --> 00:05:13.220 Sorry,

NOTE Confidence: 0.9312649275

00:05:13.220 --> 00:05:14.360 one second here.

NOTE Confidence: 0.804088352857143

00:05:16.670 --> 00:05:18.266 It seemed to have. There we go.

NOTE Confidence: 0.804088352857143

00:05:18.270 --> 00:05:21.246 It's it's only 5%.

NOTE Confidence: 0.804088352857143

00:05:21.246 --> 00:05:24.630 However, if you are giving 1 regimen and

NOTE Confidence: 0.804088352857143

00:05:24.630 --> 00:05:27.210 you notice that there's no pet response,

NOTE Confidence: 0.804088352857143

00:05:27.210 --> 00:05:31.314 but change to a different chemotherapy

NOTE Confidence: 0.804088352857143

00:05:31.314 --> 00:05:34.410 regimen for the chemo radiation phase,

NOTE Confidence: 0.804088352857143

00:05:34.410 --> 00:05:36.986 the null hypothesis is that we can take

NOTE Confidence: 0.804088352857143

00:05:36.986 --> 00:05:41.050 this 5% path CR rate and bump it up to 20%.

NOTE Confidence: 0.804088352857143

00:05:41.050 --> 00:05:42.770 So that was the foundation

NOTE Confidence: 0.804088352857143

00:05:42.770 --> 00:05:44.490 for the CL GB study,

NOTE Confidence: 0.804088352857143

00:05:44.490 --> 00:05:47.290 and so this was in adenocarcinoma patients,

NOTE Confidence: 0.804088352857143

00:05:47.290 --> 00:05:49.369 was a phase two trial they had

NOTE Confidence: 0.804088352857143

00:05:49.369 --> 00:05:51.750 to at least be clinical stage T.

NOTE Confidence: 0.804088352857143

00:05:51.750 --> 00:05:57.054 To and or have lymph node metastases now.

NOTE Confidence: 0.804088352857143

00:05:57.060 --> 00:05:58.795 One thing that's just really

NOTE Confidence: 0.804088352857143

00:05:58.795 --> 00:06:00.887 important is you could get into

NOTE Confidence: 0.804088352857143

00:06:00.887 --> 00:06:02.875 this trial being a T2 and zero.

NOTE Confidence: 0.804088352857143

00:06:02.880 --> 00:06:05.050 That was the the minority of the

NOTE Confidence: 0.804088352857143

00:06:05.050 --> 00:06:07.598 patients and I would say this study was

NOTE Confidence: 0.804088352857143

00:06:07.598 --> 00:06:10.140 not powered to look at that subgroup.

NOTE Confidence: 0.804088352857143

00:06:10.140 --> 00:06:12.480 So just because a group is in a trial

NOTE Confidence: 0.804088352857143

00:06:12.480 --> 00:06:14.671 does not mean the trial findings

NOTE Confidence: 0.804088352857143

00:06:14.671 --> 00:06:17.160 universally apply to every small subgroup.

NOTE Confidence: 0.804088352857143

00:06:17.160 --> 00:06:19.674 I think that's important, and that's

NOTE Confidence: 0.804088352857143

00:06:19.674 --> 00:06:22.010 I think been misinterpreted and that.

NOTE Confidence: 0.804088352857143

00:06:22.010 --> 00:06:23.276 The patients had have a distal,

NOTE Confidence: 0.804088352857143

00:06:23.280 --> 00:06:26.660 esophageal, or GE junction cancer,

NOTE Confidence: 0.804088352857143

00:06:26.660 --> 00:06:28.281 and again, as I mentioned,

NOTE Confidence: 0.804088352857143

00:06:28.281 --> 00:06:29.469 they would get chemo.

NOTE Confidence: 0.804088352857143

00:06:29.470 --> 00:06:32.430 There would be an early pet assessment and

NOTE Confidence: 0.804088352857143

00:06:32.430 --> 00:06:35.905 if they had a response you would keep going.

NOTE Confidence: 0.804088352857143

00:06:35.910 --> 00:06:38.070 If you didn't,

NOTE Confidence: 0.804088352857143

00:06:38.070 --> 00:06:40.932 you would change to another chemo

NOTE Confidence: 0.804088352857143

00:06:40.932 --> 00:06:43.885 form of chemo radiation and then

NOTE Confidence: 0.804088352857143

00:06:43.885 --> 00:06:46.275 have an esophagectomy and about

NOTE Confidence: 0.804088352857143

00:06:46.280 --> 00:06:48.513 3/4 of the patients in both arms

NOTE Confidence: 0.804088352857143

00:06:48.513 --> 00:06:51.188 went on to have an esophagectomy,

NOTE Confidence: 0.804088352857143

00:06:51.190 --> 00:06:53.530 so there's certainly was some fallout.

NOTE Confidence: 0.804088352857143

00:06:53.530 --> 00:06:56.374 Between induction and moving

NOTE Confidence: 0.804088352857143

00:06:56.374 --> 00:06:58.507 on to Esophagectomy,

NOTE Confidence: 0.804088352857143

00:06:58.510 --> 00:07:00.670 and again the primary endpoint

NOTE Confidence: 0.804088352857143

00:07:00.670 --> 00:07:03.160 of this study was path CR.

NOTE Confidence: 0.804088352857143

00:07:03.160 --> 00:07:04.945 In the patients who were

NOTE Confidence: 0.804088352857143

00:07:04.945 --> 00:07:06.016 deemed non responders.

NOTE Confidence: 0.804088352857143

00:07:06.020 --> 00:07:06.632 So again,

NOTE Confidence: 0.804088352857143

00:07:06.632 --> 00:07:08.774 that's that group we thought would have

NOTE Confidence: 0.804088352857143

00:07:08.774 --> 00:07:12.140 a 5% path CR rate and so could we bump

NOTE Confidence: 0.804088352857143

00:07:12.140 --> 00:07:15.759 that up by changing the chemotherapy so.

NOTE Confidence: 0.804088352857143

00:07:15.760 --> 00:07:19.420 Green is starting with full Fox,

NOTE Confidence: 0.804088352857143

00:07:19.420 --> 00:07:24.019 but responding and continuing with full Fox.

NOTE Confidence: 0.804088352857143

00:07:24.020 --> 00:07:26.799 The the yellow is starting with folfox,

NOTE Confidence: 0.804088352857143

00:07:26.800 --> 00:07:30.064 but then changing the carboplatin paclitaxel

NOTE Confidence: 0.804088352857143

00:07:30.064 --> 00:07:33.320 blue is starting with Carbo Taxol,

NOTE Confidence: 0.804088352857143

00:07:33.320 --> 00:07:35.804 and if you continue in blue

NOTE Confidence: 0.804088352857143

00:07:35.804 --> 00:07:37.460 then you were responder.

NOTE Confidence: 0.804088352857143

00:07:37.460 --> 00:07:38.480 If you did not respond,

NOTE Confidence: 0.804088352857143

00:07:38.480 --> 00:07:40.646 then you changed a full box.

NOTE Confidence: 0.804088352857143

00:07:40.650 --> 00:07:42.687 So if you look at the path

NOTE Confidence: 0.804088352857143

00:07:42.687 --> 00:07:44.829 CR rate in the responders,

NOTE Confidence: 0.804088352857143

00:07:44.830 --> 00:07:46.410 there's a pretty big difference.

NOTE Confidence: 0.804088352857143

00:07:46.410 --> 00:07:48.979 So of the people that got folfox,

NOTE Confidence: 0.804088352857143

00:07:48.980 --> 00:07:50.498 these are adenocarcinomas.

NOTE Confidence: 0.804088352857143

00:07:50.498 --> 00:07:54.040 If you started with Folfox and you

NOTE Confidence: 0.804088352857143

00:07:54.125 --> 00:07:56.778 responded and that was 73 out of

NOTE Confidence: 0.804088352857143

00:07:56.780 --> 00:07:58.886 129 were responders and you kept

NOTE Confidence: 0.804088352857143

00:07:58.886 --> 00:08:01.278 going the path CR rate was 40%,

NOTE Confidence: 0.804088352857143

00:08:01.280 --> 00:08:02.480 so that's pretty good.

NOTE Confidence: 0.804088352857143

00:08:02.480 --> 00:08:03.980 So that's higher than that

NOTE Confidence: 0.804088352857143

00:08:03.980 --> 00:08:06.689 25% historical number.

NOTE Confidence: 0.804088352857143

00:08:06.690 --> 00:08:08.728 If you started with carboplatin,

NOTE Confidence: 0.804088352857143

00:08:08.728 --> 00:08:12.022 paclitaxel, and you responded and kept

NOTE Confidence: 0.804088352857143

00:08:12.022 --> 00:08:15.318 going with Carbo Taxol, you're past CR.

NOTE Confidence: 0.804088352857143

00:08:15.318 --> 00:08:16.458 It was 14%.

NOTE Confidence: 0.804088352857143

00:08:16.458 --> 00:08:18.010 That's pretty darn low,

NOTE Confidence: 0.804088352857143

00:08:18.010 --> 00:08:20.466 and I'm going to give you some context

NOTE Confidence: 0.804088352857143

00:08:20.466 --> 00:08:22.647 in terms of other recent trials.

NOTE Confidence: 0.804088352857143

00:08:22.650 --> 00:08:23.886 Now, the non responders.

NOTE Confidence: 0.804088352857143

00:08:23.886 --> 00:08:25.740 Now this is the group we

NOTE Confidence: 0.804088352857143

00:08:25.804 --> 00:08:27.568 were trying to bump up from.

NOTE Confidence: 0.804088352857143

00:08:27.570 --> 00:08:30.570 5% so if you started green,

NOTE Confidence: 0.804088352857143

00:08:30.570 --> 00:08:32.386 if you started folfox,

NOTE Confidence: 0.804088352857143

00:08:32.386 --> 00:08:35.110 you were deemed a non responder

NOTE Confidence: 0.804088352857143

00:08:35.201 --> 00:08:37.385 and changed the path CR 8.

NOTE Confidence: 0.804088352857143

00:08:37.390 --> 00:08:40.950 18% so that's pretty darn close to 20%.

NOTE Confidence: 0.824055006

00:08:40.950 --> 00:08:43.362 And however, if you were a

NOTE Confidence: 0.824055006

00:08:43.362 --> 00:08:44.970 non responder to carboplatin,

NOTE Confidence: 0.824055006

00:08:44.970 --> 00:08:47.130 paclitaxel, and you switched,

NOTE Confidence: 0.824055006

00:08:47.130 --> 00:08:49.290 you actually got 20%,

NOTE Confidence: 0.824055006

00:08:49.290 --> 00:08:52.650 so this was actually.

NOTE Confidence: 0.824055006

00:08:52.650 --> 00:08:55.107 This actually met criteria for both arms,

NOTE Confidence: 0.824055006

00:08:55.110 --> 00:08:57.168 so this was actually a positive study.

NOTE Confidence: 0.824055006

00:08:57.170 --> 00:08:59.627 Again, because we were expecting a 5%

NOTE Confidence: 0.824055006

00:08:59.630 --> 00:09:03.622 path CR rate from historical data and

NOTE Confidence: 0.824055006

00:09:03.622 --> 00:09:05.878 both of these were significantly higher

NOTE Confidence: 0.824055006

00:09:05.878 --> 00:09:08.379 than what we would have anticipated.

NOTE Confidence: 0.824055006

00:09:08.380 --> 00:09:12.764 So I'm just some stats from CL GB 80803.

NOTE Confidence: 0.824055006

00:09:12.764 --> 00:09:14.316 The complete resection rate.

NOTE Confidence: 0.824055006

00:09:14.320 --> 00:09:16.960 So granted 3 out of four patients that

NOTE Confidence: 0.824055006

00:09:16.960 --> 00:09:19.574 started in each arm went on to get

NOTE Confidence: 0.824055006

00:09:19.574 --> 00:09:22.012 into Sophie Ectomy the path CR that

NOTE Confidence: 0.824055006

00:09:22.012 --> 00:09:24.282 the complete resection rate was 94%.

NOTE Confidence: 0.824055006

00:09:24.282 --> 00:09:25.488 That's pretty good.

NOTE Confidence: 0.824055006

00:09:25.488 --> 00:09:27.096 That's that's pretty average.

NOTE Confidence: 0.824055006

00:09:27.100 --> 00:09:28.330 The mortality rate.

NOTE Confidence: 0.824055006

00:09:28.330 --> 00:09:31.719 This is the 90 day mortality rate is 3.3%.

NOTE Confidence: 0.824055006

00:09:31.719 --> 00:09:32.556 That's quite low,

NOTE Confidence: 0.824055006

00:09:32.556 --> 00:09:35.060 so in the French and German trials though,

NOTE Confidence: 0.824055006

00:09:35.060 --> 00:09:38.644 they had double digit 30 day mortality.

NOTE Confidence: 0.824055006

00:09:38.650 --> 00:09:39.930 So this is quite low.

NOTE Confidence: 0.824055006

00:09:39.930 --> 00:09:41.745 Usually the 90 day mortality

NOTE Confidence: 0.824055006

00:09:41.745 --> 00:09:43.955 mortality is twice the 30 day

NOTE Confidence: 0.824055006

00:09:43.955 --> 00:09:46.244 mortality and so this is quite low.

NOTE Confidence: 0.824055006

00:09:46.250 --> 00:09:48.620 Five or six started with

NOTE Confidence: 0.824055006

00:09:48.620 --> 00:09:49.568 Carboplatinum paclitaxel,

NOTE Confidence: 0.824055006

00:09:49.570 --> 00:09:52.146 so that's I think that's just a statistical.

NOTE Confidence: 0.824055006

00:09:52.150 --> 00:09:53.890 I think that's just an aberration,

NOTE Confidence: 0.824055006

00:09:53.890 --> 00:09:57.373 but maybe a light signal and the five year

NOTE Confidence: 0.824055006

00:09:57.373 --> 00:10:00.176 survival for this study was about 45%.

NOTE Confidence: 0.824055006

00:10:00.176 --> 00:10:03.718 So if you look at the difference

NOTE Confidence: 0.824055006

00:10:03.718 --> 00:10:06.549 between responders and non responders.

NOTE Confidence: 0.824055006

00:10:06.550 --> 00:10:08.909 So again, how did people do based

NOTE Confidence: 0.824055006

00:10:08.909 --> 00:10:11.090 on whether they respond to that?

NOTE Confidence: 0.824055006

00:10:11.090 --> 00:10:12.842 Early pet, the responders,

NOTE Confidence: 0.824055006

00:10:12.842 --> 00:10:14.594 as you might think,

NOTE Confidence: 0.824055006

00:10:14.600 --> 00:10:18.878 would have had a better outcome.

NOTE Confidence: 0.824055006

00:10:18.880 --> 00:10:22.040 49% five year survival versus 39% and

NOTE Confidence: 0.824055006

00:10:22.040 --> 00:10:25.448 the median survival was almost twice as long.

NOTE Confidence: 0.824055006

00:10:25.448 --> 00:10:27.230 Now if you look at the

NOTE Confidence: 0.824055006

00:10:27.304 --> 00:10:29.128 different treatment groups,

NOTE Confidence: 0.824055006

00:10:29.130 --> 00:10:33.240 so the red is full fox.

NOTE Confidence: 0.824055006

00:10:33.240 --> 00:10:35.538 The dash is responder the the

NOTE Confidence: 0.824055006

00:10:35.538 --> 00:10:38.220 solid line is the nonresponder,

NOTE Confidence: 0.824055006

00:10:38.220 --> 00:10:40.868 so you can see those are the those

NOTE Confidence: 0.824055006

00:10:40.868 --> 00:10:43.120 are wider than the blue lines,

NOTE Confidence: 0.824055006

00:10:43.120 --> 00:10:47.056 which are the people that started

NOTE Confidence: 0.824055006

00:10:47.056 --> 00:10:49.024 with carboplatinum paclitaxel.

NOTE Confidence: 0.824055006

00:10:49.030 --> 00:10:51.571 So here's how I put this study

NOTE Confidence: 0.824055006

00:10:51.571 --> 00:10:54.037 together so that that if you the

NOTE Confidence: 0.824055006

00:10:54.037 --> 00:10:56.451 path CR was more likely if you

NOTE Confidence: 0.824055006

00:10:56.451 --> 00:10:59.153 started with full fox of all the

NOTE Confidence: 0.824055006

00:10:59.153 --> 00:11:01.214 patients that started with full Fox,

NOTE Confidence: 0.824055006

00:11:01.214 --> 00:11:03.829 they were more likely to have a path CR.

NOTE Confidence: 0.824055006

00:11:03.830 --> 00:11:06.200 So when you combine an average

NOTE Confidence: 0.824055006

00:11:06.200 --> 00:11:09.915 this out 31% versus 14% in the

NOTE Confidence: 0.824055006

00:11:09.915 --> 00:11:11.670 carboplatinum paclitaxel group,

NOTE Confidence: 0.824055006

00:11:11.670 --> 00:11:16.262 Now this is a bit odd because sorry,

NOTE Confidence: 0.824055006

00:11:16.262 --> 00:11:19.146 the in the cross trial which was.

NOTE Confidence: 0.824055006

00:11:19.150 --> 00:11:20.188 Carboplatinum, paclitaxel,

NOTE Confidence: 0.824055006

00:11:20.188 --> 00:11:23.302 the all the way through the

NOTE Confidence: 0.824055006

00:11:23.302 --> 00:11:25.041 paths CR8 was 29%.

NOTE Confidence: 0.824055006

00:11:25.041 --> 00:11:27.180 So something's funny in that 14%.

NOTE Confidence: 0.824055006

00:11:27.180 --> 00:11:30.120 So it's hard to know what to make of that.

NOTE Confidence: 0.824055006

00:11:30.120 --> 00:11:32.736 But at least in the in this study

NOTE Confidence: 0.824055006

00:11:32.740 --> 00:11:34.948 there was a difference based on

NOTE Confidence: 0.824055006

00:11:34.948 --> 00:11:37.071 whether you started with folfox

NOTE Confidence: 0.824055006

00:11:37.071 --> 00:11:38.799 or carboplatinum paclitaxel.

NOTE Confidence: 0.824055006

00:11:38.800 --> 00:11:41.138 But paths yard does not tell the

NOTE Confidence: 0.824055006

00:11:41.138 --> 00:11:42.994 story because when you actually

NOTE Confidence: 0.824055006

00:11:42.994 --> 00:11:44.959 look at the overall survival,

NOTE Confidence: 0.824055006

00:11:44.960 --> 00:11:47.536 this is the five year overall survival.

NOTE Confidence: 0.824055006

00:11:47.540 --> 00:11:48.518 The the.

NOTE Confidence: 0.824055006

00:11:48.518 --> 00:11:50.963 The mustard and there's probably

NOTE Confidence: 0.824055006

00:11:50.963 --> 00:11:53.888 a fancy name for that color.

NOTE Confidence: 0.824055006

00:11:53.890 --> 00:11:58.050 Maybe no, I forget what you call that color,

NOTE Confidence: 0.824055006

00:11:58.050 --> 00:12:02.798 but brownish yellow, the.

NOTE Confidence: 0.824055006

00:12:02.800 --> 00:12:06.105 They're both around 4142%,

NOTE Confidence: 0.824055006

00:12:06.105 --> 00:12:08.100 and if you look at the Greens,

NOTE Confidence: 0.824055006

00:12:08.100 --> 00:12:09.748 the full fox patients,

NOTE Confidence: 0.824055006

00:12:09.748 --> 00:12:12.220 they're all in the same ballpark,

NOTE Confidence: 0.824055006

00:12:12.220 --> 00:12:14.050 so I don't think if anything

NOTE Confidence: 0.824055006

00:12:14.050 --> 00:12:15.270 you know we were.

NOTE Confidence: 0.86021555

00:12:15.270 --> 00:12:18.192 We were expecting this this carboplatin

NOTE Confidence: 0.86021555

00:12:18.192 --> 00:12:20.200 group, which went all the way

NOTE Confidence: 0.86021555

00:12:20.200 --> 00:12:22.408 through without a Pats CR of 14%.

NOTE Confidence: 0.86021555

00:12:22.408 --> 00:12:25.827 They still had a 44 percent five

NOTE Confidence: 0.86021555

00:12:25.827 --> 00:12:28.749 year survival, so path CR definitely

NOTE Confidence: 0.86021555

00:12:28.749 --> 00:12:31.718 does not tell the whole story.

NOTE Confidence: 0.86021555

00:12:31.720 --> 00:12:34.345 Now the other question is this study.

NOTE Confidence: 0.86021555

00:12:34.350 --> 00:12:36.429 The biggest part of this study was a pivot,

NOTE Confidence: 0.86021555

00:12:36.430 --> 00:12:39.254 meaning if you use a pet to change

NOTE Confidence: 0.86021555

00:12:39.254 --> 00:12:41.657 what you're going to give people,

NOTE Confidence: 0.86021555

00:12:41.660 --> 00:12:42.910 does that help you know?

NOTE Confidence: 0.86021555

00:12:42.910 --> 00:12:45.670 So these were two common chemotherapy

NOTE Confidence: 0.86021555

00:12:45.670 --> 00:12:47.510 regimens used with radiation

NOTE Confidence: 0.86021555

00:12:47.580 --> 00:12:49.806 that there was a pivot in place.

NOTE Confidence: 0.86021555

00:12:49.810 --> 00:12:51.346 So with this pivot,

NOTE Confidence: 0.86021555

00:12:51.346 --> 00:12:53.266 did we make anything better?

NOTE Confidence: 0.86021555

00:12:53.270 --> 00:12:55.514 So overall, the five year survival

NOTE Confidence: 0.86021555

00:12:55.514 --> 00:12:57.924 in this study was about 45%,

NOTE Confidence: 0.86021555

00:12:57.924 --> 00:13:01.364 so the pivot gets you about 45%.

NOTE Confidence: 0.86021555

00:13:01.364 --> 00:13:03.740 However, the cross trial,

NOTE Confidence: 0.86021555

00:13:03.740 --> 00:13:04.910 it's pretty much the same,

NOTE Confidence: 0.86021555

00:13:04.910 --> 00:13:06.575 and there that was carboplatinum

NOTE Confidence: 0.86021555

00:13:06.575 --> 00:13:08.240 paclitaxel all the way through,

NOTE Confidence: 0.86021555

00:13:08.240 --> 00:13:10.880 so it's hard for me to say that

NOTE Confidence: 0.86021555

00:13:10.880 --> 00:13:13.398 using PET to guide your therapy,

NOTE Confidence: 0.86021555

00:13:13.400 --> 00:13:15.920 at least in this context,

NOTE Confidence: 0.86021555

00:13:15.920 --> 00:13:18.678 that it really changed the overall survival.

NOTE Confidence: 0.86021555

00:13:18.680 --> 00:13:20.612 Now that that doesn't mean that

NOTE Confidence: 0.86021555

00:13:20.612 --> 00:13:22.519 there's never a role for this,

NOTE Confidence: 0.86021555

00:13:22.520 --> 00:13:25.175 but it does mean pivoting

NOTE Confidence: 0.86021555

00:13:25.175 --> 00:13:27.299 between these two regimens,

NOTE Confidence: 0.86021555

00:13:27.300 --> 00:13:32.288 carboplatin and paclitaxel, and full fox.

NOTE Confidence: 0.86021555

00:13:32.288 --> 00:13:34.486 Using trying to mimic this and thinking

NOTE Confidence: 0.86021555

00:13:34.486 --> 00:13:36.706 you're going to make people live longer.

NOTE Confidence: 0.86021555

00:13:36.710 --> 00:13:39.209 I think that's that's a hard sell.

NOTE Confidence: 0.86021555

00:13:39.210 --> 00:13:41.429 So what are the take home messages

NOTE Confidence: 0.86021555

00:13:41.430 --> 00:13:42.970 that the pet does predict?

NOTE Confidence: 0.86021555

00:13:42.970 --> 00:13:43.287 Resistance?

NOTE Confidence: 0.86021555

00:13:43.287 --> 00:13:46.140 So I think that of the non responders in

NOTE Confidence: 0.86021555

00:13:46.208 --> 00:13:48.530 general they had lower response rates.

NOTE Confidence: 0.86021555

00:13:48.530 --> 00:13:51.704 So if there was a better pivot,

NOTE Confidence: 0.86021555

00:13:51.704 --> 00:13:55.172 potentially this this there is potential

NOTE Confidence: 0.86021555

00:13:55.172 --> 00:13:59.270 for pet early pet response to predict

NOTE Confidence: 0.86021555

00:13:59.270 --> 00:14:02.610 overall response to chemo radiation.

NOTE Confidence: 0.86021555

00:14:02.610 --> 00:14:05.556 I think that this adds to a signal.

NOTE Confidence: 0.86021555

00:14:05.560 --> 00:14:06.056 Now, again,

NOTE Confidence: 0.86021555

00:14:06.056 --> 00:14:07.544 this is a very soft call,

NOTE Confidence: 0.86021555

00:14:07.550 --> 00:14:09.176 and and Jill I'd love to

NOTE Confidence: 0.86021555

00:14:09.176 --> 00:14:10.630 get your feedback on this,

NOTE Confidence: 0.86021555

00:14:10.630 --> 00:14:13.462 but I think this adds to a signal that

NOTE Confidence: 0.86021555

00:14:13.462 --> 00:14:15.660 if you have a squamous cell carcinoma

NOTE Confidence: 0.86021555

00:14:15.730 --> 00:14:17.358 that that really carboplatinum

NOTE Confidence: 0.86021555

00:14:17.358 --> 00:14:19.393 paclitaxel makes the most sense

NOTE Confidence: 0.86021555

00:14:19.393 --> 00:14:21.544 and so this is the cross study.

NOTE Confidence: 0.86021555

00:14:21.544 --> 00:14:21.808 Again,

NOTE Confidence: 0.86021555

00:14:21.808 --> 00:14:24.479 this is I'm just saying it adds to a signal.

NOTE Confidence: 0.86021555

00:14:24.480 --> 00:14:27.315 I'm not saying that this is an

NOTE Confidence: 0.86021555

00:14:27.315 --> 00:14:30.609 absolute but this is the the the

NOTE Confidence: 0.86021555

00:14:30.609 --> 00:14:33.094 squamous cell that got chemoradiation.

NOTE Confidence: 0.86021555

00:14:33.100 --> 00:14:35.340 And squamous cell that got surgery only.

NOTE Confidence: 0.86021555

00:14:35.340 --> 00:14:38.068 And you could see how wide apart those

NOTE Confidence: 0.86021555

00:14:38.068 --> 00:14:40.834 bars are. The lighter Gray bars.

NOTE Confidence: 0.86021555

00:14:40.834 --> 00:14:43.436 Those are the adenocarcinoma with

NOTE Confidence: 0.86021555

00:14:43.436 --> 00:14:45.500 and without induction therapy.

NOTE Confidence: 0.86021555

00:14:45.500 --> 00:14:48.580 So I think this is pretty impressive

NOTE Confidence: 0.86021555

00:14:48.580 --> 00:14:51.684 that with squamous cell the induction

NOTE Confidence: 0.86021555

00:14:51.684 --> 00:14:53.388 carboplatinum paclitaxel really

NOTE Confidence: 0.86021555

00:14:53.388 --> 00:14:56.460 does have a profound widening.

NOTE Confidence: 0.86021555

00:14:56.460 --> 00:14:58.892 I think this adds to a signal

NOTE Confidence: 0.86021555

00:14:58.892 --> 00:15:01.360 that full Fox is better with AD.

NOTE Confidence: 0.86021555

00:15:01.360 --> 00:15:05.720 No that compared to.

NOTE Confidence: 0.86021555

00:15:05.720 --> 00:15:06.300 Carboplatin,

NOTE Confidence: 0.86021555

00:15:06.300 --> 00:15:06.880 paclitaxel,

NOTE Confidence: 0.86021555

00:15:06.880 --> 00:15:09.780 there are studies like protect

NOTE Confidence: 0.86021555

00:15:09.780 --> 00:15:13.911 fourteen O2 that are going to compare

NOTE Confidence: 0.86021555

00:15:13.911 --> 00:15:15.639 different induction regimens,

NOTE Confidence: 0.86021555

00:15:15.640 --> 00:15:17.960 but I think this adds to that signal.

NOTE Confidence: 0.86021555

00:15:17.960 --> 00:15:19.160 So why do I say that?

NOTE Confidence: 0.86021555

00:15:19.160 --> 00:15:22.900 So if you look at the full fox,

NOTE Confidence: 0.86021555

00:15:22.900 --> 00:15:25.780 the people that started with full

NOTE Confidence: 0.86021555

00:15:25.780 --> 00:15:28.936 Fox the the lines are just more

NOTE Confidence: 0.86021555

00:15:28.936 --> 00:15:30.720 separated based on response,

NOTE Confidence: 0.86021555

00:15:30.720 --> 00:15:33.016 and so I think it does a better

NOTE Confidence: 0.86021555

00:15:33.016 --> 00:15:34.650 job stratifying people that are

NOTE Confidence: 0.86021555

00:15:34.650 --> 00:15:36.642 going to respond and not respond.

NOTE Confidence: 0.86021555

00:15:36.650 --> 00:15:37.252 So again,

NOTE Confidence: 0.86021555

00:15:37.252 --> 00:15:38.757 that's not telling you prognostically,

NOTE Confidence: 0.917023269

00:15:38.760 --> 00:15:40.728 it's just saying if the whole point of

NOTE Confidence: 0.917023269

00:15:40.728 --> 00:15:42.971 this study is to be able to separate

NOTE Confidence: 0.917023269

00:15:42.971 --> 00:15:44.099 responders and non responders,

NOTE Confidence: 0.917023269

00:15:44.100 --> 00:15:46.590 it's the the pet format.

NOTE Confidence: 0.917023269

00:15:46.590 --> 00:15:48.816 Seems to be better with folfox.

NOTE Confidence: 0.917023269

00:15:48.820 --> 00:15:50.830 The blue lines are people that

NOTE Confidence: 0.917023269

00:15:50.830 --> 00:15:52.170 started with carboplatinum paclitaxel.

NOTE Confidence: 0.84344467

00:15:54.300 --> 00:15:57.954 This is the cross study and if

NOTE Confidence: 0.84344467

00:15:57.954 --> 00:16:00.780 you this is the forest which

NOTE Confidence: 0.84344467

00:16:00.780 --> 00:16:02.460 basically looks at unplanned,

NOTE Confidence: 0.84344467

00:16:02.460 --> 00:16:04.440 these are unplanned subset

NOTE Confidence: 0.84344467

00:16:04.440 --> 00:16:06.915 analysis from the cross study.

NOTE Confidence: 0.84344467

00:16:06.920 --> 00:16:09.827 This is old now, but if you actually look

NOTE Confidence: 0.84344467

00:16:09.827 --> 00:16:12.936 at by the Histology and and to be clear,

NOTE Confidence: 0.84344467

00:16:12.940 --> 00:16:15.100 the majority of these patients

NOTE Confidence: 0.84344467

00:16:15.100 --> 00:16:16.396 were adenocarcinoma patients,

NOTE Confidence: 0.84344467

00:16:16.400 --> 00:16:18.580 it actually was not statistically

NOTE Confidence: 0.84344467

00:16:18.580 --> 00:16:20.760 significant in the ADNO group.

NOTE Confidence: 0.84344467

00:16:20.760 --> 00:16:23.816 Clearly the mortality reduction.

NOTE Confidence: 0.84344467

00:16:23.816 --> 00:16:26.814 Is less impressive in adeno

NOTE Confidence: 0.84344467

00:16:26.814 --> 00:16:28.878 versus squamous cell, so again,

NOTE Confidence: 0.84344467

00:16:28.878 --> 00:16:32.406 I'm not saying it's wrong to give

NOTE Confidence: 0.84344467

00:16:32.406 --> 00:16:34.690 carboplatinum paclitaxel to adno,

NOTE Confidence: 0.84344467

00:16:34.690 --> 00:16:38.101 but I do believe this the the CGB study

NOTE Confidence: 0.84344467

00:16:38.101 --> 00:16:41.288 adds to a signal that in adno full

NOTE Confidence: 0.84344467

00:16:41.288 --> 00:16:44.176 fox is actually a better way to go.

NOTE Confidence: 0.84344467

00:16:44.180 --> 00:16:46.609 So now I'm going to pivot to

NOTE Confidence: 0.84344467

00:16:46.609 --> 00:16:48.848 postoperative therapy and I'm going to

NOTE Confidence: 0.84344467

00:16:48.848 --> 00:16:51.240 talk just briefly about checkmates 577,

NOTE Confidence: 0.84344467

00:16:51.240 --> 00:16:53.740 and this was giving nivolumab

NOTE Confidence: 0.84344467

00:16:53.740 --> 00:16:55.240 after completely resected,

NOTE Confidence: 0.84344467

00:16:55.240 --> 00:16:58.500 so they had negative margins.

NOTE Confidence: 0.84344467

00:16:58.500 --> 00:17:03.409 Esophageal cancer that had

NOTE Confidence: 0.84344467

00:17:03.409 --> 00:17:05.308 some residual disease.

NOTE Confidence: 0.84344467

00:17:05.310 --> 00:17:06.434 They were not anybody.

NOTE Confidence: 0.84344467

00:17:06.434 --> 00:17:08.120 That was anything other than a

NOTE Confidence: 0.84344467

00:17:08.177 --> 00:17:09.770 pathologic complete responder.

NOTE Confidence: 0.84344467

00:17:09.770 --> 00:17:15.062 So this this they accrued between 16 and 19,

NOTE Confidence: 0.84344467

00:17:15.070 --> 00:17:17.370 a lot of different centers.

NOTE Confidence: 0.84344467

00:17:17.370 --> 00:17:20.448 They had to be clinical stage two or three.

NOTE Confidence: 0.84344467

00:17:20.450 --> 00:17:22.962 They received induction chemo

NOTE Confidence: 0.84344467

00:17:22.962 --> 00:17:26.102 radiation with two common backbones

NOTE Confidence: 0.84344467

00:17:26.110 --> 00:17:29.236 of chemo that was platinum based.

NOTE Confidence: 0.84344467

00:17:29.240 --> 00:17:31.568 They again they had to have

NOTE Confidence: 0.84344467

00:17:31.568 --> 00:17:32.732 a complete resection.

NOTE Confidence: 0.84344467

00:17:32.740 --> 00:17:35.866 No positive margins and then they

NOTE Confidence: 0.84344467

00:17:35.866 --> 00:17:38.732 were randomized whether or not to

NOTE Confidence: 0.84344467

00:17:38.732 --> 00:17:41.245 start between one and four months

NOTE Confidence: 0.84344467

00:17:41.245 --> 00:17:42.977 after the complete resection,

NOTE Confidence: 0.84344467

00:17:42.980 --> 00:17:45.476 and again they had to have some residual

NOTE Confidence: 0.84344467

00:17:45.476 --> 00:17:47.818 disease in the pathologic or specimen,

NOTE Confidence: 0.84344467

00:17:47.820 --> 00:17:51.627 so it could not be a a a complete

NOTE Confidence: 0.84344467

00:17:51.627 --> 00:17:55.640 pathologic response. And so.

NOTE Confidence: 0.84344467

00:17:55.640 --> 00:17:58.646 It was nivolumab for four months.

NOTE Confidence: 0.866352902727273

00:18:00.780 --> 00:18:03.195 That was given every two weeks and

NOTE Confidence: 0.866352902727273

00:18:03.195 --> 00:18:06.171 then it became monthly after that and

NOTE Confidence: 0.866352902727273

00:18:06.171 --> 00:18:08.456 it continued either to progression

NOTE Confidence: 0.866352902727273

00:18:08.456 --> 00:18:11.578 or if it was terminated for toxicity

NOTE Confidence: 0.866352902727273

00:18:11.578 --> 00:18:15.030 or patients got to a year and again.

NOTE Confidence: 0.866352902727273

00:18:15.030 --> 00:18:17.850 This was designed for disease free

NOTE Confidence: 0.866352902727273

00:18:17.850 --> 00:18:21.530 survival and so this just highlights

NOTE Confidence: 0.866352902727273

00:18:21.530 --> 00:18:26.870 where the patients came from the.

NOTE Confidence: 0.866352902727273

00:18:26.870 --> 00:18:31.230 About 40% were from Europe.

NOTE Confidence: 0.866352902727273

00:18:31.230 --> 00:18:34.090 60% were esophageal and 40%

NOTE Confidence: 0.866352902727273

00:18:34.090 --> 00:18:37.519 were gastroesophageal junction.

NOTE Confidence: 0.866352902727273

00:18:37.520 --> 00:18:39.716 71% were adenocarcinoma.

NOTE Confidence: 0.866352902727273

00:18:39.716 --> 00:18:45.634 Now the the PDL 1 count so was

NOTE Confidence: 0.866352902727273

00:18:45.634 --> 00:18:48.600 about 16% were PDL 1 positive.

NOTE Confidence: 0.866352902727273

00:18:48.600 --> 00:18:49.863 Now that's different.

NOTE Confidence: 0.866352902727273

00:18:49.863 --> 00:18:51.968 Something Doctor Robert is going

NOTE Confidence: 0.866352902727273

00:18:51.968 --> 00:18:55.772 to talk about which is a which

NOTE Confidence: 0.866352902727273

00:18:55.772 --> 00:18:58.962 is a complete positive score.

NOTE Confidence: 0.866352902727273

00:18:58.970 --> 00:19:01.623 A composite positive score which is a

NOTE Confidence: 0.866352902727273

00:19:01.623 --> 00:19:04.651 different and in just to be clear in a

NOTE Confidence: 0.866352902727273

00:19:04.651 --> 00:19:06.988 post hoc analysis the that score was.

NOTE Confidence: 0.866352902727273

00:19:06.990 --> 00:19:09.558 Positive in about 57% had five

NOTE Confidence: 0.866352902727273

00:19:09.558 --> 00:19:12.100 or more percent cells positive,

NOTE Confidence: 0.866352902727273

00:19:12.100 --> 00:19:13.726 so this looks like there was

NOTE Confidence: 0.866352902727273

00:19:13.726 --> 00:19:14.810 very little PDL one.

NOTE Confidence: 0.866352902727273

00:19:14.810 --> 00:19:18.236 But actually when you use the.

NOTE Confidence: 0.866352902727273

00:19:18.240 --> 00:19:21.838 The composite score it's actually was higher.

NOTE Confidence: 0.332944005

00:19:25.060 --> 00:19:32.971 So the. So this was well tolerated so the

NOTE Confidence: 0.332944005

00:19:32.971 --> 00:19:38.030 there were no grade 5 adverse events.

NOTE Confidence: 0.332944005

00:19:38.030 --> 00:19:40.058 About 1/3 of patients had any

NOTE Confidence: 0.332944005

00:19:40.058 --> 00:19:41.940 three or four adverse events.

NOTE Confidence: 0.332944005

00:19:41.940 --> 00:19:43.830 It was actually pretty similar between

NOTE Confidence: 0.332944005

00:19:43.830 --> 00:19:46.169 the placebo and then the volume Nob arm.

NOTE Confidence: 0.332944005

00:19:46.170 --> 00:19:49.149 This continued treatment.

NOTE Confidence: 0.332944005

00:19:49.150 --> 00:19:53.007 Was 9% in the Nomad and 3%

NOTE Confidence: 0.332944005

00:19:53.010 --> 00:19:56.100 in the placebo group. Umm?

NOTE Confidence: 0.8029525384

00:19:58.210 --> 00:20:02.522 The sorry, so when we look at disease

NOTE Confidence: 0.8029525384

00:20:02.522 --> 00:20:05.125 free survival, the blue line is the

NOTE Confidence: 0.8029525384

00:20:05.125 --> 00:20:07.780 nivolumab arm and the red line is placebo.

NOTE Confidence: 0.8029525384

00:20:07.780 --> 00:20:10.316 So you can see there was a really

NOTE Confidence: 0.8029525384

00:20:10.316 --> 00:20:11.859 significant difference in the disease.

NOTE Confidence: 0.8029525384

00:20:11.860 --> 00:20:15.212 Free survival if you look at the median

NOTE Confidence: 0.8029525384

00:20:15.212 --> 00:20:18.856 disease free survival in the nivolumab group,

NOTE Confidence: 0.8029525384

00:20:18.856 --> 00:20:21.451 it was basically twice that

NOTE Confidence: 0.8029525384

00:20:21.451 --> 00:20:23.800 of the placebo group.

NOTE Confidence: 0.8029525384

00:20:23.800 --> 00:20:27.730 When you look by Histology so.

NOTE Confidence: 0.8029525384

00:20:27.730 --> 00:20:31.937 The the the the blue lines are

NOTE Confidence: 0.8029525384

00:20:31.937 --> 00:20:35.669 the patients who got nivolumab.

NOTE Confidence: 0.8029525384

00:20:35.670 --> 00:20:39.720 The red lines are the placebo groups and when

NOTE Confidence: 0.8029525384

00:20:39.720 --> 00:20:44.029 you actually just break it down by Histology.

NOTE Confidence: 0.8029525384

00:20:44.030 --> 00:20:45.950 So if you look at adenocarcinoma,

NOTE Confidence: 0.8029525384

00:20:45.950 --> 00:20:47.790 the median disease free survival

NOTE Confidence: 0.8029525384

00:20:47.790 --> 00:20:49.630 was 19 versus 11 months.

NOTE Confidence: 0.8029525384

00:20:49.630 --> 00:20:51.240 And when you look at

NOTE Confidence: 0.8029525384

00:20:51.240 --> 00:20:53.221 squamous it was actually 29,

NOTE Confidence: 0.8029525384

00:20:53.221 --> 00:20:57.367 almost 30 months versus 11 months.

NOTE Confidence: 0.8029525384

00:20:57.370 --> 00:20:59.165 Which is something we've seen

NOTE Confidence: 0.8029525384

00:20:59.165 --> 00:21:01.661 before where there seems to be a

NOTE Confidence: 0.8029525384

00:21:01.661 --> 00:21:03.551 little bit more activity in the

NOTE Confidence: 0.8029525384

00:21:03.551 --> 00:21:05.448 squamous cell patients and again,

NOTE Confidence: 0.8029525384

00:21:05.450 --> 00:21:07.688 70% of the patients in the

NOTE Confidence: 0.8029525384

00:21:07.688 --> 00:21:09.180 study were actually adino.

NOTE Confidence: 0.8029525384

00:21:09.180 --> 00:21:11.036 When you look at the forest plot again,

NOTE Confidence: 0.8029525384

00:21:11.040 --> 00:21:15.036 these are all unplanned subset analysis.

NOTE Confidence: 0.8029525384

00:21:15.040 --> 00:21:17.504 When you look at Adno versus Swain,

NOTE Confidence: 0.8029525384

00:21:17.510 --> 00:21:20.610 they were both significant.

NOTE Confidence: 0.8029525384

00:21:20.610 --> 00:21:24.892 Adno was flirting with a non

NOTE Confidence: 0.8029525384

00:21:24.892 --> 00:21:27.624 significance but was significant.

NOTE Confidence: 0.8029525384

00:21:27.630 --> 00:21:29.550 When you look at PDL one,

NOTE Confidence: 0.8029525384

00:21:29.550 --> 00:21:32.970 so the people that had PDL 1 less than

NOTE Confidence: 0.8029525384

00:21:32.970 --> 00:21:36.379 one now granted this is probably just

NOTE Confidence: 0.8029525384

00:21:36.379 --> 00:21:39.566 a power analysis but the people with

NOTE Confidence: 0.8029525384

00:21:39.566 --> 00:21:42.647 PDL 1 less than one it was significant

NOTE Confidence: 0.8029525384

00:21:42.647 --> 00:21:45.566 but they had 600 patients versus the

NOTE Confidence: 0.8029525384

00:21:45.566 --> 00:21:47.833 patients who were greater than one

NOTE Confidence: 0.8029525384

00:21:47.833 --> 00:21:50.230 and these are tumor cell PDL one.

NOTE Confidence: 0.8029525384

00:21:50.230 --> 00:21:53.236 It's it actually was not significant.

NOTE Confidence: 0.8029525384

00:21:53.240 --> 00:21:55.010 That doesn't necessarily make sense,

NOTE Confidence: 0.8029525384

00:21:55.010 --> 00:21:57.960 but I think it's got to be a power issue.

NOTE Confidence: 0.8029525384

00:21:57.960 --> 00:21:59.604 And interestingly,

NOTE Confidence: 0.8029525384

00:21:59.604 --> 00:22:05.358 if you the people who had node

NOTE Confidence: 0.8029525384

00:22:05.358 --> 00:22:06.724 positive pathologic specimens,

NOTE Confidence: 0.8029525384

00:22:06.724 --> 00:22:08.628 they seem to do a little bit

NOTE Confidence: 0.8029525384

00:22:08.628 --> 00:22:10.137 better and have a bigger impact.

NOTE Confidence: 0.8029525384

00:22:10.140 --> 00:22:11.598 The people that were no negative.

NOTE Confidence: 0.8029525384

00:22:11.600 --> 00:22:14.108 Actually it did not reach significance.

NOTE Confidence: 0.8029525384

00:22:14.110 --> 00:22:15.820 And again these are unplanned

NOTE Confidence: 0.8029525384

00:22:15.820 --> 00:22:16.504 subset analysis.

NOTE Confidence: 0.8029525384

00:22:16.510 --> 00:22:19.036 So it's I don't think these

NOTE Confidence: 0.8029525384

00:22:19.036 --> 00:22:20.720 should be practice changing,

NOTE Confidence: 0.8029525384

00:22:20.720 --> 00:22:23.640 but should inspire future

NOTE Confidence: 0.8029525384

00:22:23.640 --> 00:22:26.560 deliberation and future trials.

NOTE Confidence: 0.8029525384

00:22:26.560 --> 00:22:29.376 And if you were really on the fence.

NOTE Confidence: 0.8029525384

00:22:29.380 --> 00:22:31.150 As to what should somebody get

NOTE Confidence: 0.8029525384

00:22:31.150 --> 00:22:33.359 immunotherapy if they were in a group

NOTE Confidence: 0.8029525384

00:22:33.359 --> 00:22:34.979 where there really wasn't significance,

NOTE Confidence: 0.8029525384

00:22:34.980 --> 00:22:37.324 I think you can.

NOTE Confidence: 0.8029525384

00:22:37.324 --> 00:22:40.254 That's one perspective to consider.

NOTE Confidence: 0.8029525384

00:22:40.260 --> 00:22:44.194 Older patients we've seen this before in

NOTE Confidence: 0.8029525384

00:22:44.194 --> 00:22:46.500 different immunotherapy adjuvant trials.

NOTE Confidence: 0.8029525384

00:22:46.500 --> 00:22:48.710 the IT was not significant,

NOTE Confidence: 0.8029525384

00:22:48.710 --> 00:22:50.074 although it was a.

NOTE Confidence: 0.8029525384

00:22:50.074 --> 00:22:52.878 A hazard ratio less than one and this

NOTE Confidence: 0.8029525384

00:22:52.878 --> 00:22:55.606 very well may have been a power issue,

NOTE Confidence: 0.8029525384

00:22:55.610 --> 00:22:57.605 but again, if you had an older

NOTE Confidence: 0.8029525384

00:22:57.605 --> 00:22:59.647 patient and you were on the fence,

NOTE Confidence: 0.8029525384

00:22:59.650 --> 00:23:01.630 you know I think you could.

NOTE Confidence: 0.8029525384

00:23:01.630 --> 00:23:03.740 You can consider that the

NOTE Confidence: 0.8029525384

00:23:03.740 --> 00:23:05.428 impact might be less,

NOTE Confidence: 0.8029525384

00:23:05.430 --> 00:23:09.738 and if you're her two positive.

NOTE Confidence: 0.8029525384

00:23:09.740 --> 00:23:11.420 This was a very small group.

NOTE Confidence: 0.8029525384

00:23:11.420 --> 00:23:14.084 There were only 63 patients so I don't

NOTE Confidence: 0.8029525384

00:23:14.084 --> 00:23:16.817 know how much stock to put into this,

NOTE Confidence: 0.8029525384

00:23:16.820 --> 00:23:18.740 but just something to think about.

NOTE Confidence: 0.8029525384

00:23:18.740 --> 00:23:20.693 So there are a couple of there's

NOTE Confidence: 0.8029525384

00:23:20.693 --> 00:23:22.640 a bunch of ongoing studies.

NOTE Confidence: 0.8029525384

00:23:22.640 --> 00:23:25.118 These are a couple interesting ones,

NOTE Confidence: 0.8029525384

00:23:25.120 --> 00:23:30.364 which is flot versus Cisplatinum 5 FU and

NOTE Confidence: 0.8029525384

00:23:30.364 --> 00:23:33.640 in patients that have resectable gastric

NOTE Confidence: 0.692280666764286

00:23:33.738 --> 00:23:35.798 and GE junction cancer,

NOTE Confidence: 0.692280666764286

00:23:35.800 --> 00:23:37.810 getting adjuvant Pembroke

NOTE Confidence: 0.692280666764286

00:23:37.810 --> 00:23:41.160 versus placebo and then keynote.

NOTE Confidence: 0.692280666764286

00:23:41.160 --> 00:23:43.590 975, which is for either people

NOTE Confidence: 0.692280666764286

00:23:43.590 --> 00:23:45.793 who are have unresectable disease

NOTE Confidence: 0.692280666764286

00:23:45.793 --> 00:23:47.837 or don't want esophagectomy,

NOTE Confidence: 0.692280666764286

00:23:47.840 --> 00:23:50.036 which I don't know why anybody

NOTE Confidence: 0.692280666764286

00:23:50.036 --> 00:23:51.980 wouldn't want an esophagectomy I

NOTE Confidence: 0.692280666764286

00:23:51.980 --> 00:23:53.420 giving definitive chemoradiation

NOTE Confidence: 0.692280666764286

00:23:53.420 --> 00:23:56.848 again with a one of the common

NOTE Confidence: 0.692280666764286

00:23:56.848 --> 00:23:59.128 backbones and then Pembroke or

NOTE Confidence: 0.692280666764286

00:23:59.128 --> 00:24:02.120 not so a lot of information.

NOTE Confidence: 0.692280666764286

00:24:02.120 --> 00:24:04.200 I appreciate your time.

NOTE Confidence: 0.692280666764286

00:24:04.200 --> 00:24:06.419 So this was a a chemotherapy talk

NOTE Confidence: 0.692280666764286

00:24:06.419 --> 00:24:08.328 by a non chemotherapy ologist

NOTE Confidence: 0.692280666764286

00:24:08.328 --> 00:24:11.387 so take it for what it's worth.

NOTE Confidence: 0.692280666764286

00:24:11.390 --> 00:24:12.160 But again,

NOTE Confidence: 0.692280666764286

00:24:12.160 --> 00:24:14.470 thank you for your your attention.

NOTE Confidence: 0.847582673333333

00:24:17.110 --> 00:24:18.730 Dan, thank you. That was great.

NOTE Confidence: 0.847582673333333

00:24:18.730 --> 00:24:20.690 Really nice review of

NOTE Confidence: 0.847582673333333

00:24:20.690 --> 00:24:23.162 some very very important.

NOTE Confidence: 0.847582673333333

00:24:23.162 --> 00:24:25.435 Studies, one of which is clearly

NOTE Confidence: 0.847582673333333

00:24:25.435 --> 00:24:26.759 practice changing adjuvant neevo

NOTE Confidence: 0.847582673333333

00:24:26.759 --> 00:24:28.659 huge advance in the field and

NOTE Confidence: 0.847582673333333

00:24:28.659 --> 00:24:30.481 advance that we've been waiting for

NOTE Confidence: 0.847582673333333

00:24:30.481 --> 00:24:32.189 for I think a couple of decades,

NOTE Confidence: 0.847582673333333

00:24:32.190 --> 00:24:35.284 so really exciting to have the adjuvant

NOTE Confidence: 0.847582673333333

00:24:35.284 --> 00:24:37.461 therapy option with the volume

NOTE Confidence: 0.847582673333333

00:24:37.461 --> 00:24:40.495 up in these patients we are happy

NOTE Confidence: 0.847582673333333

00:24:40.495 --> 00:24:43.465 to take questions in this format.

NOTE Confidence: 0.847582673333333

00:24:43.470 --> 00:24:45.982 It's in the chat box so please put

NOTE Confidence: 0.847582673333333

00:24:45.982 --> 00:24:48.058 any questions in that you may have.

NOTE Confidence: 0.838753273333333

00:24:50.080 --> 00:24:52.654 Dan, if I may, I have. I have a couple

NOTE Confidence: 0.838753273333333

00:24:52.654 --> 00:24:56.470 of for for you, so the C LGB study.

NOTE Confidence: 0.906410566666667

00:24:58.650 --> 00:25:01.332 Left us hanging with a lot

NOTE Confidence: 0.906410566666667

00:25:01.332 --> 00:25:02.673 of unanswered questions.

NOTE Confidence: 0.906410566666667

00:25:02.680 --> 00:25:04.456 And and wish A wish list for maybe

NOTE Confidence: 0.906410566666667

00:25:04.456 --> 00:25:06.140 how they had designed the study.

NOTE Confidence: 0.906410566666667

00:25:06.140 --> 00:25:08.648 But one just your opinion on

NOTE Confidence: 0.906410566666667

00:25:08.648 --> 00:25:11.280 the the question of induction,

NOTE Confidence: 0.906410566666667

00:25:11.280 --> 00:25:14.537 chemo versus prior to chemo radiotherapy.

NOTE Confidence: 0.906410566666667

00:25:14.537 --> 00:25:17.171 There's been no study that's compared

NOTE Confidence: 0.906410566666667

00:25:17.171 --> 00:25:19.625 adding induction chemo priority if

NOTE Confidence: 0.906410566666667

00:25:19.625 --> 00:25:21.125 therapy versus just chemoradiotherapy

NOTE Confidence: 0.906410566666667

00:25:21.125 --> 00:25:22.250 followed by esophagectomy.

NOTE Confidence: 0.890596526

00:25:24.280 --> 00:25:26.360 It's from a pragmatic perspective.

NOTE Confidence: 0.890596526

00:25:26.360 --> 00:25:28.160 We find it useful to start

NOTE Confidence: 0.890596526

00:25:28.160 --> 00:25:29.206 with induction, chemo,

NOTE Confidence: 0.890596526

00:25:29.206 --> 00:25:31.436 because often dysphagia resolves rapidly,

NOTE Confidence: 0.890596526

00:25:31.440 --> 00:25:33.060 so we do it pretty routinely,

NOTE Confidence: 0.890596526

00:25:33.060 --> 00:25:35.676 and I think based on the study you reviewed,

NOTE Confidence: 0.890596526

00:25:35.676 --> 00:25:38.172 we have shifted towards full

NOTE Confidence: 0.890596526

00:25:38.172 --> 00:25:42.230 Fox in the adenocarcinomas.

NOTE Confidence: 0.890596526

00:25:42.230 --> 00:25:43.556 Do do you have an opinion?

NOTE Confidence: 0.890596526

00:25:43.560 --> 00:25:45.170 I'll just I will just ask for

NOTE Confidence: 0.890596526

00:25:45.170 --> 00:25:47.105 your opinion on whether you think

NOTE Confidence: 0.890596526

00:25:47.105 --> 00:25:48.685 induction chemotherapy is important.

NOTE Confidence: 0.890596526

00:25:48.690 --> 00:25:49.898 The survival statistics from

NOTE Confidence: 0.890596526

00:25:49.898 --> 00:25:51.106 that study were impressive.

NOTE Confidence: 0.890596526

00:25:51.110 --> 00:25:54.170 I think better than prior studies.

NOTE Confidence: 0.890596526

00:25:54.170 --> 00:25:57.644 Could that in part be due to the induction.

NOTE Confidence: 0.890596526

00:25:57.650 --> 00:25:59.110 The inclusion of induction, chemo?

NOTE Confidence: 0.890596526

00:25:59.110 --> 00:26:00.503 Or do you think it just has

NOTE Confidence: 0.890596526

00:26:00.503 --> 00:26:02.433 more to do with maybe full Fox

NOTE Confidence: 0.890596526

00:26:02.433 --> 00:26:03.713 in the adenocarcinoma subset?

NOTE Confidence: 0.843689094782609

00:26:05.230 --> 00:26:09.217 So, so the fact that there were that that

NOTE Confidence: 0.843689094782609

00:26:09.217 --> 00:26:13.126 you know roughly 1/4 of patients did

NOTE Confidence: 0.843689094782609

00:26:13.126 --> 00:26:16.848 not get an esophagectomy could be that.

NOTE Confidence: 0.843689094782609

00:26:16.850 --> 00:26:19.480 You know, anytime there's attrition

NOTE Confidence: 0.843689094782609

00:26:19.480 --> 00:26:22.233 that could be could be appropriate.

NOTE Confidence: 0.843689094782609

00:26:22.233 --> 00:26:24.891 Patient selection patients progress and they

NOTE Confidence: 0.843689094782609

00:26:24.891 --> 00:26:27.588 avoided a surgery that didn't help them.

NOTE Confidence: 0.843689094782609

00:26:27.590 --> 00:26:32.266 I think in my experience there are

NOTE Confidence: 0.843689094782609

00:26:32.266 --> 00:26:35.434 definitely patients who achieved a a

NOTE Confidence: 0.843689094782609

00:26:35.434 --> 00:26:37.762 superior nutritional status and had a

NOTE Confidence: 0.843689094782609

00:26:37.762 --> 00:26:40.488 they were better surgical candidates,

NOTE Confidence: 0.843689094782609

00:26:40.490 --> 00:26:42.250 ultimately because they got induction,

NOTE Confidence: 0.843689094782609

00:26:42.250 --> 00:26:45.154 chemo and then moved on to chemo radiation

NOTE Confidence: 0.843689094782609

00:26:45.154 --> 00:26:48.209 instead of just getting hammered right away.

NOTE Confidence: 0.843689094782609

00:26:48.210 --> 00:26:49.878 Clearly there also had patients that

NOTE Confidence: 0.843689094782609

00:26:49.878 --> 00:26:52.009 got so much chemo by the time they

NOTE Confidence: 0.843689094782609

00:26:52.009 --> 00:26:53.770 got to the operating room they were.

NOTE Confidence: 0.843689094782609

00:26:53.770 --> 00:26:55.480 So they just really didn't.

NOTE Confidence: 0.843689094782609

00:26:55.480 --> 00:26:56.772 They distorted, never recovered.

NOTE Confidence: 0.843689094782609

00:26:56.772 --> 00:26:59.040 And it and it increased the risk.

NOTE Confidence: 0.843689094782609

00:26:59.040 --> 00:27:03.616 And so one thing I love about Connecticut,

NOTE Confidence: 0.843689094782609

00:27:03.620 --> 00:27:05.852 I've practiced in a couple of

NOTE Confidence: 0.843689094782609

00:27:05.852 --> 00:27:06.596 different places.

NOTE Confidence: 0.843689094782609

00:27:06.600 --> 00:27:08.616 The medical oncologists have been really

NOTE Confidence: 0.843689094782609

00:27:08.616 --> 00:27:11.203 engaged and just say you know and I and

NOTE Confidence: 0.843689094782609

00:27:11.203 --> 00:27:13.160 been really open to this conversation.

NOTE Confidence: 0.843689094782609

00:27:13.160 --> 00:27:14.312 And often, you know,

NOTE Confidence: 0.843689094782609

00:27:14.312 --> 00:27:16.360 there's no scientific way of doing this,

NOTE Confidence: 0.843689094782609

00:27:16.360 --> 00:27:19.538 but but a gestalt of are they?

NOTE Confidence: 0.843689094782609

00:27:19.540 --> 00:27:21.444 What's the regimen that's going to really

NOTE Confidence: 0.843689094782609

00:27:21.444 --> 00:27:24.009 get them to take advantage of all modalities?

NOTE Confidence: 0.843689094782609

00:27:24.010 --> 00:27:26.376 And so I do think if they're

NOTE Confidence: 0.843689094782609

00:27:26.376 --> 00:27:28.220 obstructive and then nutritions.

NOTE Confidence: 0.843689094782609

00:27:28.220 --> 00:27:30.728 An issue trying to optimize them,

NOTE Confidence: 0.843689094782609

00:27:30.730 --> 00:27:33.478 I think in our experience the

NOTE Confidence: 0.843689094782609

00:27:33.478 --> 00:27:36.260 induction chemo is very effective.

NOTE Confidence: 0.843689094782609

00:27:36.260 --> 00:27:40.365 But I do think there are people who

NOTE Confidence: 0.843689094782609

00:27:40.365 --> 00:27:42.742 just get so debilitated from all

NOTE Confidence: 0.843689094782609

00:27:42.742 --> 00:27:45.390 of the induction to try to to to

NOTE Confidence: 0.843689094782609

00:27:45.480 --> 00:27:48.149 identify those people so that they

NOTE Confidence: 0.843689094782609

00:27:48.149 --> 00:27:50.087 don't miss out on an opportunity

NOTE Confidence: 0.843689094782609

00:27:50.087 --> 00:27:52.168 of a curative and resection.

NOTE Confidence: 0.814064201111111

00:27:54.490 --> 00:27:58.612 I have a question before we let Dan go,

NOTE Confidence: 0.814064201111111

00:27:58.620 --> 00:28:01.250 I don't know how close to this part

NOTE Confidence: 0.814064201111111

00:28:01.250 --> 00:28:03.890 of the data that you might be,

NOTE Confidence: 0.814064201111111

00:28:03.890 --> 00:28:08.178 but in the trial with Nivolumab did anyone

NOTE Confidence: 0.814064201111111

00:28:08.178 --> 00:28:12.192 have to withdraw due to immune related

NOTE Confidence: 0.814064201111111

00:28:12.192 --> 00:28:15.247 adverse events from the checkpoint?

NOTE Confidence: 0.814064201111111

00:28:15.250 --> 00:28:17.100 Or was there a significant?

NOTE Confidence: 0.814064201111111

00:28:17.100 --> 00:28:19.062 Was there any incidents or could

NOTE Confidence: 0.814064201111111

00:28:19.062 --> 00:28:20.394 you talk about that at all?

NOTE Confidence: 0.857597785

00:28:21.880 --> 00:28:24.268 Great question and and I'm gonna.

NOTE Confidence: 0.857597785

00:28:24.270 --> 00:28:27.035 I'm Jill is going to know exactly

NOTE Confidence: 0.857597785

00:28:27.035 --> 00:28:29.169 what I'm talking about here,

NOTE Confidence: 0.857597785

00:28:29.170 --> 00:28:32.824 but we so. So in the trial,

NOTE Confidence: 0.857597785

00:28:32.830 --> 00:28:35.230 discontinuation of therapy was about

NOTE Confidence: 0.857597785

00:28:35.230 --> 00:28:39.665 10 percent 910% and and I would say. I,

NOTE Confidence: 0.857597785

00:28:39.665 --> 00:28:43.577 I think that is an overly optimistic number.

NOTE Confidence: 0.857597785

00:28:43.577 --> 00:28:47.713 We've now had the advantage of seeing people

NOTE Confidence: 0.857597785

00:28:47.720 --> 00:28:50.348 on on nivolumab after Esophagectomy and

NOTE Confidence: 0.857597785

00:28:50.348 --> 00:28:54.100 I I don't think it's a walk in the park.

NOTE Confidence: 0.857597785

00:28:54.100 --> 00:28:55.520 I think it's tolerated,

NOTE Confidence: 0.857597785

00:28:55.520 --> 00:28:57.856 but I think it does. You know?

NOTE Confidence: 0.857597785

00:28:57.856 --> 00:28:59.246 Unlike because we've because I

NOTE Confidence: 0.857597785

00:28:59.246 --> 00:29:01.560 do a lot of lung cancer and we

NOTE Confidence: 0.857597785

00:29:01.560 --> 00:29:02.980 give a ton of immunotherapy.

NOTE Confidence: 0.857597785

00:29:02.980 --> 00:29:06.228 I personally think it is a it is a

NOTE Confidence: 0.857597785

00:29:06.228 --> 00:29:09.619 real thing to go through immunotherapy.

NOTE Confidence: 0.857597785

00:29:09.620 --> 00:29:14.138 After off Ectomy and I would guess

NOTE Confidence: 0.857597785

00:29:14.138 --> 00:29:17.800 that that more than 10% of people

NOTE Confidence: 0.857597785

00:29:17.800 --> 00:29:19.696 have a hard time with it.

NOTE Confidence: 0.857597785

00:29:19.700 --> 00:29:21.032 But but Joe, what?

NOTE Confidence: 0.857597785

00:29:21.032 --> 00:29:23.030 What is your sense of that?

NOTE Confidence: 0.921176828571429

00:29:24.840 --> 00:29:26.499 This is a learning curve for all

NOTE Confidence: 0.921176828571429

00:29:26.499 --> 00:29:28.147 of us because this is very new,

NOTE Confidence: 0.921176828571429

00:29:28.150 --> 00:29:31.398 so I I think we don't have vast

NOTE Confidence: 0.921176828571429

00:29:31.398 --> 00:29:33.158 experience yet in that study I

NOTE Confidence: 0.921176828571429

00:29:33.158 --> 00:29:34.494 think was about 10% discontinuation

NOTE Confidence: 0.921176828571429

00:29:34.494 --> 00:29:36.030 for treatment related areas,

NOTE Confidence: 0.921176828571429

00:29:36.030 --> 00:29:37.738 and I would imagine that most of

NOTE Confidence: 0.921176828571429

00:29:37.738 --> 00:29:39.597 those were felt to be immune related.

NOTE Confidence: 0.921176828571429

00:29:39.600 --> 00:29:41.256 So I mean, I think in general we

NOTE Confidence: 0.921176828571429

00:29:41.256 --> 00:29:42.928 think Nevo is a well tolerated drug,

NOTE Confidence: 0.921176828571429

00:29:42.930 --> 00:29:45.604 a single agent with a low incidence

NOTE Confidence: 0.921176828571429

00:29:45.604 --> 00:29:47.620 of serious immune related AE,

NOTE Confidence: 0.921176828571429

00:29:47.620 --> 00:29:49.310 but I think you're right, Dan.

NOTE Confidence: 0.921176828571429

00:29:49.310 --> 00:29:50.690 This is a new patient population.

NOTE Confidence: 0.921176828571429

00:29:50.690 --> 00:29:52.394 We've not done this before in large numbers,

NOTE Confidence: 0.921176828571429

00:29:52.400 --> 00:29:54.698 so I think to be continued,

NOTE Confidence: 0.921176828571429

00:29:54.700 --> 00:29:57.112 we'll we'll have to see how it plays out.

NOTE Confidence: 0.921176828571429

00:29:57.120 --> 00:29:58.292 Just one final question,

NOTE Confidence: 0.921176828571429

00:29:58.292 --> 00:30:00.642 and maybe this is the lead in for

NOTE Confidence: 0.921176828571429

00:30:00.642 --> 00:30:02.226 Marie's talk you you you showed

NOTE Confidence: 0.921176828571429

00:30:02.226 --> 00:30:03.778 some of the information about

NOTE Confidence: 0.921176828571429

00:30:03.778 --> 00:30:05.692 PDL 1 scoring in this study?

NOTE Confidence: 0.921176828571429

00:30:05.700 --> 00:30:08.409 Was that done in the post treatment

NOTE Confidence: 0.921176828571429

00:30:08.409 --> 00:30:09.570 Pathologic specimen stand?

NOTE Confidence: 0.921176828571429

00:30:09.570 --> 00:30:11.217 Do you know off the top of your head?

NOTE Confidence: 0.918834906

00:30:12.170 --> 00:30:14.249 Yeah, that's a great question, I don't know.

NOTE Confidence: 0.830067296666667

00:30:15.210 --> 00:30:17.894 Because, you know, going to,

NOTE Confidence: 0.830067296666667

00:30:17.894 --> 00:30:19.798 I think educate us all about some

NOTE Confidence: 0.830067296666667

00:30:19.798 --> 00:30:21.787 of the challenges with PDL one,

NOTE Confidence: 0.830067296666667

00:30:21.790 --> 00:30:25.535 but I think 1 issue is that.

NOTE Confidence: 0.830067296666667

00:30:25.540 --> 00:30:26.520 We don't really have a.

NOTE Confidence: 0.830067296666667

00:30:26.520 --> 00:30:28.886 I don't think a clear understanding of

NOTE Confidence: 0.830067296666667

00:30:28.886 --> 00:30:32.182 what we would see with PDL 1 scoring

NOTE Confidence: 0.830067296666667

00:30:32.182 --> 00:30:34.392 pretreatment and then post chemoradiotherapy,

NOTE Confidence: 0.830067296666667

00:30:34.400 --> 00:30:35.954 but you have to imagine it's

NOTE Confidence: 0.830067296666667

00:30:35.954 --> 00:30:37.480 going to affect the results.

NOTE Confidence: 0.830067296666667

00:30:37.480 --> 00:30:38.784 So all right, Dan,

NOTE Confidence: 0.830067296666667

00:30:38.784 --> 00:30:40.088 thank you very much.

NOTE Confidence: 0.830067296666667

00:30:40.090 --> 00:30:42.652 That was really a great review

NOTE Confidence: 0.830067296666667

00:30:42.652 --> 00:30:44.360 of really important studies.

NOTE Confidence: 0.830067296666667

00:30:44.360 --> 00:30:47.360 So we're going to move on to our second talk.

NOTE Confidence: 0.830067296666667

00:30:47.360 --> 00:30:49.824 We're going to shift directions now and

NOTE Confidence: 0.830067296666667

00:30:49.824 --> 00:30:52.949 take a very deep dive into immunotherapy.

NOTE Confidence: 0.830067296666667

00:30:52.950 --> 00:30:54.838 And as I think, most of you know,

NOTE Confidence: 0.830067296666667

00:30:54.840 --> 00:30:57.010 in the last two years we have

NOTE Confidence: 0.830067296666667

00:30:57.010 --> 00:30:59.511 heard a lot about immunotherapy

NOTE Confidence: 0.830067296666667

00:30:59.511 --> 00:31:01.740 and gastroesophageal cancers.

NOTE Confidence: 0.830067296666667

00:31:01.740 --> 00:31:04.386 And we are deploying it quite regularly

NOTE Confidence: 0.830067296666667

00:31:04.386 --> 00:31:07.038 now in the first line setting.

NOTE Confidence: 0.830067296666667

00:31:07.040 --> 00:31:10.460 And there's a lot of chatter about.

NOTE Confidence: 0.830067296666667

00:31:10.460 --> 00:31:13.662 How do we use PDL one as a

NOTE Confidence: 0.830067296666667

00:31:13.662 --> 00:31:15.194 predictive biomarker in choosing

NOTE Confidence: 0.830067296666667

00:31:15.194 --> 00:31:17.269 an patients for immunotherapy in

NOTE Confidence: 0.830067296666667

00:31:17.269 --> 00:31:19.735 the first line setting and beyond.

NOTE Confidence: 0.830067296666667

00:31:19.740 --> 00:31:22.001 And Marie is going to shed some

NOTE Confidence: 0.830067296666667

00:31:22.001 --> 00:31:24.558 light on that very confusing topic.

NOTE Confidence: 0.830067296666667

00:31:24.560 --> 00:31:27.424 And then with that backdrop then I will

NOTE Confidence: 0.830067296666667

00:31:27.424 --> 00:31:30.456 then review some of the more recent studies.

NOTE Confidence: 0.830067296666667

00:31:30.460 --> 00:31:32.092 So Marie Doctor Robert,

NOTE Confidence: 0.830067296666667

00:31:32.092 --> 00:31:34.540 another wonderful colleague of mine that

NOTE Confidence: 0.830067296666667

00:31:34.612 --> 00:31:37.033 I get to work with on a regular basis.

NOTE Confidence: 0.830067296666667

00:31:37.040 --> 00:31:38.840 Is professor of pathology,

NOTE Confidence: 0.830067296666667

00:31:38.840 --> 00:31:39.290 medicine,

NOTE Confidence: 0.830067296666667

00:31:39.290 --> 00:31:42.068 and human and translational immunology here.

NOTE Confidence: 0.830067296666667

00:31:42.070 --> 00:31:44.966 And she directs our GI pathology program and,

NOTE Confidence: 0.830067296666667

00:31:44.970 --> 00:31:47.588 very importantly and relevant to her topic.

NOTE Confidence: 0.830067296666667

00:31:47.590 --> 00:31:51.517 Tonight she is Co leading an important

NOTE Confidence: 0.830067296666667

00:31:51.517 --> 00:31:53.903 international study on interobserver

NOTE Confidence: 0.830067296666667

00:31:53.903 --> 00:31:57.545 agreement in PDL one CPS scoring

NOTE Confidence: 0.830067296666667

00:31:57.545 --> 00:32:00.420 and gastric cancer, so Marie.

NOTE Confidence: 0.830067296666667

00:32:00.420 --> 00:32:01.470 Thank you.

NOTE Confidence: 0.953792594

00:32:02.150 --> 00:32:04.430 Thank you so much, Jill.

NOTE Confidence: 0.953792594

00:32:04.430 --> 00:32:07.415 And I'm still smiling despite

NOTE Confidence: 0.953792594

00:32:07.415 --> 00:32:10.400 being on doing that study.

NOTE Confidence: 0.953792594

00:32:10.400 --> 00:32:14.180 OK, so I think you can see my screen.

NOTE Confidence: 0.953792594

00:32:14.180 --> 00:32:17.628 Well, I'm delighted to be here with you

NOTE Confidence: 0.953792594

00:32:17.628 --> 00:32:20.220 today in person and those watching later on.

NOTE Confidence: 0.953792594

00:32:20.220 --> 00:32:24.172 And I want to thank Doctor Lacey for the

NOTE Confidence: 0.953792594

00:32:24.172 --> 00:32:28.330 invitation and Doctor Boffa for sharing the.

NOTE Confidence: 0.953792594

00:32:28.330 --> 00:32:30.978 Virtual podium this evening.

NOTE Confidence: 0.953792594

00:32:30.980 --> 00:32:34.679 I hope that I will only spend about 20

NOTE Confidence: 0.953792594

00:32:34.679 --> 00:32:38.090 maximum 25 minutes discussing really the

NOTE Confidence: 0.953792594

00:32:38.090 --> 00:32:42.780 inside baseball nitty gritty in the weeds.

NOTE Confidence: 0.953792594

00:32:42.780 --> 00:32:46.175 What does it mean to score a

NOTE Confidence: 0.953792594

00:32:46.175 --> 00:32:47.630 PD1 immunohistochemical stain

NOTE Confidence: 0.953792594

00:32:47.722 --> 00:32:50.434 in gastric cancer and this would

NOTE Confidence: 0.953792594

00:32:50.434 --> 00:32:53.000 apply to other tumors as well,

NOTE Confidence: 0.953792594

00:32:53.000 --> 00:32:55.864 and so the subtitle is the challenges and

NOTE Confidence: 0.953792594

00:32:55.864 --> 00:32:57.837 interpretation and how for a clinician,

NOTE Confidence: 0.953792594

00:32:57.840 --> 00:32:59.736 how should one decipher the report?

NOTE Confidence: 0.953792594

00:32:59.740 --> 00:33:02.240 These are my disclosures.

NOTE Confidence: 0.953792594

00:33:02.240 --> 00:33:03.640 So by way of outline,

NOTE Confidence: 0.953792594

00:33:03.640 --> 00:33:05.760 I'm just going to spend a moment just

NOTE Confidence: 0.953792594

00:33:05.760 --> 00:33:07.699 second on things you already know,

NOTE Confidence: 0.953792594

00:33:07.700 --> 00:33:09.008 way better than me.

NOTE Confidence: 0.953792594

00:33:09.008 --> 00:33:10.970 The rationale for blocking PD one

NOTE Confidence: 0.953792594

00:33:11.036 --> 00:33:14.340 receptors on immune cells in cancer.

NOTE Confidence: 0.953792594

00:33:14.340 --> 00:33:18.036 Spend the bulk of the time talking about.

NOTE Confidence: 0.953792594

00:33:18.040 --> 00:33:21.925 An overview of the development of the

NOTE Confidence: 0.953792594

00:33:21.925 --> 00:33:24.617 PO1 immunohistochemical stain as a

NOTE Confidence: 0.953792594

00:33:24.617 --> 00:33:26.505 companion or complementary diagnostic

NOTE Confidence: 0.953792594

00:33:26.505 --> 00:33:30.300 for the use of checkpoint inhibitors,

NOTE Confidence: 0.953792594

00:33:30.300 --> 00:33:32.540 and we're really going to look very,

NOTE Confidence: 0.953792594

00:33:32.540 --> 00:33:35.156 very intensely at how Pedial Wednesdays

NOTE Confidence: 0.953792594

00:33:35.156 --> 00:33:37.750 are interpreted at the microscope,

NOTE Confidence: 0.953792594

00:33:37.750 --> 00:33:39.759 and I will show you examples and

NOTE Confidence: 0.953792594

00:33:39.759 --> 00:33:43.248 ask you to do this with me.

NOTE Confidence: 0.953792594

00:33:43.250 --> 00:33:47.120 And in doing so, I hope to.

NOTE Confidence: 0.953792594

00:33:47.120 --> 00:33:48.148 Sort of.

NOTE Confidence: 0.953792594

00:33:48.148 --> 00:33:50.718 Unveil the challenges in applying

NOTE Confidence: 0.953792594

00:33:50.718 --> 00:33:53.277 the scoring criteria that are

NOTE Confidence: 0.953792594

00:33:53.277 --> 00:33:55.607 recommended by the Agilent Dako

NOTE Confidence: 0.953792594

00:33:55.610 --> 00:33:58.982 group for two are proportions.

NOTE Confidence: 0.953792594

00:33:58.982 --> 00:34:01.250 Score what we're really about today.

NOTE Confidence: 0.953792594

00:34:01.250 --> 00:34:03.906 The combined positive score and all of that

NOTE Confidence: 0.953792594

00:34:03.906 --> 00:34:06.936 is about scoring tumor cells in immune cells.

NOTE Confidence: 0.953792594

00:34:06.940 --> 00:34:09.789 And this will get to the question

NOTE Confidence: 0.953792594

00:34:09.789 --> 00:34:11.602 of Interobserver agreement and

NOTE Confidence: 0.953792594

00:34:11.602 --> 00:34:13.177 reproducibility of results.

NOTE Confidence: 0.953792594

00:34:13.180 --> 00:34:16.638 Finally, I'll hope to help decipher reports,

NOTE Confidence: 0.953792594

00:34:16.640 --> 00:34:20.216 at least the Yale reports and.

NOTE Confidence: 0.953792594

00:34:20.220 --> 00:34:21.879 Touch on what I think would be,

NOTE Confidence: 0.953792594

00:34:21.880 --> 00:34:24.036 I think what everyone thinks who does

NOTE Confidence: 0.953792594

00:34:24.036 --> 00:34:26.945 this for a living is what would be great.

NOTE Confidence: 0.953792594

00:34:26.950 --> 00:34:28.510 A future directions.

NOTE Confidence: 0.953792594

00:34:28.510 --> 00:34:33.090 So this is the tried and true example.

NOTE Confidence: 0.953792594

00:34:33.090 --> 00:34:34.035 There's a cartoon.

NOTE Confidence: 0.953792594

00:34:34.035 --> 00:34:34.980 There are many.

NOTE Confidence: 0.953792594

00:34:34.980 --> 00:34:38.196 This happens to be photos from the Agilent

NOTE Confidence: 0.953792594

00:34:38.200 --> 00:34:40.960 Vehicle Training manual for pathologists.

NOTE Confidence: 0.953792594

00:34:40.960 --> 00:34:42.680 I, just to remind everyone what are we?

NOTE Confidence: 0.953792594

00:34:42.680 --> 00:34:43.660 What are we standing here?

NOTE Confidence: 0.953792594

00:34:43.660 --> 00:34:44.660 What are we talking about?

NOTE Confidence: 0.953792594

00:34:44.660 --> 00:34:48.848 So PDL one and also PDL 2 Stanford

NOTE Confidence: 0.953792594

00:34:48.848 --> 00:34:50.960 Program cell death ligand.

NOTE Confidence: 0.953792594

00:34:50.960 --> 00:34:53.306 So the ligand is the thing

NOTE Confidence: 0.953792594

00:34:53.306 --> 00:34:55.380 sticking out of the cell.

NOTE Confidence: 0.953792594

00:34:55.380 --> 00:34:58.490 On the membrane and it's expressed

NOTE Confidence: 0.953792594

00:34:58.490 --> 00:35:00.463 normally in normal cells,

NOTE Confidence: 0.953792594

00:35:00.463 --> 00:35:01.636 normal immune cells,

NOTE Confidence: 0.953792594

00:35:01.640 --> 00:35:02.906 epithelial cells,

NOTE Confidence: 0.953792594

00:35:02.906 --> 00:35:05.438 fibroblasts and endothelial cells

NOTE Confidence: 0.953792594

00:35:05.438 --> 00:35:07.337 and the ligate.

NOTE Confidence: 0.953792594

00:35:07.340 --> 00:35:09.452 The the receptor for this to the PD

NOTE Confidence: 0.953792594

00:35:09.452 --> 00:35:11.713 one which is the program cell death

NOTE Confidence: 0.953792594

00:35:11.713 --> 00:35:14.690 receptor is expressed on the surface of.

NOTE Confidence: 0.953792594

00:35:14.690 --> 00:35:17.189 Inflammatory cells CD 4 positive and CD

NOTE Confidence: 0.953792594

00:35:17.189 --> 00:35:20.190 8 positive T cells natural killer cells,

NOTE Confidence: 0.953792594

00:35:20.190 --> 00:35:21.504 B cells,

NOTE Confidence: 0.953792594

00:35:21.504 --> 00:35:22.161 macrophages,

NOTE Confidence: 0.953792594

00:35:22.161 --> 00:35:26.103 and dendritic cells and in health.

NOTE Confidence: 0.953792594

00:35:26.110 --> 00:35:29.673 The purpose of the PD one ligand

NOTE Confidence: 0.953792594

00:35:29.673 --> 00:35:34.748 is to bind to a T cell receptor

NOTE Confidence: 0.953792594

00:35:34.750 --> 00:35:38.369 and and and tell it I'm OK.

NOTE Confidence: 0.953792594

00:35:38.370 --> 00:35:39.408 This is me.

NOTE Confidence: 0.953792594

00:35:39.408 --> 00:35:43.070 This is you stop and cease and desist friend.

NOTE Confidence: 0.953792594

00:35:43.070 --> 00:35:47.570 And this prevents autoimmunity.

NOTE Confidence: 0.821920152857143

00:35:47.570 --> 00:35:50.006 Interesting when that breaks down not just

NOTE Confidence: 0.821920152857143

00:35:50.006 --> 00:35:52.529 because of drugs but from other diseases.

NOTE Confidence: 0.821920152857143

00:35:52.530 --> 00:35:57.206 The then you can get bad autoimmunity.

NOTE Confidence: 0.821920152857143

00:35:57.210 --> 00:35:58.904 It is one of the mechanisms actually.

NOTE Confidence: 0.821920152857143

00:35:58.910 --> 00:36:00.695 As a side point is there's the

NOTE Confidence: 0.821920152857143

00:36:00.695 --> 00:36:02.390 CLA 4 deficiency that can lead

NOTE Confidence: 0.821920152857143

00:36:02.390 --> 00:36:05.110 to severe colitis, for example.

NOTE Confidence: 0.821920152857143

00:36:05.110 --> 00:36:07.530 But in tumor growth,

NOTE Confidence: 0.821920152857143

00:36:07.530 --> 00:36:10.766 some tumor cells develop the ability

NOTE Confidence: 0.821920152857143

00:36:10.766 --> 00:36:14.070 and mimic normal cells by up regulating

NOTE Confidence: 0.821920152857143

00:36:14.070 --> 00:36:17.210 PD1 ligand on their membranes,

NOTE Confidence: 0.821920152857143

00:36:17.210 --> 00:36:19.849 and then they trick the cytotoxic T

NOTE Confidence: 0.821920152857143

00:36:19.849 --> 00:36:22.510 cell which binds via the PD1 receptor

NOTE Confidence: 0.821920152857143

00:36:22.510 --> 00:36:24.827 and it activates the cytotoxic T cell

NOTE Confidence: 0.821920152857143

00:36:24.827 --> 00:36:27.313 which is supposed to recognize this as

NOTE Confidence: 0.821920152857143

00:36:27.313 --> 00:36:29.449 something that doesn't belong and kill

NOTE Confidence: 0.821920152857143

00:36:29.509 --> 00:36:32.238 it and so you all know this very very

NOTE Confidence: 0.821920152857143

00:36:32.238 --> 00:36:35.616 well and therefore the the rationale behind.

NOTE Confidence: 0.821920152857143

00:36:35.620 --> 00:36:39.986 Anti PD One therapy is to give an

NOTE Confidence: 0.821920152857143

00:36:39.986 --> 00:36:42.104 antibody that will bind instead of

NOTE Confidence: 0.821920152857143

00:36:42.104 --> 00:36:45.179 the PD one ligand on a tumor cell

NOTE Confidence: 0.821920152857143

00:36:45.179 --> 00:36:47.438 will block these receptors and allow

NOTE Confidence: 0.821920152857143

00:36:47.438 --> 00:36:49.734 these cells to then not to say,

NOTE Confidence: 0.821920152857143

00:36:49.740 --> 00:36:50.700 hey, you're not me,

NOTE Confidence: 0.821920152857143

00:36:50.700 --> 00:36:52.690 you're not self and and attack.

NOTE Confidence: 0.821920152857143

00:36:52.690 --> 00:36:54.050 That's the rationale.

NOTE Confidence: 0.78120005

00:36:57.270 --> 00:37:02.636 So. I'm trying to put my pictures somewhere.

NOTE Confidence: 0.78120005

00:37:02.640 --> 00:37:05.244 This led to this these the discoveries

NOTE Confidence: 0.78120005

00:37:05.244 --> 00:37:06.740 about this, the wonderful science,

NOTE Confidence: 0.78120005

00:37:06.740 --> 00:37:11.020 some of a lot of which done it, Yale.

NOTE Confidence: 0.78120005

00:37:11.020 --> 00:37:13.402 The development led to the development

NOTE Confidence: 0.78120005

00:37:13.402 --> 00:37:14.593 of immunohistochemical PDL.

NOTE Confidence: 0.78120005

00:37:14.600 --> 00:37:17.372 One stain as a companion or companion

NOTE Confidence: 0.78120005

00:37:17.372 --> 00:37:18.980 meaning companion diagnostic means.

NOTE Confidence: 0.78120005

00:37:18.980 --> 00:37:20.758 If you don't have this result you

NOTE Confidence: 0.78120005

00:37:20.758 --> 00:37:22.739 can't give the drug or complementary.

NOTE Confidence: 0.78120005

00:37:22.740 --> 00:37:23.910 We want to know the result,

NOTE Confidence: 0.78120005

00:37:23.910 --> 00:37:25.690 but either way we'll still

NOTE Confidence: 0.78120005

00:37:25.690 --> 00:37:27.114 use the drug diagnostic,

NOTE Confidence: 0.78120005

00:37:27.120 --> 00:37:29.940 so immunohistochemical stains

NOTE Confidence: 0.78120005

00:37:29.940 --> 00:37:31.416 if you don't know, they're very.

NOTE Confidence: 0.78120005

00:37:31.420 --> 00:37:32.860 I think you all do.

NOTE Confidence: 0.78120005

00:37:32.860 --> 00:37:35.730 These are these are a series of

NOTE Confidence: 0.78120005

00:37:35.730 --> 00:37:37.790 antibodies linked together to identify

NOTE Confidence: 0.78120005

00:37:37.790 --> 00:37:40.070 a molecule on a formalin fixed,

NOTE Confidence: 0.78120005

00:37:40.070 --> 00:37:42.040 or it could be frozen,

NOTE Confidence: 0.78120005

00:37:42.040 --> 00:37:44.882 fixed piece of human tissue or any

NOTE Confidence: 0.78120005

00:37:44.882 --> 00:37:48.340 tissue that is in mostly in this setting.

NOTE Confidence: 0.78120005

00:37:48.340 --> 00:37:49.956 Formalin fixed and paraffin

NOTE Confidence: 0.78120005

00:37:49.956 --> 00:37:52.380 embedded and cut onto a slide.

NOTE Confidence: 0.78120005

00:37:52.380 --> 00:37:54.372 And this is the of course on the

NOTE Confidence: 0.78120005

00:37:54.372 --> 00:37:56.118 manual they show beautiful stain.

NOTE Confidence: 0.78120005

00:37:56.120 --> 00:37:57.674 This is an example of a PD.

NOTE Confidence: 0.78120005

00:37:57.680 --> 00:38:01.713 One stain on a cancer and you see

NOTE Confidence: 0.78120005

00:38:01.713 --> 00:38:03.579 the brown is positive stain and

NOTE Confidence: 0.78120005

00:38:03.579 --> 00:38:05.778 it's outlining the cell membrane,

NOTE Confidence: 0.78120005

00:38:05.780 --> 00:38:07.940 so it's membranous, strong,

NOTE Confidence: 0.78120005

00:38:07.940 --> 00:38:09.020 membranous staining.

NOTE Confidence: 0.78120005

00:38:09.020 --> 00:38:12.156 If anyone looks at her too immunostains,

NOTE Confidence: 0.78120005

00:38:12.160 --> 00:38:14.078 it's very similar when it's this strong,

NOTE Confidence: 0.78120005

00:38:14.080 --> 00:38:16.424 it's similar to what up 3 plus positive

NOTE Confidence: 0.78120005

00:38:16.424 --> 00:38:18.817 her two stain would look like strong

NOTE Confidence: 0.78120005

00:38:18.817 --> 00:38:21.000 member to staining on tumor cells.

NOTE Confidence: 0.78120005

00:38:21.000 --> 00:38:21.290 OK,

NOTE Confidence: 0.78120005

00:38:21.290 --> 00:38:22.450 but that's the manual.

NOTE Confidence: 0.78120005

00:38:22.450 --> 00:38:24.724 And then there's real life so,

NOTE Confidence: 0.78120005

00:38:24.724 --> 00:38:26.236 but this development,

NOTE Confidence: 0.78120005

00:38:26.236 --> 00:38:29.260 I was very successful and LED

NOTE Confidence: 0.78120005

00:38:29.352 --> 00:38:31.409 to in 2015 the Deco,

NOTE Confidence: 0.78120005

00:38:31.409 --> 00:38:36.519 which is bought by Agilent few years later.

NOTE Confidence: 0.78120005

00:38:36.519 --> 00:38:40.190 Firm DX anti PD122C3 assay which

NOTE Confidence: 0.78120005

00:38:40.190 --> 00:38:42.240 was first developed and FDA

NOTE Confidence: 0.78120005

00:38:42.240 --> 00:38:44.842 approved for lung cancer in 2017.

NOTE Confidence: 0.78120005

00:38:44.842 --> 00:38:46.766 The combined positive score

NOTE Confidence: 0.78120005

00:38:46.766 --> 00:38:49.460 I'll be defining all of this.

NOTE Confidence: 0.78120005

00:38:49.460 --> 00:38:52.281 Was FDA approved for gastric and GJ

NOTE Confidence: 0.78120005

00:38:52.281 --> 00:38:55.308 had no person Noma after phase two?

NOTE Confidence: 0.78120005

00:38:55.310 --> 00:38:56.909 Keynote 59 trial.

NOTE Confidence: 0.743889245

00:38:59.090 --> 00:39:01.865 So Agilent or Dayco developed

NOTE Confidence: 0.743889245

00:39:01.865 --> 00:39:04.640 and and but this this.

NOTE Confidence: 0.743889245

00:39:04.640 --> 00:39:07.503 This approval was based on pathologist at

NOTE Confidence: 0.743889245

00:39:07.503 --> 00:39:10.857 Merck and I'll talk about this in a moment.

NOTE Confidence: 0.743889245

00:39:10.860 --> 00:39:14.371 The the scoring, the the the putting

NOTE Confidence: 0.743889245

00:39:14.371 --> 00:39:16.326 together of combined positive score.

NOTE Confidence: 0.743889245

00:39:16.330 --> 00:39:19.260 What was it? How to do it was done in

NOTE Confidence: 0.743889245

00:39:19.345 --> 00:39:22.439 the confines of a single company Merck.

NOTE Confidence: 0.743889245

00:39:22.440 --> 00:39:25.674 And and the FDA approved their methodology.

NOTE Confidence: 0.743889245

00:39:25.680 --> 00:39:26.970 That's how that got going.

NOTE Confidence: 0.743889245

00:39:26.970 --> 00:39:30.804 That's how CPS came to be as a requirement.

NOTE Confidence: 0.743889245

00:39:30.810 --> 00:39:33.690 Was not tested outside of that.

NOTE Confidence: 0.743889245

00:39:33.690 --> 00:39:35.946 It's important to know that so,

NOTE Confidence: 0.743889245

00:39:35.950 --> 00:39:36.942 but nonetheless,

NOTE Confidence: 0.743889245

00:39:36.942 --> 00:39:38.926 Agilent then developed training

NOTE Confidence: 0.743889245

00:39:38.926 --> 00:39:41.919 modules for work and day pathologists

NOTE Confidence: 0.743889245

00:39:41.919 --> 00:39:44.896 like myself and others to to

NOTE Confidence: 0.743889245

00:39:44.896 --> 00:39:48.767 train and learn how to look at.

NOTE Confidence: 0.743889245

00:39:48.770 --> 00:39:51.810 Video 1 stains and produce these scores from

NOTE Confidence: 0.743889245

00:39:51.810 --> 00:39:54.539 the methods developed in house at Merck.

NOTE Confidence: 0.743889245

00:39:54.540 --> 00:39:56.232 I will just mention that now

NOTE Confidence: 0.743889245

00:39:56.232 --> 00:39:57.360 there are multiple antibodies.

NOTE Confidence: 0.743889245

00:39:57.360 --> 00:39:59.580 I purposefully mentioned the specific

NOTE Confidence: 0.743889245

00:39:59.580 --> 00:40:02.195 antibody 22 C three because that's

NOTE Confidence: 0.743889245

00:40:02.195 --> 00:40:04.442 the one that was approved by the

NOTE Confidence: 0.743889245

00:40:04.442 --> 00:40:06.797 FDA for this purpose and with CPS

NOTE Confidence: 0.743889245

00:40:06.797 --> 00:40:08.948 score and also TPS and inland.

NOTE Confidence: 0.743889245

00:40:08.948 --> 00:40:11.488 There are multiple antibodies available

NOTE Confidence: 0.743889245

00:40:11.488 --> 00:40:16.650 and at Yale we use the E1L 3N.

NOTE Confidence: 0.743889245

00:40:16.650 --> 00:40:20.690 Antibody that has been shown to have a

NOTE Confidence: 0.743889245

00:40:20.690 --> 00:40:24.772 homology and to work equally well as 22C3,

NOTE Confidence: 0.743889245

00:40:24.772 --> 00:40:28.300 and there's also 28 eight SP 142.

NOTE Confidence: 0.743889245

00:40:28.300 --> 00:40:30.340 Many proof of concept studies since

NOTE Confidence: 0.743889245

00:40:30.340 --> 00:40:32.582 I was not involved in those I

NOTE Confidence: 0.743889245

00:40:32.582 --> 00:40:35.120 feel I can brag for my colleagues.

NOTE Confidence: 0.743889245

00:40:35.120 --> 00:40:37.820 We're actually performed by Yale Smilow

NOTE Confidence: 0.743889245

00:40:37.820 --> 00:40:39.620 and pathology department faculty,

NOTE Confidence: 0.743889245

00:40:39.620 --> 00:40:43.240 and so it's a nice legacy of progress.

NOTE Confidence: 0.94158229

00:40:47.480 --> 00:40:48.810 But I think it's important

NOTE Confidence: 0.583820656666667

00:40:48.820 --> 00:40:50.209 is so so.

NOTE Confidence: 0.855144970666667

00:40:52.320 --> 00:40:54.744 Those of us who look at this stain

NOTE Confidence: 0.855144970666667

00:40:54.744 --> 00:40:57.379 on a daily basis have come to,

NOTE Confidence: 0.855144970666667

00:40:57.380 --> 00:40:59.240 I would say almost universally,

NOTE Confidence: 0.855144970666667

00:40:59.240 --> 00:41:00.496 across the United States.

NOTE Confidence: 0.855144970666667

00:41:00.496 --> 00:41:02.469 In any case, and opinions are

NOTE Confidence: 0.855144970666667

00:41:02.469 --> 00:41:04.527 slightly different in Europe from the

NOTE Confidence: 0.855144970666667

00:41:04.527 --> 00:41:06.277 pathologist with whom I interact with.

NOTE Confidence: 0.796600026666667

00:41:08.510 --> 00:41:12.308 That what we are having trouble.

NOTE Confidence: 0.796600026666667

00:41:12.310 --> 00:41:14.006 With reproducibility and with

NOTE Confidence: 0.796600026666667

00:41:14.006 --> 00:41:16.550 frankly performing the stain as it

NOTE Confidence: 0.796600026666667

00:41:16.618 --> 00:41:19.066 is laid out in the in the guidelines,

NOTE Confidence: 0.796600026666667

00:41:19.070 --> 00:41:20.870 I just like to share this with you.

NOTE Confidence: 0.796600026666667

00:41:20.870 --> 00:41:24.710 We do it, we we we do our very best.

NOTE Confidence: 0.796600026666667

00:41:24.710 --> 00:41:27.496 We follow the guidelines but I would

NOTE Confidence: 0.796600026666667

00:41:27.496 --> 00:41:30.848 like you to know about some concerns.

NOTE Confidence: 0.796600026666667

00:41:30.850 --> 00:41:32.540 About relying on this immunostain

NOTE Confidence: 0.796600026666667

00:41:32.540 --> 00:41:34.780 because I think we can move on,

NOTE Confidence: 0.796600026666667

00:41:34.780 --> 00:41:36.670 hopefully in the not so far

NOTE Confidence: 0.796600026666667

00:41:36.670 --> 00:41:37.930 future to something else,

NOTE Confidence: 0.796600026666667

00:41:37.930 --> 00:41:41.240 so it starts back from 2017 at ASCO.

NOTE Confidence: 0.796600026666667

00:41:41.240 --> 00:41:43.190 This presentation by Merck about

NOTE Confidence: 0.796600026666667

00:41:43.190 --> 00:41:45.077 the development of the combined

NOTE Confidence: 0.796600026666667

00:41:45.077 --> 00:41:46.807 positive score for the evaluation

NOTE Confidence: 0.796600026666667

00:41:46.807 --> 00:41:48.887 of PD one and solid tumors.

NOTE Confidence: 0.796600026666667

00:41:48.890 --> 00:41:51.254 Using this antibody and what they

NOTE Confidence: 0.796600026666667

00:41:51.254 --> 00:41:53.965 discussed is that they had an

NOTE Confidence: 0.796600026666667

00:41:53.965 --> 00:41:55.549 interobserver agreement amongst

NOTE Confidence: 0.796600026666667

00:41:55.549 --> 00:41:57.670 their pathologists of 88%,

NOTE Confidence: 0.796600026666667

00:41:57.670 --> 00:42:00.283 which sounds pretty good further.

NOTE Confidence: 0.796600026666667

00:42:00.283 --> 00:42:05.080 For a cut off of of Cpia score of 1,

NOTE Confidence: 0.796600026666667

00:42:05.080 --> 00:42:07.971 about 57% of the gastric cancers in

NOTE Confidence: 0.796600026666667

00:42:07.971 --> 00:42:10.680 their hands had a positive score.

NOTE Confidence: 0.796600026666667

00:42:10.680 --> 00:42:12.636 I've seen in in the literature

NOTE Confidence: 0.796600026666667

00:42:12.636 --> 00:42:15.485 and I would say in our hands it's

NOTE Confidence: 0.796600026666667

00:42:15.485 --> 00:42:17.693 somewhere more between 30 and 50%,

NOTE Confidence: 0.796600026666667

00:42:17.700 --> 00:42:20.170 but that's what they found.

NOTE Confidence: 0.796600026666667

00:42:20.170 --> 00:42:22.782 So that's interesting that in their

NOTE Confidence: 0.796600026666667

00:42:22.782 --> 00:42:25.290 hands they got an 88% agreement.

NOTE Confidence: 0.796600026666667

00:42:25.290 --> 00:42:30.110 As at a cutoff of 1. But what what?

NOTE Confidence: 0.796600026666667

00:42:30.110 --> 00:42:32.065 There are a few questions that this

NOTE Confidence: 0.796600026666667

00:42:32.065 --> 00:42:34.112 raises once we get into start doing

NOTE Confidence: 0.796600026666667

00:42:34.112 --> 00:42:36.740 this as we've been doing for some years now,

NOTE Confidence: 0.796600026666667

00:42:36.740 --> 00:42:38.336 there's not much data on agreement

NOTE Confidence: 0.796600026666667

00:42:38.336 --> 00:42:40.300 at other cut offs,

NOTE Confidence: 0.796600026666667

00:42:40.300 --> 00:42:42.756 nor at what if and what if the

NOTE Confidence: 0.796600026666667

00:42:42.756 --> 00:42:43.840 case will come,

NOTE Confidence: 0.796600026666667

00:42:43.840 --> 00:42:46.381 which it may be coming that oncologists

NOTE Confidence: 0.796600026666667

00:42:46.381 --> 00:42:48.919 would like to have an exact value,

NOTE Confidence: 0.796600026666667

00:42:48.920 --> 00:42:49.768 not a cut off,

NOTE Confidence: 0.796600026666667

00:42:49.768 --> 00:42:50.828 like greater than one greater

NOTE Confidence: 0.796600026666667

00:42:50.828 --> 00:42:51.997 than five greater than 10.

NOTE Confidence: 0.796600026666667

00:42:52.000 --> 00:42:56.398 But was it 8 or 45?

NOTE Confidence: 0.796600026666667

00:42:56.400 --> 00:42:58.423 And and I've heard I'm in discussions

NOTE Confidence: 0.796600026666667

00:42:58.423 --> 00:42:59.290 now with with.

NOTE Confidence: 0.796600026666667

00:42:59.290 --> 00:43:01.354 Gynecology here at Yale about what

NOTE Confidence: 0.796600026666667

00:43:01.354 --> 00:43:03.534 we should be providing and this

NOTE Confidence: 0.796600026666667

00:43:03.534 --> 00:43:05.374 is because the indications keep

NOTE Confidence: 0.796600026666667

00:43:05.374 --> 00:43:07.369 changing and there's new protocols

NOTE Confidence: 0.796600026666667

00:43:07.369 --> 00:43:09.013 and wonderful opportunities for

NOTE Confidence: 0.796600026666667

00:43:09.013 --> 00:43:11.702 patients to be treated with these

NOTE Confidence: 0.796600026666667

00:43:11.702 --> 00:43:15.349 medicines that may or may not depend

NOTE Confidence: 0.796600026666667

00:43:15.349 --> 00:43:18.478 upon certain criteria of MCPS.

NOTE Confidence: 0.796600026666667

00:43:18.480 --> 00:43:19.840 And I'm just very curious.

NOTE Confidence: 0.796600026666667

00:43:19.840 --> 00:43:21.247 I think we have the answer and

NOTE Confidence: 0.796600026666667

00:43:21.247 --> 00:43:22.340 we ask this question.

NOTE Confidence: 0.796600026666667

00:43:22.340 --> 00:43:24.855 How does agreement on combined

NOTE Confidence: 0.796600026666667

00:43:24.855 --> 00:43:26.364 positive score differ?

NOTE Confidence: 0.796600026666667

00:43:26.370 --> 00:43:28.590 From agreement on tumor proportion score,

NOTE Confidence: 0.796600026666667

00:43:28.590 --> 00:43:30.294 which is simply the percent of

NOTE Confidence: 0.796600026666667

00:43:30.294 --> 00:43:31.755 positive tumor cells over the

NOTE Confidence: 0.796600026666667

00:43:31.755 --> 00:43:33.105 total number of tumor cells,

NOTE Confidence: 0.796600026666667

00:43:33.110 --> 00:43:34.895 simple straight percentage and the

NOTE Confidence: 0.796600026666667

00:43:34.895 --> 00:43:37.200 hint is you're not surprised by this.

NOTE Confidence: 0.796600026666667

00:43:37.200 --> 00:43:40.404 You already know is that pathologists

NOTE Confidence: 0.796600026666667

00:43:40.404 --> 00:43:43.252 agree much better on TPS.

NOTE Confidence: 0.796600026666667

00:43:43.252 --> 00:43:46.725 If you have 10 pathologists look at

NOTE Confidence: 0.796600026666667

00:43:46.725 --> 00:43:50.238 the same sample then they would on CPS.

NOTE Confidence: 0.796600026666667

00:43:50.240 --> 00:43:52.478 We're going to go into why?

NOTE Confidence: 0.796600026666667

00:43:52.480 --> 00:43:54.475 But the the other you know concepts

NOTE Confidence: 0.796600026666667

00:43:54.475 --> 00:43:56.916 to to put out here is when when one

NOTE Confidence: 0.796600026666667

00:43:56.916 --> 00:43:59.138 puts out in an abstract that hey,

NOTE Confidence: 0.796600026666667

00:43:59.140 --> 00:44:01.540 this works and there's great

NOTE Confidence: 0.796600026666667

00:44:01.540 --> 00:44:03.015 interobserver agreement, well.

NOTE Confidence: 0.796600026666667

00:44:03.015 --> 00:44:05.590 What was your training methodology

NOTE Confidence: 0.796600026666667

00:44:05.590 --> 00:44:09.053 in this specific setting and what is

NOTE Confidence: 0.796600026666667

00:44:09.053 --> 00:44:11.552 the training methodology in the the

NOTE Confidence: 0.796600026666667

00:44:11.552 --> 00:44:14.480 rest of the world and in practicing medicine?

NOTE Confidence: 0.796600026666667

00:44:14.480 --> 00:44:15.740 In fact,

NOTE Confidence: 0.796600026666667

00:44:15.740 --> 00:44:18.260 the methodology is voluntary.

NOTE Confidence: 0.796600026666667

00:44:18.260 --> 00:44:20.260 It the rigor varies widely,

NOTE Confidence: 0.796600026666667

00:44:20.260 --> 00:44:22.160 there's no requirement that that

NOTE Confidence: 0.796600026666667

00:44:22.160 --> 00:44:24.060 it's not registered with the

NOTE Confidence: 0.798921287222222

00:44:24.126 --> 00:44:26.614 FDA that we've done our training or not.

NOTE Confidence: 0.798921287222222

00:44:26.620 --> 00:44:27.448 This is honor system,

NOTE Confidence: 0.798921287222222

00:44:27.448 --> 00:44:29.277 so we've all done it all the graphologists

NOTE Confidence: 0.798921287222222

00:44:29.277 --> 00:44:31.437 if you all have gone through the training,

NOTE Confidence: 0.798921287222222

00:44:31.440 --> 00:44:32.780 but there's no requirement that

NOTE Confidence: 0.798921287222222

00:44:32.780 --> 00:44:33.852 you repeated every year.

NOTE Confidence: 0.798921287222222

00:44:33.860 --> 00:44:36.457 What about drift over time after training,

NOTE Confidence: 0.798921287222222

00:44:36.460 --> 00:44:39.246 so it's there's a lot of questions.

NOTE Confidence: 0.798921287222222

00:44:39.250 --> 00:44:41.440 And the unfortunate fact that we

NOTE Confidence: 0.798921287222222

00:44:41.440 --> 00:44:44.502 seem to notice is that many samples.

NOTE Confidence: 0.798921287222222

00:44:44.502 --> 00:44:48.185 Hover near the cutoff so when it's

NOTE Confidence: 0.798921287222222

00:44:48.185 --> 00:44:50.210 negative we're all in agreement.

NOTE Confidence: 0.798921287222222

00:44:50.210 --> 00:44:52.014 When it's wildly positive,

NOTE Confidence: 0.798921287222222

00:44:52.014 --> 00:44:53.818 and clearly you know.

NOTE Confidence: 0.798921287222222

00:44:53.820 --> 00:44:56.251 1020, etcetera score that's easy

NOTE Confidence: 0.798921287222222

00:44:56.251 --> 00:44:58.008 because you're way above any cut off.

NOTE Confidence: 0.798921287222222

00:44:58.010 --> 00:45:00.327 But we do have many samples that

NOTE Confidence: 0.798921287222222

00:45:00.327 --> 00:45:02.569 hover near a CPS cutoff of 1.

NOTE Confidence: 0.798921287222222

00:45:02.570 --> 00:45:05.740 And I know new cut offs of five are coming.

NOTE Confidence: 0.798921287222222

00:45:05.740 --> 00:45:07.060 I'm just going to highlight here.

NOTE Confidence: 0.798921287222222

00:45:07.060 --> 00:45:08.698 This is the manual that we use,

NOTE Confidence: 0.798921287222222

00:45:08.700 --> 00:45:12.696 and I'm going to show some figures and and

NOTE Confidence: 0.798921287222222

00:45:12.700 --> 00:45:15.535 language from this from the Agilent Deco.

NOTE Confidence: 0.798921287222222

00:45:15.540 --> 00:45:18.366 This is what we read and is a gorgeous

NOTE Confidence: 0.798921287222222

00:45:18.366 --> 00:45:20.454 picture of PD one standings pristine

NOTE Confidence: 0.798921287222222

00:45:20.454 --> 00:45:22.940 and I'm also going to use material

NOTE Confidence: 0.798921287222222

00:45:22.940 --> 00:45:25.780 from a book written by friends of Mine,

NOTE Confidence: 0.798921287222222

00:45:25.780 --> 00:45:26.276 Sunil,

NOTE Confidence: 0.798921287222222

00:45:26.276 --> 00:45:29.252 Bobby and George Kumar predicted biomarkers

NOTE Confidence: 0.798921287222222

00:45:29.252 --> 00:45:32.400 in oncology and this is an excellent.

NOTE Confidence: 0.798921287222222

00:45:32.400 --> 00:45:35.548 Treatise of the topic.

NOTE Confidence: 0.798921287222222

00:45:35.550 --> 00:45:39.526 This is not to get into the test

NOTE Confidence: 0.798921287222222

00:45:39.526 --> 00:45:42.648 tube and pipette phase of things,

NOTE Confidence: 0.798921287222222

00:45:42.648 --> 00:45:45.866 but it is important that we all remember

NOTE Confidence: 0.798921287222222

00:45:45.866 --> 00:45:49.282 that in any test that's done in a

NOTE Confidence: 0.798921287222222

00:45:49.282 --> 00:45:51.410 laboratory there are called there's

NOTE Confidence: 0.798921287222222

00:45:51.410 --> 00:45:53.960 a quality assurance aspect and this

NOTE Confidence: 0.798921287222222

00:45:54.035 --> 00:45:56.475 is they they in in the and kumars

NOTE Confidence: 0.798921287222222

00:45:56.475 --> 00:45:59.279 book they talk about the predictive

NOTE Confidence: 0.798921287222222

00:45:59.279 --> 00:46:01.403 biomarker quality assurance cycle,

NOTE Confidence: 0.798921287222222

00:46:01.410 --> 00:46:03.458 and I think it's important to know that

NOTE Confidence: 0.798921287222222

00:46:03.458 --> 00:46:05.577 when you're taking a sample from a patient.

NOTE Confidence: 0.798921287222222

00:46:05.580 --> 00:46:08.058 Usually in this setting it's an

NOTE Confidence: 0.798921287222222

00:46:08.058 --> 00:46:09.659 endoscopic mucosal biopsy that

NOTE Confidence: 0.798921287222222

00:46:09.659 --> 00:46:10.736 undergoes tissue processing,

NOTE Confidence: 0.798921287222222

00:46:10.736 --> 00:46:12.531 first in formalin and through

NOTE Confidence: 0.798921287222222

00:46:12.531 --> 00:46:14.060 a series of solutions.

NOTE Confidence: 0.798921287222222

00:46:14.060 --> 00:46:16.275 In the regular Histology laboratory

NOTE Confidence: 0.798921287222222

00:46:16.275 --> 00:46:18.490 that have to be controlled.

NOTE Confidence: 0.798921287222222

00:46:18.490 --> 00:46:21.689 It's put into paraffin, cut into sections,

NOTE Confidence: 0.798921287222222

00:46:21.690 --> 00:46:23.856 and then that's the tissue processing.

NOTE Confidence: 0.798921287222222

00:46:23.860 --> 00:46:25.384 The pre analytic phase.

NOTE Confidence: 0.798921287222222

00:46:25.384 --> 00:46:26.908 Then there's sustaining the

NOTE Confidence: 0.798921287222222

00:46:26.908 --> 00:46:28.250 analytic phase that has.

NOTE Confidence: 0.798921287222222

00:46:28.250 --> 00:46:31.616 There has to be QC and quality assurance of

NOTE Confidence: 0.798921287222222

00:46:31.616 --> 00:46:35.186 both the controls and the test tissue sample.

NOTE Confidence: 0.798921287222222

00:46:35.190 --> 00:46:37.230 And then there's post analytic.

NOTE Confidence: 0.798921287222222

00:46:37.230 --> 00:46:38.694 That's the interpretation,

NOTE Confidence: 0.798921287222222

00:46:38.694 --> 00:46:40.158 scoring and reporting.

NOTE Confidence: 0.798921287222222

00:46:40.160 --> 00:46:43.405 So what kind of QC can we really apply?

NOTE Confidence: 0.798921287222222

00:46:43.405 --> 00:46:45.660 And that's a question to pose

NOTE Confidence: 0.798921287222222

00:46:45.660 --> 00:46:47.865 yourself when I take you through this.

NOTE Confidence: 0.798921287222222

00:46:47.870 --> 00:46:49.140 All of this leads to.

NOTE Confidence: 0.798921287222222

00:46:49.140 --> 00:46:51.678 No matter what.

NOTE Confidence: 0.798921287222222

00:46:51.680 --> 00:46:54.490 A decision for a patient.

NOTE Confidence: 0.798921287222222

00:46:54.490 --> 00:46:57.234 So think about compare this if you will

NOTE Confidence: 0.798921287222222

00:46:57.234 --> 00:47:00.425 as I go through what goes into this.

NOTE Confidence: 0.798921287222222

00:47:00.430 --> 00:47:02.590 The result of a CPS score,

NOTE Confidence: 0.798921287222222

00:47:02.590 --> 00:47:03.500 for example,

NOTE Confidence: 0.798921287222222

00:47:03.500 --> 00:47:06.230 compared to a chemistry test of

NOTE Confidence: 0.798921287222222

00:47:06.230 --> 00:47:09.696 a blood test in the lab and and

NOTE Confidence: 0.798921287222222

00:47:09.696 --> 00:47:12.190 what kinds of decisions might be

NOTE Confidence: 0.798921287222222

00:47:12.190 --> 00:47:15.038 made and how that's done.

NOTE Confidence: 0.798921287222222

00:47:15.040 --> 00:47:16.587 I won't walk through all this side,

NOTE Confidence: 0.798921287222222

00:47:16.590 --> 00:47:18.795 but but just to say those people

NOTE Confidence: 0.798921287222222

00:47:18.795 --> 00:47:20.984 who do just know that at the

NOTE Confidence: 0.798921287222222

00:47:20.984 --> 00:47:23.595 back of a test like this one and

NOTE Confidence: 0.798921287222222

00:47:23.595 --> 00:47:25.535 and hopefully every other one.

NOTE Confidence: 0.798921287222222

00:47:25.540 --> 00:47:29.124 Is a whole are people who understand.

NOTE Confidence: 0.798921287222222

00:47:29.130 --> 00:47:31.902 What needs to go into the pre

NOTE Confidence: 0.798921287222222

00:47:31.902 --> 00:47:34.260 analytic analytic and post analytic?

NOTE Confidence: 0.798921287222222

00:47:34.260 --> 00:47:36.055 Quality checks such that there

NOTE Confidence: 0.798921287222222

00:47:36.055 --> 00:47:37.850 are things that would indicators

NOTE Confidence: 0.880474148461538

00:47:37.915 --> 00:47:40.148 of unacceptable results that would cause us

NOTE Confidence: 0.880474148461538

00:47:40.148 --> 00:47:42.940 to pause and not report that and start over.

NOTE Confidence: 0.880474148461538

00:47:42.940 --> 00:47:45.229 I just want to highlight one here.

NOTE Confidence: 0.880474148461538

00:47:45.230 --> 00:47:48.690 Quality of tissue morphology.

NOTE Confidence: 0.880474148461538

00:47:48.690 --> 00:47:53.044 So the tissue morphology in a biopsy.

NOTE Confidence: 0.880474148461538

00:47:53.050 --> 00:47:56.776 Is is sort of decided by things that are

NOTE Confidence: 0.880474148461538

00:47:56.776 --> 00:48:00.387 out of our hands that they're sample.

NOTE Confidence: 0.880474148461538

00:48:00.390 --> 00:48:02.364 How much tumor is in it versus

NOTE Confidence: 0.880474148461538

00:48:02.364 --> 00:48:03.750 normal benign or incites?

NOTE Confidence: 0.880474148461538

00:48:03.750 --> 00:48:07.050 You crush artifact from the biopsy,

NOTE Confidence: 0.880474148461538

00:48:07.050 --> 00:48:07.950 forceps, necrosis,

NOTE Confidence: 0.880474148461538

00:48:07.950 --> 00:48:10.650 thermal injury if caught early was

NOTE Confidence: 0.880474148461538

00:48:10.650 --> 00:48:13.329 used in obtaining the specimen,

NOTE Confidence: 0.880474148461538

00:48:13.330 --> 00:48:14.968 so we have no control over

NOTE Confidence: 0.880474148461538

00:48:14.968 --> 00:48:16.530 this and we we don't.

NOTE Confidence: 0.880474148461538

00:48:16.530 --> 00:48:18.234 We try very hard not to ask folks

NOTE Confidence: 0.880474148461538

00:48:18.234 --> 00:48:20.752 to go back and get more samples and

NOTE Confidence: 0.880474148461538

00:48:20.752 --> 00:48:22.108 put patients through procedures.

NOTE Confidence: 0.880474148461538

00:48:22.110 --> 00:48:23.098 We deal with what?

NOTE Confidence: 0.880474148461538

00:48:23.098 --> 00:48:25.728 We have by and large and do the best we can,

NOTE Confidence: 0.880474148461538

00:48:25.730 --> 00:48:27.650 but it's something to know about,

NOTE Confidence: 0.880474148461538

00:48:27.650 --> 00:48:30.569 so these are some statements from the.

NOTE Confidence: 0.880474148461538

00:48:30.570 --> 00:48:34.618 Agilent Manual and this is the the most

NOTE Confidence: 0.880474148461538

00:48:34.618 --> 00:48:37.262 important equation that we are are

NOTE Confidence: 0.880474148461538

00:48:37.262 --> 00:48:40.270 living by for gastric and GJ cancer.

NOTE Confidence: 0.880474148461538

00:48:40.270 --> 00:48:42.384 So what is the combined positive score?

NOTE Confidence: 0.880474148461538

00:48:42.390 --> 00:48:45.435 It is as you know the number.

NOTE Confidence: 0.880474148461538

00:48:45.440 --> 00:48:48.578 Of Pedial 1 staining tumor cells,

NOTE Confidence: 0.880474148461538

00:48:48.580 --> 00:48:51.385 lymphocytes and macrophages over divided

NOTE Confidence: 0.880474148461538

00:48:51.385 --> 00:48:55.978 by the total number of viable tumor cells,

NOTE Confidence: 0.880474148461538

00:48:55.980 --> 00:48:57.804 and then we multiply that times 100 so

NOTE Confidence: 0.880474148461538

00:48:57.804 --> 00:48:59.654 you can see that we we ought to be,

NOTE Confidence: 0.880474148461538

00:48:59.660 --> 00:49:00.110 you know,

NOTE Confidence: 0.880474148461538

00:49:00.110 --> 00:49:01.685 shouldn't be too hard to get to

NOTE Confidence: 0.880474148461538

00:49:01.685 --> 00:49:03.054 something greater than one because

NOTE Confidence: 0.880474148461538

00:49:03.054 --> 00:49:04.154 we're multiplying by 100.

NOTE Confidence: 0.880474148461538

00:49:04.160 --> 00:49:05.906 So they they want us to get to 1.

NOTE Confidence: 0.795424178888889

00:49:08.170 --> 00:49:11.266 So let's take some definitions now for PDL 1,

NOTE Confidence: 0.795424178888889

00:49:11.270 --> 00:49:12.878 scorning tumor cell.

NOTE Confidence: 0.795424178888889

00:49:12.878 --> 00:49:14.781 OK, well, what is that?

NOTE Confidence: 0.795424178888889

00:49:14.781 --> 00:49:16.166 Well, it sounds pretty obvious,

NOTE Confidence: 0.795424178888889

00:49:16.170 --> 00:49:18.830 but there are some caveats.

NOTE Confidence: 0.795424178888889

00:49:18.830 --> 00:49:21.924 Not inside you, not dysplasia or carcinoma,

NOTE Confidence: 0.795424178888889

00:49:21.930 --> 00:49:24.422 incites you and in the esophageal cancer

NOTE Confidence: 0.795424178888889

00:49:24.422 --> 00:49:26.968 or gastric cancer coming from a backward,

NOTE Confidence: 0.795424178888889

00:49:26.970 --> 00:49:28.880 often a dysplastic background on

NOTE Confidence: 0.795424178888889

00:49:28.880 --> 00:49:30.790 top and the superficial mucosa

NOTE Confidence: 0.795424178888889

00:49:30.853 --> 00:49:32.425 that is not to be counted,

NOTE Confidence: 0.795424178888889

00:49:32.430 --> 00:49:34.686 and that is to be distinguished

NOTE Confidence: 0.795424178888889

00:49:34.686 --> 00:49:37.164 from the invasive self coming right

NOTE Confidence: 0.795424178888889

00:49:37.164 --> 00:49:40.086 off of that inside your component.

NOTE Confidence: 0.795424178888889

00:49:40.090 --> 00:49:42.510 That's very challenging at times.

NOTE Confidence: 0.795424178888889

00:49:42.510 --> 00:49:45.142 Areas of necrosis are to be avoided

NOTE Confidence: 0.795424178888889

00:49:45.142 --> 00:49:48.190 and one must have a minimum of 100

NOTE Confidence: 0.795424178888889

00:49:48.190 --> 00:49:50.660 viable tumor cells in the sample.

NOTE Confidence: 0.795424178888889

00:49:50.660 --> 00:49:53.940 To to perform the stain.

NOTE Confidence: 0.795424178888889

00:49:53.940 --> 00:49:56.604 What is an immune cell for the purposes

NOTE Confidence: 0.795424178888889

00:49:56.604 --> 00:49:59.621 of this for CPS it's consists only

NOTE Confidence: 0.795424178888889

00:49:59.621 --> 00:50:01.445 of lymphocytes and macrophages,

NOTE Confidence: 0.795424178888889

00:50:01.450 --> 00:50:02.810 plasma cells and neutrophils

NOTE Confidence: 0.795424178888889

00:50:02.810 --> 00:50:04.510 are not to be counted.

NOTE Confidence: 0.795424178888889

00:50:04.510 --> 00:50:06.758 Those are very common cells in the mucosa,

NOTE Confidence: 0.795424178888889

00:50:06.760 --> 00:50:07.906 especially plasma cells,

NOTE Confidence: 0.795424178888889

00:50:07.906 --> 00:50:09.816 fibroblasts and endothelial cells which

NOTE Confidence: 0.795424178888889

00:50:09.816 --> 00:50:12.156 are not inflammatory cells but are other

NOTE Confidence: 0.795424178888889

00:50:12.156 --> 00:50:14.309 stromal cells are not to be counted.

NOTE Confidence: 0.795424178888889

00:50:14.310 --> 00:50:18.174 All of these things can pick up stain.

NOTE Confidence: 0.795424178888889

00:50:18.180 --> 00:50:19.836 All of them can pick up a PD.

NOTE Confidence: 0.795424178888889

00:50:19.840 --> 00:50:22.730 One stain can be positive.

NOTE Confidence: 0.795424178888889

00:50:22.730 --> 00:50:25.990 So we already said what 2 reports and CPS is.

NOTE Confidence: 0.795424178888889

00:50:25.990 --> 00:50:28.153 I want to just point that outside

NOTE Confidence: 0.795424178888889

00:50:28.153 --> 00:50:30.850 of the GE of the GE junction and

NOTE Confidence: 0.795424178888889

00:50:30.850 --> 00:50:33.050 gastric cancer in the GI tract,

NOTE Confidence: 0.795424178888889

00:50:33.050 --> 00:50:35.780 we're doing PD one on many things

NOTE Confidence: 0.795424178888889

00:50:35.780 --> 00:50:38.142 and there because CPS or TPS

NOTE Confidence: 0.795424178888889

00:50:38.142 --> 00:50:39.626 have not been codified.

NOTE Confidence: 0.795424178888889

00:50:39.630 --> 00:50:42.156 We report simply the percent immune

NOTE Confidence: 0.795424178888889

00:50:42.156 --> 00:50:44.990 cells and percent tumor cells staining,

NOTE Confidence: 0.795424178888889

00:50:44.990 --> 00:50:46.170 and we'll talk about that

NOTE Confidence: 0.795424178888889

00:50:46.170 --> 00:50:47.712 when we get to reports, OK?

NOTE Confidence: 0.795424178888889

00:50:47.712 --> 00:50:48.074 Fine,

NOTE Confidence: 0.795424178888889

00:50:48.074 --> 00:50:50.608 so that's those are our marching orders.

NOTE Confidence: 0.795424178888889

00:50:50.610 --> 00:50:51.430 How do we do it?

NOTE Confidence: 0.795424178888889

00:50:51.430 --> 00:50:51.784 Well,

NOTE Confidence: 0.795424178888889

00:50:51.784 --> 00:50:53.908 the minimum of 100 cells we

NOTE Confidence: 0.795424178888889

00:50:53.908 --> 00:50:56.130 look at various magnifications.

NOTE Confidence: 0.795424178888889

00:50:56.130 --> 00:50:58.314 This is important if the specimen includes

NOTE Confidence: 0.795424178888889

00:50:58.314 --> 00:51:00.706 more than one biopsy in the in the jar,

NOTE Confidence: 0.795424178888889

00:51:00.710 --> 00:51:03.290 which it always does.

NOTE Confidence: 0.795424178888889

00:51:03.290 --> 00:51:04.970 And we put all that on one slide,

NOTE Confidence: 0.795424178888889

00:51:04.970 --> 00:51:06.338 all the tissue on the slide

NOTE Confidence: 0.795424178888889

00:51:06.338 --> 00:51:07.250 needs to be evaluated.

NOTE Confidence: 0.795424178888889

00:51:07.250 --> 00:51:10.520 Generate a single CPS score.

NOTE Confidence: 0.795424178888889

00:51:10.520 --> 00:51:12.400 And if we're doing it on a resection,

NOTE Confidence: 0.795424178888889

00:51:12.400 --> 00:51:14.878 the entire every single tumor cell,

NOTE Confidence: 0.795424178888889

00:51:14.880 --> 00:51:16.866 every immune cell should be evaluated.

NOTE Confidence: 0.795424178888889

00:51:16.870 --> 00:51:18.680 And that's when in tumor.

NOTE Confidence: 0.795424178888889

00:51:18.680 --> 00:51:21.515 We have a lot of of a little table

NOTE Confidence: 0.795424178888889

00:51:21.515 --> 00:51:24.827 of dos and don'ts include and don't

NOTE Confidence: 0.795424178888889

00:51:24.827 --> 00:51:28.219 include in the numerator and denominator.

NOTE Confidence: 0.795424178888889

00:51:28.220 --> 00:51:29.210 For immune cells.

NOTE Confidence: 0.8214599

00:51:31.890 --> 00:51:34.758 And specifically, what are we grading?

NOTE Confidence: 0.8214599

00:51:34.760 --> 00:51:36.575 Well, for tumor cells we're

NOTE Confidence: 0.8214599

00:51:36.575 --> 00:51:38.027 looking at membranous staining,

NOTE Confidence: 0.8214599

00:51:38.030 --> 00:51:39.425 only not cytoplasmic.

NOTE Confidence: 0.8214599

00:51:39.425 --> 00:51:43.253 And we are to count a cell as

NOTE Confidence: 0.8214599

00:51:43.253 --> 00:51:46.079 positive if it has any partial.

NOTE Confidence: 0.8214599

00:51:46.080 --> 00:51:47.920 Or complete linear membrane staining.

NOTE Confidence: 0.8214599

00:51:47.920 --> 00:51:49.736 So half the cell or the whole cell.

NOTE Confidence: 0.8214599

00:51:49.740 --> 00:51:51.756 Any part of the cell any

NOTE Confidence: 0.8214599

00:51:51.756 --> 00:51:52.764 membrane is staining.

NOTE Confidence: 0.8214599

00:51:52.770 --> 00:51:56.496 Of greater than one plus intensity.

NOTE Confidence: 0.8214599

00:51:56.500 --> 00:51:57.788 So what's interesting is

NOTE Confidence: 0.8214599

00:51:57.788 --> 00:51:59.398 that this is not defined.

NOTE Confidence: 0.8214599

00:51:59.400 --> 00:52:01.380 This is a completely subjective

NOTE Confidence: 0.8214599

00:52:01.380 --> 00:52:06.240 1 + 2 + 3 plus partial complete.

NOTE Confidence: 0.8214599

00:52:06.240 --> 00:52:09.408 And for the immune cell lymphocyte

NOTE Confidence: 0.8214599

00:52:09.408 --> 00:52:11.520 or macrophage membranous staining

NOTE Confidence: 0.8214599

00:52:11.601 --> 00:52:14.009 and cytoplasmic staining count,

NOTE Confidence: 0.8214599

00:52:14.010 --> 00:52:15.735 again with with any basically

NOTE Confidence: 0.8214599

00:52:15.735 --> 00:52:17.115 any amount of staining.

NOTE Confidence: 0.8214599

00:52:17.120 --> 00:52:19.110 You're to count that cell.

NOTE Confidence: 0.8214599

00:52:19.110 --> 00:52:21.549 So let's go through now and see how to

NOTE Confidence: 0.8214599

00:52:21.549 --> 00:52:24.145 do this with some real world samples.

NOTE Confidence: 0.8214599

00:52:24.150 --> 00:52:26.328 Here's a biopsy set of biopsies

NOTE Confidence: 0.8214599

00:52:26.328 --> 00:52:27.780 all in one jar,

NOTE Confidence: 0.924939705714286

00:52:31.070 --> 00:52:33.905 123456789, ten eleven you know 12 ish.

NOTE Confidence: 0.924939705714286

00:52:33.910 --> 00:52:36.630 Biopsy fragments of various sizes.

NOTE Confidence: 0.924939705714286

00:52:36.630 --> 00:52:38.961 I can tell at this magnification that

NOTE Confidence: 0.924939705714286

00:52:38.961 --> 00:52:41.376 they basically all came all have tumor

NOTE Confidence: 0.924939705714286

00:52:41.376 --> 00:52:43.410 in them is very generous endoscopist,

NOTE Confidence: 0.924939705714286

00:52:43.410 --> 00:52:45.874 so we're meant to do an immunostain and

NOTE Confidence: 0.924939705714286

00:52:45.874 --> 00:52:48.186 count every single one of these pieces.

NOTE Confidence: 0.924939705714286

00:52:48.190 --> 00:52:50.128 So let's see how that's done.

NOTE Confidence: 0.924939705714286

00:52:50.130 --> 00:52:52.632 This is one piece at a

NOTE Confidence: 0.924939705714286

00:52:52.632 --> 00:52:53.883 slightly higher magnification.

NOTE Confidence: 0.924939705714286

00:52:53.890 --> 00:52:57.488 The bigger poofy cells are tumor cells.

NOTE Confidence: 0.924939705714286

00:52:57.490 --> 00:53:01.928 The small purple dots are inflammatory cells.

NOTE Confidence: 0.924939705714286

00:53:01.930 --> 00:53:03.826 Here it is at higher magnification.

NOTE Confidence: 0.924939705714286

00:53:03.830 --> 00:53:06.230 These are tumor cells the the bigger cells,

NOTE Confidence: 0.924939705714286

00:53:06.230 --> 00:53:08.827 they're bigger nuclei, a little bit paler,

NOTE Confidence: 0.924939705714286

00:53:08.830 --> 00:53:12.630 and the smaller purple dots are immune cells,

NOTE Confidence: 0.924939705714286

00:53:12.630 --> 00:53:14.800 so I just want you to know

NOTE Confidence: 0.924939705714286

00:53:14.800 --> 00:53:16.589 the oncologist watching.

NOTE Confidence: 0.924939705714286

00:53:16.590 --> 00:53:20.856 There is no ocular micrometer or

NOTE Confidence: 0.924939705714286

00:53:20.856 --> 00:53:23.334 software to do this counting.

NOTE Confidence: 0.924939705714286

00:53:23.334 --> 00:53:25.980 We are literally at a microscope

NOTE Confidence: 0.924939705714286

00:53:26.065 --> 00:53:27.729 with maybe an arrow.

NOTE Confidence: 0.924939705714286

00:53:27.730 --> 00:53:29.446 Basically, guesstimating estimating

NOTE Confidence: 0.924939705714286

00:53:29.446 --> 00:53:32.878 that that the numbers of denominator

NOTE Confidence: 0.924939705714286

00:53:32.878 --> 00:53:35.486 how many tumor cells are here.

NOTE Confidence: 0.924939705714286

00:53:35.490 --> 00:53:37.682 So that is what I want to communicate

NOTE Confidence: 0.924939705714286

00:53:37.682 --> 00:53:39.539 to you about the precision.

NOTE Confidence: 0.924939705714286

00:53:39.540 --> 00:53:40.430 How do we do this?

NOTE Confidence: 0.924939705714286

00:53:40.430 --> 00:53:42.570 Some people do a gestalt.

NOTE Confidence: 0.924939705714286

00:53:42.570 --> 00:53:44.685 I do a counting guesstimate

NOTE Confidence: 0.924939705714286

00:53:44.685 --> 00:53:47.485 and on the training in in the

NOTE Confidence: 0.924939705714286

00:53:47.485 --> 00:53:50.010 online training with a guide,

NOTE Confidence: 0.924939705714286

00:53:50.010 --> 00:53:51.490 someone teaching us how to

NOTE Confidence: 0.924939705714286

00:53:51.490 --> 00:53:52.970 train at Agilent at Dayco.

NOTE Confidence: 0.924939705714286

00:53:52.970 --> 00:53:54.706 That's as good as they had to offer.

NOTE Confidence: 0.924939705714286

00:53:54.710 --> 00:53:56.908 That's what we are meant to do,

NOTE Confidence: 0.924939705714286

00:53:56.910 --> 00:54:01.986 so I will count off 100 cells by hand,

NOTE Confidence: 0.924939705714286

00:54:01.990 --> 00:54:04.629 12345 at the microscope with the fellow.

NOTE Confidence: 0.924939705714286

00:54:04.630 --> 00:54:07.238 Count to 100 and then I do this.

NOTE Confidence: 0.924939705714286

00:54:07.240 --> 00:54:08.260 I don't want to scare you,

NOTE Confidence: 0.924939705714286

00:54:08.260 --> 00:54:09.540 but that's what we do.

NOTE Confidence: 0.924939705714286

00:54:09.540 --> 00:54:12.930 203 hundred, 405 hundred 600.

NOTE Confidence: 0.924939705714286

00:54:12.930 --> 00:54:13.260 Literally,

NOTE Confidence: 0.924939705714286

00:54:13.260 --> 00:54:15.900 this is what we have to work with.

NOTE Confidence: 0.924939705714286

00:54:15.900 --> 00:54:17.428 There is nothing better.

NOTE Confidence: 0.90163192

00:54:19.610 --> 00:54:21.128 Then when we put side by

NOTE Confidence: 0.90163192

00:54:21.128 --> 00:54:22.510 side as I've done here,

NOTE Confidence: 0.90163192

00:54:22.510 --> 00:54:24.870 the tumor cells a high power view of

NOTE Confidence: 0.90163192

00:54:24.870 --> 00:54:27.388 the tumor cells with some immune cells.

NOTE Confidence: 0.90163192

00:54:27.390 --> 00:54:29.613 I would just like to point out that some

NOTE Confidence: 0.90163192

00:54:29.613 --> 00:54:31.990 of these immune cells are plasma cells,

NOTE Confidence: 0.90163192

00:54:31.990 --> 00:54:34.048 and we're not to count plasma cells,

NOTE Confidence: 0.90163192

00:54:34.050 --> 00:54:35.554 only lymphocytes and macrophages.

NOTE Confidence: 0.90163192

00:54:35.554 --> 00:54:37.810 The the macrophages are always quite

NOTE Confidence: 0.90163192

00:54:37.873 --> 00:54:40.003 hard to recognize and distinguish from

NOTE Confidence: 0.90163192

00:54:40.003 --> 00:54:41.750 a fibroblast or endothelial cell.

NOTE Confidence: 0.90163192

00:54:41.750 --> 00:54:44.828 This is the PDL one stain in this example.

NOTE Confidence: 0.90163192

00:54:44.830 --> 00:54:47.436 So we get a sense.

NOTE Confidence: 0.90163192

00:54:47.436 --> 00:54:49.050 Here's a Member in this staining,

NOTE Confidence: 0.90163192

00:54:49.050 --> 00:54:51.836 probably a tumor cell, so that's one.

NOTE Confidence: 0.90163192

00:54:51.840 --> 00:54:53.541 There are some other cells with some

NOTE Confidence: 0.90163192

00:54:53.541 --> 00:54:55.518 membrane and I'm not sure what this one is,

NOTE Confidence: 0.90163192

00:54:55.520 --> 00:54:56.474 but you know,

NOTE Confidence: 0.90163192

00:54:56.474 --> 00:54:58.700 chances are it's meant to be counted.

NOTE Confidence: 0.90163192

00:54:58.700 --> 00:55:00.314 That's two and we're getting into

NOTE Confidence: 0.90163192

00:55:00.314 --> 00:55:02.368 some things here that have a lot of

NOTE Confidence: 0.90163192

00:55:02.368 --> 00:55:03.748 stain that's very dark where it's

NOTE Confidence: 0.90163192

00:55:03.804 --> 00:55:05.214 hard to distinguish what cell type

NOTE Confidence: 0.90163192

00:55:05.214 --> 00:55:07.548 it is and how many cells are here.

NOTE Confidence: 0.90163192

00:55:07.548 --> 00:55:09.630 So this is what is challenging

NOTE Confidence: 0.90163192

00:55:09.703 --> 00:55:12.020 when you get big clumps like this,

NOTE Confidence: 0.90163192

00:55:12.020 --> 00:55:13.838 there's a lot of standing here.

NOTE Confidence: 0.90163192

00:55:13.840 --> 00:55:16.040 This is this is here's that same vessel.

NOTE Confidence: 0.90163192

00:55:16.040 --> 00:55:17.066 It's stuff here.

NOTE Confidence: 0.90163192

00:55:17.066 --> 00:55:18.434 It's probably immune cells,

NOTE Confidence: 0.90163192

00:55:18.440 --> 00:55:20.420 and some of them are lymphocytes,

NOTE Confidence: 0.90163192

00:55:20.420 --> 00:55:24.934 some are not. So we do the best we can.

NOTE Confidence: 0.90163192

00:55:24.940 --> 00:55:27.538 In this example, there's some pretty,

NOTE Confidence: 0.90163192

00:55:27.540 --> 00:55:29.658 you know, honeycomb pretty clear cut,

NOTE Confidence: 0.90163192

00:55:29.660 --> 00:55:30.866 membranous tumor staining.

NOTE Confidence: 0.90163192

00:55:30.866 --> 00:55:33.278 And we could probably could certainly

NOTE Confidence: 0.90163192

00:55:33.278 --> 00:55:35.526 get to cut offs where we're helped a

NOTE Confidence: 0.90163192

00:55:35.526 --> 00:55:37.987 lot by the fact that we are only for

NOTE Confidence: 0.90163192

00:55:37.987 --> 00:55:40.160 the most part giving a cut off of less

NOTE Confidence: 0.90163192

00:55:40.160 --> 00:55:42.330 than or greater than one not an exact number.

NOTE Confidence: 0.90163192

00:55:42.330 --> 00:55:44.714 So one can guess that this degree of

NOTE Confidence: 0.90163192

00:55:44.714 --> 00:55:46.646 staining and then your time timing

NOTE Confidence: 0.90163192

00:55:46.646 --> 00:55:48.548 that by 100 the equation we're

NOTE Confidence: 0.90163192

00:55:48.608 --> 00:55:50.617 going to get to greater than one.

NOTE Confidence: 0.90163192

00:55:50.620 --> 00:55:52.120 So I think this saves us.

NOTE Confidence: 0.90163192

00:55:52.120 --> 00:55:54.390 But if we're going to get to cut off some 5.

NOTE Confidence: 0.90163192

00:55:54.390 --> 00:55:56.454 And and exact numbers.

NOTE Confidence: 0.90163192

00:55:56.454 --> 00:55:57.486 It's different.

NOTE Confidence: 0.90163192

00:55:57.490 --> 00:56:00.122 In this example, the tumor cells are are

NOTE Confidence: 0.90163192

00:56:00.122 --> 00:56:03.065 here and these are this very nice example,

NOTE Confidence: 0.90163192

00:56:03.070 --> 00:56:04.590 because these are all lymphocytes.

NOTE Confidence: 0.90163192

00:56:04.590 --> 00:56:05.010 Morphologically,

NOTE Confidence: 0.90163192

00:56:05.010 --> 00:56:07.530 I feel pretty comfortable about that.

NOTE Confidence: 0.90163192

00:56:07.530 --> 00:56:10.450 And the PDL one stain in this area

NOTE Confidence: 0.90163192

00:56:10.450 --> 00:56:13.129 anyway shows negative tumor staining,

NOTE Confidence: 0.90163192

00:56:13.130 --> 00:56:14.940 but lots of lymphocytes staining,

NOTE Confidence: 0.90163192

00:56:14.940 --> 00:56:17.196 so even if I'm not sure it's really

NOTE Confidence: 0.90163192

00:56:17.196 --> 00:56:19.428 impossible to count how many are positive,

NOTE Confidence: 0.90163192

00:56:19.430 --> 00:56:22.038 but one can do their best with this

NOTE Confidence: 0.90163192

00:56:22.038 --> 00:56:25.120 sort of an estimate and get to a score.

NOTE Confidence: 0.90163192

00:56:25.120 --> 00:56:27.504 In terms of a cutoff of greater less

NOTE Confidence: 0.90163192

00:56:27.504 --> 00:56:28.961 than one. Couple more examples.

NOTE Confidence: 0.90163192

00:56:28.961 --> 00:56:31.480 I want to show this is a biopsy,

NOTE Confidence: 0.90163192

00:56:31.480 --> 00:56:33.880 which is real life biopsy with the usual.

NOTE Confidence: 0.90163192

00:56:33.880 --> 00:56:36.360 Sometimes we get folds in the slide etcetera.

NOTE Confidence: 0.90163192

00:56:36.360 --> 00:56:38.789 In the section there's a lot of

NOTE Confidence: 0.90163192

00:56:38.789 --> 00:56:40.570 insights you display Asia here.

NOTE Confidence: 0.90163192

00:56:40.570 --> 00:56:42.526 This is not cancer, that's dysplasia.

NOTE Confidence: 0.90163192

00:56:42.530 --> 00:56:45.914 This is cancer. There is some cancer here.

NOTE Confidence: 0.90163192

00:56:45.920 --> 00:56:47.768 This probably is cancer.

NOTE Confidence: 0.90163192

00:56:47.768 --> 00:56:49.154 These three glands.

NOTE Confidence: 0.90163192

00:56:49.160 --> 00:56:50.680 Then there's some inside you.

NOTE Confidence: 0.90163192

00:56:50.680 --> 00:56:53.270 So when you. Pivot to the PDL.

NOTE Confidence: 0.90163192

00:56:53.270 --> 00:56:55.208 One stain one has to be.

NOTE Confidence: 0.90163192

00:56:55.210 --> 00:56:56.810 It's challenging to count only

NOTE Confidence: 0.90163192

00:56:56.810 --> 00:56:58.870 what we think is invasive cancer,

NOTE Confidence: 0.90163192

00:56:58.870 --> 00:56:59.642 not dysplasia.

NOTE Confidence: 0.90163192

00:56:59.642 --> 00:57:02.730 And only the immune cells around the cancer,

NOTE Confidence: 0.872605534285714

00:57:02.730 --> 00:57:05.677 not the immune cells around the dysplasia.

NOTE Confidence: 0.872605534285714

00:57:05.680 --> 00:57:08.200 So these are just some of the challenges.

NOTE Confidence: 0.872605534285714

00:57:08.200 --> 00:57:11.744 In this example, these again are tumor cells.

NOTE Confidence: 0.872605534285714

00:57:11.750 --> 00:57:14.448 And there's some stroma around this is

NOTE Confidence: 0.872605534285714

00:57:14.448 --> 00:57:16.440 the PDL one stain and there is some

NOTE Confidence: 0.872605534285714

00:57:16.498 --> 00:57:18.928 positive staining and this is cytoplasmic,

NOTE Confidence: 0.872605534285714

00:57:18.930 --> 00:57:19.410 not membranous.

NOTE Confidence: 0.872605534285714

00:57:19.410 --> 00:57:21.090 So if this is a tumor cell,

NOTE Confidence: 0.872605534285714

00:57:21.090 --> 00:57:22.548 it is not to be counted.

NOTE Confidence: 0.872605534285714

00:57:22.550 --> 00:57:24.190 Here's some membranous staining,

NOTE Confidence: 0.872605534285714

00:57:24.190 --> 00:57:25.830 probably a tumor cell.

NOTE Confidence: 0.872605534285714

00:57:25.830 --> 00:57:27.978 But there's some other staining that

NOTE Confidence: 0.872605534285714

00:57:27.978 --> 00:57:30.036 is cytoplasmic here and there and

NOTE Confidence: 0.872605534285714

00:57:30.036 --> 00:57:31.989 I don't know what the cells are.

NOTE Confidence: 0.872605534285714

00:57:31.990 --> 00:57:34.685 I don't know. I can't tell morphologically.

NOTE Confidence: 0.872605534285714

00:57:34.690 --> 00:57:36.225 Even going back and forth

NOTE Confidence: 0.872605534285714

00:57:36.225 --> 00:57:37.146 are those lymphocytes.

NOTE Confidence: 0.872605534285714

00:57:37.150 --> 00:57:38.462 These are actually smooth

NOTE Confidence: 0.872605534285714

00:57:38.462 --> 00:57:40.430 muscle cells with a faint stain.

NOTE Confidence: 0.872605534285714

00:57:40.430 --> 00:57:43.580 So it it does. Get quite challenging.

NOTE Confidence: 0.872605534285714

00:57:43.580 --> 00:57:43.935 Finally,

NOTE Confidence: 0.872605534285714

00:57:43.935 --> 00:57:46.065 we're asked this is a metastatic

NOTE Confidence: 0.872605534285714

00:57:46.065 --> 00:57:47.820 colon cancer to the liver.

NOTE Confidence: 0.872605534285714

00:57:47.820 --> 00:57:50.160 Just the concept of.

NOTE Confidence: 0.872605534285714

00:57:50.160 --> 00:57:52.878 How much material there can be?

NOTE Confidence: 0.872605534285714

00:57:52.880 --> 00:57:55.358 This is only about 1/5 of the

NOTE Confidence: 0.872605534285714

00:57:55.358 --> 00:57:57.020 tumor on the slide,

NOTE Confidence: 0.872605534285714

00:57:57.020 --> 00:57:59.834 and here we're counting just percent

NOTE Confidence: 0.872605534285714

00:57:59.834 --> 00:58:02.992 tumor and percent immune cells and making

NOTE Confidence: 0.872605534285714

00:58:02.992 --> 00:58:05.834 them very specific point on this slide.

NOTE Confidence: 0.872605534285714

00:58:05.840 --> 00:58:06.650 There's not a lot of.

NOTE Confidence: 0.872605534285714

00:58:06.650 --> 00:58:08.575 There's almost no tumor cell staining here,

NOTE Confidence: 0.872605534285714

00:58:08.580 --> 00:58:11.320 but you can see some faint brown even at this

NOTE Confidence: 0.872605534285714

00:58:11.387 --> 00:58:14.590 magnification surrounding some of the cancer,

NOTE Confidence: 0.872605534285714

00:58:14.590 --> 00:58:15.886 and there these are immune cells

NOTE Confidence: 0.872605534285714

00:58:15.886 --> 00:58:17.858 and a lot of these are lymphocytes,

NOTE Confidence: 0.872605534285714

00:58:17.860 --> 00:58:20.209 others are neutrophils.

NOTE Confidence: 0.872605534285714

00:58:20.210 --> 00:58:22.009 And this is the PDL one stain.

NOTE Confidence: 0.872605534285714

00:58:22.010 --> 00:58:23.648 This is a vessel that's staining

NOTE Confidence: 0.872605534285714

00:58:23.648 --> 00:58:25.178 and there is some cytoplasmic

NOTE Confidence: 0.872605534285714

00:58:25.178 --> 00:58:27.088 staining of variety of things.

NOTE Confidence: 0.872605534285714

00:58:27.090 --> 00:58:28.406 Not sure what all these cells are,

NOTE Confidence: 0.872605534285714

00:58:28.410 --> 00:58:31.010 but you know we we would do our best but

NOTE Confidence: 0.872605534285714

00:58:31.075 --> 00:58:33.603 the the other point about this is that.

NOTE Confidence: 0.872605534285714

00:58:33.610 --> 00:58:34.828 When we're giving.

NOTE Confidence: 0.872605534285714

00:58:34.828 --> 00:58:36.858 A PDL one CPS score.

NOTE Confidence: 0.872605534285714

00:58:36.860 --> 00:58:39.002 We just have to guesstimate the

NOTE Confidence: 0.872605534285714

00:58:39.002 --> 00:58:41.225 number of positive tumor and the

NOTE Confidence: 0.872605534285714

00:58:41.225 --> 00:58:43.045 number of positive immune cells.

NOTE Confidence: 0.872605534285714

00:58:43.050 --> 00:58:45.206 We don't have to give the denominator

NOTE Confidence: 0.872605534285714

00:58:45.206 --> 00:58:47.843 of what is the total immune cell count

NOTE Confidence: 0.872605534285714

00:58:47.843 --> 00:58:49.846 and you can imagine how challenging

NOTE Confidence: 0.872605534285714

00:58:49.846 --> 00:58:52.510 it would be for us to try to count

NOTE Confidence: 0.872605534285714

00:58:52.510 --> 00:58:54.848 the immune cells in in any section,

NOTE Confidence: 0.872605534285714

00:58:54.850 --> 00:58:56.750 let alone a large section.

NOTE Confidence: 0.872605534285714

00:58:56.750 --> 00:59:00.278 So percent immune cell is is really

NOTE Confidence: 0.872605534285714

00:59:00.278 --> 00:59:04.046 quite challenging to feel good about.

NOTE Confidence: 0.872605534285714

00:59:04.050 --> 00:59:05.199 So in summary.

NOTE Confidence: 0.872605534285714

00:59:05.199 --> 00:59:07.880 I think I'm being the bearer of

NOTE Confidence: 0.872605534285714

00:59:07.880 --> 00:59:11.220 of not very comforting news here.

NOTE Confidence: 0.872605534285714

00:59:11.220 --> 00:59:13.796 This is our reality in every academic

NOTE Confidence: 0.872605534285714

00:59:13.796 --> 00:59:15.796 pathologist with whom I've ever

NOTE Confidence: 0.872605534285714

00:59:15.796 --> 00:59:17.926 spoken across numerous centers is in

NOTE Confidence: 0.872605534285714

00:59:17.926 --> 00:59:19.557 complete agreement with this and we are.

NOTE Confidence: 0.872605534285714

00:59:19.560 --> 00:59:21.835 We are really rattling the

NOTE Confidence: 0.872605534285714

00:59:21.835 --> 00:59:23.655 cage for something better.

NOTE Confidence: 0.872605534285714

00:59:23.660 --> 00:59:24.731 So in summary,

NOTE Confidence: 0.872605534285714

00:59:24.731 --> 00:59:27.880 there are the challenges with PDL 1 scoring.

NOTE Confidence: 0.872605534285714

00:59:27.880 --> 00:59:29.064 Are in the denominator.

NOTE Confidence: 0.872605534285714

00:59:29.064 --> 00:59:29.656 You know,

NOTE Confidence: 0.872605534285714

00:59:29.660 --> 00:59:32.540 recognizing tumor cells from stroma,

NOTE Confidence: 0.872605534285714

00:59:32.540 --> 00:59:34.296 cautery and other artifacts,

NOTE Confidence: 0.872605534285714

00:59:34.296 --> 00:59:36.930 faint staining and in the immune

NOTE Confidence: 0.872605534285714

00:59:37.009 --> 00:59:39.517 cells it's really hard to distinguish

NOTE Confidence: 0.872605534285714

00:59:39.517 --> 00:59:42.014 the limbs and macros from other

NOTE Confidence: 0.872605534285714

00:59:42.014 --> 00:59:44.646 cells and a variety of other things.

NOTE Confidence: 0.872605534285714

00:59:44.650 --> 00:59:47.802 The agreement at cut offs is, I think,

NOTE Confidence: 0.872605534285714

00:59:47.802 --> 00:59:49.307 already can be quite challenging,

NOTE Confidence: 0.872605534285714

00:59:49.310 --> 00:59:52.480 but reproducibility for exact scores.

NOTE Confidence: 0.872605534285714

00:59:52.480 --> 00:59:55.610 Should that be be requested,

NOTE Confidence: 0.872605534285714

00:59:55.610 --> 00:59:57.948 would I would expect that to be

NOTE Confidence: 0.872605534285714

00:59:57.948 --> 00:59:59.990 even less agreements and I'm saying,

NOTE Confidence: 0.872605534285714

00:59:59.990 --> 01:00:00.968 well, I think it's an 8.

NOTE Confidence: 0.872605534285714

01:00:00.970 --> 01:00:03.387 Well, I think it's a 25, you know.

NOTE Confidence: 0.872605534285714

01:00:03.387 --> 01:00:05.760 So I think that would be troublesome.

NOTE Confidence: 0.805837805833333

01:00:05.760 --> 01:00:08.322 And Jill mentioned something that I

NOTE Confidence: 0.805837805833333

01:00:08.322 --> 01:00:10.649 think there's basically no data on.

NOTE Confidence: 0.805837805833333

01:00:10.650 --> 01:00:15.024 What about the variability within the tumor?

NOTE Confidence: 0.805837805833333

01:00:15.024 --> 01:00:17.803 Even even in a single tumor within

NOTE Confidence: 0.805837805833333

01:00:17.803 --> 01:00:20.728 biopsy fragments or within a resection.

NOTE Confidence: 0.805837805833333

01:00:20.730 --> 01:00:21.555 And what about?

NOTE Confidence: 0.805837805833333

01:00:21.555 --> 01:00:24.250 Should we do a primary or a metastasis?

NOTE Confidence: 0.805837805833333

01:00:24.250 --> 01:00:26.246 Pre or post therapy?

NOTE Confidence: 0.805837805833333

01:00:26.246 --> 01:00:29.240 So those are really valid questions.

NOTE Confidence: 0.805837805833333

01:00:29.240 --> 01:00:30.380 Uh, almost done.

NOTE Confidence: 0.805837805833333

01:00:30.380 --> 01:00:32.280 Just how to decipher report.

NOTE Confidence: 0.805837805833333

01:00:32.280 --> 01:00:33.939 OK, we're giving it our best shot.

NOTE Confidence: 0.805837805833333

01:00:33.940 --> 01:00:36.372 We do this test every day and we

NOTE Confidence: 0.805837805833333

01:00:36.372 --> 01:00:38.934 will continue to do so as requested

NOTE Confidence: 0.805837805833333

01:00:38.934 --> 01:00:40.819 until something better comes along.

NOTE Confidence: 0.805837805833333

01:00:40.820 --> 01:00:42.416 But at Yale, in any case,

NOTE Confidence: 0.805837805833333

01:00:42.420 --> 01:00:43.948 our reports, I think,

NOTE Confidence: 0.805837805833333

01:00:43.948 --> 01:00:45.858 can probably be somewhat confusing,

NOTE Confidence: 0.805837805833333

01:00:45.860 --> 01:00:47.659 and I'm sorry if that's the case.

NOTE Confidence: 0.805837805833333

01:00:47.660 --> 01:00:51.156 We try to give for gastric and GGJ

NOTE Confidence: 0.805837805833333

01:00:51.160 --> 01:00:54.664 a score based upon the cutoff of 1

NOTE Confidence: 0.805837805833333

01:00:54.664 --> 01:00:58.369 and say it's positive or negative.

NOTE Confidence: 0.805837805833333

01:00:58.370 --> 01:01:00.062 And what the what?

NOTE Confidence: 0.805837805833333

01:01:00.062 --> 01:01:01.754 The equation consists of?

NOTE Confidence: 0.7271570746

01:01:03.910 --> 01:01:06.073 In, in, and in isopropyl that cut

NOTE Confidence: 0.7271570746

01:01:06.073 --> 01:01:08.310 off his ten etcetera depends on

NOTE Confidence: 0.7271570746

01:01:08.310 --> 01:01:11.062 the organ system elsewhere in the

NOTE Confidence: 0.7271570746

01:01:11.062 --> 01:01:14.560 GI tract we when asked to do this.

NOTE Confidence: 0.7271570746

01:01:14.560 --> 01:01:16.480 Since there's no cutoff agreement,

NOTE Confidence: 0.7271570746

01:01:16.480 --> 01:01:18.044 one just gives the.

NOTE Confidence: 0.7271570746

01:01:18.044 --> 01:01:20.390 The percent of immune cells and

NOTE Confidence: 0.7271570746

01:01:20.467 --> 01:01:22.917 percent of tumor cells staining,

NOTE Confidence: 0.7271570746

01:01:22.920 --> 01:01:24.940 albeit the challenges that I,

NOTE Confidence: 0.7271570746

01:01:24.940 --> 01:01:28.860 despite the challenges that I've mentioned.

NOTE Confidence: 0.7271570746

01:01:28.860 --> 01:01:30.732 And I just want to make a point

NOTE Confidence: 0.7271570746

01:01:30.732 --> 01:01:32.900 here that while you can impute.

NOTE Confidence: 0.7271570746

01:01:32.900 --> 01:01:35.025 A tumor proportion score from

NOTE Confidence: 0.7271570746

01:01:35.025 --> 01:01:37.287 this information because the the

NOTE Confidence: 0.7271570746

01:01:37.287 --> 01:01:39.927 percent of tumor cells is TPS.

NOTE Confidence: 0.7271570746

01:01:39.930 --> 01:01:41.970 That is what TPS is.

NOTE Confidence: 0.7271570746

01:01:41.970 --> 01:01:44.290 But you can't impute a CPS should

NOTE Confidence: 0.7271570746

01:01:44.290 --> 01:01:46.372 you want to from this, because.

NOTE Confidence: 0.7271570746

01:01:46.372 --> 01:01:49.264 The CPS is just the absolute

NOTE Confidence: 0.7271570746

01:01:49.264 --> 01:01:51.286 number of positive immune cells.

NOTE Confidence: 0.7271570746

01:01:51.286 --> 01:01:53.302 It is nothing to do with the

NOTE Confidence: 0.7271570746

01:01:53.302 --> 01:01:55.003 denominator of the total number of

NOTE Confidence: 0.7271570746

01:01:55.003 --> 01:01:56.950 immune cells staining at any intensity,

NOTE Confidence: 0.7271570746

01:01:56.950 --> 01:01:59.036 so you can't add these together or

NOTE Confidence: 0.7271570746

01:01:59.036 --> 01:02:01.200 in some way figure out you're not

NOTE Confidence: 0.7271570746

01:02:01.200 --> 01:02:02.850 getting the number of immune cells,

NOTE Confidence: 0.7271570746

01:02:02.850 --> 01:02:04.280 which is what you need.

NOTE Confidence: 0.7271570746

01:02:04.280 --> 01:02:05.012 The absolute number,

NOTE Confidence: 0.7271570746

01:02:05.012 --> 01:02:06.970 which is what you need for a CPS.

NOTE Confidence: 0.7271570746

01:02:06.970 --> 01:02:08.770 You're getting the percent of

NOTE Confidence: 0.7271570746

01:02:08.770 --> 01:02:09.850 immune cells stain.

NOTE Confidence: 0.858679203333333

01:02:13.260 --> 01:02:18.594 Future directions we would be thrilled to

NOTE Confidence: 0.858679203333333

01:02:18.594 --> 01:02:23.186 get as quickly as possible to automation with

NOTE Confidence: 0.858679203333333

01:02:23.190 --> 01:02:26.110 artificial intelligence and other software,

NOTE Confidence: 0.858679203333333

01:02:26.110 --> 01:02:29.035 and I think this is coming to remove the

NOTE Confidence: 0.858679203333333

01:02:29.035 --> 01:02:31.540 subjective interpretation from this process.

NOTE Confidence: 0.858679203333333

01:02:31.540 --> 01:02:33.532 I'm always comforted to hear from

NOTE Confidence: 0.858679203333333

01:02:33.532 --> 01:02:36.863 Jill that if if one needs to treat a

NOTE Confidence: 0.858679203333333

01:02:36.863 --> 01:02:38.793 patient with a checkpoint inhibitor,

NOTE Confidence: 0.858679203333333

01:02:38.800 --> 01:02:42.020 it is possible to do so regardless.

NOTE Confidence: 0.858679203333333

01:02:42.020 --> 01:02:43.570 Of what the score is,

NOTE Confidence: 0.858679203333333

01:02:43.570 --> 01:02:46.498 but we still feel quite a burden that

NOTE Confidence: 0.858679203333333

01:02:46.498 --> 01:02:50.003 we may be giving a result that is,

NOTE Confidence: 0.858679203333333

01:02:50.003 --> 01:02:53.430 is not could potentially not be accurate

NOTE Confidence: 0.858679203333333

01:02:53.430 --> 01:02:56.129 about a cutoff that you're counting on,

NOTE Confidence: 0.858679203333333

01:02:56.130 --> 01:02:59.018 and therefore the the sort of the hope

NOTE Confidence: 0.858679203333333

01:02:59.018 --> 01:03:02.050 given to the patient about a response.

NOTE Confidence: 0.858679203333333

01:03:02.050 --> 01:03:04.850 We would like that to be real.

NOTE Confidence: 0.858679203333333

01:03:04.850 --> 01:03:06.890 But it does beg the question.

NOTE Confidence: 0.858679203333333

01:03:06.890 --> 01:03:09.368 Are there situations where PD one stain?

NOTE Confidence: 0.858679203333333

01:03:09.370 --> 01:03:11.169 It may not be needed to treat,

NOTE Confidence: 0.858679203333333

01:03:11.170 --> 01:03:12.110 and if that's the case,

NOTE Confidence: 0.858679203333333

01:03:12.110 --> 01:03:14.938 be great not to ask for it.

NOTE Confidence: 0.858679203333333

01:03:14.940 --> 01:03:15.235 Further,

NOTE Confidence: 0.858679203333333

01:03:15.235 --> 01:03:17.890 in addition to what I I think you know,

NOTE Confidence: 0.858679203333333

01:03:17.890 --> 01:03:18.950 and I have to mention,

NOTE Confidence: 0.858679203333333

01:03:18.950 --> 01:03:20.616 Dave Rim always in a talk like

NOTE Confidence: 0.858679203333333

01:03:20.616 --> 01:03:22.204 this for all the wonderful work

NOTE Confidence: 0.858679203333333

01:03:22.204 --> 01:03:24.101 that he and his lab have done.

NOTE Confidence: 0.858679203333333

01:03:24.110 --> 01:03:26.861 And I he has a quantitative pathology

NOTE Confidence: 0.858679203333333

01:03:26.861 --> 01:03:28.908 laboratory yield that I hope will,

NOTE Confidence: 0.858679203333333

01:03:28.910 --> 01:03:30.728 I assume is working very hard

NOTE Confidence: 0.858679203333333

01:03:30.728 --> 01:03:32.730 on on getting to automation.

NOTE Confidence: 0.858679203333333

01:03:32.730 --> 01:03:34.560 But in in fact there's other

NOTE Confidence: 0.858679203333333

01:03:34.560 --> 01:03:36.513 research and Kurt Shelper in our

NOTE Confidence: 0.858679203333333

01:03:36.513 --> 01:03:37.865 department with Leaping Chen.

NOTE Confidence: 0.858679203333333

01:03:37.870 --> 01:03:39.742 Of course they recently

NOTE Confidence: 0.858679203333333

01:03:39.742 --> 01:03:42.120 published in Cell in 2019.

NOTE Confidence: 0.858679203333333

01:03:42.120 --> 01:03:44.060 They're digging even deeper,

NOTE Confidence: 0.858679203333333

01:03:44.060 --> 01:03:44.460 you know,

NOTE Confidence: 0.858679203333333

01:03:44.460 --> 01:03:45.660 because after all there are those.

NOTE Confidence: 0.858679203333333

01:03:45.660 --> 01:03:47.152 Folks with checkpoint inhibitors

NOTE Confidence: 0.858679203333333

01:03:47.152 --> 01:03:49.390 who don't respond and he's there,

NOTE Confidence: 0.858679203333333

01:03:49.390 --> 01:03:52.820 the group is getting into other discoveries

NOTE Confidence: 0.858679203333333

01:03:52.820 --> 01:03:57.240 of other potential important molecules.

NOTE Confidence: 0.858679203333333

01:03:57.240 --> 01:03:59.965 Such as fibrogenic like fibrinogen

NOTE Confidence: 0.858679203333333

01:03:59.965 --> 01:04:02.690 like protein and its interaction

NOTE Confidence: 0.858679203333333

01:04:02.780 --> 01:04:05.550 with lymphocyte activation gene 3.

NOTE Confidence: 0.858679203333333

01:04:05.550 --> 01:04:06.910 So that's very exciting,

NOTE Confidence: 0.858679203333333

01:04:06.910 --> 01:04:08.950 and hopefully they'll be more things.

NOTE Confidence: 0.858679203333333

01:04:08.950 --> 01:04:12.358 I just wanted to share some references that

NOTE Confidence: 0.858679203333333

01:04:12.358 --> 01:04:16.468 I referred to in this talk and thank you.

NOTE Confidence: 0.858679203333333

01:04:16.470 --> 01:04:19.230 I hope it's not too alarming,

NOTE Confidence: 0.858679203333333

01:04:19.230 --> 01:04:23.024 but I it's a great opportunity for

NOTE Confidence: 0.858679203333333

01:04:23.024 --> 01:04:25.364 pathologist to share what's really

NOTE Confidence: 0.858679203333333

01:04:25.364 --> 01:04:27.506 going on behind that CPS clip.

NOTE Confidence: 0.858679203333333

01:04:27.510 --> 01:04:28.010 Thank you.

NOTE Confidence: 0.035580188

01:04:31.150 --> 01:04:34.520 Summary that was awesome and maybe

NOTE Confidence: 0.035580188

01:04:34.520 --> 01:04:37.260 a little alarming. I'm sorry.

NOTE Confidence: 0.858157674736842

01:04:37.260 --> 01:04:38.364 Thank you for clarification.

NOTE Confidence: 0.858157674736842

01:04:38.364 --> 01:04:40.977 There was a question in the chat box which

NOTE Confidence: 0.858157674736842

01:04:40.977 --> 01:04:42.783 I think you preemptively answered about.

NOTE Confidence: 0.858157674736842

01:04:42.790 --> 01:04:44.332 There must be scanning software and

NOTE Confidence: 0.858157674736842

01:04:44.332 --> 01:04:45.709 artificial intelligence that can do this.

NOTE Confidence: 0.858157674736842

01:04:45.710 --> 01:04:47.330 This just seems like such an

NOTE Confidence: 0.858157674736842

01:04:47.330 --> 01:04:48.680 onerous burden on you all.

NOTE Confidence: 0.858157674736842

01:04:48.680 --> 01:04:50.755 And at the end of the day, as you said,

NOTE Confidence: 0.858157674736842

01:04:50.755 --> 01:04:52.345 it's not really as quantitative as

NOTE Confidence: 0.858157674736842

01:04:52.345 --> 01:04:54.299 we all think it might be when we

NOTE Confidence: 0.858157674736842

01:04:54.299 --> 01:04:56.118 look at forest plots with cut offs.

NOTE Confidence: 0.858157674736842

01:04:56.120 --> 01:04:57.548 So it looks like that is something

NOTE Confidence: 0.858157674736842

01:04:57.548 --> 01:04:59.430 that's in the works, and I

NOTE Confidence: 0.8389574734

01:04:59.490 --> 01:05:02.232 think people. I know people are

NOTE Confidence: 0.8389574734

01:05:02.232 --> 01:05:05.983 working on this and and it I agree

NOTE Confidence: 0.8389574734

01:05:05.983 --> 01:05:08.725 with the person asking the question.

NOTE Confidence: 0.8389574734

01:05:08.730 --> 01:05:09.966 There will be a better way.

NOTE Confidence: 0.918112289

01:05:11.390 --> 01:05:12.660 All right, well I will

NOTE Confidence: 0.918112289

01:05:12.660 --> 01:05:13.930 carry on and thank you.

NOTE Confidence: 0.918112289

01:05:13.930 --> 01:05:18.018 That really lays the foundation for my talk.

NOTE Confidence: 0.918112289

01:05:18.020 --> 01:05:20.092 And now we're going to talk about how

NOTE Confidence: 0.918112289

01:05:20.092 --> 01:05:23.018 we use this information in making very

NOTE Confidence: 0.918112289

01:05:23.018 --> 01:05:25.348 important decisions for our patients.

NOTE Confidence: 0.881233578571429

01:05:27.860 --> 01:05:31.535 So we can all see my screen.

NOTE Confidence: 0.881233578571429

01:05:31.540 --> 01:05:32.784 So I'm Jill Lacey.

NOTE Confidence: 0.881233578571429

01:05:32.784 --> 01:05:35.474 I'm a medical oncologist at the Yale School

NOTE Confidence: 0.881233578571429

01:05:35.474 --> 01:05:37.760 of Medicine and Smilow Cancer Center.

NOTE Confidence: 0.881233578571429

01:05:37.760 --> 01:05:40.840 I'm involved in caring for patients with

NOTE Confidence: 0.881233578571429

01:05:40.840 --> 01:05:43.182 gastrointestinal cancers and do have a

NOTE Confidence: 0.881233578571429

01:05:43.182 --> 01:05:45.716 strong interest in gastroesophageal cancers.

NOTE Confidence: 0.881233578571429

01:05:45.716 --> 01:05:48.876 So my topic tonight is,

NOTE Confidence: 0.881233578571429

01:05:48.880 --> 01:05:50.734 is it time for chemo immunotherapy

NOTE Confidence: 0.881233578571429

01:05:50.734 --> 01:05:52.610 for all of our patients,

NOTE Confidence: 0.881233578571429

01:05:52.610 --> 01:05:55.828 or should we slow down, put the brakes on?

NOTE Confidence: 0.881233578571429

01:05:55.828 --> 01:05:58.812 Not so fast. And here are my.

NOTE Confidence: 0.881233578571429

01:05:58.812 --> 01:06:02.252 Conflicts, so I'm going to be focusing

NOTE Confidence: 0.881233578571429

01:06:02.252 --> 01:06:05.390 solely on first line treatment,

NOTE Confidence: 0.881233578571429

01:06:05.390 --> 01:06:07.250 not second line and beyond,

NOTE Confidence: 0.881233578571429

01:06:07.250 --> 01:06:09.280 and the role of immunotherapy

NOTE Confidence: 0.881233578571429

01:06:09.280 --> 01:06:12.076 in the first line treatment of

NOTE Confidence: 0.881233578571429

01:06:12.076 --> 01:06:14.158 metastatic gastroesophageal cancers.

NOTE Confidence: 0.881233578571429

01:06:14.160 --> 01:06:16.758 I'm going to review the data

NOTE Confidence: 0.881233578571429

01:06:16.758 --> 01:06:17.624 for chemoimmunotherapy,

NOTE Confidence: 0.881233578571429

01:06:17.630 --> 01:06:19.580 and when I say chemoimmunotherapy here,

NOTE Confidence: 0.881233578571429

01:06:19.580 --> 01:06:22.130 I'm talking about a standard

NOTE Confidence: 0.881233578571429

01:06:22.130 --> 01:06:24.734 chemotherapy doublet with or without

NOTE Confidence: 0.881233578571429

01:06:24.734 --> 01:06:26.846 an immune checkpoint inhibitor.

NOTE Confidence: 0.881233578571429

01:06:26.850 --> 01:06:28.789 And all the studies have been with.

NOTE Confidence: 0.881233578571429

01:06:28.790 --> 01:06:29.842 PD1 inhibitors to date.

NOTE Confidence: 0.881233578571429

01:06:29.842 --> 01:06:31.420 I'm going to talk about the

NOTE Confidence: 0.881233578571429

01:06:31.480 --> 01:06:33.110 data in squamous cell carcinoma

NOTE Confidence: 0.881233578571429

01:06:33.110 --> 01:06:34.740 and the data in adenocarcinoma,

NOTE Confidence: 0.881233578571429

01:06:34.740 --> 01:06:35.865 which is different.

NOTE Confidence: 0.881233578571429

01:06:35.865 --> 01:06:38.520 Then I'm going to review some of

NOTE Confidence: 0.881233578571429

01:06:38.520 --> 01:06:40.470 the data for chemotherapy free

NOTE Confidence: 0.881233578571429

01:06:40.470 --> 01:06:42.969 immunotherapy in the first line setting.

NOTE Confidence: 0.881233578571429

01:06:42.970 --> 01:06:45.154 We've heard a lot about the controversy

NOTE Confidence: 0.881233578571429

01:06:45.154 --> 01:06:47.240 surrounding PDL ones predictive biomarker,

NOTE Confidence: 0.881233578571429

01:06:47.240 --> 01:06:50.565 so I will just highlight those and

NOTE Confidence: 0.881233578571429

01:06:50.565 --> 01:06:53.188 then I will have some conclusions of

NOTE Confidence: 0.881233578571429

01:06:53.188 --> 01:06:56.471 my own and some of the questions and

NOTE Confidence: 0.881233578571429

01:06:56.471 --> 01:06:59.123 future directions that we are facing.

NOTE Confidence: 0.881233578571429

01:06:59.130 --> 01:07:00.040 So.

NOTE Confidence: 0.021532059

01:07:03.630 --> 01:07:04.280 Enhancing

NOTE Confidence: 0.917321995

01:07:06.850 --> 01:07:08.290 did you click on your talk?

NOTE Confidence: 0.917321995

01:07:08.290 --> 01:07:09.240 I had. There you go

NOTE Confidence: 0.743765947333333

01:07:09.360 --> 01:07:12.390 there you go. OK, so immune.

NOTE Confidence: 0.743765947333333

01:07:12.390 --> 01:07:13.236 Checkpoint inhibitors.

NOTE Confidence: 0.743765947333333

01:07:13.236 --> 01:07:16.197 I think as many know in gastroesophageal

NOTE Confidence: 0.743765947333333

01:07:16.197 --> 01:07:18.825 cancers have really had a checkered history.

NOTE Confidence: 0.743765947333333

01:07:18.830 --> 01:07:20.670 Had some pretty inconsistent

NOTE Confidence: 0.743765947333333

01:07:20.670 --> 01:07:22.050 and conflicting results.

NOTE Confidence: 0.743765947333333

01:07:22.050 --> 01:07:23.688 Certainly in the second and third line

NOTE Confidence: 0.743765947333333

01:07:23.688 --> 01:07:25.550 setting and also in the first line setting.

NOTE Confidence: 0.743765947333333

01:07:25.550 --> 01:07:27.668 There are many reasons for this.

NOTE Confidence: 0.743765947333333

01:07:27.670 --> 01:07:28.878 This is really a

NOTE Confidence: 0.743765947333333

01:07:28.878 --> 01:07:30.086 heterogeneous group of tumors.

NOTE Confidence: 0.743765947333333

01:07:30.090 --> 01:07:32.082 In every respect we've just heard

NOTE Confidence: 0.743765947333333

01:07:32.082 --> 01:07:33.909 about the imperfections of PDL one,

NOTE Confidence: 0.743765947333333

01:07:33.910 --> 01:07:35.938 and yet we are continue to.

NOTE Confidence: 0.743765947333333

01:07:35.940 --> 01:07:37.942 Use it to make to design studies

NOTE Confidence: 0.743765947333333

01:07:37.942 --> 01:07:40.105 and to make treatment decisions and

NOTE Confidence: 0.743765947333333

01:07:40.105 --> 01:07:42.577 then of course the trial designs.

NOTE Confidence: 0.743765947333333

01:07:42.580 --> 01:07:44.110 Any trial design is never perfect

NOTE Confidence: 0.743765947333333

01:07:44.110 --> 01:07:46.362 and I think there have been a lot of

NOTE Confidence: 0.743765947333333

01:07:46.362 --> 01:07:48.170 imperfections in in the ways that the

NOTE Confidence: 0.743765947333333

01:07:48.170 --> 01:07:49.898 studies have have have been designed.

NOTE Confidence: 0.743765947333333

01:07:49.900 --> 01:07:50.370 You know,

NOTE Confidence: 0.743765947333333

01:07:50.370 --> 01:07:51.780 in large part baked into the

NOTE Confidence: 0.743765947333333

01:07:51.780 --> 01:07:53.398 cake and for pragmatic reasons.

NOTE Confidence: 0.743765947333333

01:07:53.400 --> 01:07:54.567 But that said,

NOTE Confidence: 0.743765947333333

01:07:54.567 --> 01:07:57.290 I think in the first line setting

NOTE Confidence: 0.743765947333333

01:07:57.379 --> 01:07:59.743 some consistent and reproducible

NOTE Confidence: 0.743765947333333

01:07:59.743 --> 01:08:01.516 data have emerged,

NOTE Confidence: 0.743765947333333

01:08:01.520 --> 01:08:05.500 especially in squamous cell carcinomas.

NOTE Confidence: 0.743765947333333

01:08:05.500 --> 01:08:06.295 As I said,

NOTE Confidence: 0.743765947333333

01:08:06.295 --> 01:08:08.150 I'm focusing on the first line setting

NOTE Confidence: 0.743765947333333

01:08:08.207 --> 01:08:09.935 at present in the United States,

NOTE Confidence: 0.743765947333333

01:08:09.940 --> 01:08:12.732 we have FDA approvals for two iOS in

NOTE Confidence: 0.743765947333333

01:08:12.732 --> 01:08:15.297 the second line setting and beyond,

NOTE Confidence: 0.743765947333333

01:08:15.300 --> 01:08:17.385 both in squamous cell carcinomas

NOTE Confidence: 0.743765947333333

01:08:17.385 --> 01:08:18.636 of the esophagus,

NOTE Confidence: 0.743765947333333

01:08:18.640 --> 01:08:20.615 one with pembrolizumab with the

NOTE Confidence: 0.743765947333333

01:08:20.615 --> 01:08:23.786 PDL 1 score is 10% or greater.

NOTE Confidence: 0.743765947333333

01:08:23.786 --> 01:08:27.329 That's CPS and neevo PDL 1 agnostic,

NOTE Confidence: 0.743765947333333

01:08:27.329 --> 01:08:30.599 so I'm going to talk now about the

NOTE Confidence: 0.743765947333333

01:08:30.599 --> 01:08:33.099 data in squamous cell carcinoma.

NOTE Confidence: 0.743765947333333

01:08:33.100 --> 01:08:36.092 So I just need to remind you as we go

NOTE Confidence: 0.743765947333333

01:08:36.092 --> 01:08:38.710 through this that when we talk about

NOTE Confidence: 0.743765947333333

01:08:38.710 --> 01:08:41.300 esophageal cancer so often historically,

NOTE Confidence: 0.743765947333333

01:08:41.300 --> 01:08:43.675 the studies have included both

NOTE Confidence: 0.743765947333333

01:08:43.675 --> 01:08:45.575 squamous cell and adenocarcinoma.

NOTE Confidence: 0.743765947333333

01:08:45.580 --> 01:08:47.248 So mixed Histology studies

NOTE Confidence: 0.743765947333333

01:08:47.248 --> 01:08:49.333 really based on the anatomy,

NOTE Confidence: 0.743765947333333

01:08:49.340 --> 01:08:51.125 but in reality these are

NOTE Confidence: 0.743765947333333

01:08:51.125 --> 01:08:52.196 very different diseases.

NOTE Confidence: 0.743765947333333

01:08:52.200 --> 01:08:54.978 Many differences as are highlighted here

NOTE Confidence: 0.743765947333333

01:08:54.978 --> 01:08:58.259 and actually not that many similarities,

NOTE Confidence: 0.743765947333333

01:08:58.260 --> 01:09:00.660 symptoms, overarching treatment algorithms

NOTE Confidence: 0.743765947333333

01:09:00.660 --> 01:09:03.756 and and prognosis, and I think.

NOTE Confidence: 0.743765947333333

01:09:03.756 --> 01:09:06.261 What's really emerged is that, yes,

NOTE Confidence: 0.743765947333333

01:09:06.261 --> 01:09:07.966 these are very different diseases.

NOTE Confidence: 0.743765947333333

01:09:07.970 --> 01:09:11.568 This is from the tumor profiling and

NOTE Confidence: 0.743765947333333

01:09:11.568 --> 01:09:14.874 molecular analysis that we're seeing with

NOTE Confidence: 0.743765947333333

01:09:14.874 --> 01:09:17.226 esophageal squamous and adenocarcinoma.

NOTE Confidence: 0.743765947333333

01:09:17.230 --> 01:09:19.050 So the squamous subtype really

NOTE Confidence: 0.743765947333333

01:09:19.050 --> 01:09:22.070 resembles from A at a molecular level,

NOTE Confidence: 0.743765947333333

01:09:22.070 --> 01:09:24.070 and a genomic profiling level,

NOTE Confidence: 0.743765947333333

01:09:24.070 --> 01:09:25.321 squamous cell carcinomas

NOTE Confidence: 0.743765947333333

01:09:25.321 --> 01:09:26.989 of other organ sites.

NOTE Confidence: 0.743765947333333

01:09:26.990 --> 01:09:30.280 Whereas adenocarcinomas of the esophagus

NOTE Confidence: 0.743765947333333

01:09:30.280 --> 01:09:33.570 resemble the chromosomal instability subtype.

NOTE Confidence: 0.743765947333333

01:09:33.570 --> 01:09:35.868 The four subtypes of gastric cancer.

NOTE Confidence: 0.743765947333333

01:09:35.870 --> 01:09:37.334 The chromosomal instability

NOTE Confidence: 0.743765947333333

01:09:37.334 --> 01:09:39.286 subtype of gastric cancer.

NOTE Confidence: 0.743765947333333

01:09:39.290 --> 01:09:41.625 So really there's no biologic

NOTE Confidence: 0.743765947333333

01:09:41.625 --> 01:09:43.026 or scientific rationale,

NOTE Confidence: 0.743765947333333

01:09:43.030 --> 01:09:45.767 I think at this point in clinical

NOTE Confidence: 0.743765947333333

01:09:45.767 --> 01:09:47.566 trials for combining squamous

NOTE Confidence: 0.743765947333333

01:09:47.566 --> 01:09:49.766 and adeno esophageal cancers.

NOTE Confidence: 0.743765947333333

01:09:49.770 --> 01:09:51.630 It's a maybe a pragmatic reason,

NOTE Confidence: 0.743765947333333

01:09:51.630 --> 01:09:53.460 but not really a biological reason.

NOTE Confidence: 0.743765947333333

01:09:53.460 --> 01:09:55.852 And I think if that's important to keep

NOTE Confidence: 0.743765947333333

01:09:55.852 --> 01:09:58.560 in mind as we look at some of this data.

NOTE Confidence: 0.743765947333333

01:09:58.560 --> 01:10:01.430 So turning now to squamous cell carcinomas.

NOTE Confidence: 0.743765947333333

01:10:01.430 --> 01:10:02.435 This is remarkable.

NOTE Confidence: 0.743765947333333

01:10:02.435 --> 01:10:05.811 There have been in the last two years 5

NOTE Confidence: 0.743765947333333

01:10:05.811 --> 01:10:08.206 completed published large randomized phase.

NOTE Confidence: 0.743765947333333

01:10:08.210 --> 01:10:10.158 Three trials of chemotherapy

NOTE Confidence: 0.743765947333333

01:10:10.158 --> 01:10:12.106 doublets versus a chemotherapy

NOTE Confidence: 0.743765947333333

01:10:12.106 --> 01:10:14.228 doublet plus a PD1 inhibitor,

NOTE Confidence: 0.743765947333333

01:10:14.230 --> 01:10:15.990 and they are listed here,

NOTE Confidence: 0.743765947333333

01:10:15.990 --> 01:10:18.307 and these studies have all shown really

NOTE Confidence: 0.743765947333333

01:10:18.307 --> 01:10:19.910 a consistent improvement in overall

NOTE Confidence: 0.743765947333333

01:10:19.910 --> 01:10:21.578 survival with the addition of a.

NOTE Confidence: 0.743765947333333

01:10:21.580 --> 01:10:24.716 I'm sorry that is PD1 inhibitor to

NOTE Confidence: 0.743765947333333

01:10:24.716 --> 01:10:26.060 chemotherapy remarkable consistency

NOTE Confidence: 0.743765947333333

01:10:26.124 --> 01:10:28.044 and two of these studies have

NOTE Confidence: 0.743765947333333

01:10:28.044 --> 01:10:29.324 led to FDA approvals

NOTE Confidence: 0.862154936071429

01:10:29.388 --> 01:10:31.308 in the United States in

NOTE Confidence: 0.862154936071429

01:10:31.308 --> 01:10:32.460 squamous cell carcinoma.

NOTE Confidence: 0.862154936071429

01:10:32.460 --> 01:10:34.938 I'm going to focus in on Checkmate 648.

NOTE Confidence: 0.862154936071429

01:10:34.938 --> 01:10:36.954 This is the largest study by far,

NOTE Confidence: 0.862154936071429

01:10:36.960 --> 01:10:38.892 and this is the study that led

NOTE Confidence: 0.862154936071429

01:10:38.892 --> 01:10:41.502 to the FDA approval of Nevo with

NOTE Confidence: 0.862154936071429

01:10:41.502 --> 01:10:43.637 chemo and squamous cell carcinomas.

NOTE Confidence: 0.862154936071429

01:10:43.640 --> 01:10:45.985 I think you've seen the study design

NOTE Confidence: 0.862154936071429

01:10:45.985 --> 01:10:48.740 is this was a three arm study

NOTE Confidence: 0.862154936071429

01:10:48.740 --> 01:10:50.115 with chemotherapy, fluorouracil,

NOTE Confidence: 0.862154936071429

01:10:50.115 --> 01:10:52.790 cisplatinum as a control against

NOTE Confidence: 0.862154936071429

01:10:52.790 --> 01:10:56.201 chemo plus Nevo and then a third

NOTE Confidence: 0.862154936071429

01:10:56.201 --> 01:10:58.176 arm without chemo of Nevo.

NOTE Confidence: 0.862154936071429

01:10:58.180 --> 01:11:00.856 Plus Skippy and the results are

NOTE Confidence: 0.862154936071429

01:11:00.856 --> 01:11:02.640 highlighted in this somewhat.

NOTE Confidence: 0.862154936071429

01:11:02.640 --> 01:11:03.824 Disease slide,

NOTE Confidence: 0.862154936071429

01:11:03.824 --> 01:11:07.968 so in terms of the overall survival,

NOTE Confidence: 0.862154936071429

01:11:07.970 --> 01:11:12.106 there was a benefit in both the PDL

NOTE Confidence: 0.862154936071429

01:11:12.106 --> 01:11:14.150 one TPS 1% or greater population,

NOTE Confidence: 0.862154936071429

01:11:14.150 --> 01:11:16.334 which was their first primary endpoint

NOTE Confidence: 0.862154936071429

01:11:16.334 --> 01:11:19.419 about a six month improvement in survival.

NOTE Confidence: 0.862154936071429

01:11:19.420 --> 01:11:22.381 Truly a stunning result with a hazard

NOTE Confidence: 0.862154936071429

01:11:22.381 --> 01:11:24.670 ratio of .54 and also improved

NOTE Confidence: 0.862154936071429

01:11:24.670 --> 01:11:26.830 progression free survival and response rate.

NOTE Confidence: 0.862154936071429

01:11:26.830 --> 01:11:30.141 This is really dramatic data for this

NOTE Confidence: 0.862154936071429

01:11:30.141 --> 01:11:32.899 very difficult disease and again major.

NOTE Confidence: 0.862154936071429

01:11:32.900 --> 01:11:34.292 Events in the field.

NOTE Confidence: 0.862154936071429

01:11:34.292 --> 01:11:36.380 Also there was benefit in terms

NOTE Confidence: 0.862154936071429

01:11:36.454 --> 01:11:38.634 of survival for all randomized

NOTE Confidence: 0.862154936071429

01:11:38.634 --> 01:11:41.422 patients of about two 2 1/2 months

NOTE Confidence: 0.862154936071429

01:11:41.422 --> 01:11:45.040 with a hazard ratio .74.

NOTE Confidence: 0.862154936071429

01:11:45.040 --> 01:11:47.074 And of course everyone is interested

NOTE Confidence: 0.862154936071429

01:11:47.074 --> 01:11:48.794 in the subset analysis that

NOTE Confidence: 0.862154936071429

01:11:48.794 --> 01:11:50.308 are often flawed small numbers.

NOTE Confidence: 0.862154936071429

01:11:50.308 --> 01:11:52.740 But if you look at the subsets here,

NOTE Confidence: 0.862154936071429

01:11:52.740 --> 01:11:55.586 I think what jumps out is that

NOTE Confidence: 0.862154936071429

01:11:55.586 --> 01:11:57.598 almost all subsets benefited.

NOTE Confidence: 0.862154936071429

01:11:57.600 --> 01:12:00.589 Interestingly, females and it's a small set.

NOTE Confidence: 0.862154936071429

01:12:00.590 --> 01:12:02.324 A number of patients in squamous

NOTE Confidence: 0.862154936071429

01:12:02.324 --> 01:12:04.622 there did not appear to be a benefit

NOTE Confidence: 0.862154936071429

01:12:04.622 --> 01:12:06.254 that's been seen in other studies,

NOTE Confidence: 0.862154936071429

01:12:06.260 --> 01:12:07.106 and importantly,

NOTE Confidence: 0.862154936071429

01:12:07.106 --> 01:12:09.221 that very important biomarker that

NOTE Confidence: 0.862154936071429

01:12:09.221 --> 01:12:11.798 we're all now relying on PDL one.

NOTE Confidence: 0.862154936071429

01:12:11.800 --> 01:12:13.528 And so that's that's blown up

NOTE Confidence: 0.862154936071429

01:12:13.528 --> 01:12:14.680 here on this slide.

NOTE Confidence: 0.862154936071429

01:12:14.680 --> 01:12:17.896 And so if you look at CPS first.

NOTE Confidence: 0.862154936071429

01:12:17.900 --> 01:12:20.133 The only group that did not appear

NOTE Confidence: 0.862154936071429

01:12:20.133 --> 01:12:22.355 to benefit in terms of hazard ratio

NOTE Confidence: 0.862154936071429

01:12:22.355 --> 01:12:25.149 less than one was a CPS less than one,

NOTE Confidence: 0.862154936071429

01:12:25.150 --> 01:12:27.473 and that was only 9% of the patient,

NOTE Confidence: 0.862154936071429

01:12:27.473 --> 01:12:28.978 so all the others were.

NOTE Confidence: 0.862154936071429

01:12:28.980 --> 01:12:32.436 The hazard ratio was was less than one.

NOTE Confidence: 0.862154936071429

01:12:32.440 --> 01:12:34.040 If you look at TPS,

NOTE Confidence: 0.862154936071429

01:12:34.040 --> 01:12:36.105 this is interesting in the

NOTE Confidence: 0.862154936071429

01:12:36.105 --> 01:12:37.757 group less than one.

NOTE Confidence: 0.862154936071429

01:12:37.760 --> 01:12:39.552 There did not appear to be a

NOTE Confidence: 0.862154936071429

01:12:39.552 --> 01:12:41.474 benefit and and by TPS less than

NOTE Confidence: 0.862154936071429

01:12:41.474 --> 01:12:43.112 one is about half the patient,

NOTE Confidence: 0.862154936071429

01:12:43.120 --> 01:12:45.094 so the data is a little bit,

NOTE Confidence: 0.862154936071429

01:12:45.100 --> 01:12:47.984 I think hard director head around, but.

NOTE Confidence: 0.862154936071429

01:12:47.984 --> 01:12:50.048 In the CPS less than one,

NOTE Confidence: 0.862154936071429

01:12:50.050 --> 01:12:52.126 there was a higher response rate.

NOTE Confidence: 0.862154936071429

01:12:52.130 --> 01:12:54.290 There was longer response duration,

NOTE Confidence: 0.862154936071429

01:12:54.290 --> 01:12:57.062 and it's possible that a survival survival

NOTE Confidence: 0.862154936071429

01:12:57.062 --> 01:12:59.748 benefit may emerge with longer follow-up.

NOTE Confidence: 0.862154936071429

01:12:59.750 --> 01:13:02.430 So in the other studies, just to run through,

NOTE Confidence: 0.862154936071429

01:13:02.430 --> 01:13:04.650 you know what these look like.

NOTE Confidence: 0.862154936071429

01:13:04.650 --> 01:13:06.180 Three of them conducted in Asia,

NOTE Confidence: 0.862154936071429

01:13:06.180 --> 01:13:06.850 three global.

NOTE Confidence: 0.862154936071429

01:13:06.850 --> 01:13:08.525 These are all big studies.

NOTE Confidence: 0.862154936071429

01:13:08.530 --> 01:13:11.221 Keynote 590 stands out in that it was a

NOTE Confidence: 0.862154936071429

01:13:11.221 --> 01:13:13.789 mixed Histology study of adenosquamous.

NOTE Confidence: 0.862154936071429

01:13:13.790 --> 01:13:16.910 The 2/3 of them being squamous.

NOTE Confidence: 0.862154936071429

01:13:16.910 --> 01:13:18.486 Different PD1 inhibitors were

NOTE Confidence: 0.862154936071429

01:13:18.486 --> 01:13:20.850 used in each of these studies.

NOTE Confidence: 0.862154936071429

01:13:20.850 --> 01:13:23.370 Different chemotherapy backbones were used,

NOTE Confidence: 0.862154936071429

01:13:23.370 --> 01:13:24.770 although most were cisplatinum,

NOTE Confidence: 0.862154936071429

01:13:24.770 --> 01:13:26.870 based with either 5 or fewer

NOTE Confidence: 0.862154936071429

01:13:26.870 --> 01:13:28.338 CARBO paclitaxel.

NOTE Confidence: 0.862154936071429

01:13:28.338 --> 01:13:29.806 Different PDL,

NOTE Confidence: 0.862154936071429

01:13:29.806 --> 01:13:34.210 one cut points for primary analysis,

NOTE Confidence: 0.862154936071429

01:13:34.210 --> 01:13:35.336 different assays.

NOTE Confidence: 0.862154936071429

01:13:35.336 --> 01:13:38.151 But what's remarkable is the

NOTE Confidence: 0.862154936071429

01:13:38.151 --> 01:13:40.676 similarity in survival benefit in

NOTE Confidence: 0.862154936071429

01:13:40.676 --> 01:13:43.676 all of these studies of a couple of

NOTE Confidence: 0.905483848461538

01:13:43.764 --> 01:13:47.028 months with quite similar hazard ratios.

NOTE Confidence: 0.905483848461538

01:13:47.030 --> 01:13:49.550 Jupiter 06 being most impressive,

NOTE Confidence: 0.905483848461538

01:13:49.550 --> 01:13:51.713 so this is a very consistent finding

NOTE Confidence: 0.905483848461538

01:13:51.713 --> 01:13:53.652 and I think that really drives

NOTE Confidence: 0.905483848461538

01:13:53.652 --> 01:13:56.346 home the point of the value PD 1

NOTE Confidence: 0.905483848461538

01:13:56.346 --> 01:13:58.436 inhibitors and squamous cell cancers.

NOTE Confidence: 0.905483848461538

01:13:58.440 --> 01:14:00.640 And for those of you that like Kaplan

NOTE Confidence: 0.905483848461538

01:14:00.640 --> 01:14:02.669 Meier plots, those are depicted

NOTE Confidence: 0.905483848461538

01:14:02.669 --> 01:14:05.134 graphically here for these studies.

NOTE Confidence: 0.905483848461538

01:14:05.140 --> 01:14:07.660 Now how does PDL 1 fit into this?

NOTE Confidence: 0.905483848461538

01:14:07.660 --> 01:14:10.678 So again we're getting conflicting results.

NOTE Confidence: 0.905483848461538

01:14:10.680 --> 01:14:13.804 I reviewed the PDL one story with 648

NOTE Confidence: 0.905483848461538

01:14:13.804 --> 01:14:16.492 where did appear that the benefit was

NOTE Confidence: 0.905483848461538

01:14:16.492 --> 01:14:18.827 greater with higher PL and scores,

NOTE Confidence: 0.905483848461538

01:14:18.830 --> 01:14:19.716 especially TPS.

NOTE Confidence: 0.905483848461538

01:14:19.716 --> 01:14:23.260 We did not appear to see that same

NOTE Confidence: 0.905483848461538

01:14:23.352 --> 01:14:26.960 phenomenon in Jupiter 06 or in Orient 15,

NOTE Confidence: 0.905483848461538

01:14:26.960 --> 01:14:29.633 but there was an association with Epoxy

NOTE Confidence: 0.905483848461538

01:14:29.633 --> 01:14:32.657 and PDL one and escort the escort study.

NOTE Confidence: 0.905483848461538

01:14:32.660 --> 01:14:35.020 So again not completely consistent.

NOTE Confidence: 0.905483848461538

01:14:35.020 --> 01:14:35.616 But overall,

NOTE Confidence: 0.905483848461538

01:14:35.616 --> 01:14:37.702 I think these are really impressive results,

NOTE Confidence: 0.905483848461538

01:14:37.710 --> 01:14:38.222 and again,

NOTE Confidence: 0.905483848461538

01:14:38.222 --> 01:14:40.014 if you look at the forest plots

NOTE Confidence: 0.905483848461538

01:14:40.014 --> 01:14:41.932 and again the the big picture here

NOTE Confidence: 0.905483848461538

01:14:41.932 --> 01:14:43.811 is the the hazard ratio is less

NOTE Confidence: 0.905483848461538

01:14:43.811 --> 01:14:45.561 than one in almost all of these

NOTE Confidence: 0.905483848461538

01:14:45.570 --> 01:14:48.288 studies in all PDL 1 subsets.

NOTE Confidence: 0.905483848461538

01:14:48.290 --> 01:14:50.514 So my take away message is that PD

NOTE Confidence: 0.905483848461538

01:14:50.514 --> 01:14:52.225 one inhibitors added to chemotherapy

NOTE Confidence: 0.905483848461538

01:14:52.225 --> 01:14:54.045 and this disease improves survival

NOTE Confidence: 0.905483848461538

01:14:54.045 --> 01:14:56.354 and the magnitude of benefit has

NOTE Confidence: 0.905483848461538

01:14:56.354 --> 01:14:58.259 been similar across different studies

NOTE Confidence: 0.905483848461538

01:14:58.259 --> 01:15:00.256 with different PD1 inhibitors and

NOTE Confidence: 0.905483848461538

01:15:00.256 --> 01:15:02.562 different chemo backbones and the 648

NOTE Confidence: 0.905483848461538

01:15:02.562 --> 01:15:05.110 study did lead to the FDA approval.

NOTE Confidence: 0.905483848461538

01:15:05.110 --> 01:15:09.700 For me, vote and that is a a PDL 1 agnostic.

NOTE Confidence: 0.905483848461538

01:15:09.700 --> 01:15:13.354 So your respective of PDL one expression.

NOTE Confidence: 0.905483848461538

01:15:13.360 --> 01:15:15.772 And we also have an approval

NOTE Confidence: 0.905483848461538

01:15:15.772 --> 01:15:18.580 from Keynote 590 for Pembroke.

NOTE Confidence: 0.905483848461538

01:15:18.580 --> 01:15:19.164 Also,

NOTE Confidence: 0.905483848461538

01:15:19.164 --> 01:15:22.668 irrespective of PD L1 expression in

NOTE Confidence: 0.905483848461538

01:15:22.668 --> 01:15:25.799 esophageal squamous as well as adeno.

NOTE Confidence: 0.905483848461538

01:15:25.800 --> 01:15:28.280 So I'm going to pivot now to adenocarcinoma,

NOTE Confidence: 0.905483848461538

01:15:28.280 --> 01:15:31.580 and here the story is a little less clear.

NOTE Confidence: 0.905483848461538

01:15:31.580 --> 01:15:34.954 The data is more conflicted and I

NOTE Confidence: 0.905483848461538

01:15:34.954 --> 01:15:37.848 would say that conclusions certainly

NOTE Confidence: 0.905483848461538

01:15:37.848 --> 01:15:41.218 can be made with caveats,

NOTE Confidence: 0.905483848461538

01:15:41.220 --> 01:15:43.020 but it's it's this is a little bit

NOTE Confidence: 0.905483848461538

01:15:43.020 --> 01:15:45.478 more of a challenging story, I think.

NOTE Confidence: 0.905483848461538

01:15:45.478 --> 01:15:48.112 So here we have 5 randomized

NOTE Confidence: 0.905483848461538

01:15:48.112 --> 01:15:49.800 phase three studies,

NOTE Confidence: 0.905483848461538

01:15:49.800 --> 01:15:53.115 all similar designs of chemotherapy

NOTE Confidence: 0.905483848461538

01:15:53.115 --> 01:15:55.104 doublets against chemotherapy.

NOTE Confidence: 0.905483848461538

01:15:55.110 --> 01:15:58.569 Plus PD1 inhibitor.

NOTE Confidence: 0.905483848461538

01:15:58.570 --> 01:16:00.022 Two of these studies,

NOTE Confidence: 0.905483848461538

01:16:00.022 --> 01:16:00.748 keynote 62,

NOTE Confidence: 0.905483848461538

01:16:00.750 --> 01:16:02.700 which was using Pembroke with

NOTE Confidence: 0.905483848461538

01:16:02.700 --> 01:16:05.650 chemo and also had a chemo through

NOTE Confidence: 0.905483848461538

01:16:05.650 --> 01:16:07.935 free arm of Pembroke alone.

NOTE Confidence: 0.905483848461538

01:16:07.940 --> 01:16:10.175 Traction four was a negative

NOTE Confidence: 0.905483848461538

01:16:10.175 --> 01:16:12.390 study and then checkmate 649,

NOTE Confidence: 0.905483848461538

01:16:12.390 --> 01:16:13.230 keynote 590,

NOTE Confidence: 0.905483848461538

01:16:13.230 --> 01:16:15.330 and adenocarcinoma subset and Orient

NOTE Confidence: 0.905483848461538

01:16:15.330 --> 01:16:18.083 16 were all viewed as positive studies

NOTE Confidence: 0.905483848461538

01:16:18.083 --> 01:16:21.713 and the two the two Checkmate 649 and

NOTE Confidence: 0.905483848461538

01:16:21.713 --> 01:16:26.060 590 like to FDA approval in adenocarcinoma.

NOTE Confidence: 0.905483848461538

01:16:26.060 --> 01:16:27.060 I think in the aggregate,

NOTE Confidence: 0.905483848461538

01:16:27.060 --> 01:16:28.860 even though there is conflicting

NOTE Confidence: 0.905483848461538

01:16:28.860 --> 01:16:29.580 results here,

NOTE Confidence: 0.905483848461538

01:16:29.580 --> 01:16:31.325 there's a trend towards improved

NOTE Confidence: 0.905483848461538

01:16:31.325 --> 01:16:33.531 outcomes with the addition of PD1

NOTE Confidence: 0.905483848461538

01:16:33.531 --> 01:16:35.506 inhibitors to chemotherapy in the

NOTE Confidence: 0.905483848461538

01:16:35.506 --> 01:16:37.819 adenocarcinoma Histology as well as squamous,

NOTE Confidence: 0.905483848461538

01:16:37.820 --> 01:16:39.920 and again I'm going to

NOTE Confidence: 0.905483848461538

01:16:39.920 --> 01:16:41.178 highlight Checkmate 649.

NOTE Confidence: 0.905483848461538

01:16:41.178 --> 01:16:42.014 And because,

NOTE Confidence: 0.905483848461538

01:16:42.014 --> 01:16:42.432 again,

NOTE Confidence: 0.905483848461538

01:16:42.432 --> 01:16:45.672 this led to an FDA approval and you

NOTE Confidence: 0.905483848461538

01:16:45.672 --> 01:16:48.460 you have seen the design of 648,

NOTE Confidence: 0.905483848461538

01:16:48.460 --> 01:16:51.552 this is very similar chemo as

NOTE Confidence: 0.905483848461538

01:16:51.552 --> 01:16:53.748 the control arm chemo plus anevo

NOTE Confidence: 0.905483848461538

01:16:53.748 --> 01:16:56.020 and then a chemo free arm of.

NOTE Confidence: 0.905483848461538

01:16:56.020 --> 01:16:58.638 Nivo and IPI and here the ippy

NOTE Confidence: 0.905483848461538

01:16:58.638 --> 01:17:01.589 doses 3 megs per keg and neevo 1.

NOTE Confidence: 0.905483848461538

01:17:01.590 --> 01:17:03.678 The chemotherapy free arm was closed

NOTE Confidence: 0.905483848461538

01:17:03.678 --> 01:17:05.984 early due to futility and they carried

NOTE Confidence: 0.905483848461538

01:17:05.984 --> 01:17:07.958 on with the other two arms and

NOTE Confidence: 0.877736327666666

01:17:08.024 --> 01:17:09.788 then the key points in terms

NOTE Confidence: 0.877736327666666

01:17:09.788 --> 01:17:11.296 of results are shown here.

NOTE Confidence: 0.877736327666666

01:17:11.296 --> 01:17:13.252 They primary end point was in

NOTE Confidence: 0.877736327666666

01:17:13.252 --> 01:17:15.818 the CPS 5 or greater subset and

NOTE Confidence: 0.877736327666666

01:17:15.818 --> 01:17:18.080 that was positive with a three

NOTE Confidence: 0.877736327666666

01:17:18.158 --> 01:17:20.518 month improvement in survival and

NOTE Confidence: 0.877736327666666

01:17:20.518 --> 01:17:23.186 again this is in in this disease.

NOTE Confidence: 0.877736327666666

01:17:23.190 --> 01:17:23.912 Pretty impressive.

NOTE Confidence: 0.877736327666666

01:17:23.912 --> 01:17:26.439 We haven't seen this kind of result.

NOTE Confidence: 0.877736327666666

01:17:26.440 --> 01:17:27.664 In in decades,

NOTE Confidence: 0.877736327666666

01:17:27.664 --> 01:17:30.112 except in the her two positive

NOTE Confidence: 0.877736327666666

01:17:30.112 --> 01:17:32.200 group with a hazard ratio,

NOTE Confidence: 0.877736327666666

01:17:32.200 --> 01:17:34.582 .71 was also positive study in

NOTE Confidence: 0.877736327666666

01:17:34.582 --> 01:17:36.601 all randomized patients about a

NOTE Confidence: 0.877736327666666

01:17:36.601 --> 01:17:38.421 two month improvement in survival

NOTE Confidence: 0.877736327666666

01:17:38.421 --> 01:17:40.339 with a hazard ratio of .8.

NOTE Confidence: 0.877736327666666

01:17:40.340 --> 01:17:42.938 So this was a positive study.

NOTE Confidence: 0.877736327666666

01:17:42.940 --> 01:17:45.712 Now everybody is interested in the PDL

NOTE Confidence: 0.877736327666666

01:17:45.712 --> 01:17:48.959 1 subsets and is there a benefit in PDL?

NOTE Confidence: 0.877736327666666

01:17:48.960 --> 01:17:51.725 One negative and low and that data

NOTE Confidence: 0.877736327666666

01:17:51.725 --> 01:17:54.865 is shown here and so you can see that

NOTE Confidence: 0.877736327666666

01:17:54.865 --> 01:17:57.488 in the PDL one CPS less than one,

NOTE Confidence: 0.877736327666666

01:17:57.488 --> 01:17:59.983 the hazard ratio just is just under

NOTE Confidence: 0.877736327666666

01:17:59.983 --> 01:18:02.203 one but not impressive and the

NOTE Confidence: 0.877736327666666

01:18:02.203 --> 01:18:04.459 same thing with less than five.

NOTE Confidence: 0.877736327666666

01:18:04.460 --> 01:18:07.449 But if you look at responses the

NOTE Confidence: 0.877736327666666

01:18:07.449 --> 01:18:09.948 response rates are higher in all

NOTE Confidence: 0.877736327666666

01:18:09.948 --> 01:18:11.752 PDL 1 subsets including less

NOTE Confidence: 0.877736327666666

01:18:11.752 --> 01:18:13.768 than one and less than five.

NOTE Confidence: 0.877736327666666

01:18:13.770 --> 01:18:14.526 So again,

NOTE Confidence: 0.877736327666666

01:18:14.526 --> 01:18:16.416 this study strongly suggests that

NOTE Confidence: 0.877736327666666

01:18:16.416 --> 01:18:19.460 there is a relationship between PD

NOTE Confidence: 0.877736327666666

01:18:19.460 --> 01:18:21.610 L1 expression and efficacy from

NOTE Confidence: 0.877736327666666

01:18:21.610 --> 01:18:24.570 the addition of a PD1 inhibitor.

NOTE Confidence: 0.877736327666666

01:18:24.570 --> 01:18:28.738 So again, here are the the five studies.

NOTE Confidence: 0.877736327666666

01:18:28.740 --> 01:18:31.960 And in terms of how they look

NOTE Confidence: 0.877736327666666

01:18:31.960 --> 01:18:33.448 in terms of geography,

NOTE Confidence: 0.877736327666666

01:18:33.448 --> 01:18:36.247 there they were all large studies except

NOTE Confidence: 0.877736327666666

01:18:36.247 --> 01:18:38.737 the keynote 590 adenocarcinoma subset.

NOTE Confidence: 0.877736327666666

01:18:38.740 --> 01:18:40.434 Most of them were focused on GE,

NOTE Confidence: 0.877736327666666

01:18:40.440 --> 01:18:41.608 J gastric,

NOTE Confidence: 0.877736327666666

01:18:41.608 --> 01:18:43.944 but Checkmate 649 fortunately

NOTE Confidence: 0.877736327666666

01:18:43.944 --> 01:18:46.280 included Asopus and keynote.

NOTE Confidence: 0.877736327666666

01:18:46.280 --> 01:18:49.799 590 excluded gastric.

NOTE Confidence: 0.877736327666666

01:18:49.800 --> 01:18:52.890 And they used again different chemo

NOTE Confidence: 0.877736327666666

01:18:52.890 --> 01:18:55.940 backbones and different PD1 inhibitors,

NOTE Confidence: 0.877736327666666

01:18:55.940 --> 01:18:57.962 and for the positive studies the

NOTE Confidence: 0.877736327666666

01:18:57.962 --> 01:19:00.338 hazard ratios in the overall patient

NOTE Confidence: 0.877736327666666

01:19:00.338 --> 01:19:02.888 population were quite similar and

NOTE Confidence: 0.877736327666666

01:19:02.888 --> 01:19:06.078 hazard ratios are not significant

NOTE Confidence: 0.877736327666666

01:19:06.078 --> 01:19:10.259 in keynote 62 and Attraction 4.

NOTE Confidence: 0.877736327666666

01:19:10.260 --> 01:19:11.562 And these are the Kaplan Meier

NOTE Confidence: 0.877736327666666

01:19:11.562 --> 01:19:13.230 curves for the two negative studies.

NOTE Confidence: 0.877736327666666

01:19:13.230 --> 01:19:16.998 They really, really were negative studies.

NOTE Confidence: 0.877736327666666

01:19:17.000 --> 01:19:18.365 When you look at the hazard ratio

NOTE Confidence: 0.877736327666666

01:19:18.365 --> 01:19:19.560 you you ask the question.

NOTE Confidence: 0.877736327666666

01:19:19.560 --> 01:19:19.825 Well,

NOTE Confidence: 0.877736327666666

01:19:19.825 --> 01:19:21.150 the negative studies did the

NOTE Confidence: 0.877736327666666

01:19:21.150 --> 01:19:22.770 PDL 1 high subset benefited?

NOTE Confidence: 0.877736327666666

01:19:22.770 --> 01:19:28.638 That did not seem to be the case and in the.

NOTE Confidence: 0.877736327666666

01:19:28.640 --> 01:19:32.560 Other studies we don't really have good

NOTE Confidence: 0.877736327666666

01:19:32.560 --> 01:19:35.220 data in the PDL negative or low subset,

NOTE Confidence: 0.877736327666666

01:19:35.220 --> 01:19:37.740 so it's hard to draw a lot of conclusions

NOTE Confidence: 0.877736327666666

01:19:37.740 --> 01:19:41.110 other than from Checkmate 649 about

NOTE Confidence: 0.877736327666666

01:19:41.110 --> 01:19:44.890 PDL quantification and benefit.

NOTE Confidence: 0.877736327666666

01:19:44.890 --> 01:19:47.538 Now it's a different story in patients who

NOTE Confidence: 0.877736327666666

01:19:47.538 --> 01:19:49.887 are mismatched pair definition or MSI high,

NOTE Confidence: 0.877736327666666

01:19:49.890 --> 01:19:52.203 and I think this is a really interesting and

NOTE Confidence: 0.877736327666666

01:19:52.203 --> 01:19:54.087 important story that deserves highlighting.

NOTE Confidence: 0.877736327666666

01:19:54.090 --> 01:19:56.512 So in in both Keynote 62 which

NOTE Confidence: 0.877736327666666

01:19:56.512 --> 01:19:58.524 looked at Pembroke chemo versus

NOTE Confidence: 0.877736327666666

01:19:58.524 --> 01:20:01.251 chemo and Checkmate 649 Nevo chemo.

NOTE Confidence: 0.877736327666666

01:20:01.251 --> 01:20:03.993 They looked at retrospectively at the

NOTE Confidence: 0.877736327666666

01:20:03.993 --> 01:20:07.545 small numbers of patients that were MSI high.

NOTE Confidence: 0.877736327666666

01:20:07.550 --> 01:20:08.980 These numbers are small but

NOTE Confidence: 0.877736327666666

01:20:08.980 --> 01:20:10.124 look at these results.

NOTE Confidence: 0.877736327666666

01:20:10.130 --> 01:20:12.218 They're really dramatically.

NOTE Confidence: 0.877736327666666

01:20:12.218 --> 01:20:15.002 Favorable and dramatically similar

NOTE Confidence: 0.877736327666666

01:20:15.002 --> 01:20:18.319 with almost identical hazard ratios,

NOTE Confidence: 0.877736327666666

01:20:18.320 --> 01:20:20.770 and so I think there's no question

NOTE Confidence: 0.877736327666666

01:20:20.770 --> 01:20:22.233 that chemoimmunotherapy should be

NOTE Confidence: 0.877736327666666

01:20:22.233 --> 01:20:24.333 given to all patients without other

NOTE Confidence: 0.877736327666666

01:20:24.333 --> 01:20:26.310 contraindications who have mismatch repair,

NOTE Confidence: 0.877736327666666

01:20:26.310 --> 01:20:27.674 deficient MSI high tumors.

NOTE Confidence: 0.877736327666666

01:20:27.674 --> 01:20:29.379 This is a huge story,

NOTE Confidence: 0.877736327666666

01:20:29.380 --> 01:20:29.836 I think.

NOTE Confidence: 0.877736327666666

01:20:29.836 --> 01:20:30.520 In my opinion,

NOTE Confidence: 0.877736327666666

01:20:30.520 --> 01:20:33.058 New England Journal of Medicine Worthy,

NOTE Confidence: 0.901667813333333

01:20:33.060 --> 01:20:36.120 but I think definitely worth highlighting.

NOTE Confidence: 0.901667813333333

01:20:36.120 --> 01:20:37.885 So can we explain the

NOTE Confidence: 0.901667813333333

01:20:37.885 --> 01:20:39.297 discrepancies in these studies?

NOTE Confidence: 0.901667813333333

01:20:39.300 --> 01:20:41.755 I would say I'm challenged

NOTE Confidence: 0.901667813333333

01:20:41.755 --> 01:20:43.228 to really rationally.

NOTE Confidence: 0.901667813333333

01:20:43.230 --> 01:20:45.960 Explain the discrepancies.

NOTE Confidence: 0.901667813333333

01:20:45.960 --> 01:20:48.456 We can talk about biology because

NOTE Confidence: 0.901667813333333

01:20:48.456 --> 01:20:50.120 gastroesophageal adenocarcinoma from a

NOTE Confidence: 0.901667813333333

01:20:50.179 --> 01:20:52.779 biological perspective is very heterogeneous.

NOTE Confidence: 0.901667813333333

01:20:52.780 --> 01:20:54.492 We've identified the four

NOTE Confidence: 0.901667813333333

01:20:54.492 --> 01:20:55.776 major molecular phenotypes,

NOTE Confidence: 0.901667813333333

01:20:55.780 --> 01:20:58.052 but that's just I think the tip of

NOTE Confidence: 0.901667813333333

01:20:58.052 --> 01:20:59.680 the iceberg, and we know, of course,

NOTE Confidence: 0.901667813333333

01:20:59.680 --> 01:21:01.878 that MSI high and B positives will

NOTE Confidence: 0.901667813333333

01:21:01.878 --> 01:21:04.120 be the ones likely to respond.

NOTE Confidence: 0.901667813333333

01:21:04.120 --> 01:21:07.376 A lot of challenges in the trial design.

NOTE Confidence: 0.901667813333333

01:21:07.380 --> 01:21:09.516 You know, excluding esophageal

NOTE Confidence: 0.901667813333333

01:21:09.516 --> 01:21:11.118 adenocarcinoma or excluding,

NOTE Confidence: 0.901667813333333

01:21:11.120 --> 01:21:13.224 gastric, different chemo backbones.

NOTE Confidence: 0.901667813333333

01:21:13.224 --> 01:21:15.328 And then of course,

NOTE Confidence: 0.901667813333333

01:21:15.330 --> 01:21:17.106 the impact of post study treatment.

NOTE Confidence: 0.901667813333333

01:21:17.110 --> 01:21:20.253 I think the explanation for the very

NOTE Confidence: 0.901667813333333

01:21:20.253 --> 01:21:22.315 negative attraction for study was

NOTE Confidence: 0.901667813333333

01:21:22.315 --> 01:21:23.905 that that many of those patients

NOTE Confidence: 0.901667813333333

01:21:23.905 --> 01:21:25.691 did get PD1 inhibitors in the

NOTE Confidence: 0.901667813333333

01:21:25.691 --> 01:21:27.563 second and third line and beyond.

NOTE Confidence: 0.83674636375

01:21:30.210 --> 01:21:32.892 Now, how about her two positive

NOTE Confidence: 0.83674636375

01:21:32.892 --> 01:21:33.786 gastroesophageal cancer?

NOTE Confidence: 0.83674636375

01:21:33.790 --> 01:21:35.834 All those studies that we just reviewed

NOTE Confidence: 0.83674636375

01:21:35.834 --> 01:21:37.709 excluded her two positive patients,

NOTE Confidence: 0.83674636375

01:21:37.710 --> 01:21:39.396 so we now have pretty exciting

NOTE Confidence: 0.83674636375

01:21:39.396 --> 01:21:41.190 data in this patient population,

NOTE Confidence: 0.83674636375

01:21:41.190 --> 01:21:43.577 with the inclusion of a PD1 inhibitor

NOTE Confidence: 0.83674636375

01:21:43.577 --> 01:21:45.360 with chemotherapy and trastuzumab.

NOTE Confidence: 0.83674636375

01:21:45.360 --> 01:21:47.946 This is the keynote 811 study.

NOTE Confidence: 0.83674636375

01:21:47.950 --> 01:21:50.449 Also got a lot of publicity appropriately,

NOTE Confidence: 0.83674636375

01:21:50.450 --> 01:21:53.410 so simple design, trastuzumab,

NOTE Confidence: 0.83674636375

01:21:53.410 --> 01:21:55.630 chemo versus trastuzumab,

NOTE Confidence: 0.83674636375

01:21:55.630 --> 01:21:59.389 chemo and Pembroke, and on what we.

NOTE Confidence: 0.83674636375

01:21:59.390 --> 01:22:01.665 See here are the response data and

NOTE Confidence: 0.83674636375

01:22:01.665 --> 01:22:04.409 you can see very high response rate.

NOTE Confidence: 0.83674636375

01:22:04.410 --> 01:22:07.375 Very deep responses with Pembroke

NOTE Confidence: 0.83674636375

01:22:07.375 --> 01:22:09.806 added to chemo and Herceptin.

NOTE Confidence: 0.83674636375

01:22:09.806 --> 01:22:11.638 Higher response rate and

NOTE Confidence: 0.83674636375

01:22:11.638 --> 01:22:13.470 a complete response rate.

NOTE Confidence: 0.83674636375

01:22:13.470 --> 01:22:17.776 That's very impressive at 11% versus 3%.

NOTE Confidence: 0.83674636375

01:22:17.776 --> 01:22:20.575 This study led to the provisional

NOTE Confidence: 0.83674636375

01:22:20.575 --> 01:22:21.610 approval of Pembroke,

NOTE Confidence: 0.83674636375

01:22:21.610 --> 01:22:23.566 added to trastuzumab and

NOTE Confidence: 0.83674636375

01:22:23.566 --> 01:22:26.011 chemo and her two positive

NOTE Confidence: 0.83674636375

01:22:26.011 --> 01:22:27.730 gastroesophageal adenocarcinomas.

NOTE Confidence: 0.83674636375

01:22:27.730 --> 01:22:29.300 So obviously this is provisional.

NOTE Confidence: 0.83674636375

01:22:29.300 --> 01:22:30.684 We are waiting for.

NOTE Confidence: 0.83674636375

01:22:30.684 --> 01:22:32.760 PFS data and overall survival data.

NOTE Confidence: 0.83674636375

01:22:32.760 --> 01:22:34.810 To see what the final impact is going to be.

NOTE Confidence: 0.786749505

01:22:37.440 --> 01:22:41.654 So we have three FDA approvals now

NOTE Confidence: 0.786749505

01:22:41.654 --> 01:22:43.460 and gastroesophageal adenocarcinomas.

NOTE Confidence: 0.786749505

01:22:43.460 --> 01:22:45.710 So Pembroke from Keynote 590,

NOTE Confidence: 0.786749505

01:22:45.710 --> 01:22:48.416 which did not include gastric cancers.

NOTE Confidence: 0.786749505

01:22:48.420 --> 01:22:52.108 Neevo based on Checkmate 649 and

NOTE Confidence: 0.786749505

01:22:52.108 --> 01:22:54.060 Pembroke added to trastuzumab.

NOTE Confidence: 0.786749505

01:22:54.060 --> 01:22:57.000 Chemo based on keynote 811.

NOTE Confidence: 0.786749505

01:22:57.000 --> 01:22:58.812 All of these studies.

NOTE Confidence: 0.786749505

01:22:58.812 --> 01:23:01.077 All of these approvals by

NOTE Confidence: 0.786749505

01:23:01.077 --> 01:23:03.670 the FDA are PDL 1 agnostic.

NOTE Confidence: 0.786749505

01:23:03.670 --> 01:23:05.198 Which is, I think,

NOTE Confidence: 0.786749505

01:23:05.198 --> 01:23:07.490 interesting and and can be debated.

NOTE Confidence: 0.786749505

01:23:07.490 --> 01:23:11.882 So my take away message in the last few

NOTE Confidence: 0.786749505

01:23:11.882 --> 01:23:15.120 minutes is that adding a PD1 inhibitor.

NOTE Confidence: 0.786749505

01:23:15.120 --> 01:23:17.432 To chemotherapy and adenocarcinomas

NOTE Confidence: 0.786749505

01:23:17.432 --> 01:23:20.900 improves overall survival in most studies,

NOTE Confidence: 0.786749505

01:23:20.900 --> 01:23:22.679 but not all.

NOTE Confidence: 0.786749505

01:23:22.680 --> 01:23:23.990 That benefit has been seen

NOTE Confidence: 0.786749505

01:23:23.990 --> 01:23:25.038 with different PD1 inhibitors.

NOTE Confidence: 0.786749505

01:23:25.040 --> 01:23:26.460 Chemo doublets and different PD,

NOTE Confidence: 0.786749505

01:23:26.460 --> 01:23:27.936 one cut offs.

NOTE Confidence: 0.786749505

01:23:27.936 --> 01:23:32.390 I think we can conclude safely that efficacy.

NOTE Confidence: 0.786749505

01:23:32.390 --> 01:23:36.350 Diminishes with decreasing PD L1 expression.

NOTE Confidence: 0.786749505

01:23:36.350 --> 01:23:38.966 And so, how do we use this information?

NOTE Confidence: 0.786749505

01:23:38.970 --> 01:23:41.987 So I think that most patients with

NOTE Confidence: 0.786749505

01:23:41.987 --> 01:23:44.048 adenocarcinoma should be offered

NOTE Confidence: 0.786749505

01:23:44.048 --> 01:23:46.130 first line chemoimmunotherapy.

NOTE Confidence: 0.786749505

01:23:46.130 --> 01:23:49.161 But I I recognize that we are

NOTE Confidence: 0.786749505

01:23:49.161 --> 01:23:51.362 conflicted about what to do

NOTE Confidence: 0.786749505

01:23:51.362 --> 01:23:54.211 with patients who have no PD L1

NOTE Confidence: 0.786749505

01:23:54.211 --> 01:23:56.746 expression or low PD L1 expression.

NOTE Confidence: 0.786749505

01:23:56.750 --> 01:23:58.894 So just for a few minutes for the

NOTE Confidence: 0.786749505

01:23:58.894 --> 01:24:00.996 last few minutes I'm going to pivot

NOTE Confidence: 0.786749505

01:24:00.996 --> 01:24:03.050 to the data in guest Russophile

NOTE Confidence: 0.786749505

01:24:03.050 --> 01:24:06.042 deal cancers for first line

NOTE Confidence: 0.786749505

01:24:06.042 --> 01:24:08.010 immunotherapy without chemotherapy.

NOTE Confidence: 0.786749505

01:24:08.010 --> 01:24:09.902 So chemotherapy free immunotherapy

NOTE Confidence: 0.786749505

01:24:09.902 --> 01:24:12.740 and there are three randomized phase

NOTE Confidence: 0.786749505

01:24:12.815 --> 01:24:15.335 three trials that have addressed this

NOTE Confidence: 0.786749505

01:24:15.335 --> 01:24:18.045 question with the control arm of

NOTE Confidence: 0.786749505

01:24:18.045 --> 01:24:20.445 chemotherapy against an experimental arm

NOTE Confidence: 0.786749505

01:24:20.445 --> 01:24:22.590 of immunotherapy without chemotherapy.

NOTE Confidence: 0.786749505

01:24:22.590 --> 01:24:26.516 So we've heard about Checkmate 648.

NOTE Confidence: 0.786749505

01:24:26.516 --> 01:24:28.646 Squamous cell carcinoma that had

NOTE Confidence: 0.786749505

01:24:28.646 --> 01:24:31.099 the ippy Nevo chemo free arm.

NOTE Confidence: 0.786749505

01:24:31.100 --> 01:24:33.746 We'll discuss in a minute led to

NOTE Confidence: 0.786749505

01:24:33.746 --> 01:24:35.994 FDA approval just this past month

NOTE Confidence: 0.786749505

01:24:35.994 --> 01:24:39.150 for it being EVO in squamous cell

NOTE Confidence: 0.786749505

01:24:39.150 --> 01:24:40.920 carcinomas for adenocarcinomas.

NOTE Confidence: 0.786749505

01:24:40.920 --> 01:24:44.483 We have Checkmate 62 which looked at

NOTE Confidence: 0.786749505

01:24:44.483 --> 01:24:47.761 chemo versus Pembroke and Checkmate 649

NOTE Confidence: 0.786749505

01:24:47.761 --> 01:24:50.887 again which looked at a chemotherapy

NOTE Confidence: 0.786749505

01:24:50.887 --> 01:24:52.940 free dual immunotherapy Nevo.

NOTE Confidence: 0.786749505

01:24:52.940 --> 01:24:55.352 These studies in adenocarcinoma

NOTE Confidence: 0.786749505

01:24:55.352 --> 01:24:56.558 were considered.

NOTE Confidence: 0.786749505

01:24:56.560 --> 01:24:58.618 Negative studies and we do not

NOTE Confidence: 0.786749505

01:24:58.618 --> 01:24:59.647 have FDA approval.

NOTE Confidence: 0.786749505

01:24:59.650 --> 01:25:02.415 And then again I'm going to highlight

NOTE Confidence: 0.786749505

01:25:02.415 --> 01:25:05.709 the data in MSI high adenocarcinomas.

NOTE Confidence: 0.786749505

01:25:05.710 --> 01:25:08.734 So we've seen the Checkmate 648 and

NOTE Confidence: 0.786749505

01:25:08.734 --> 01:25:10.994 649 designs very similar except

NOTE Confidence: 0.786749505

01:25:10.994 --> 01:25:13.688 for the dosing of Yippee Nevo,

NOTE Confidence: 0.786749505

01:25:13.690 --> 01:25:16.450 3 megs per kig in adenocarcinoma,

NOTE Confidence: 0.786749505

01:25:16.450 --> 01:25:19.558 one Mig per kig ippy in squamous

NOTE Confidence: 0.786749505

01:25:19.558 --> 01:25:22.006 cell carcinomas, and side by side.

NOTE Confidence: 0.786749505

01:25:22.006 --> 01:25:24.941 Here are the Captain Meyer plots for

NOTE Confidence: 0.786749505

01:25:24.941 --> 01:25:28.188 overall survival and in their primary

NOTE Confidence: 0.786749505

01:25:28.188 --> 01:25:32.251 endpoint of PD L1 positive tumors and

NOTE Confidence: 0.786749505

01:25:32.251 --> 01:25:36.109 then down below all randomized patients.

NOTE Confidence: 0.786749505

01:25:36.110 --> 01:25:37.838 And so, in adenocarcinomas,

NOTE Confidence: 0.786749505

01:25:37.838 --> 01:25:40.960 this was viewed as a negative study,

NOTE Confidence: 0.786749505

01:25:40.960 --> 01:25:41.806 median survival,

NOTE Confidence: 0.786749505

01:25:41.806 --> 01:25:42.652 the same.

NOTE Confidence: 0.786749505

01:25:42.652 --> 01:25:45.190 Although you can see the curves

NOTE Confidence: 0.786749505

01:25:45.270 --> 01:25:47.676 do separate at later time points,

NOTE Confidence: 0.786749505

01:25:47.680 --> 01:25:50.040 I think which is interesting.

NOTE Confidence: 0.786749505

01:25:50.040 --> 01:25:51.925 The response rate was notably

NOTE Confidence: 0.786749505

01:25:51.925 --> 01:25:52.679 substantially lower.

NOTE Confidence: 0.786749505

01:25:52.680 --> 01:25:55.314 Would it be neevo different story

NOTE Confidence: 0.786749505

01:25:55.314 --> 01:25:57.070 and squamous cell carcinoma?

NOTE Confidence: 0.786749505

01:25:57.070 --> 01:26:00.178 This is a positive study with a

NOTE Confidence: 0.786749505

01:26:00.178 --> 01:26:02.025 significant improvement in overall

NOTE Confidence: 0.786749505

01:26:02.025 --> 01:26:04.205 survival in PDL and positive

NOTE Confidence: 0.786749505

01:26:04.205 --> 01:26:07.179 patients and also in all randomized.

NOTE Confidence: 0.786749505

01:26:07.180 --> 01:26:10.738 Patients so no approval for apnea

NOTE Confidence: 0.786749505

01:26:10.738 --> 01:26:11.924 and adenocarcinoma,

NOTE Confidence: 0.786749505

01:26:11.930 --> 01:26:13.682 but it is approved in squamous

NOTE Confidence: 0.786749505

01:26:13.682 --> 01:26:14.266 cell carcinomas.

NOTE Confidence: 0.786749505

01:26:14.270 --> 01:26:16.944 Now what are the red flags here

NOTE Confidence: 0.786749505

01:26:16.950 --> 01:26:18.358 for squamous cell carcinoma?

NOTE Confidence: 0.786749505

01:26:18.358 --> 01:26:21.410 So a big red flag is this crossing

NOTE Confidence: 0.786749505

01:26:21.410 --> 01:26:24.166 of the curve survival curves in the

NOTE Confidence: 0.786749505

01:26:24.166 --> 01:26:26.550 first six months so a higher rate of

NOTE Confidence: 0.860198533888889

01:26:26.622 --> 01:26:29.527 death and patients getting immunotherapy

NOTE Confidence: 0.860198533888889

01:26:29.527 --> 01:26:31.270 alone versus chemotherapy.

NOTE Confidence: 0.860198533888889

01:26:31.270 --> 01:26:32.758 And we don't know the full

NOTE Confidence: 0.860198533888889

01:26:32.758 --> 01:26:33.502 explanation for that.

NOTE Confidence: 0.860198533888889

01:26:33.510 --> 01:26:35.310 We can come up with some

NOTE Confidence: 0.860198533888889

01:26:35.310 --> 01:26:35.910 plausible explanations,

NOTE Confidence: 0.860198533888889

01:26:35.910 --> 01:26:37.358 but we're not certain.

NOTE Confidence: 0.860198533888889

01:26:37.358 --> 01:26:39.530 I think we'll get more information

NOTE Confidence: 0.860198533888889

01:26:39.602 --> 01:26:41.317 from this study about that.

NOTE Confidence: 0.860198533888889

01:26:41.320 --> 01:26:43.735 If you compare immunotherapy alone

NOTE Confidence: 0.860198533888889

01:26:43.735 --> 01:26:46.018 versus chemotherapy immunotherapy in 648,

NOTE Confidence: 0.860198533888889

01:26:46.018 --> 01:26:48.454 which is not fair by our statistically,

NOTE Confidence: 0.860198533888889

01:26:48.460 --> 01:26:50.770 it does look like the

NOTE Confidence: 0.860198533888889

01:26:50.770 --> 01:26:52.618 survival curves are similar,

NOTE Confidence: 0.860198533888889

01:26:52.620 --> 01:26:55.399 but the duration of response and the

NOTE Confidence: 0.860198533888889

01:26:55.399 --> 01:26:57.540 responders does appear to be longer.

NOTE Confidence: 0.860198533888889

01:26:57.540 --> 01:26:59.622 With dual immunotherapy

NOTE Confidence: 0.860198533888889

01:26:59.622 --> 01:27:01.010 versus chemoimmunotherapy.

NOTE Confidence: 0.860198533888889

01:27:01.010 --> 01:27:02.907 When you look at immunotherapy versus chemo,

NOTE Confidence: 0.860198533888889

01:27:02.910 --> 01:27:05.484 you have the very predictable expected

NOTE Confidence: 0.860198533888889

01:27:05.484 --> 01:27:07.450 differences in treatment related AE.

NOTE Confidence: 0.860198533888889

01:27:07.450 --> 01:27:09.105 But there were fewer treatment

NOTE Confidence: 0.860198533888889

01:27:09.105 --> 01:27:11.616 related AE's leading to treatment

NOTE Confidence: 0.860198533888889

01:27:11.616 --> 01:27:13.850 discontinuation with dual immunotherapy.

NOTE Confidence: 0.860198533888889

01:27:13.850 --> 01:27:16.850 So this is really exciting.

NOTE Confidence: 0.860198533888889

01:27:16.850 --> 01:27:19.506 This has led to the first FDA approval

NOTE Confidence: 0.860198533888889

01:27:19.506 --> 01:27:21.394 of chemotherapy free treatment for

NOTE Confidence: 0.860198533888889

01:27:21.394 --> 01:27:23.319 squamous cell of the esophagus,

NOTE Confidence: 0.860198533888889

01:27:23.320 --> 01:27:24.976 and for those that like the

NOTE Confidence: 0.860198533888889

01:27:24.976 --> 01:27:26.310 forest plots here we go.

NOTE Confidence: 0.860198533888889

01:27:26.310 --> 01:27:30.966 Most subsets benefited, but again in the TPS.

NOTE Confidence: 0.860198533888889

01:27:30.970 --> 01:27:36.160 Less than one, the hazard ratio was .96.

NOTE Confidence: 0.860198533888889

01:27:36.160 --> 01:27:38.065 Now in adenocarcinomas we have

NOTE Confidence: 0.860198533888889

01:27:38.065 --> 01:27:40.363 another study and this was did

NOTE Confidence: 0.860198533888889

01:27:40.363 --> 01:27:41.978 not lead to FDA approval.

NOTE Confidence: 0.860198533888889

01:27:41.980 --> 01:27:44.640 That was Pembroke versus chemo.

NOTE Confidence: 0.860198533888889

01:27:44.640 --> 01:27:47.175 Pembroke was non inferior to

NOTE Confidence: 0.860198533888889

01:27:47.175 --> 01:27:50.547 chemo but again you see those

NOTE Confidence: 0.860198533888889

01:27:50.547 --> 01:27:52.432 troubling survival curves crossing.

NOTE Confidence: 0.860198533888889

01:27:52.432 --> 01:27:55.120 So with the higher rate of death

NOTE Confidence: 0.860198533888889

01:27:55.192 --> 01:27:57.460 early on and so right now there's

NOTE Confidence: 0.860198533888889

01:27:57.460 --> 01:27:59.171 no approval for immunotherapy

NOTE Confidence: 0.860198533888889

01:27:59.171 --> 01:28:01.160 alone and adenocarcinomas.

NOTE Confidence: 0.860198533888889

01:28:01.160 --> 01:28:03.968 We have to talk about the MSI high patients

NOTE Confidence: 0.860198533888889

01:28:03.968 --> 01:28:06.287 though with adenocarcinomas and again.

NOTE Confidence: 0.860198533888889

01:28:06.290 --> 01:28:07.994 We have keynote 62 where they

NOTE Confidence: 0.860198533888889

01:28:07.994 --> 01:28:10.091 went back and looked at this and

NOTE Confidence: 0.860198533888889

01:28:10.091 --> 01:28:14.238 Checkmate 649 again small numbers.

NOTE Confidence: 0.860198533888889

01:28:14.240 --> 01:28:17.670 But really impressive survival curves

NOTE Confidence: 0.860198533888889

01:28:17.670 --> 01:28:20.640 and very similar outcomes with really

NOTE Confidence: 0.860198533888889

01:28:20.640 --> 01:28:22.620 virtually identical hazard ratios.

NOTE Confidence: 0.860198533888889

01:28:22.620 --> 01:28:23.033 Again,

NOTE Confidence: 0.860198533888889

01:28:23.033 --> 01:28:26.337 I think this is a a huge story,

NOTE Confidence: 0.860198533888889

01:28:26.340 --> 01:28:28.972 and so it it begs the question

NOTE Confidence: 0.860198533888889

01:28:28.972 --> 01:28:30.100 could could we?

NOTE Confidence: 0.860198533888889

01:28:30.100 --> 01:28:33.020 Should we consider immunotherapy loan

NOTE Confidence: 0.860198533888889

01:28:33.020 --> 01:28:35.211 as first line treatment in patients with

NOTE Confidence: 0.860198533888889

01:28:35.211 --> 01:28:37.520 MSI high guest Raphael adenocarcinoma?

NOTE Confidence: 0.860198533888889

01:28:37.520 --> 01:28:39.740 So a story to be continued.

NOTE Confidence: 0.860198533888889

01:28:39.740 --> 01:28:41.228 And also I think of course

NOTE Confidence: 0.860198533888889

01:28:41.228 --> 01:28:42.540 begs the question you know,

NOTE Confidence: 0.860198533888889

01:28:42.540 --> 01:28:44.700 are we going to be curing these patients?

NOTE Confidence: 0.860198533888889

01:28:44.700 --> 01:28:47.290 With MSI high guest reseal endocarp sinoma,

NOTE Confidence: 0.860198533888889

01:28:47.290 --> 01:28:49.090 either with immunotherapy

NOTE Confidence: 0.860198533888889

01:28:49.090 --> 01:28:50.890 alone or chemoimmunotherapy,

NOTE Confidence: 0.860198533888889

01:28:50.890 --> 01:28:53.402 so to to conclude to the

NOTE Confidence: 0.860198533888889

01:28:53.402 --> 01:28:54.706 base to the question.

NOTE Confidence: 0.860198533888889

01:28:54.710 --> 01:28:57.328 Chemoimmunotherapy for all or not so fast.

NOTE Confidence: 0.860198533888889

01:28:57.330 --> 01:29:00.004 So I think here are the considerations

NOTE Confidence: 0.860198533888889

01:29:00.004 --> 01:29:01.849 squamous versus adeno it matters

NOTE Confidence: 0.860198533888889

01:29:01.850 --> 01:29:03.450 PDL one matters I think,

NOTE Confidence: 0.860198533888889

01:29:03.450 --> 01:29:04.608 especially in adenocarcinoma,

NOTE Confidence: 0.860198533888889

01:29:04.608 --> 01:29:07.310 but as we heard so brilliantly from

NOTE Confidence: 0.860198533888889

01:29:07.373 --> 01:29:09.746 Marie it is such an imperfect biomarker.

NOTE Confidence: 0.860198533888889

01:29:09.750 --> 01:29:13.329 Is it good enough to guide us to

NOTE Confidence: 0.860198533888889

01:29:13.329 --> 01:29:15.543 select patients in whom we will

NOTE Confidence: 0.860198533888889

01:29:15.543 --> 01:29:16.650 not give immunotherapy?

NOTE Confidence: 0.860198533888889

01:29:16.650 --> 01:29:18.990 This is a really troubling question

NOTE Confidence: 0.860198533888889

01:29:18.990 --> 01:29:21.552 for us as clinicians in terms of

NOTE Confidence: 0.860198533888889

01:29:21.552 --> 01:29:22.888 anatomic site for adenocarcinomas.

NOTE Confidence: 0.860198533888889

01:29:22.890 --> 01:29:25.290 I don't think we have any data yet

NOTE Confidence: 0.860198533888889

01:29:25.290 --> 01:29:27.002 that esophagus versus GE junction

NOTE Confidence: 0.860198533888889

01:29:27.002 --> 01:29:29.445 versus Gastro is gastric is the issue.

NOTE Confidence: 0.860198533888889

01:29:29.450 --> 01:29:31.460 I think MSI mismatch repair

NOTE Confidence: 0.860198533888889

01:29:31.460 --> 01:29:33.068 deficiency Trump's PDL one.

NOTE Confidence: 0.860198533888889

01:29:33.070 --> 01:29:35.600 All those patients should get

NOTE Confidence: 0.860198533888889

01:29:35.600 --> 01:29:37.118 chemoimmunotherapy and similarly

NOTE Confidence: 0.860198533888889

01:29:37.118 --> 01:29:39.947 for her too regardless of PD L1.

NOTE Confidence: 0.860198533888889

01:29:39.950 --> 01:29:42.190 Those patients now inclusion of

NOTE Confidence: 0.860198533888889

01:29:42.190 --> 01:29:44.430 Pembroke I think is reasonable.

NOTE Confidence: 0.860198533888889

01:29:44.430 --> 01:29:47.330 We're waiting for survival data.

NOTE Confidence: 0.860198533888889

01:29:47.330 --> 01:29:49.780 So here are my conclusions.

NOTE Confidence: 0.860198533888889

01:29:49.780 --> 01:29:53.175 So for a sophal squamous I am

NOTE Confidence: 0.860198533888889

01:29:53.175 --> 01:29:54.630 offering chemoimmunotherapy to

NOTE Confidence: 0.75372688523125

01:29:54.711 --> 01:29:57.537 most of my patients irrespective of

NOTE Confidence: 0.75372688523125

01:29:57.540 --> 01:30:01.108 PD L1 and for the adenocarcinomas I I

NOTE Confidence: 0.75372688523125

01:30:01.108 --> 01:30:05.228 am taking a similar approach but I am

NOTE Confidence: 0.75372688523125

01:30:05.228 --> 01:30:08.359 very circumspect about what we may be,

NOTE Confidence: 0.75372688523125

01:30:08.360 --> 01:30:10.478 how, how much we're helping patients.

NOTE Confidence: 0.75372688523125

01:30:10.480 --> 01:30:14.270 If the PDL 1 score is 0 or very low.

NOTE Confidence: 0.704306465833333

01:30:16.400 --> 01:30:18.386 So again, the question should should

NOTE Confidence: 0.704306465833333

01:30:18.386 --> 01:30:21.164 we use PDL one course to exclude

NOTE Confidence: 0.704306465833333

01:30:21.164 --> 01:30:23.474 patients from frontline PD1 inhibitors?

NOTE Confidence: 0.704306465833333

01:30:23.480 --> 01:30:25.550 If if we do I think it has to be

NOTE Confidence: 0.704306465833333

01:30:25.622 --> 01:30:27.698 with circumspection and caution.

NOTE Confidence: 0.704306465833333

01:30:27.700 --> 01:30:30.955 I think particularly you know after the

NOTE Confidence: 0.704306465833333

01:30:30.955 --> 01:30:34.161 information that we heard from Marie about

NOTE Confidence: 0.704306465833333

01:30:34.161 --> 01:30:37.630 some of the challenges with this biomarker.

NOTE Confidence: 0.704306465833333

01:30:37.630 --> 01:30:40.190 Chemotherapy free immunotherapy, for whom?

NOTE Confidence: 0.704306465833333

01:30:40.190 --> 01:30:41.282 And in what settings?

NOTE Confidence: 0.704306465833333

01:30:41.282 --> 01:30:42.647 So this is very exciting.

NOTE Confidence: 0.704306465833333

01:30:42.650 --> 01:30:45.362 It is approved it be neevo and squamous

NOTE Confidence: 0.704306465833333

01:30:45.362 --> 01:30:47.549 cell carcinoma irrespective of PD one.

NOTE Confidence: 0.704306465833333

01:30:47.550 --> 01:30:49.494 But again that cautionary note we

NOTE Confidence: 0.704306465833333

01:30:49.494 --> 01:30:51.132 are seeing increased deaths compared

NOTE Confidence: 0.704306465833333

01:30:51.132 --> 01:30:53.085 to chemo in the first six months.

NOTE Confidence: 0.704306465833333

01:30:53.090 --> 01:30:55.110 So that gives one pause.

NOTE Confidence: 0.704306465833333

01:30:55.110 --> 01:30:56.682 And so I think careful patient

NOTE Confidence: 0.704306465833333

01:30:56.682 --> 01:30:57.730 selection is the key.

NOTE Confidence: 0.704306465833333

01:30:57.730 --> 01:30:59.613 But I don't think we know yet

NOTE Confidence: 0.704306465833333

01:30:59.613 --> 01:31:01.050 how to select patients.

NOTE Confidence: 0.704306465833333

01:31:01.050 --> 01:31:02.718 Is it PD one or PDL?

NOTE Confidence: 0.704306465833333

01:31:02.720 --> 01:31:03.378 One score?

NOTE Confidence: 0.704306465833333

01:31:03.378 --> 01:31:06.530 Is it the tumor burden so you know again,

NOTE Confidence: 0.704306465833333

01:31:06.530 --> 01:31:07.900 I think. To be continued.

NOTE Confidence: 0.704306465833333

01:31:07.900 --> 01:31:10.060 This is an interesting story.

NOTE Confidence: 0.704306465833333

01:31:10.060 --> 01:31:11.740 And then for gastric adenocarcinomas,

NOTE Confidence: 0.704306465833333

01:31:11.740 --> 01:31:15.170 we're not there yet for immunotherapy alone,

NOTE Confidence: 0.704306465833333

01:31:15.170 --> 01:31:16.406 as the initial treatment.

NOTE Confidence: 0.704306465833333

01:31:16.406 --> 01:31:20.414 I think even in MSI high patients, I think

NOTE Confidence: 0.704306465833333

01:31:20.414 --> 01:31:24.249 it's still would be chemoimmunotherapy.

NOTE Confidence: 0.704306465833333

01:31:24.250 --> 01:31:25.666 So where we go from here?

NOTE Confidence: 0.704306465833333

01:31:25.670 --> 01:31:29.247 I think the questions are are obvious.

NOTE Confidence: 0.704306465833333

01:31:29.250 --> 01:31:30.990 I think adenocarcinoma we just

NOTE Confidence: 0.704306465833333

01:31:30.990 --> 01:31:33.130 we do need more better data.

NOTE Confidence: 0.704306465833333

01:31:33.130 --> 01:31:35.384 We have the keynote 859 and other

NOTE Confidence: 0.704306465833333

01:31:35.384 --> 01:31:37.064 large randomized phase three trial

NOTE Confidence: 0.704306465833333

01:31:37.064 --> 01:31:38.730 of chemo versus chemo, plus pember.

NOTE Confidence: 0.704306465833333

01:31:38.730 --> 01:31:40.430 We're going to learn a lot from that study.

NOTE Confidence: 0.704306465833333

01:31:40.430 --> 01:31:42.622 It's a huge study.

NOTE Confidence: 0.704306465833333

01:31:42.622 --> 01:31:43.170 Clearly,

NOTE Confidence: 0.704306465833333

01:31:43.170 --> 01:31:45.618 as Marie articulated we we do

NOTE Confidence: 0.704306465833333

01:31:45.618 --> 01:31:47.870 need a better biomarker period.

NOTE Confidence: 0.704306465833333

01:31:47.870 --> 01:31:50.294 Full stop writ large.

NOTE Confidence: 0.704306465833333

01:31:50.294 --> 01:31:53.324 And now the next phase.

NOTE Confidence: 0.704306465833333

01:31:53.330 --> 01:31:54.530 This is a big advance.

NOTE Confidence: 0.704306465833333

01:31:54.530 --> 01:31:55.358 Forward for us.

NOTE Confidence: 0.704306465833333

01:31:55.358 --> 01:31:58.014 I mean really huge when you look at the

NOTE Confidence: 0.704306465833333

01:31:58.014 --> 01:32:00.012 history of the treatment of metastatic

NOTE Confidence: 0.704306465833333

01:32:00.012 --> 01:32:02.180 and advanced gastroesophageal cancers.

NOTE Confidence: 0.704306465833333

01:32:02.180 --> 01:32:05.155 So now we need we want more.

NOTE Confidence: 0.704306465833333

01:32:05.160 --> 01:32:08.568 So we need more effective immunotherapy

NOTE Confidence: 0.704306465833333

01:32:08.568 --> 01:32:10.840 agents or immunotherapy combinations.

NOTE Confidence: 0.704306465833333

01:32:10.840 --> 01:32:13.072 And now we're going to be moving into

NOTE Confidence: 0.704306465833333

01:32:13.072 --> 01:32:15.014 the realm of adding immunotherapy

NOTE Confidence: 0.704306465833333

01:32:15.014 --> 01:32:16.778 to other targeted therapies.

NOTE Confidence: 0.704306465833333

01:32:16.780 --> 01:32:19.475 So some studies that were planned or

NOTE Confidence: 0.704306465833333

01:32:19.475 --> 01:32:22.198 underway have now had to be redesigned.

NOTE Confidence: 0.704306465833333

01:32:22.200 --> 01:32:24.540 In light of this data.

NOTE Confidence: 0.704306465833333

01:32:24.540 --> 01:32:26.830 Adding immunotherapy to a targeted

NOTE Confidence: 0.704306465833333

01:32:26.830 --> 01:32:28.204 therapy and chemotherapy,

NOTE Confidence: 0.704306465833333

01:32:28.210 --> 01:32:30.904 and I've highlighted 2 studies such

NOTE Confidence: 0.704306465833333

01:32:30.904 --> 01:32:33.749 studies that will be open here

NOTE Confidence: 0.704306465833333

01:32:33.749 --> 01:32:36.154 at Smilow Cancer Center shortly.

NOTE Confidence: 0.704306465833333

01:32:36.160 --> 01:32:37.072 And of course,

NOTE Confidence: 0.704306465833333

01:32:37.072 --> 01:32:38.896 now the widespread use of PD1

NOTE Confidence: 0.704306465833333

01:32:38.896 --> 01:32:40.839 inhibitors in the first line setting

NOTE Confidence: 0.704306465833333

01:32:40.839 --> 01:32:42.756 really changes the landscape in the

NOTE Confidence: 0.704306465833333

01:32:42.756 --> 01:32:44.418 second line setting and beyond in

NOTE Confidence: 0.704306465833333

01:32:44.418 --> 01:32:46.322 terms of how we design those studies

NOTE Confidence: 0.704306465833333

01:32:46.322 --> 01:32:48.276 and how we're going to be treating

NOTE Confidence: 0.704306465833333

01:32:48.276 --> 01:32:50.604 those patients so much work to be done.

NOTE Confidence: 0.704306465833333

01:32:50.610 --> 01:32:53.585 But this is an incredibly exciting era.

NOTE Confidence: 0.704306465833333

01:32:53.590 --> 01:32:54.658 For those of us.

NOTE Confidence: 0.704306465833333

01:32:54.660 --> 01:32:57.024 Who treat this these diseases

NOTE Confidence: 0.704306465833333

01:32:57.024 --> 01:32:59.832 and thank you for your attention,

NOTE Confidence: 0.704306465833333

01:32:59.840 --> 01:33:03.396 and I'm happy to take any questions

NOTE Confidence: 0.704306465833333

01:33:03.396 --> 01:33:05.460 in the chat box,

NOTE Confidence: 0.704306465833333

01:33:05.460 --> 01:33:09.400 but I know we are overtime so I'm

NOTE Confidence: 0.704306465833333

01:33:09.400 --> 01:33:12.100 happy to take questions by e-mail.

NOTE Confidence: 0.704306465833333

01:33:12.100 --> 01:33:15.924 I know Dan shared his mind as the

NOTE Confidence: 0.704306465833333

01:33:15.924 --> 01:33:17.640 typical Yale e-mail jill.lacey@yale.edu

NOTE Confidence: 0.6983145

01:33:22.030 --> 01:33:22.878 Still, I will ask

NOTE Confidence: 0.93279395

01:33:22.890 --> 01:33:26.120 a question to close. Thank

NOTE Confidence: 0.982170548

01:33:26.130 --> 01:33:27.390 you so much for that.

NOTE Confidence: 0.9483689

01:33:28.940 --> 01:33:32.630 Really. Sort of exhaustive and and

NOTE Confidence: 0.9483689

01:33:32.630 --> 01:33:34.240 deep dive into the differences

NOTE Confidence: 0.9483689

01:33:34.299 --> 01:33:36.389 between squamous and the salvageable.

NOTE Confidence: 0.9483689

01:33:36.390 --> 01:33:38.882 And it's so interesting to see about

NOTE Confidence: 0.9483689

01:33:38.882 --> 01:33:41.968 the PDL 1 scores and where they are

NOTE Confidence: 0.9483689

01:33:41.970 --> 01:33:44.420 making sense and where they may not.

NOTE Confidence: 0.9483689

01:33:44.420 --> 01:33:45.520 Might not be making sense.

NOTE Confidence: 0.894460095

01:33:46.460 --> 01:33:48.110 Are you ever in a situation

NOTE Confidence: 0.928063653333333

01:33:48.120 --> 01:33:51.023 where, Despite that, it's sort of the

NOTE Confidence: 0.928063653333333

01:33:51.023 --> 01:33:53.105 deregulated to order this the PDL?

NOTE Confidence: 0.928063653333333

01:33:53.105 --> 01:33:54.920 One stain that you might say you

NOTE Confidence: 0.928063653333333

01:33:54.920 --> 01:33:56.660 know I'm going to proceed without it?

NOTE Confidence: 0.928063653333333

01:33:56.660 --> 01:33:59.000 I'm going to do for XYZ.

NOTE Confidence: 0.928063653333333

01:33:59.000 --> 01:34:01.168 Reason is that is that ever a part

NOTE Confidence: 0.928063653333333

01:34:01.170 --> 01:34:03.228 of the conversation at this point.

NOTE Confidence: 0.92267488

01:34:05.600 --> 01:34:07.744 Yeah, so you're getting at the heart of

NOTE Confidence: 0.92267488

01:34:07.744 --> 01:34:14.200 what we struggle with in the clinic. I.

NOTE Confidence: 0.92267488

01:34:14.200 --> 01:34:17.280 My my bias is to to include immunotherapy

NOTE Confidence: 0.92267488

01:34:17.280 --> 01:34:21.042 as I I concluded in in the slides for

NOTE Confidence: 0.92267488

01:34:21.042 --> 01:34:23.290 most patients with gastroesophageal

NOTE Confidence: 0.92267488

01:34:23.290 --> 01:34:25.538 cancers with metastatic disease.

NOTE Confidence: 0.92267488

01:34:25.540 --> 01:34:27.997 Not that I know that it's benefiting

NOTE Confidence: 0.92267488

01:34:27.997 --> 01:34:29.331 everybody, because I certainly

NOTE Confidence: 0.92267488

01:34:29.331 --> 01:34:31.293 know that it is absolutely not,

NOTE Confidence: 0.92267488

01:34:31.300 --> 01:34:35.656 but I just don't have confidence that we are.

NOTE Confidence: 0.92267488

01:34:35.660 --> 01:34:37.208 Able to sort out those patients

NOTE Confidence: 0.92267488

01:34:37.208 --> 01:34:38.700 that are getting no benefit,

NOTE Confidence: 0.92267488

01:34:38.700 --> 01:34:41.598 so this is not like a K rest mutation

NOTE Confidence: 0.92267488

01:34:41.598 --> 01:34:44.124 in colorectal cancer that's very

NOTE Confidence: 0.92267488

01:34:44.124 --> 01:34:46.356 black and white and very clear.

NOTE Confidence: 0.92267488

01:34:46.360 --> 01:34:49.035 There's not benefit to adding

NOTE Confidence: 0.92267488

01:34:49.035 --> 01:34:50.640 cetuximab or panitumumab.

NOTE Confidence: 0.92267488

01:34:50.640 --> 01:34:53.538 This is much more ambiguous and nuanced,

NOTE Confidence: 0.92267488

01:34:53.540 --> 01:34:57.500 so I I think we're just not there yet.

NOTE Confidence: 0.92267488

01:34:57.500 --> 01:35:00.580 I do know that.

NOTE Confidence: 0.92267488

01:35:00.580 --> 01:35:03.202 Key opinion leaders you know will

NOTE Confidence: 0.92267488

01:35:03.202 --> 01:35:05.879 agree to disagree about this point,

NOTE Confidence: 0.92267488

01:35:05.880 --> 01:35:08.876 and I know that people have different

NOTE Confidence: 0.92267488

01:35:08.880 --> 01:35:14.528 approaches to how to use immunotherapy

NOTE Confidence: 0.92267488

01:35:14.528 --> 01:35:16.576 in this patient population.

NOTE Confidence: 0.92267488

01:35:16.580 --> 01:35:19.051 We're we're all I would say we're

NOTE Confidence: 0.92267488

01:35:19.051 --> 01:35:21.755 all struggling and so I think at

NOTE Confidence: 0.92267488

01:35:21.755 --> 01:35:24.399 this point it's just keep at it.

NOTE Confidence: 0.92267488

01:35:24.400 --> 01:35:26.344 More studies, more data.

NOTE Confidence: 0.92267488

01:35:26.344 --> 01:35:28.288 Looking for better biomarkers?

NOTE Confidence: 0.867063336

01:35:29.160 --> 01:35:30.540 Useful for us to know.

NOTE Confidence: 0.867063336

01:35:30.540 --> 01:35:32.180 This pathologist, because of

NOTE Confidence: 0.867063336

01:35:32.180 --> 01:35:34.640 the the because of our struggles

NOTE Confidence: 0.867063336

01:35:34.710 --> 01:35:36.658 with interpreting that stain.

NOTE Confidence: 0.867063336

01:35:36.660 --> 01:35:39.569 Eventually I it's not needed.

NOTE Confidence: 0.867063336

01:35:39.569 --> 01:35:40.628 That'll be great.

NOTE Confidence: 0.892203288333333

01:35:41.060 --> 01:35:42.938 I can't speak for all oncologists.

NOTE Confidence: 0.892203288333333

01:35:42.940 --> 01:35:45.130 Obviously. I do know that some

NOTE Confidence: 0.892203288333333

01:35:45.130 --> 01:35:46.792 oncologists if the PDL ones,

NOTE Confidence: 0.892203288333333

01:35:46.792 --> 01:35:49.560 if there is no PDL one anywhere,

NOTE Confidence: 0.892203288333333

01:35:49.560 --> 01:35:51.408 it's just flat out,

NOTE Confidence: 0.892203288333333

01:35:51.408 --> 01:35:55.280 no PDL one are are not including

NOTE Confidence: 0.892203288333333

01:35:55.280 --> 01:35:56.954 immunotherapy because there's

NOTE Confidence: 0.892203288333333

01:35:56.954 --> 01:35:59.744 there there there are toxicities

NOTE Confidence: 0.892203288333333

01:35:59.744 --> 01:36:02.316 the treatment discontinuation rate

NOTE Confidence: 0.892203288333333

01:36:02.316 --> 01:36:03.972 was higher in all these studies

NOTE Confidence: 0.892203288333333

01:36:03.972 --> 01:36:05.411 in the immunotherapy arm and

NOTE Confidence: 0.892203288333333

01:36:05.411 --> 01:36:06.796 that makes sense because you're.

NOTE Confidence: 0.892203288333333

01:36:06.800 --> 01:36:09.352 Adding in a whole another class of

NOTE Confidence: 0.892203288333333

01:36:09.352 --> 01:36:12.184 toxicities that may lead to treatment

NOTE Confidence: 0.892203288333333

01:36:12.184 --> 01:36:14.164 discontinuation and of course

NOTE Confidence: 0.892203288333333

01:36:14.164 --> 01:36:16.599 we're all now experiencing that.

NOTE Confidence: 0.892203288333333

01:36:16.600 --> 01:36:19.785 We start chemo immuno and have a

NOTE Confidence: 0.892203288333333

01:36:19.785 --> 01:36:21.918 treatment related immune adverse event

NOTE Confidence: 0.892203288333333

01:36:21.918 --> 01:36:24.760 and and are are withdrawing the drug.

NOTE Confidence: 0.892203288333333

01:36:24.760 --> 01:36:28.016 It's also a cost issue but I think

NOTE Confidence: 0.892203288333333

01:36:28.020 --> 01:36:31.870 I I think that's a health economics

NOTE Confidence: 0.892203288333333

01:36:31.870 --> 01:36:33.611 issue for individual decision

NOTE Confidence: 0.892203288333333

01:36:33.611 --> 01:36:35.993 making for patients you know unless

NOTE Confidence: 0.892203288333333

01:36:35.993 --> 01:36:38.190 it's personal financial toxicity.

NOTE Confidence: 0.892203288333333

01:36:38.190 --> 01:36:39.422 I think it's a little hard for

NOTE Confidence: 0.892203288333333

01:36:39.422 --> 01:36:40.210 me to argue well,

NOTE Confidence: 0.892203288333333

01:36:40.210 --> 01:36:42.550 it's costly to our healthcare system,

NOTE Confidence: 0.892203288333333

01:36:42.550 --> 01:36:45.154 so I'm going to withhold immunotherapy

NOTE Confidence: 0.892203288333333

01:36:45.154 --> 01:36:47.560 if it's personal financial toxicity.

NOTE Confidence: 0.892203288333333

01:36:47.560 --> 01:36:48.928 That's of course a different story,

NOTE Confidence: 0.892203288333333

01:36:48.930 --> 01:36:50.766 so that's kind of how I think about it.

NOTE Confidence: 0.892203288333333

01:36:50.770 --> 01:36:53.493 But everybody I think looks at this

NOTE Confidence: 0.892203288333333

01:36:53.493 --> 01:36:56.039 differently and right now I don't think

NOTE Confidence: 0.892203288333333

01:36:56.039 --> 01:36:57.888 anyone has has the right right answer,

NOTE Confidence: 0.892203288333333

01:36:57.890 --> 01:37:00.277 or there's a truly a wrong answer.

NOTE Confidence: 0.912903464444444

01:37:00.850 --> 01:37:02.325 Well, you touched on something

NOTE Confidence: 0.912903464444444

01:37:02.325 --> 01:37:04.803 that we can do, and that is

NOTE Confidence: 0.912903464444444

01:37:04.803 --> 01:37:06.527 the completely negative stain.

NOTE Confidence: 0.912903464444444

01:37:06.530 --> 01:37:07.900 We can agree on that

NOTE Confidence: 0.8398851

01:37:08.440 --> 01:37:10.276 and and definitely I know they're

NOTE Confidence: 0.8398851

01:37:10.276 --> 01:37:12.384 oncologists and some of our key opinion

NOTE Confidence: 0.8398851

01:37:12.384 --> 01:37:14.570 leaders in the field who feel we should.

NOTE Confidence: 0.8398851

01:37:14.570 --> 01:37:16.850 That's a setting where very

NOTE Confidence: 0.8398851

01:37:16.850 --> 01:37:18.218 comfortable withholding anything

NOTE Confidence: 0.660685752642857

01:37:18.230 --> 01:37:20.225 you can rely on. Our result is

NOTE Confidence: 0.660685752642857

01:37:20.225 --> 01:37:22.550 what I meant that we can reliably.

NOTE Confidence: 0.660685752642857

01:37:22.550 --> 01:37:23.960 We can agree this is negative.

NOTE Confidence: 0.769834255

01:37:25.440 --> 01:37:26.976 That's that is important to know.

NOTE Confidence: 0.769834255

01:37:26.980 --> 01:37:28.186 Actually all right,

NOTE Confidence: 0.769834255

01:37:28.186 --> 01:37:30.196 we are beyond the hour.

NOTE Confidence: 0.769834255

01:37:30.200 --> 01:37:31.600 Thanks everyone who stayed to

NOTE Confidence: 0.769834255

01:37:31.600 --> 01:37:33.000 the end for your attention.

NOTE Confidence: 0.769834255

01:37:33.000 --> 01:37:34.668 And again, I think we're all

NOTE Confidence: 0.769834255

01:37:34.668 --> 01:37:36.320 happy to take questions by e-mail

NOTE Confidence: 0.769834255

01:37:36.320 --> 01:37:38.010 and have a good evening. Thank

NOTE Confidence: 0.938615604285714

01:37:38.020 --> 01:37:40.190 you very much everyone. Thank you Jill.