WEBVTT

NOTE duration:"00:54:33.2160000"

NOTE language:en-us

NOTE Confidence: 0.8051051

00:00:00.000 --> 00:00:04.578 OK, so you know if you instant.

NOTE Confidence: 0.8051051

00:00:04.580 --> 00:00:07.140 We will be starting.

NOTE Confidence: 0.67705846

00:00:09.260 --> 00:00:13.660 So this is the server.

NOTE Confidence: 0.67705846

00:00:13.660 --> 00:00:16.124 Seminar on the liver.

NOTE Confidence: 0.67705846

00:00:16.124 --> 00:00:19.820 Tumor lecture we've launched in January

NOTE Confidence: 0.67705846

00:00:19.924 --> 00:00:23.459 and today we will have FaceTime to.

NOTE Confidence: 0.67705846

00:00:23.460 --> 00:00:27.620 The medical treatment of HCC.

NOTE Confidence: 0.67705846

00:00:27.620 --> 00:00:30.063 I remind you that this is part

NOTE Confidence: 0.67705846

00:00:30.063 --> 00:00:32.010 of our liver cancer program

NOTE Confidence: 0.67705846

00:00:32.010 --> 00:00:34.852 and it takes a village to treat

NOTE Confidence: 0.67705846

00:00:34.852 --> 00:00:37.458 the patient with liver cancer.

NOTE Confidence: 0.67705846

00:00:37.460 --> 00:00:40.860 You see, on the left all the different

NOTE Confidence: 0.67705846

00:00:40.860 --> 00:00:43.497 approaches that needs to be considered

NOTE Confidence: 0.67705846

00:00:43.497 --> 00:00:46.047 when we discuss the patient and

NOTE Confidence: 0.67705846

00:00:46.133 --> 00:00:49.029 and on the right part of the people

NOTE Confidence: 0.67705846

00:00:49.029 --> 00:00:51.400 that takes part to our program.

NOTE Confidence: 0.67705846

00:00:51.400 --> 00:00:52.220 Between surgeons,

NOTE Confidence: 0.67705846

00:00:52.220 --> 00:00:53.860 interventional is the medical

NOTE Confidence: 0.67705846

00:00:53.860 --> 00:00:55.500 oncologist at geologies pathologist,

NOTE Confidence: 0.67705846

00:00:55.500 --> 00:00:58.398 and so on and so forth.

NOTE Confidence: 0.67705846

00:00:58.400 --> 00:01:02.390 And in the two prior seminars,

NOTE Confidence: 0.67705846

00:01:02.390 --> 00:01:06.524 we have the Doctor Billingslea from

NOTE Confidence: 0.67705846

00:01:06.524 --> 00:01:09.710 Service Surgical oncology Ann Dr.

NOTE Confidence: 0.67705846

00:01:09.710 --> 00:01:13.910 Model from interventional radiology today.

NOTE Confidence: 0.67705846

00:01:13.910 --> 00:01:15.558 We will have Stacy,

NOTE Confidence: 0.67705846

00:01:15.558 --> 00:01:18.588 which is a format of just so

NOTE Confidence: 0.67705846

00:01:18.588 --> 00:01:21.336 that to remind you very briefly

NOTE Confidence: 0.67705846

00:01:21.336 --> 00:01:23.360 how the program works.

NOTE Confidence: 0.67705846

00:01:23.360 --> 00:01:26.424 We have a a comment intake line and

NOTE Confidence: 0.67705846

00:01:26.424 --> 00:01:29.620 the patient is seeing in in the liver

NOTE Confidence: 0.67705846

00:01:29.620 --> 00:01:32.480 cancer clinic and then discuss the

NOTE Confidence: 0.67705846

00:01:32.480 --> 00:01:35.505 tumor board where everybody participate.

NOTE Confidence: 0.67705846

00:01:35.510 --> 00:01:38.548 You see here on all the discipline

NOTE Confidence: 0.67705846

00:01:38.548 --> 00:01:41.340 that take part to our discussion

NOTE Confidence: 0.67705846

00:01:41.340 --> 00:01:43.665 and then a treatment is.

NOTE Confidence: 0.67705846

00:01:43.670 --> 00:01:45.752 Is discussed among us an and

NOTE Confidence: 0.67705846

00:01:45.752 --> 00:01:47.875 the patient is referred for the

NOTE Confidence: 0.67705846

00:01:47.875 --> 00:01:49.873 treatment and and the follow up.

NOTE Confidence: 0.67705846

00:01:49.880 --> 00:01:53.016 So today I am very happy to

NOTE Confidence: 0.67705846

00:01:53.016 --> 00:01:54.360 present Doctor Spacetime.

NOTE Confidence: 0.67705846

00:01:54.360 --> 00:01:58.392 Stacy is is a very valued member of our

NOTE Confidence: 0.67705846

00:01:58.392 --> 00:02:01.080 program. She had this battle studies.

NOTE Confidence: 0.67705846

00:02:01.080 --> 00:02:04.056 I looked gassed in New York she got

NOTE Confidence: 0.67705846

00:02:04.056 --> 00:02:06.951 the ND in the University University

NOTE Confidence: 0.67705846

00:02:06.951 --> 00:02:10.035 and then a master in science.

NOTE Confidence: 0.67705846

00:02:10.040 --> 00:02:13.365 She did her residency in the Montefiore

NOTE Confidence: 0.67705846

00:02:13.365 --> 00:02:16.718 Medical Center in New York City and

NOTE Confidence: 0.67705846

00:02:16.718 --> 00:02:19.890 your college fellowship are and where you?

NOTE Confidence: 0.67705846

00:02:19.890 --> 00:02:21.906 She donyale in 2010.

NOTE Confidence: 0.67705846

00:02:21.906 --> 00:02:24.426 And she's now associate professor

NOTE Confidence: 0.67705846

00:02:24.426 --> 00:02:27.318 of internal medicine ecology.

NOTE Confidence: 0.67705846

00:02:27.320 --> 00:02:29.816 She has leadership positions at the

NOTE Confidence: 0.67705846

00:02:29.816 --> 00:02:31.924 Center for Gas, intestinal cancer,

NOTE Confidence: 0.67705846

00:02:31.924 --> 00:02:34.913 and she's a member of our steering

NOTE Confidence: 0.67705846

00:02:34.913 --> 00:02:37.306 committee of our Liver Cancer program,

NOTE Confidence: 0.67705846

00:02:37.310 --> 00:02:41.045 and she is one of the person that actually.

NOTE Confidence: 0.7733291

00:02:43.430 --> 00:02:46.075 Give us their guidelines through

NOTE Confidence: 0.7733291

00:02:46.075 --> 00:02:48.720 her activity in the effort

NOTE Confidence: 0.7733291

00:02:48.817 --> 00:02:51.417 Ability Cancer panel ansehen.

NOTE Confidence: 0.7733291

00:02:51.420 --> 00:02:55.612 In addition, Stacy is one of the really

NOTE Confidence: 0.7733291

00:02:55.612 --> 00:02:59.198 few medical oncologist who are expert

NOTE Confidence: 0.7733291

00:02:59.198 --> 00:03:02.840 in the treatment of liver cancer,

NOTE Confidence: 0.7733291

00:03:02.840 --> 00:03:05.875 which is a particularly difficult

NOTE Confidence: 0.7733291

00:03:05.875 --> 00:03:10.115 condition to to treat because of the

NOTE Confidence: 0.7733291

00:03:10.115 --> 00:03:13.439 combined liver and an ecology diseases.

NOTE Confidence: 0.7733291

00:03:13.440 --> 00:03:15.050 And in addition to that,

NOTE Confidence: 0.7733291

00:03:15.050 --> 00:03:17.927 she has the time to be the.

NOTE Confidence: 0.7733291

00:03:17.930 --> 00:03:21.486 Principal investigator or one of the Co.

NOTE Confidence: 0.7733291

00:03:21.490 --> 00:03:24.322 Investigator in about 30 different clinical

NOTE Confidence: 0.7733291

00:03:24.322 --> 00:03:27.070 trials and it's really impressive.

NOTE Confidence: 0.7733291

00:03:27.070 --> 00:03:29.610 And so without further ado,

NOTE Confidence: 0.7733291

00:03:29.610 --> 00:03:32.949 let me share my screen Anne and

NOTE Confidence: 0.7733291

00:03:32.949 --> 00:03:35.710 let Stacy begin his lecture.

NOTE Confidence: 0.92804784

00:03:46.160 --> 00:03:48.827 OK great. Can you see it now?

NOTE Confidence: 0.92804784

00:03:48.830 --> 00:03:50.090 Yep OK perfect.

NOTE Confidence: 0.92804784

00:03:50.090 --> 00:03:52.610 Alright thanks Mario for the introduction,

NOTE Confidence: 0.92804784

00:03:52.610 --> 00:03:55.270 so I'm really excited to be talking

NOTE Confidence: 0.92804784

00:03:55.270 --> 00:03:57.425 to you about combination therapy

NOTE Confidence: 0.92804784

00:03:57.425 --> 00:03:59.745 for HCC and you know,

NOTE Confidence: 0.92804784

00:03:59.750 --> 00:04:02.207 I usually start talks by giving a

NOTE Confidence: 0.92804784

00:04:02.207 --> 00:04:04.304 lot of background information and

NOTE Confidence: 0.92804784

00:04:04.304 --> 00:04:07.685 really explaining why this is such a

NOTE Confidence: 0.92804784

00:04:07.685 --> 00:04:09.410 multidisciplinary disease to treat.

NOTE Confidence: 0.92804784

00:04:09.410 --> 00:04:12.770 But this group is well aware of that,

NOTE Confidence: 0.92804784

00:04:12.770 --> 00:04:15.528 and so I'm going to jump right

NOTE Confidence: 0.92804784

00:04:15.528 --> 00:04:17.722 into really thinking about the

NOTE Confidence: 0.92804784

00:04:17.722 --> 00:04:19.578 medical oncology piece of.

NOTE Confidence: 0.92804784

00:04:19.580 --> 00:04:21.500 Of treatment and so you know,

NOTE Confidence: 0.92804784

00:04:21.500 --> 00:04:23.885 I like to start with looking at the BC

NOTE Confidence: 0.92804784

00:04:23.885 --> 00:04:26.297 else staging system because I think this

NOTE Confidence: 0.92804784

00:04:26.297 --> 00:04:28.860 really shows kind of where things were,

NOTE Confidence: 0.92804784

00:04:28.860 --> 00:04:29.456 you know,

NOTE Confidence: 0.92804784

00:04:29.456 --> 00:04:30.946 and then thinking about where

NOTE Confidence: 0.92804784

00:04:30.946 --> 00:04:32.933 things are and then really thinking

NOTE Confidence: 0.92804784

00:04:32.933 --> 00:04:34.648 more broadly about where things

NOTE Confidence: 0.92804784

00:04:34.648 --> 00:04:36.218 are going in the feature.

NOTE Confidence: 0.92804784

00:04:36.220 --> 00:04:38.780 So we'll come back to this slide later.

NOTE Confidence: 0.92804784

00:04:38.780 --> 00:04:40.040 But you know also,

NOTE Confidence: 0.92804784

00:04:40.040 --> 00:04:41.930 I feel like this reflects the

NOTE Confidence: 0.92804784

00:04:42.005 --> 00:04:43.888 time when I came to Yale 10

NOTE Confidence: 0.92804784

00:04:43.888 --> 00:04:46.229 years ago and it was really a

NOTE Confidence: 0.92804784

00:04:46.229 --> 00:04:48.054 transplant conference at the time,

NOTE Confidence: 0.92804784

00:04:48.060 --> 00:04:50.030 not a liver tumor board.

NOTE Confidence: 0.92804784

00:04:50.030 --> 00:04:53.282 But I went to weekly and I kind of sat in

NOTE Confidence: 0.92804784

00:04:53.282 --> 00:04:56.486 the back of the room right out of fellowship.

NOTE Confidence: 0.92804784

00:04:56.490 --> 00:04:58.105 And when someone kind of

NOTE Confidence: 0.92804784

00:04:58.105 --> 00:04:59.720 came off the transplant list,

NOTE Confidence: 0.92804784

00:04:59.720 --> 00:05:01.646 you know someone would look back

NOTE Confidence: 0.92804784

00:05:01.646 --> 00:05:04.566 at me in the in the corner and say,

NOTE Confidence: 0.92804784

00:05:04.570 --> 00:05:06.656 do you want to see this patient

NOTE Confidence: 0.92804784

00:05:06.656 --> 00:05:08.439 and put them on Seraphim?

NOTE Confidence: 0.92804784

00:05:08.440 --> 00:05:10.807 And so I feel like the story that I

NOTE Confidence: 0.92804784

00:05:10.807 --> 00:05:13.211 could present today is kind of all

NOTE Confidence: 0.92804784

00:05:13.211 --> 00:05:15.357 the new treatment options really come

NOTE Confidence: 0.92804784

00:05:15.357 --> 00:05:17.433 in parallel with my experience and

NOTE Confidence: 0.92804784

00:05:17.433 --> 00:05:20.080 kind of growth here in this field.

NOTE Confidence: 0.92804784

00:05:20.080 --> 00:05:21.073 So you know,

NOTE Confidence: 0.92804784

00:05:21.073 --> 00:05:23.059 really seraphim's been the one drug

NOTE Confidence: 0.92804784

00:05:23.059 --> 00:05:25.201 that's been around for awhile and

NOTE Confidence: 0.92804784

00:05:25.201 --> 00:05:26.946 now we have different treatment

NOTE Confidence: 0.92804784

00:05:27.013 --> 00:05:29.194 options and we're kind of, you know,

NOTE Confidence: 0.92804784

00:05:29.194 --> 00:05:30.729 sandwich done after the cure

NOTE Confidence: 0.92804784

00:05:30.729 --> 00:05:32.320 it if intent therapies,

NOTE Confidence: 0.92804784

00:05:32.320 --> 00:05:32.672 right?

NOTE Confidence: 0.92804784

00:05:32.672 --> 00:05:35.488 And then the local regional therapies for the

NOTE Confidence: 0.92804784

00:05:35.488 --> 00:05:38.094 Child Pugh for the for the BCLCB patients.

NOTE Confidence: 0.92804784

00:05:38.100 --> 00:05:39.460 And so you know,

NOTE Confidence: 0.92804784

00:05:39.460 --> 00:05:40.140 I think.

NOTE Confidence: 0.92804784

00:05:40.140 --> 00:05:40.480 Also,

NOTE Confidence: 0.92804784

00:05:40.480 --> 00:05:42.520 although this staging system isn't perfect,

NOTE Confidence: 0.92804784

00:05:42.520 --> 00:05:43.788 it really reflects right?

NOTE Confidence: 0.92804784

00:05:43.788 --> 00:05:46.466 The you know the importance of thinking of

NOTE Confidence: 0.92804784

00:05:46.466 --> 00:05:48.972 the underlying liver function of the patient,

NOTE Confidence: 0.92804784

00:05:48.980 --> 00:05:50.424 their performance status and.

NOTE Confidence: 0.92804784

00:05:50.424 --> 00:05:52.590 The tumor characteristics and so starting

NOTE Confidence: 0.92804784

00:05:52.649 --> 00:05:54.833 at the beginning here with the sharp study,

NOTE Confidence: 0.92804784

00:05:54.840 --> 00:05:56.415 which I'm sure everyone is

NOTE Confidence: 0.92804784

00:05:56.415 --> 00:05:57.360 familiar with rates,

NOTE Confidence: 0.92804784

00:05:57.360 --> 00:05:59.552 so this goes back to 2008 and this

NOTE Confidence: 0.92804784

00:05:59.552 --> 00:06:02.203 was the first study to show a survival

NOTE Confidence: 0.92804784

00:06:02.203 --> 00:06:04.608 benefit of a systemic therapy in HCC.

NOTE Confidence: 0.92804784

00:06:04.610 --> 00:06:06.160 So other drugs like doxorubicin

NOTE Confidence: 0.92804784

00:06:06.160 --> 00:06:08.070 had been used in the past,

NOTE Confidence: 0.92804784

00:06:08.070 --> 00:06:09.726 but they had ever never actually

NOTE Confidence: 0.92804784

00:06:09.726 --> 00:06:11.618 been shown in a randomized child

NOTE Confidence: 0.92804784

00:06:11.618 --> 00:06:13.428 to show a survival benefit.

NOTE Confidence: 0.92804784

00:06:13.430 --> 00:06:15.542 So in this study you could see that

NOTE Confidence: 0.92804784

00:06:15.542 --> 00:06:17.839 Seraphim was actually randomized to placebo,

NOTE Confidence: 0.92804784

00:06:17.840 --> 00:06:18.179 right?

NOTE Confidence: 0.92804784

00:06:18.179 --> 00:06:20.213 Which is unusual for a first

NOTE Confidence: 0.92804784

00:06:20.213 --> 00:06:21.710 line systemic therapy option.

NOTE Confidence: 0.92804784

00:06:21.710 --> 00:06:24.414 An in this study we saw an overall

NOTE Confidence: 0.92804784

00:06:24.414 --> 00:06:26.219 survival benefit going from 7.9

NOTE Confidence: 0.92804784

00:06:26.219 --> 00:06:27.979 months with placebo to 10.7

NOTE Confidence: 0.92804784

00:06:27.979 --> 00:06:30.209 months and so based on this data,

NOTE Confidence: 0.92804784

00:06:30.210 --> 00:06:32.166 this became the new standard of

NOTE Confidence: 0.92804784

00:06:32.166 --> 00:06:34.499 care option and you could see also

NOTE Confidence: 0.92804784

00:06:34.499 --> 00:06:36.739 that there was a time to radiologic

NOTE Confidence: 0.92804784

00:06:36.805 --> 00:06:38.977 progression on this on this drug

NOTE Confidence: 0.92804784

00:06:38.977 --> 00:06:40.063 and just remember,

NOTE Confidence: 0.82814777

00:06:40.070 --> 00:06:41.502 you know Seraphim, right?

NOTE Confidence: 0.82814777

00:06:41.502 --> 00:06:43.650 It's not chemotherapy in the exact

NOTE Confidence: 0.82814777

00:06:43.717 --> 00:06:45.505 strict sense of the term rate,

NOTE Confidence: 0.82814777

00:06:45.510 --> 00:06:47.934 but it's a it's a TKI and multi

NOTE Confidence: 0.82814777

00:06:47.934 --> 00:06:49.250 tyrosine kinase inhibitor,

NOTE Confidence: 0.82814777

00:06:49.250 --> 00:06:51.483 and because of that you know it's

NOTE Confidence: 0.82814777

00:06:51.483 --> 00:06:52.990 really targeting multiple pathways.

NOTE Confidence: 0.82814777

00:06:52.990 --> 00:06:55.280 It's kind of a dirty.

NOTE Confidence: 0.82814777

00:06:55.280 --> 00:06:57.938 Drug and you know they're not.

NOTE Confidence: 0.82814777

00:06:57.940 --> 00:07:01.048 Although their oral and they're taken daily,

NOTE Confidence: 0.82814777

00:07:01.050 --> 00:07:04.002 and they may not have some of the

NOTE Confidence: 0.82814777

00:07:04.002 --> 00:07:06.442 more serious side effects that

NOTE Confidence: 0.82814777

00:07:06.442 --> 00:07:08.598 some chemotherapy drugs have.

NOTE Confidence: 0.82814777

00:07:08.600 --> 00:07:12.047 They do have a lot of great two toxicities

NOTE Confidence: 0.82814777

00:07:12.047 --> 00:07:15.697 that often affect our patients like fatigue.

NOTE Confidence: 0.82814777

00:07:15.700 --> 00:07:17.032 Sometimes decreased appetite,

NOTE Confidence: 0.82814777

00:07:17.032 --> 00:07:18.840 hand foot, skin reaction,

NOTE Confidence: 0.82814777

00:07:18.840 --> 00:07:19.760 diarrhea, right?

NOTE Confidence: 0.82814777

00:07:19.760 --> 00:07:22.520 Which are definitely important in the

NOTE Confidence: 0.82814777

00:07:22.593 --> 00:07:25.526 management of these of these patients still.

NOTE Confidence: 0.82814777

00:07:25.530 --> 00:07:27.679 Stay on therapy and I'm just going

NOTE Confidence: 0.82814777

00:07:27.679 --> 00:07:29.948 to focus now on first line therapy

NOTE Confidence: 0.82814777

00:07:29.948 --> 00:07:32.330 and then we could talk more about.

NOTE Confidence: 0.82814777

00:07:32.330 --> 00:07:34.500 The second line therapy option so Lynn

NOTE Confidence: 0.82814777

00:07:34.500 --> 00:07:37.010 van if another tyrosine kinase inhibitor,

NOTE Confidence: 0.82814777

00:07:37.010 --> 00:07:39.834 was the next drug that had a positive

NOTE Confidence: 0.82814777

00:07:39.834 --> 00:07:42.049 result in a first line study,

NOTE Confidence: 0.82814777

00:07:42.050 --> 00:07:44.143 and so this study is actually powered

NOTE Confidence: 0.82814777

00:07:44.143 --> 00:07:45.984 to look for either superiority

NOTE Confidence: 0.82814777

00:07:45.984 --> 00:07:48.169 or non inferiority to Seraphim.

NOTE Confidence: 0.82814777

00:07:48.170 --> 00:07:50.866 And this is the reflect study and I'm

NOTE Confidence: 0.82814777

00:07:50.866 --> 00:07:53.928 just going to manage mention for this study.

NOTE Confidence: 0.82814777

00:07:53.930 --> 00:07:56.762 Some of the criteria and then you could

NOTE Confidence: 0.82814777

00:07:56.762 --> 00:07:59.548 see that really all of the systemic

NOTE Confidence: 0.82814777

00:07:59.548 --> 00:08:02.359 therapy studies in HTC kind of follow.

NOTE Confidence: 0.82814777

00:08:02.360 --> 00:08:04.204 Pretty closely this standard

NOTE Confidence: 0.82814777

00:08:04.204 --> 00:08:06.509 criteria so you know patients

NOTE Confidence: 0.82814777

00:08:06.509 --> 00:08:09.020 have to have measurable lesions.

NOTE Confidence: 0.82814777

00:08:09.020 --> 00:08:11.876 BBC else stage B or C.

NOTE Confidence: 0.82814777

00:08:11.880 --> 00:08:14.260 Usually child Pugh a disease.

NOTE Confidence: 0.82814777

00:08:14.260 --> 00:08:16.640 Some studies may have included

NOTE Confidence: 0.82814777

00:08:16.640 --> 00:08:19.020 some patients with B7 disease,

NOTE Confidence: 0.82814777

00:08:19.020 --> 00:08:21.876 but most are primarily child Pugh.

NOTE Confidence: 0.82814777

00:08:21.880 --> 00:08:25.680 A good performance status of zero or one,

NOTE Confidence: 0.82814777

00:08:25.680 --> 00:08:29.400 and then you know usual parameters

NOTE Confidence: 0.82814777

00:08:29.400 --> 00:08:31.880 for adequate organ function.

NOTE Confidence: 0.82814777

00:08:31.880 --> 00:08:33.980 They excluded patients that had,

NOTE Confidence: 0.82814777

00:08:33.980 --> 00:08:36.070 you know more more advanced

NOTE Confidence: 0.82814777

00:08:36.070 --> 00:08:37.324 disease like Portal,

NOTE Confidence: 0.82814777

00:08:37.330 --> 00:08:39.420 vein invasion and then they

NOTE Confidence: 0.82814777

00:08:39.420 --> 00:08:41.092 were stratified by region,

NOTE Confidence: 0.82814777

00:08:41.100 --> 00:08:43.084 whether they had Macrovascular

NOTE Confidence: 0.82814777

00:08:43.084 --> 00:08:45.068 invasion or extrahepatic spread

NOTE Confidence: 0.82814777

00:08:45.068 --> 00:08:47.964 and E COGS status and they were

NOTE Confidence: 0.82814777

00:08:47.964 --> 00:08:50.740 randomized one to one to live at nib,

NOTE Confidence: 0.82814777

00:08:50.740 --> 00:08:53.314 which you know most patients received

NOTE Confidence: 0.82814777

00:08:53.314 --> 00:08:55.759 the 12 milligram dose to start,

NOTE Confidence: 0.82814777

00:08:55.760 --> 00:08:58.142 or saraf nib and the primary

NOTE Confidence: 0.82814777

00:08:58.142 --> 00:08:59.730 endpoint was overall survival

NOTE Confidence: 0.82814777

00:08:59.808 --> 00:09:02.140 with multiple secondary endpoints.

NOTE Confidence: 0.82814777

00:09:02.140 --> 00:09:04.294 And you could see that basically

NOTE Confidence: 0.82814777

00:09:04.294 --> 00:09:06.758 you know they didn't show that it

NOTE Confidence: 0.82814777

00:09:06.758 --> 00:09:08.984 was superior and the lines cross a

NOTE Confidence: 0.82814777

00:09:09.061 --> 00:09:11.287 few times but it was non inferior

NOTE Confidence: 0.82814777

00:09:11.287 --> 00:09:12.924 so the median overall survival

NOTE Confidence: 0.82814777

00:09:12.924 --> 00:09:14.946 is very similar between the two.

NOTE Confidence: 0.82814777

00:09:14.950 --> 00:09:17.323 But the reason why many people would

NOTE Confidence: 0.82814777

00:09:17.323 --> 00:09:19.520 consider this a better option for

NOTE Confidence: 0.82814777

00:09:19.520 --> 00:09:21.746 first line therapy for patients who

NOTE Confidence: 0.82814777

00:09:21.746 --> 00:09:24.486 are going to start therapy on a TKI is

NOTE Confidence: 0.82814777

00:09:24.486 --> 00:09:26.740 that even though the survival was similar,

NOTE Confidence: 0.82814777

00:09:26.740 --> 00:09:28.756 the progression free survival was better.

NOTE Confidence: 0.82814777

00:09:28.760 --> 00:09:30.788 Although the study was not powered.

NOTE Confidence: 0.82814777

00:09:30.790 --> 00:09:32.980 You know to have this as

NOTE Confidence: 0.82814777

00:09:32.980 --> 00:09:34.075 the primary endpoint.

NOTE Confidence: 0.82814777

00:09:34.080 --> 00:09:36.446 And if you look at the bottom,

NOTE Confidence: 0.82814777

00:09:36.450 --> 00:09:37.810 the overall response rate,

NOTE Confidence: 0.82814777

00:09:37.810 --> 00:09:40.518 which 9% to me is high for seraphon.

NOTE Confidence: 0.82814777

00:09:40.520 --> 00:09:42.898 But it was up to 24% with

NOTE Confidence: 0.82814777

00:09:42.898 --> 00:09:44.250 the Lynn Vatanen arm.

NOTE Confidence: 0.82814777

00:09:44.250 --> 00:09:46.746 And so you know you could argue without

NOTE Confidence: 0.82814777

00:09:46.746 --> 00:09:48.659 the benefit of overall survival.

NOTE Confidence: 0.82814777

00:09:48.660 --> 00:09:50.355 Whether there really is a

NOTE Confidence: 0.82814777

00:09:50.355 --> 00:09:52.050 benefit of having a response.

NOTE Confidence: 0.82814777

00:09:52.050 --> 00:09:54.288 But I think most most people

NOTE Confidence: 0.82814777

00:09:54.288 --> 00:09:55.780 that take care of

NOTE Confidence: 0.8380414

00:09:55.869 --> 00:09:58.469 these patients would think that.

NOTE Confidence: 0.8380414

00:09:58.470 --> 00:10:00.770 Potentially having a response.

NOTE Confidence: 0.8380414

00:10:00.770 --> 00:10:03.645 May help with better symptom

NOTE Confidence: 0.8380414

00:10:03.645 --> 00:10:06.510 you know symptom management.

NOTE Confidence: 0.8380414

00:10:06.510 --> 00:10:09.464 And this just showed a subset analysis

NOTE Confidence: 0.8380414

00:10:09.464 --> 00:10:11.579 looking at multiple different groups

NOTE Confidence: 0.8380414

00:10:11.579 --> 00:10:14.281 that in all the groups in the

NOTE Confidence: 0.8380414

00:10:14.281 --> 00:10:16.559 subset they favored linv at NAB.

NOTE Confidence: 0.8380414

00:10:16.560 --> 00:10:22.560 And so so now moving to immune therapy.

NOTE Confidence: 0.8380414

00:10:22.560 --> 00:10:24.822 So obviously this is an exciting

NOTE Confidence: 0.8380414

00:10:24.822 --> 00:10:27.322 area for HCC and there's multiple

NOTE Confidence: 0.8380414

00:10:27.322 --> 00:10:30.500 ways rate that we could think about.

NOTE Confidence: 0.8380414

00:10:30.500 --> 00:10:32.590 You know using immune therapy

NOTE Confidence: 0.8380414

00:10:32.590 --> 00:10:33.844 for different targets.

NOTE Confidence: 0.8380414

00:10:33.850 --> 00:10:35.995 Immune therapy was a little

NOTE Confidence: 0.8380414

00:10:35.995 --> 00:10:38.860 bit late in the game to HCC,

NOTE Confidence: 0.8380414

00:10:38.860 --> 00:10:40.945 I think largely because before

NOTE Confidence: 0.8380414

00:10:40.945 --> 00:10:42.613 there were drug approvals,

NOTE Confidence: 0.8380414

00:10:42.620 --> 00:10:46.052 it seemed like a risky choice to give

NOTE Confidence: 0.8380414

00:10:46.052 --> 00:10:48.473 to patients who had either hepatitis

NOTE Confidence: 0.8380414

00:10:48.473 --> 00:10:51.819 B or C or were at higher risk,

NOTE Confidence: 0.8380414

00:10:51.820 --> 00:10:53.540 potentially for D compensation.

NOTE Confidence: 0.8380414

00:10:53.540 --> 00:10:55.260 If they had autoimmune.

NOTE Confidence: 0.8380414

00:10:55.260 --> 00:10:56.700 Effects to the liver,

NOTE Confidence: 0.8380414

00:10:56.700 --> 00:10:58.860 and so these studies weren't really

NOTE Confidence: 0.8380414

00:10:58.924 --> 00:11:01.384 started until they already had FDA

NOTE Confidence: 0.8380414

00:11:01.384 --> 00:11:03.486 approval for other indications and

NOTE Confidence: 0.8380414

00:11:03.486 --> 00:11:05.844 out of the concern for potential

NOTE Confidence: 0.8380414

00:11:05.844 --> 00:11:06.630 viral reactivation.

NOTE Confidence: 0.8380414

00:11:06.630 --> 00:11:08.705 These initial studies in the

NOTE Confidence: 0.8380414

00:11:08.705 --> 00:11:10.780 Phase one setting separated the

NOTE Confidence: 0.8380414

00:11:10.849 --> 00:11:12.961 patients out into a hepatitis C

NOTE Confidence: 0.8380414

00:11:12.961 --> 00:11:14.860 Group A hepatitis B group,

NOTE Confidence: 0.8380414

00:11:14.860 --> 00:11:17.540 and then you see they had some patients

NOTE Confidence: 0.8380414

00:11:17.540 --> 00:11:19.960 who have progressed on sorafenib.

NOTE Confidence: 0.8380414

00:11:19.960 --> 00:11:22.620 But then there's also this fourth group

NOTE Confidence: 0.8380414

00:11:22.620 --> 00:11:25.061 of some patients who actually we're

NOTE Confidence: 0.8380414

00:11:25.061 --> 00:11:27.509 getting this as first line therapy.

NOTE Confidence: 0.8380414

00:11:27.510 --> 00:11:30.310 And what you could see?

NOTE Confidence: 0.8380414

00:11:30.310 --> 00:11:32.718 You know on these on these patient bars

NOTE Confidence: 0.8380414

00:11:32.718 --> 00:11:35.334 is that the four groups are pretty

NOTE Confidence: 0.8380414

00:11:35.334 --> 00:11:37.284 much superimposable on each other,

NOTE Confidence: 0.8380414

00:11:37.290 --> 00:11:39.999 and so you know there were many

NOTE Confidence: 0.8380414

00:11:39.999 --> 00:11:41.950 patients that were on treatment

NOTE Confidence: 0.8380414

00:11:41.950 --> 00:11:44.798 for at least a year and they were

NOTE Confidence: 0.8380414

00:11:44.876 --> 00:11:47.426 pretty similar across the groups.

NOTE Confidence: 0.8380414

00:11:47.430 --> 00:11:49.642 And this just shows on the left

NOTE Confidence: 0.8380414

00:11:49.642 --> 00:11:50.590 the spider plots,

NOTE Confidence: 0.8380414

00:11:50.590 --> 00:11:52.795 so anything that goes below the 30%

NOTE Confidence: 0.8380414

00:11:52.800 --> 00:11:54.963 response there on the bottom was at

NOTE Confidence: 0.8380414

00:11:54.963 --> 00:11:56.980 least a partial response and you

NOTE Confidence: 0.8380414

00:11:56.980 --> 00:11:59.020 could see that those are pretty

NOTE Confidence: 0.8380414

00:11:59.020 --> 00:12:00.849 similar across the groups and then

NOTE Confidence: 0.8380414

00:12:00.849 --> 00:12:03.204 on the right is just another form of

NOTE Confidence: 0.8380414

00:12:03.204 --> 00:12:05.360 looking at the data in a waterfall

NOTE Confidence: 0.8380414

00:12:05.427 --> 00:12:07.747 plot and you could see from the red

NOTE Confidence: 0.8380414

00:12:07.747 --> 00:12:09.869 dotted line going across the bottom.

NOTE Confidence: 0.8380414

00:12:09.870 --> 00:12:12.061 All the patients that went below that

NOTE Confidence: 0.8380414

00:12:12.061 --> 00:12:14.475 had had at least a partial response

NOTE Confidence: 0.8380414

00:12:14.475 --> 00:12:17.004 to the drug and basically the four

NOTE Confidence: 0.8380414

00:12:17.004 --> 00:12:19.484 graphs are. Very similar and so.

NOTE Confidence: 0.8380414

00:12:19.484 --> 00:12:21.268 Based on this data,

NOTE Confidence: 0.8380414

00:12:21.270 --> 00:12:24.036 the FDA approved Nuvola MAB with

NOTE Confidence: 0.8380414

00:12:24.036 --> 00:12:26.372 the conditional approval that there

NOTE Confidence: 0.8380414

00:12:26.372 --> 00:12:29.298 would be randomized data in the future,

NOTE Confidence: 0.8380414

00:12:29.300 --> 00:12:32.078 but this allowed patients to have

NOTE Confidence: 0.8380414

00:12:32.078 --> 00:12:34.649 access to immune therapy for HCC,

NOTE Confidence: 0.8380414

00:12:34.650 --> 00:12:36.880 an in a similar study.

NOTE Confidence: 0.8380414

00:12:36.880 --> 00:12:39.995 The keynote 224 study very similar design.

NOTE Confidence: 0.8380414

00:12:40.000 --> 00:12:42.355 This looked at pembrolizumab and

NOTE Confidence: 0.8380414

00:12:42.355 --> 00:12:45.182 they separated the patients out in

NOTE Confidence: 0.8380414

00:12:45.182 --> 00:12:47.576 a similar fashion with hepatitis B,

NOTE Confidence: 0.8380414

00:12:47.580 --> 00:12:50.810 hepatitis C, and uninfected group.

NOTE Confidence: 0.8380414

00:12:50.810 --> 00:12:53.354 And you could see again that in in

NOTE Confidence: 0.8380414

00:12:53.354 --> 00:12:55.689 you know this waterfall plot that

NOTE Confidence: 0.8380414

00:12:55.689 --> 00:12:58.659 there were responses in all of the

NOTE Confidence: 0.8380414

00:12:58.659 --> 00:13:01.365 groups and that they were pretty

NOTE Confidence: 0.8380414

00:13:01.365 --> 00:13:02.718 similar in distribution.

NOTE Confidence: 0.8380414

00:13:02.720 --> 00:13:05.632 And so again they got a very similar

NOTE Confidence: 0.8380414

00:13:05.632 --> 00:13:07.780 FDA approval that was conditional

NOTE Confidence: 0.8380414

00:13:07.780 --> 00:13:10.010 on having future randomized data

NOTE Confidence: 0.8380414

00:13:10.010 --> 00:13:13.167 and so now we get to more exciting

NOTE Confidence: 0.8380414

00:13:13.167 --> 00:13:15.424 data rate of thinking of combination

NOTE Confidence: 0.8380414

00:13:15.424 --> 00:13:17.409 therapy in the first line.

NOTE Confidence: 0.8380414

00:13:17.410 --> 00:13:20.441 And so this study looked at a

NOTE Confidence: 0.8380414

00:13:20.441 --> 00:13:21.740 combination of atisa

NOTE Confidence: 0.8179294

00:13:21.827 --> 00:13:24.364 Les Mab. With bevacizumab of veg

NOTE Confidence: 0.8179294

00:13:24.364 --> 00:13:26.669 F inhibitor and what's interesting

NOTE Confidence: 0.8179294

00:13:26.669 --> 00:13:28.778 is that bevacizumab had been

NOTE Confidence: 0.8179294

00:13:28.778 --> 00:13:32.054 looked at in HCC before in a small

NOTE Confidence: 0.8179294

00:13:32.054 --> 00:13:34.159 couple small phase two studies,

NOTE Confidence: 0.8179294

00:13:34.160 --> 00:13:36.740 and there was a response rate.

NOTE Confidence: 0.8179294

00:13:36.740 --> 00:13:39.757 They weren't randomized to show a clear,

NOTE Confidence: 0.8179294

00:13:39.760 --> 00:13:41.396 you know, survival benefit,

NOTE Confidence: 0.8179294

00:13:41.396 --> 00:13:44.821 but there was a signal that there was

NOTE Confidence: 0.8179294

00:13:44.821 --> 00:13:47.943 clearly benefit of giving anti VEGF therapy,

NOTE Confidence: 0.8179294

00:13:47.950 --> 00:13:50.386 but there was never approval for

NOTE Confidence: 0.8179294

00:13:50.386 --> 00:13:52.770 or an application for approval.

NOTE Confidence: 0.8179294

00:13:52.770 --> 00:13:54.710 You know for the drug.

NOTE Confidence: 0.8179294

00:13:54.710 --> 00:13:58.022 So before this berbasis map was not an

NOTE Confidence: 0.8179294

00:13:58.022 --> 00:14:00.916 approved drug for each CC and you know,

NOTE Confidence: 0.8179294

00:14:00.920 --> 00:14:03.741 it's interesting to think about why there

NOTE Confidence: 0.8179294

00:14:03.741 --> 00:14:06.116 is potentially synergy between these two

NOTE Confidence: 0.8179294

00:14:06.116 --> 00:14:08.671 drugs as opposed to an additive benefit,

NOTE Confidence: 0.8179294

00:14:08.680 --> 00:14:11.008 but it seems like Bevis is.

NOTE Confidence: 0.8179294

00:14:11.010 --> 00:14:13.326 Mab does normalize the tumor vasculature?

NOTE Confidence: 0.8179294

00:14:13.330 --> 00:14:14.882 An actually allows for

NOTE Confidence: 0.8179294

00:14:14.882 --> 00:14:16.434 more T cell infiltration,

NOTE Confidence: 0.8179294

00:14:16.440 --> 00:14:19.536 and so this is the phase one study.

NOTE Confidence: 0.8179294

00:14:19.540 --> 00:14:22.284 This is the Geo 30140 study that

NOTE Confidence: 0.8179294

00:14:22.284 --> 00:14:24.640 looked at several arms of which.

NOTE Confidence: 0.8179294

00:14:24.640 --> 00:14:28.213 HTC was one of the arms on the study,

NOTE Confidence: 0.8179294

00:14:28.220 --> 00:14:31.028 and so these were the other arms that

NOTE Confidence: 0.8179294

00:14:31.028 --> 00:14:34.436 that we also had open here are may

NOTE Confidence: 0.8179294

00:14:34.436 --> 00:14:36.580 was for unresectable advanced HCC.

NOTE Confidence: 0.8179294

00:14:36.580 --> 00:14:39.796 They did include some B7 patients

NOTE Confidence: 0.8179294

00:14:39.796 --> 00:14:41.404 on the study.

NOTE Confidence: 0.8179294

00:14:41.410 --> 00:14:46.246 To have measurable disease rate very

NOTE Confidence: 0.8179294

00:14:46.246 --> 00:14:49.470 similar eligibility criteria and.

NOTE Confidence: 0.8179294

00:14:49.470 --> 00:14:50.866 The primary endpoint here,

NOTE Confidence: 0.8179294

00:14:50.866 --> 00:14:53.493 because it was a phase one study

NOTE Confidence: 0.8179294

00:14:53.493 --> 00:14:55.337 with safety and tolerability,

NOTE Confidence: 0.8179294

00:14:55.340 --> 00:14:57.890 safety and tolerability and then

NOTE Confidence: 0.8179294

00:14:57.890 --> 00:15:00.440 looking at the overall response

NOTE Confidence: 0.8179294

00:15:00.520 --> 00:15:03.070 rate by resist 1.1 there's also.

NOTE Confidence: 0.8179294

00:15:03.070 --> 00:15:04.950 Duration of response progression.

NOTE Confidence: 0.8179294

00:15:04.950 --> 00:15:07.770 Free response time to radio graphic

NOTE Confidence: 0.8179294

00:15:07.840 --> 00:15:10.492 progression and then they also looked

NOTE Confidence: 0.8179294

00:15:10.492 --> 00:15:12.766 at modified resist criteria and

NOTE Confidence: 0.8179294

00:15:12.766 --> 00:15:15.769 overall survival so this looks at the

NOTE Confidence: 0.8179294

00:15:15.769 --> 00:15:18.004 baseline demographics of this study.

NOTE Confidence: 0.8179294

00:15:18.004 --> 00:15:20.752 So in total there were 103

NOTE Confidence: 0.8179294

00:15:20.752 --> 00:15:23.408 patients on the Phase one study,

NOTE Confidence: 0.8179294

00:15:23.410 --> 00:15:24.392 predominantly male,

NOTE Confidence: 0.8179294

00:15:24.392 --> 00:15:27.338 which is the HTC population that

NOTE Confidence: 0.8179294

00:15:27.338 --> 00:15:30.485 we see about half the patients were

NOTE Confidence: 0.8179294

00:15:30.485 --> 00:15:33.694 in Asia and the other 40% were in.

NOTE Confidence: 0.8179294

00:15:33.694 --> 00:15:36.076 Japan or the US patients were

NOTE Confidence: 0.8179294

00:15:36.076 --> 00:15:38.320 split between E kog performance,

NOTE Confidence: 0.8179294

00:15:38.320 --> 00:15:41.280 status of zero and one and the majority

NOTE Confidence: 0.8179294

00:15:41.280 --> 00:15:44.261 of the patients had child Pugh A5

NOTE Confidence: 0.8179294

00:15:44.261 --> 00:15:47.160 disease with 20% ASICS and you could

NOTE Confidence: 0.8179294

00:15:47.160 --> 00:15:50.030 see there were only six patients that

NOTE Confidence: 0.8179294

00:15:50.030 --> 00:15:52.788 wound up in rolling with B7 disease.

NOTE Confidence: 0.8179294

00:15:52.790 --> 00:15:55.604 About half the patients had hepatitis B,

NOTE Confidence: 0.8179294

00:15:55.610 --> 00:15:58.106 reflecting the you know mostly the

NOTE Confidence: 0.8179294

00:15:58.106 --> 00:16:00.431 Asian population that enrolled 30% with

NOTE Confidence: 0.8179294

00:16:00.431 --> 00:16:03.244 hepatitis C and another 20% more nonviral.

NOTE Confidence: 0.8179294

00:16:03.244 --> 00:16:05.254 The majority of the patients

NOTE Confidence: 0.8179294

00:16:05.254 --> 00:16:06.460 had extrahepatic spread.

NOTE Confidence: 0.8179294

00:16:06.460 --> 00:16:08.570 About half had Macrovascular invasion.

NOTE Confidence: 0.8179294

00:16:08.570 --> 00:16:11.333 And so when you think of those two as

NOTE Confidence: 0.8179294

00:16:11.333 --> 00:16:14.148 being kind of high risk characteristics,

NOTE Confidence: 0.8179294

00:16:14.150 --> 00:16:14.522 right,

NOTE Confidence: 0.8179294

00:16:14.522 --> 00:16:17.870 about 90% of the patients had one or both,

NOTE Confidence: 0.8179294

00:16:17.870 --> 00:16:20.985 and then they also looked at AFP

NOTE Confidence: 0.8179294

00:16:20.985 --> 00:16:24.867 to see if that was potentially a.

NOTE Confidence: 0.8179294

00:16:24.870 --> 00:16:27.636 You know show different responses and

NOTE Confidence: 0.8179294

00:16:27.636 --> 00:16:31.427 that was about half with less than 400 AFP.

NOTE Confidence: 0.8179294

00:16:31.430 --> 00:16:34.118 About half the patients had prior taste

NOTE Confidence: 0.8179294

00:16:34.118 --> 00:16:37.540 and about a third had prior radiotherapy,

NOTE Confidence: 0.8179294

00:16:37.540 --> 00:16:40.204 and this Spider plot shows the

NOTE Confidence: 0.8179294

00:16:40.204 --> 00:16:42.846 responses to treatment and you could

NOTE Confidence: 0.8179294

00:16:42.846 --> 00:16:45.576 see that the green lines or the

NOTE Confidence: 0.8179294

00:16:45.576 --> 00:16:48.346 patients who had either a partial

NOTE Confidence: 0.8179294

00:16:48.346 --> 00:16:50.646 or complete response to treatment.

NOTE Confidence: 0.8179294

00:16:50.650 --> 00:16:53.709 Then there were many patients in blue,

NOTE Confidence: 0.8179294

00:16:53.710 --> 00:16:56.566 it's stable disease than the red.

NOTE Confidence: 0.8179294

00:16:56.570 --> 00:16:58.646 The red bars show progressive disease,

NOTE Confidence: 0.85702395

00:16:58.650 --> 00:17:00.732 so you could see that for

NOTE Confidence: 0.85702395

00:17:00.732 --> 00:17:02.120 the patients you know,

NOTE Confidence: 0.85702395

00:17:02.120 --> 00:17:04.196 they often had a good response.

NOTE Confidence: 0.85702395

00:17:04.200 --> 00:17:06.162 Kind of starting pretty early into

NOTE Confidence: 0.85702395

00:17:06.162 --> 00:17:08.264 treatment and many of the patients

NOTE Confidence: 0.85702395

00:17:08.264 --> 00:17:10.099 had a quite sustained response.

NOTE Confidence: 0.85702395

00:17:10.100 --> 00:17:12.529 So if you look at the Disease

NOTE Confidence: 0.85702395

00:17:12.529 --> 00:17:14.980 Control rate, there were.

NOTE Confidence: 0.85702395

00:17:14.980 --> 00:17:17.200 There were many responders and there

NOTE Confidence: 0.85702395

00:17:17.200 --> 00:17:19.555 were many that lasted a significant

NOTE Confidence: 0.85702395

00:17:19.555 --> 00:17:22.369 amount of time with the progression free

NOTE Confidence: 0.85702395

00:17:22.369 --> 00:17:24.629 survival of 15 months and the median,

NOTE Confidence: 0.85702395

00:17:24.630 --> 00:17:26.110 overall survival had been

NOTE Confidence: 0.85702395

00:17:26.110 --> 00:17:27.590 reached at the time.

NOTE Confidence: 0.85702395

00:17:27.590 --> 00:17:29.445 When you know this was

NOTE Confidence: 0.85702395

00:17:29.445 --> 00:17:30.929 considered a positive study.

NOTE Confidence: 0.85702395

00:17:30.930 --> 00:17:32.790 So based on this Phase,

NOTE Confidence: 0.85702395

00:17:32.790 --> 00:17:35.289 one data that I am brave 150

NOTE Confidence: 0.85702395

00:17:35.289 --> 00:17:37.484 study was designed and this is

NOTE Confidence: 0.85702395

00:17:37.484 --> 00:17:39.578 a randomized study then to look

NOTE Confidence: 0.85702395

00:17:39.578 --> 00:17:42.058 at the combination of a tease.

NOTE Confidence: 0.85702395

00:17:42.060 --> 00:17:44.846 Oh Bevause was given in the Phase

NOTE Confidence: 0.85702395

00:17:44.846 --> 00:17:46.999 one study randomized to Seraphim.

NOTE Confidence: 0.85702395

00:17:47.000 --> 00:17:49.464 Which at the time when this was started,

NOTE Confidence: 0.85702395

00:17:49.470 --> 00:17:51.675 it was still the standard of care

NOTE Confidence: 0.85702395

00:17:51.675 --> 00:17:54.838 and it was randomized 2 to one and

NOTE Confidence: 0.85702395

00:17:54.838 --> 00:17:56.983 again with the same stratifications.

NOTE Confidence: 0.85702395

00:17:56.990 --> 00:18:00.671 And so the I am brave 150 study was

NOTE Confidence: 0.85702395

00:18:00.671 --> 00:18:03.640 published back in June and based on

NOTE Confidence: 0.85702395

00:18:03.640 --> 00:18:06.120 that data, there was FDA approval.

NOTE Confidence: 0.85702395

00:18:06.120 --> 00:18:08.195 I'm actually showing you here.

NOTE Confidence: 0.85702395

00:18:08.200 --> 00:18:10.490 The updated overall survival and

NOTE Confidence: 0.85702395

00:18:10.490 --> 00:18:12.322 progression free survival data

NOTE Confidence: 0.85702395

00:18:12.322 --> 00:18:14.642 that was presented at the GI

NOTE Confidence: 0.85702395

00:18:14.642 --> 00:18:16.078 ASCO meeting in January.

NOTE Confidence: 0.85702395

00:18:16.080 --> 00:18:17.868 So this is newer,

NOTE Confidence: 0.85702395

00:18:17.868 --> 00:18:21.242 newer data and you know you could

NOTE Confidence: 0.85702395

00:18:21.242 --> 00:18:24.740 see here that the overall survival.

NOTE Confidence: 0.85702395

00:18:24.740 --> 00:18:26.348 The median overall survival

NOTE Confidence: 0.85702395

00:18:26.348 --> 00:18:28.358 for Seraphim was 13.4 months,

NOTE Confidence: 0.85702395

00:18:28.360 --> 00:18:31.568 so as these studies go on in time,

NOTE Confidence: 0.85702395

00:18:31.570 --> 00:18:33.922 the median overall survival for this

NOTE Confidence: 0.85702395

00:18:33.922 --> 00:18:36.000 rafina Barb keeps getting better,

NOTE Confidence: 0.85702395

00:18:36.000 --> 00:18:37.795 reflecting that most patients are

NOTE Confidence: 0.85702395

00:18:37.795 --> 00:18:40.445 going on to at least second line

NOTE Confidence: 0.85702395

00:18:40.445 --> 00:18:42.405 therapy and the median overall

NOTE Confidence: 0.85702395

00:18:42.405 --> 00:18:44.120 survival for the combination

NOTE Confidence: 0.85702395

00:18:44.120 --> 00:18:46.450 was an impressive 19.2 months,

NOTE Confidence: 0.85702395

00:18:46.450 --> 00:18:49.061 so this is really the best data

NOTE Confidence: 0.85702395

00:18:49.061 --> 00:18:51.792 that we have so far for first

NOTE Confidence: 0.85702395

00:18:51.792 --> 00:18:54.078 line therapy for HCC and you

NOTE Confidence: 0.85702395

00:18:54.170 --> 00:18:56.800 could see the progression free.

NOTE Confidence: 0.85702395

00:18:56.800 --> 00:18:58.960 The.

NOTE Confidence: 0.85702395

00:18:58.960 --> 00:19:01.822 The PFS data for Steven it was 4.3 months,

NOTE Confidence: 0.85702395

00:19:01.830 --> 00:19:04.118 and for that is above arms 6.9 and

NOTE Confidence: 0.85702395

00:19:04.118 --> 00:19:06.410 you could see that there's a nice

NOTE Confidence: 0.85702395

00:19:06.410 --> 00:19:08.849 separation of the curves at six months,

NOTE Confidence: 0.85702395

00:19:08.850 --> 00:19:11.762 12 months going out to 18 months

NOTE Confidence: 0.85702395

00:19:11.762 --> 00:19:15.047 and on for both the OS and PFS.

NOTE Confidence: 0.85702395

00:19:15.050 --> 00:19:17.130 And looking at responses to,

NOTE Confidence: 0.85702395

00:19:17.130 --> 00:19:19.783 they looked at resist 1.1 and modified

NOTE Confidence: 0.85702395

00:19:19.783 --> 00:19:21.888 resist and the confirmed overall

NOTE Confidence: 0.85702395

00:19:21.888 --> 00:19:25.003 response rate for Seraphim is now 11%,

NOTE Confidence: 0.85702395

00:19:25.010 --> 00:19:27.500 which seems to also keep going

NOTE Confidence: 0.85702395

00:19:27.500 --> 00:19:29.160 up for Seraphim data,

NOTE Confidence: 0.85702395

00:19:29.160 --> 00:19:31.056 which I find interesting,

NOTE Confidence: 0.85702395

00:19:31.056 --> 00:19:34.532 but I'm not sure how to explain

NOTE Confidence: 0.85702395

00:19:34.532 --> 00:19:36.128 that and then.

NOTE Confidence: 0.85702395

00:19:36.130 --> 00:19:37.905 The response rate was an

NOTE Confidence: 0.85702395

00:19:37.905 --> 00:19:39.904 impressive 30% for the A tease.

NOTE Confidence: 0.85702395

00:19:39.904 --> 00:19:42.263 Oh Bev combination and you know the

NOTE Confidence: 0.85702395

00:19:42.263 --> 00:19:44.790 response rates are always a little bit

NOTE Confidence: 0.85702395

00:19:44.790 --> 00:19:47.426 higher when their looked at by modified

NOTE Confidence: 0.85702395

00:19:47.426 --> 00:19:50.380 resist as opposed to resist 1.1 and

NOTE Confidence: 0.85702395

00:19:50.380 --> 00:19:53.710 so we saw some complete responses.

NOTE Confidence: 0.85702395

00:19:53.710 --> 00:19:54.775 Several partial responses.

NOTE Confidence: 0.85702395

00:19:54.775 --> 00:19:56.550 Many patients with stable disease,

NOTE Confidence: 0.85702395

00:19:56.550 --> 00:19:59.091 and so when you look at the

NOTE Confidence: 0.85702395

00:19:59.091 --> 00:20:00.180 overall Disease Control.

NOTE Confidence: 0.85702395

00:20:00.180 --> 00:20:02.668 Rates it's an impressive.

NOTE Confidence: 0.85702395

00:20:02.668 --> 00:20:07.020 It's an impressive 74% and so the

NOTE Confidence: 0.85702395

00:20:07.020 --> 00:20:10.120 median duration of response for

NOTE Confidence: 0.85702395

00:20:10.120 --> 00:20:13.927 Seraphim was 14.9 and four that

NOTE Confidence: 0.85702395

00:20:13.927 --> 00:20:16.992 is above combination 18.1 and,

NOTE Confidence: 0.85702395

00:20:17.000 --> 00:20:17.582 importantly,

NOTE Confidence: 0.85702395

00:20:17.582 --> 00:20:18.746 you know,

NOTE Confidence: 0.85702395

00:20:18.746 --> 00:20:21.656 looking at the adverse events

NOTE Confidence: 0.85702395

00:20:21.656 --> 00:20:24.480 for for the combination.

NOTE Confidence: 0.85702395

00:20:24.480 --> 00:20:28.834 So there was some decreased appetite fatigue,

NOTE Confidence: 0.766574374

00:20:28.840 --> 00:20:30.496 pyrexia rash. Hypertension,

NOTE Confidence: 0.766574374

00:20:30.496 --> 00:20:34.360 which is mostly from the bevacizumab which

NOTE Confidence: 0.766574374

00:20:34.444 --> 00:20:37.356 we know from you know, veg F inhibition.

NOTE Confidence: 0.766574374

00:20:37.356 --> 00:20:40.693 We see this and it's easily treatable with

NOTE Confidence: 0.766574374

00:20:40.693 --> 00:20:43.566 with blood pressure medication, you know.

NOTE Confidence: 0.766574374

00:20:43.566 --> 00:20:46.830 Importantly, there is a lot of interest in

NOTE Confidence: 0.766574374

00:20:46.910 --> 00:20:50.151 looking at bleeding events in these patients

NOTE Confidence: 0.766574374

00:20:50.151 --> 00:20:53.659 because we are giving bevacizumab and the

NOTE Confidence: 0.766574374

00:20:53.659 --> 00:20:56.719 variceal hemorrhage rate was very low.

NOTE Confidence: 0.766574374

00:20:56.720 --> 00:20:59.498 Upper GI hemorrhage rate also low,

NOTE Confidence: 0.766574374

00:20:59.500 --> 00:21:02.038 and so now comparing the safety

NOTE Confidence: 0.766574374

00:21:02.038 --> 00:21:04.600 data between Saraf and amenities.

NOTE Confidence: 0.766574374

00:21:04.600 --> 00:21:06.910 Oh Bev. So not surprisingly,

NOTE Confidence: 0.766574374

00:21:06.910 --> 00:21:10.490 of course we see more.

NOTE Confidence: 0.766574374

00:21:10.490 --> 00:21:12.520 More grade one into diarrhea.

NOTE Confidence: 0.766574374

00:21:12.520 --> 00:21:15.760 It's Arafa nib and less with a tease.

NOTE Confidence: 0.766574374

00:21:15.760 --> 00:21:18.190 Oh Bev hand foot skin reaction,

NOTE Confidence: 0.766574374

00:21:18.190 --> 00:21:20.758 really exclusively with Saraf nib decreased

NOTE Confidence: 0.766574374

00:21:20.758 --> 00:21:22.905 appetite in both groups hypertension

NOTE Confidence: 0.766574374

00:21:22.905 --> 00:21:25.474 and we see that in Seraphim also.

NOTE Confidence: 0.766574374

00:21:25.480 --> 00:21:27.856 Of course, because there's

NOTE Confidence: 0.766574374

00:21:27.856 --> 00:21:30.826 partial veg F inhibition there.

NOTE Confidence: 0.766574374

00:21:30.830 --> 00:21:32.494 Some infusion related reactions,

NOTE Confidence: 0.766574374

00:21:32.494 --> 00:21:34.990 some proteinuria which we see also

NOTE Confidence: 0.766574374

00:21:35.058 --> 00:21:37.277 with veg F inhibition an are used

NOTE Confidence: 0.766574374

00:21:37.277 --> 00:21:39.389 to checking blood pressure at every

NOTE Confidence: 0.766574374

00:21:39.389 --> 00:21:41.585 visit and checking your Infor for

NOTE Confidence: 0.766574374

00:21:41.585 --> 00:21:43.820 protein as we do with bevacizumab.

NOTE Confidence: 0.766574374

00:21:43.820 --> 00:21:44.930 Another disease groups.

NOTE Confidence: 0.766574374

00:21:44.930 --> 00:21:45.670 And importantly,

NOTE Confidence: 0.766574374

00:21:45.670 --> 00:21:48.712 you know for the phase one and phase three

NOTE Confidence: 0.766574374

00:21:48.712 --> 00:21:51.539 study all patients had to have an EGD

NOTE Confidence: 0.766574374

00:21:51.539 --> 00:21:54.200 within six months of initiating therapy,

NOTE Confidence: 0.766574374

00:21:54.200 --> 00:21:55.067 so you know.

NOTE Confidence: 0.766574374

00:21:55.067 --> 00:21:57.090 Now we think of really doing that

NOTE Confidence: 0.766574374

00:21:57.162 --> 00:21:59.018 exclusively for the patients

NOTE Confidence: 0.766574374

00:21:59.018 --> 00:22:00.874 who have underlying cirrhosis.

NOTE Confidence: 0.766574374

00:22:00.880 --> 00:22:03.328 But for the studies they didn't.

NOTE Confidence: 0.766574374

00:22:03.330 --> 00:22:04.826 Distinguish between patients who

NOTE Confidence: 0.766574374

00:22:04.826 --> 00:22:07.070 did or did not have cirrhosis,

NOTE Confidence: 0.766574374

00:22:07.070 --> 00:22:09.296 so all patients had an EGD within

NOTE Confidence: 0.766574374

00:22:09.296 --> 00:22:11.600 six months of starting therapy and

NOTE Confidence: 0.766574374

00:22:11.600 --> 00:22:14.156 they had to have verisys treated

NOTE Confidence: 0.766574374

00:22:14.156 --> 00:22:16.418 according to local standard of care,

NOTE Confidence: 0.766574374

00:22:16.420 --> 00:22:17.449 and so importantly,

NOTE Confidence: 0.766574374

00:22:17.449 --> 00:22:19.850 looking at the upper GI bleeding rate

NOTE Confidence: 0.766574374

00:22:19.919 --> 00:22:22.029 in the combination versus Seraphim.

NOTE Confidence: 0.766574374

00:22:22.030 --> 00:22:24.268 EBIT increased from 4.5% in Strafford,

NOTE Confidence: 0.766574374

00:22:24.270 --> 00:22:26.520 up to 7% with a tease.

NOTE Confidence: 0.766574374

00:22:26.520 --> 00:22:27.282 Oh bed,

NOTE Confidence: 0.766574374

00:22:27.282 --> 00:22:29.568 which is considered safe and also

NOTE Confidence: 0.766574374

00:22:29.568 --> 00:22:31.748 importantly thinking about quality of life.

NOTE Confidence: 0.766574374

00:22:31.750 --> 00:22:33.454 All patients filled out.

NOTE Confidence: 0.766574374

00:22:33.454 --> 00:22:35.584 Patient reported outcomes on this

NOTE Confidence: 0.766574374

00:22:35.584 --> 00:22:37.814 study and patients reported a

NOTE Confidence: 0.766574374

00:22:37.814 --> 00:22:39.979 significantly better quality of life

NOTE Confidence: 0.766574374

00:22:39.979 --> 00:22:42.676 with a time to clinical deterioration.

NOTE Confidence: 0.766574374

00:22:42.680 --> 00:22:45.488 Much improved from 3.6 months on

NOTE Confidence: 0.766574374

00:22:45.488 --> 00:22:48.368 Seraphim to 11.2 months on a tease.

NOTE Confidence: 0.766574374

00:22:48.370 --> 00:22:49.072 Oh Bev,

NOTE Confidence: 0.766574374

00:22:49.072 --> 00:22:51.880 so not only are we seeing increases in

NOTE Confidence: 0.766574374

00:22:51.961 --> 00:22:54.936 survival and progression free survival,

NOTE Confidence: 0.766574374

00:22:54.940 --> 00:22:57.480 but we're actually seeing patients

NOTE Confidence: 0.766574374

00:22:57.480 --> 00:23:00.556 reporting that they feel like they

NOTE Confidence: 0.766574374

00:23:00.556 --> 00:23:03.720 have a better quality of life for

NOTE Confidence: 0.766574374

00:23:03.720 --> 00:23:06.537 significantly more months on this regimen.

NOTE Confidence: 0.766574374

00:23:06.540 --> 00:23:09.256 So you know, based on this data,

NOTE Confidence: 0.766574374

00:23:09.260 --> 00:23:10.022 this now is.

NOTE Confidence: 0.766574374

00:23:10.022 --> 00:23:12.802 So it is so Bev is the first line

NOTE Confidence: 0.766574374

00:23:12.802 --> 00:23:15.122 preferred option for patients who

NOTE Confidence: 0.766574374

00:23:15.122 --> 00:23:17.073 are considered good countenance

NOTE Confidence: 0.766574374

00:23:17.073 --> 00:23:18.989 for for the regiment.

NOTE Confidence: 0.766574374

00:23:18.990 --> 00:23:21.324 And this was really a game

NOTE Confidence: 0.766574374

00:23:21.324 --> 00:23:22.880 changer in the field.

NOTE Confidence: 0.766574374

00:23:22.880 --> 00:23:25.208 So so thinking about combination therapy,

NOTE Confidence: 0.766574374

00:23:25.210 --> 00:23:25.598 right?

NOTE Confidence: 0.766574374

00:23:25.598 --> 00:23:28.314 This is really the gold standard now,

NOTE Confidence: 0.766574374

00:23:28.320 --> 00:23:31.050 but will go through some emerging data.

NOTE Confidence: 0.766574374

00:23:31.050 --> 00:23:34.034 So I wanted to go back first and

NOTE Confidence: 0.766574374

00:23:34.034 --> 00:23:36.557 think about now the second line.

NOTE Confidence: 0.766574374

00:23:36.560 --> 00:23:40.133 You know the second line data that we have,

NOTE Confidence: 0.766574374

00:23:40.140 --> 00:23:40.856 so again,

NOTE Confidence: 0.766574374

00:23:40.856 --> 00:23:43.004 you know the initial studies were

NOTE Confidence: 0.766574374

00:23:43.004 --> 00:23:44.920 with tyrosine kinase inhibitors.

NOTE Confidence: 0.766574374

00:23:44.920 --> 00:23:48.301 So these studies were designed when Saraf

NOTE Confidence: 0.766574374

00:23:48.301 --> 00:23:52.347 and it was the only drug approved and.

NOTE Confidence: 0.766574374

00:23:52.350 --> 00:23:54.678 They were randomized to placebo and

NOTE Confidence: 0.766574374

00:23:54.678 --> 00:23:57.565 so in this study the celestial study

NOTE Confidence: 0.766574374

00:23:57.565 --> 00:24:00.491 patients were randomized 2 to one to

NOTE Confidence: 0.82526374

00:24:00.571 --> 00:24:03.326 khabbaz antonym or to placebo

NOTE Confidence: 0.82526374

00:24:03.326 --> 00:24:04.979 with similar stratifications.

NOTE Confidence: 0.82526374

00:24:04.980 --> 00:24:07.080 And based on this study,

NOTE Confidence: 0.82526374

00:24:07.080 --> 00:24:08.792 the progression free survival

NOTE Confidence: 0.82526374

00:24:08.792 --> 00:24:11.700 increased from about two months to 5.2.

NOTE Confidence: 0.82526374

00:24:11.700 --> 00:24:14.860 There was a very low response rate with

NOTE Confidence: 0.82526374

00:24:14.860 --> 00:24:17.501 cabozantinib that we often see with

NOTE Confidence: 0.82526374

00:24:17.501 --> 00:24:19.680 tyrosine kinase inhibitors, you know.

NOTE Confidence: 0.82526374

00:24:19.680 --> 00:24:22.200 And so very few partial responses.

NOTE Confidence: 0.82526374

00:24:22.200 --> 00:24:25.560 It was mostly stable disease that was seen,

NOTE Confidence: 0.82526374

00:24:25.560 --> 00:24:27.984 but there was an overall survival

NOTE Confidence: 0.82526374

00:24:27.984 --> 00:24:30.180 benefit of another two months.

NOTE Confidence: 0.82526374

00:24:30.180 --> 00:24:32.280 You know which is interesting.

NOTE Confidence: 0.82526374

00:24:32.280 --> 00:24:34.920 So is there something really different?

NOTE Confidence: 0.82526374

00:24:34.920 --> 00:24:37.440 About the pathways targeted with cabins,

NOTE Confidence: 0.82526374

00:24:37.440 --> 00:24:40.440 antonym or would just staying on any TKI

NOTE Confidence: 0.82526374

00:24:40.440 --> 00:24:44.155 kind of post progression still give you some.

NOTE Confidence: 0.82526374

00:24:44.160 --> 00:24:46.260 You know some survival benefit,

NOTE Confidence: 0.82526374

00:24:46.260 --> 00:24:48.360 but this was positive data.

NOTE Confidence: 0.82526374

00:24:48.360 --> 00:24:51.120 There were also mentioned some patients

NOTE Confidence: 0.82526374

00:24:51.120 --> 00:24:54.446 who received this in the third line on

NOTE Confidence: 0.82526374

00:24:54.446 --> 00:24:57.180 the study and then a similar design.

NOTE Confidence: 0.82526374

00:24:57.180 --> 00:25:00.412 The resource study looked at red graph nib

NOTE Confidence: 0.82526374

00:25:00.412 --> 00:25:03.104 versus placebo and very similar design

NOTE Confidence: 0.82526374

00:25:03.104 --> 00:25:05.822 of primary endpoint of overall survival.

NOTE Confidence: 0.82526374

00:25:05.830 --> 00:25:07.860 And you can see here that there

NOTE Confidence: 0.82526374

00:25:07.860 --> 00:25:09.806 was a survival benefit of again

NOTE Confidence: 0.82526374

00:25:09.806 --> 00:25:11.822 about a two month benefit here.

NOTE Confidence: 0.82526374

00:25:11.830 --> 00:25:13.993 This is the progression free survival curves

NOTE Confidence: 0.82526374

00:25:13.993 --> 00:25:15.939 and the probability of progression here.

NOTE Confidence: 0.82526374

00:25:15.940 --> 00:25:18.033 And if you look at all the

NOTE Confidence: 0.82526374

00:25:18.033 --> 00:25:19.730 subgroups that favored by graphene,

NOTE Confidence: 0.82526374

00:25:19.730 --> 00:25:21.942 if also so cab is answered have

NOTE Confidence: 0.82526374

00:25:21.942 --> 00:25:22.890 been red graph,

NOTE Confidence: 0.82526374

00:25:22.890 --> 00:25:24.470 and if we're both approved

NOTE Confidence: 0.82526374

00:25:24.470 --> 00:25:25.734 in the second line,

NOTE Confidence: 0.82526374

00:25:25.740 --> 00:25:27.582 you know for those who have

NOTE Confidence: 0.82526374

00:25:27.582 --> 00:25:29.210 experience with using these drugs,

NOTE Confidence: 0.82526374

00:25:29.210 --> 00:25:32.132 I would say I think that

NOTE Confidence: 0.82526374

00:25:32.132 --> 00:25:33.593 overall cabins antonym.

NOTE Confidence: 0.82526374

00:25:33.600 --> 00:25:36.472 Is probably better tolerated

NOTE Confidence: 0.82526374

00:25:36.472 --> 00:25:40.062 than than Reg Raffa nib.

NOTE Confidence: 0.82526374

00:25:40.070 --> 00:25:43.246 But a similar kind of TKI side effects,

NOTE Confidence: 0.82526374

00:25:43.250 --> 00:25:46.162 and then to mention you know other

NOTE Confidence: 0.82526374

00:25:46.162 --> 00:25:48.799 other data in the veg F area,

NOTE Confidence: 0.82526374

00:25:48.800 --> 00:25:49.596 so ramucirumab,

NOTE Confidence: 0.82526374

00:25:49.596 --> 00:25:51.188 another veg F inhibitor,

NOTE Confidence: 0.82526374

00:25:51.190 --> 00:25:53.871 was looked at in the REACH study

NOTE Confidence: 0.82526374

00:25:53.871 --> 00:25:56.314 where they looked at this in

NOTE Confidence: 0.82526374

00:25:56.314 --> 00:25:58.329 the second line versus placebo,

NOTE Confidence: 0.82526374

00:25:58.330 --> 00:26:01.109 and the study was a negative study.

NOTE Confidence: 0.82526374

00:26:01.110 --> 00:26:03.648 But in subset analysis there seemed

NOTE Confidence: 0.82526374

00:26:03.648 --> 00:26:06.992 to be a benefit in the patients who

NOTE Confidence: 0.82526374

00:26:06.992 --> 00:26:10.170 had an AFP level of greater than 400.

NOTE Confidence: 0.82526374

00:26:10.170 --> 00:26:12.970 So they went back and design the reach

NOTE Confidence: 0.82526374

00:26:12.970 --> 00:26:15.928 two study and so using similar criteria.

NOTE Confidence: 0.82526374

00:26:15.930 --> 00:26:18.667 But for this study they only included

NOTE Confidence: 0.82526374

00:26:18.667 --> 00:26:21.335 patients who had a baseline AFP level

NOTE Confidence: 0.82526374

00:26:21.335 --> 00:26:23.929 of greater than 400 and they were

NOTE Confidence: 0.82526374

00:26:23.929 --> 00:26:26.275 randomized 2 to one to ramucirumab

NOTE Confidence: 0.82526374

00:26:26.275 --> 00:26:29.050 or placebo and that study did show

NOTE Confidence: 0.82526374

00:26:29.050 --> 00:26:31.938 a survival benefit and then if you

NOTE Confidence: 0.82526374

00:26:31.938 --> 00:26:34.794 pull the data from this study plus

NOTE Confidence: 0.82526374

00:26:34.794 --> 00:26:37.658 the patients who had an AFP of over

NOTE Confidence: 0.82526374

00:26:37.658 --> 00:26:39.846 400 from the first reach study,

NOTE Confidence: 0.82526374

00:26:39.846 --> 00:26:42.036 you see that there was.

NOTE Confidence: 0.82526374

00:26:42.040 --> 00:26:42.980 Clearly, uh,

NOTE Confidence: 0.82526374

00:26:42.980 --> 00:26:45.800 you know positive benefit again in

NOTE Confidence: 0.82526374

00:26:45.800 --> 00:26:49.180 the same range of a couple of months.

NOTE Confidence: 0.82526374

00:26:49.180 --> 00:26:52.388 So for patients with an AFP level of

NOTE Confidence: 0.82526374

00:26:52.388 --> 00:26:55.417 over 400 for second line therapy,

NOTE Confidence: 0.82526374

00:26:55.420 --> 00:26:57.650 this is another potential option.

NOTE Confidence: 0.82526374

00:26:57.650 --> 00:27:00.326 So now thinking of you know.

NOTE Confidence: 0.82526374

00:27:00.330 --> 00:27:02.694 So I mentioned before that nivolumab

NOTE Confidence: 0.82526374

00:27:02.694 --> 00:27:04.846 and pembrolizumab were both approved

NOTE Confidence: 0.82526374

00:27:04.846 --> 00:27:06.886 as conditional approvals pending

NOTE Confidence: 0.82526374

00:27:06.886 --> 00:27:07.906 randomized data.

NOTE Confidence: 0.82526374

00:27:07.910 --> 00:27:10.514 So the two companies took different

NOTE Confidence: 0.82526374

00:27:10.514 --> 00:27:13.070 approaches in thinking about randomized.

NOTE Confidence: 0.82526374

00:27:13.070 --> 00:27:15.130 Studies this Checkmate 459 study

NOTE Confidence: 0.82526374

00:27:15.130 --> 00:27:17.654 looks at nivolumab versus rap native

NOTE Confidence: 0.82526374

00:27:17.654 --> 00:27:20.006 sorafenib as first line treatment and

NOTE Confidence: 0.82526374

00:27:20.006 --> 00:27:23.250 so again looks at similar patient population.

NOTE Confidence: 0.82526374

00:27:23.250 --> 00:27:25.105 They looked at primary endpoints

NOTE Confidence: 0.82526374

00:27:25.105 --> 00:27:26.960 of time to progression and

NOTE Confidence: 0.80620193

00:27:27.028 --> 00:27:28.864 overall survival and secondary

NOTE Confidence: 0.80620193

00:27:28.864 --> 00:27:30.700 endpoints of response rate

NOTE Confidence: 0.80620193

00:27:30.700 --> 00:27:32.570 and progression free survival.

NOTE Confidence: 0.80620193

00:27:32.570 --> 00:27:35.658 An you know the study did not meet

NOTE Confidence: 0.80620193

00:27:35.658 --> 00:27:38.328 its primary endpoint so you could

NOTE Confidence: 0.80620193

00:27:38.328 --> 00:27:41.046 see that the lines really cross.

NOTE Confidence: 0.80620193

00:27:41.050 --> 00:27:43.265 There's a little bit of

NOTE Confidence: 0.80620193

00:27:43.265 --> 00:27:45.037 separation at the end.

NOTE Confidence: 0.80620193

00:27:45.040 --> 00:27:46.704 You know, it's interesting

NOTE Confidence: 0.80620193

00:27:46.704 --> 00:27:49.200 because we know that there is

NOTE Confidence: 0.80620193

00:27:49.278 --> 00:27:51.456 a percent of patients right in

NOTE Confidence: 0.80620193

00:27:51.456 --> 00:27:53.732 about the 18% range that responds

NOTE Confidence: 0.80620193

00:27:53.732 --> 00:27:55.308 to pembrolizumab and nivolumab,

NOTE Confidence: 0.80620193

00:27:55.310 --> 00:27:58.326 and so you know you could argue the

NOTE Confidence: 0.80620193

00:27:58.326 --> 00:28:00.378 subtleties of the statistical analysis

NOTE Confidence: 0.80620193

00:28:00.378 --> 00:28:03.697 of the study of how it maybe could

NOTE Confidence: 0.80620193

00:28:03.697 --> 00:28:06.001 have met the primary endpoint if

NOTE Confidence: 0.80620193

00:28:06.001 --> 00:28:07.950 it had been designed differently,

NOTE Confidence: 0.80620193

00:28:07.950 --> 00:28:10.320 but it was a negative study,

NOTE Confidence: 0.80620193

00:28:10.320 --> 00:28:11.110 and similarly,

NOTE Confidence: 0.80620193

00:28:11.110 --> 00:28:13.875 you know the Pember Lizum app study.

NOTE Confidence: 0.80620193

00:28:13.880 --> 00:28:16.316 They actually went for the second

NOTE Confidence: 0.80620193

00:28:16.316 --> 00:28:17.128 line indication.

NOTE Confidence: 0.80620193

00:28:17.130 --> 00:28:19.188 And randomized to best supportive care,

NOTE Confidence: 0.80620193

00:28:19.190 --> 00:28:21.926 which seems to be a very low bar.

NOTE Confidence: 0.80620193

00:28:21.930 --> 00:28:24.336 Knowing again that we see, you know,

NOTE Confidence: 0.80620193

00:28:24.336 --> 00:28:26.384 usually about an 18% response rate.

NOTE Confidence: 0.80620193

00:28:26.384 --> 00:28:27.732 With pembrolizumab they randomized

NOTE Confidence: 0.80620193

00:28:27.732 --> 00:28:29.819 over 400 patients to Pembroke Plus

NOTE Confidence: 0.80620193

00:28:29.819 --> 00:28:31.539 best supportive care versus placebo.

NOTE Confidence: 0.80620193

00:28:31.540 --> 00:28:33.084 Plus best supportive care,

NOTE Confidence: 0.80620193

00:28:33.084 --> 00:28:35.762 but they split the primary endpoint and

NOTE Confidence: 0.80620193

00:28:35.762 --> 00:28:38.399 so even though these P values are very low,

NOTE Confidence: 0.80620193

00:28:38.400 --> 00:28:40.115 they actually did not meet

NOTE Confidence: 0.80620193

00:28:40.115 --> 00:28:41.830 the threshold for the study,

NOTE Confidence: 0.80620193

00:28:41.830 --> 00:28:44.022 and so I think one could argue that

NOTE Confidence: 0.80620193

00:28:44.022 --> 00:28:46.556 if the study had been designed a

NOTE Confidence: 0.80620193

00:28:46.556 --> 00:28:48.922 little bit differently with maybe just

NOTE Confidence: 0.80620193

00:28:48.922 --> 00:28:51.154 one primary endpoint and the other.

NOTE Confidence: 0.80620193

00:28:51.160 --> 00:28:52.644 As a secondary endpoint,

NOTE Confidence: 0.80620193

00:28:52.644 --> 00:28:54.499 it may have been positive,

NOTE Confidence: 0.80620193

00:28:54.500 --> 00:28:56.210 but basically both of these

NOTE Confidence: 0.80620193

00:28:56.210 --> 00:28:58.580 studies turned out to be negative,

NOTE Confidence: 0.80620193

00:28:58.580 --> 00:29:00.824 and it remains to be determined

NOTE Confidence: 0.80620193

00:29:00.824 --> 00:29:03.768 what the FDA will do with this data,

NOTE Confidence: 0.80620193

00:29:03.770 --> 00:29:06.274 so they may or may not continue to

NOTE Confidence: 0.80620193

00:29:06.274 --> 00:29:08.813 have an indication as as a single

NOTE Confidence: 0.80620193

00:29:08.813 --> 00:29:11.565 agent therapy in HCC so will probably

NOTE Confidence: 0.80620193

00:29:11.565 --> 00:29:14.526 know more later this year about that,

NOTE Confidence: 0.80620193

00:29:14.530 --> 00:29:16.756 but I think you know really.

NOTE Confidence: 0.80620193

00:29:16.760 --> 00:29:17.674 Excitingly though,

NOTE Confidence: 0.80620193

00:29:17.674 --> 00:29:20.873 you know there's a lot more combination

NOTE Confidence: 0.80620193

00:29:20.873 --> 00:29:22.997 therapy that's being looked at.

NOTE Confidence: 0.80620193

00:29:23.000 --> 00:29:24.620 And so you know,

NOTE Confidence: 0.80620193

00:29:24.620 --> 00:29:26.240 there's there's several studies,

NOTE Confidence: 0.80620193

00:29:26.240 --> 00:29:29.399 so one is the LEAP 02 study looking at

NOTE Confidence: 0.80620193

00:29:29.399 --> 00:29:32.693 lens at an IM plus Pember lizum app

NOTE Confidence: 0.80620193

00:29:32.693 --> 00:29:35.150 versus Limbaugh and their balloon.

NOTE Confidence: 0.80620193

00:29:35.150 --> 00:29:38.478 And so this is looking at a combination

NOTE Confidence: 0.80620193

00:29:38.478 --> 00:29:42.435 of right so so PD one inhibition plus a TKI.

NOTE Confidence: 0.80620193

00:29:42.440 --> 00:29:45.023 So this is the Keynote 524 study

NOTE Confidence: 0.80620193

00:29:45.023 --> 00:29:47.954 was the Phase 1B study and that

NOTE Confidence: 0.80620193

00:29:47.954 --> 00:29:50.134 data is already been presented.

NOTE Confidence: 0.80620193

00:29:50.140 --> 00:29:53.080 There was an overall response rate of.

NOTE Confidence: 0.80620193

00:29:53.080 --> 00:29:56.131 36% but I just caution you that when the

NOTE Confidence: 0.80620193

00:29:56.131 --> 00:29:58.987 Phase one data was initially presented,

NOTE Confidence: 0.80620193

00:29:58.990 --> 00:30:00.166 the response rate.

NOTE Confidence: 0.80620193

00:30:00.166 --> 00:30:03.340 You know from the beginning was very high,

NOTE Confidence: 0.80620193

00:30:03.340 --> 00:30:04.592 even higher than this,

NOTE Confidence: 0.80620193

00:30:04.592 --> 00:30:07.938 and so you know as you get randomized data,

NOTE Confidence: 0.80620193

00:30:07.940 --> 00:30:10.214 the response rate often comes down

NOTE Confidence: 0.80620193

00:30:10.214 --> 00:30:12.745 so you know the final data for

NOTE Confidence: 0.80620193

00:30:12.745 --> 00:30:15.380 this may not be as high as this,

NOTE Confidence: 0.80620193

00:30:15.380 --> 00:30:17.456 'cause often the patient selection for

NOTE Confidence: 0.80620193

00:30:17.456 --> 00:30:19.979 the Phase one study is very selective.

NOTE Confidence: 0.80620193

00:30:19.980 --> 00:30:22.635 An in the Phase one study they had a

NOTE Confidence: 0.80620193

00:30:22.635 --> 00:30:24.862 median overall survival of 2022 months

NOTE Confidence: 0.80620193

00:30:24.862 --> 00:30:27.410 and that was about 100 patients.

NOTE Confidence: 0.80620193

00:30:27.410 --> 00:30:30.050 And so I think it will be really

NOTE Confidence: 0.80620193

00:30:30.050 --> 00:30:31.976 interesting to see the combination

NOTE Confidence: 0.80620193

00:30:31.976 --> 00:30:33.170 data for this.

NOTE Confidence: 0.80620193

00:30:33.170 --> 00:30:33.900 You know,

NOTE Confidence: 0.80620193

00:30:33.900 --> 00:30:36.090 and then you could really kind

NOTE Confidence: 0.80620193

00:30:36.090 --> 00:30:37.790 of think about right?

NOTE Confidence: 0.82374823

00:30:37.790 --> 00:30:40.100 Which patient might be best suited

NOTE Confidence: 0.82374823

00:30:40.100 --> 00:30:41.640 for which combination therapy,

NOTE Confidence: 0.82374823

00:30:41.640 --> 00:30:43.602 and similarly the Cosmic 312 study

NOTE Confidence: 0.82374823

00:30:43.602 --> 00:30:45.953 is looking at cabins antonym plus

NOTE Confidence: 0.82374823

00:30:45.953 --> 00:30:48.282 atezolizumab versus rafanan, so again,

NOTE Confidence: 0.82374823

00:30:48.282 --> 00:30:50.437 you know another tyrosine kinase

NOTE Confidence: 0.82374823

00:30:50.437 --> 00:30:53.106 inhibitor plus plus PD one inhibitor and

NOTE Confidence: 0.82374823

00:30:53.106 --> 00:30:55.904 you know we know right cab is antonym

NOTE Confidence: 0.82374823

00:30:55.904 --> 00:30:58.196 is active in second line therapy.

NOTE Confidence: 0.82374823

00:30:58.200 --> 00:31:00.881 And as I mentioned there were some

NOTE Confidence: 0.82374823

00:31:00.881 --> 00:31:03.289 patients that had been treated as.

NOTE Confidence: 0.82374823

00:31:03.290 --> 00:31:04.547 Third line therapy.

NOTE Confidence: 0.82374823

00:31:04.547 --> 00:31:07.480 So this I think this is a

NOTE Confidence: 0.82374823

00:31:07.576 --> 00:31:09.976 promising combination also and

NOTE Confidence: 0.82374823

00:31:09.976 --> 00:31:12.976 then the other two studies.

NOTE Confidence: 0.82374823

00:31:12.980 --> 00:31:15.326 Look at the combination of with

NOTE Confidence: 0.82374823

00:31:15.326 --> 00:31:18.566 a CTL A4 antibody right and so we

NOTE Confidence: 0.82374823

00:31:18.566 --> 00:31:20.960 know from other diseases you know,

NOTE Confidence: 0.82374823

00:31:20.960 --> 00:31:23.578 adding a CTL A4 antibody often increases

NOTE Confidence: 0.82374823

00:31:23.578 --> 00:31:25.750 response rate in immune therapy,

NOTE Confidence: 0.82374823

00:31:25.750 --> 00:31:27.740 but also increases the immune

NOTE Confidence: 0.82374823

00:31:27.740 --> 00:31:28.934 related adverse events,

NOTE Confidence: 0.82374823

00:31:28.940 --> 00:31:32.084 and so the check mate and I have

NOTE Confidence: 0.82374823

00:31:32.084 --> 00:31:34.928 some slides to show you from this,

NOTE Confidence: 0.82374823

00:31:34.930 --> 00:31:37.318 But the check Mate 040 study,

NOTE Confidence: 0.82374823

00:31:37.320 --> 00:31:40.344 which was the 1B study that I showed

NOTE Confidence: 0.82374823

00:31:40.344 --> 00:31:43.087 you the single agent data for.

NOTE Confidence: 0.82374823

00:31:43.090 --> 00:31:45.946 Also had a small arm that looked

NOTE Confidence: 0.82374823

00:31:45.946 --> 00:31:48.210 at the combination of it Bluma,

NOTE Confidence: 0.82374823

00:31:48.210 --> 00:31:48.614 Mebane,

NOTE Confidence: 0.82374823

00:31:48.614 --> 00:31:51.038 nivolumab and so their response rate

NOTE Confidence: 0.82374823

00:31:51.038 --> 00:31:54.074 was up to 32% there with an impressive

NOTE Confidence: 0.82374823

00:31:54.074 --> 00:31:56.880 median overall survival of over 20 months.

NOTE Confidence: 0.82374823

00:31:56.880 --> 00:31:59.640 And so this study is looking at the

NOTE Confidence: 0.82374823

00:31:59.640 --> 00:32:02.399 combination of niveau nippy versus Seraphim,

NOTE Confidence: 0.82374823

00:32:02.400 --> 00:32:02.792 Berlin,

NOTE Confidence: 0.82374823

00:32:02.792 --> 00:32:05.144 Baton IB in the first line,

NOTE Confidence: 0.82374823

00:32:05.150 --> 00:32:07.908 and then another combination again of PD.

NOTE Confidence: 0.82374823

00:32:07.910 --> 00:32:10.966 One inhibition with a CTL A4 antibody is

NOTE Confidence: 0.82374823

00:32:10.966 --> 00:32:13.398 the durvalumab and tremelimumab study.

NOTE Confidence: 0.82374823

00:32:13.400 --> 00:32:16.552 And so this is the Himalayas study that

NOTE Confidence: 0.82374823

00:32:16.552 --> 00:32:19.430 I'll show you the study design for.

NOTE Confidence: 0.82374823

00:32:19.430 --> 00:32:22.982 As you know so far has showed a

NOTE Confidence: 0.82374823

00:32:22.982 --> 00:32:25.944 response rate of 24% and the median

NOTE Confidence: 0.82374823

00:32:25.944 --> 00:32:29.150 overall survival of 19 months with the

NOTE Confidence: 0.82374823

00:32:29.242 --> 00:32:32.266 with one of the arms of this study.

NOTE Confidence: 0.82374823

00:32:32.270 --> 00:32:33.335 So you know.

NOTE Confidence: 0.82374823

00:32:33.335 --> 00:32:36.369 There will be a lot of data coming

NOTE Confidence: 0.82374823

00:32:36.369 --> 00:32:39.087 which will be exciting to see

NOTE Confidence: 0.82374823

00:32:39.087 --> 00:32:42.176 the final data and then I think

NOTE Confidence: 0.82374823

00:32:42.176 --> 00:32:45.006 there's a lot to debate about which

NOTE Confidence: 0.82374823

00:32:45.006 --> 00:32:46.510 patients are best suited.

NOTE Confidence: 0.82374823

00:32:46.510 --> 00:32:47.264 You know,

NOTE Confidence: 0.82374823

00:32:47.264 --> 00:32:49.903 really kind of peacing out who responded,

NOTE Confidence: 0.82374823

00:32:49.910 --> 00:32:51.790 what the adverse events were.

NOTE Confidence: 0.82374823

00:32:51.790 --> 00:32:52.458 You know?

NOTE Confidence: 0.82374823

00:32:52.458 --> 00:32:54.462 What were the difference in side

NOTE Confidence: 0.82374823

00:32:54.462 --> 00:32:56.872 effects of who might be a better

NOTE Confidence: 0.82374823

00:32:56.872 --> 00:32:58.542 candidate for addition with the

NOTE Confidence: 0.82374823

00:32:58.614 --> 00:33:00.854 CTA for antibody versus bevacizumab

NOTE Confidence: 0.82374823

00:33:00.854 --> 00:33:03.094 versus a tyrosine kinase inhibitor?

NOTE Confidence: 0.82374823

00:33:03.100 --> 00:33:05.100 And those will be exciting.

NOTE Confidence: 0.82374823

00:33:05.100 --> 00:33:07.284 Discussions to have just to show

NOTE Confidence: 0.82374823

00:33:07.284 --> 00:33:10.040 you this is the Himalaya design,

NOTE Confidence: 0.82374823

00:33:10.040 --> 00:33:12.215 so the development plus Tremelimumab

NOTE Confidence: 0.82374823

00:33:12.215 --> 00:33:14.878 as first line therapy and they

NOTE Confidence: 0.82374823

00:33:14.878 --> 00:33:17.362 used a couple of different arms

NOTE Confidence: 0.82374823

00:33:17.362 --> 00:33:19.794 of tremelimumab dosing so you know

NOTE Confidence: 0.82374823

00:33:19.794 --> 00:33:22.026 in the other disease groups where

NOTE Confidence: 0.82374823

00:33:22.026 --> 00:33:24.048 there's been approval for CTA

NOTE Confidence: 0.82374823

00:33:24.048 --> 00:33:26.108 for combination like in Melanoma.

NOTE Confidence: 0.82374823

00:33:26.110 --> 00:33:28.540 Typically the patients get four

NOTE Confidence: 0.82374823

00:33:28.540 --> 00:33:30.970 cycles with the combination and

NOTE Confidence: 0.82374823

00:33:31.055 --> 00:33:33.484 then go on to the single agent

NOTE Confidence: 0.82374823

00:33:33.484 --> 00:33:35.688 drug of Nuvola MAB by itself.

NOTE Confidence: 0.82374823

00:33:35.690 --> 00:33:37.615 So in this study they did a

NOTE Confidence: 0.82374823

00:33:37.615 --> 00:33:39.030 couple of different regimens.

NOTE Confidence: 0.82374823

00:33:39.030 --> 00:33:40.734 One where there were four doses

NOTE Confidence: 0.82374823

00:33:40.734 --> 00:33:42.263 of tremelimumab and also looking

NOTE Confidence: 0.82374823

00:33:42.263 --> 00:33:43.289 at different doses.

NOTE Confidence: 0.82374823

00:33:43.290 --> 00:33:45.278 Then there was also a small cohort

NOTE Confidence: 0.82374823

00:33:45.278 --> 00:33:47.163 that looked at just one dose

NOTE Confidence: 0.82374823

00:33:47.163 --> 00:33:48.455 of tremelimumab to start,

NOTE Confidence: 0.82374823

00:33:48.460 --> 00:33:51.946 and that one actually seemed to have.

NOTE Confidence: 0.82374823

00:33:51.950 --> 00:33:53.740 More responses, but less toxicity,

NOTE Confidence: 0.82374823

00:33:53.740 --> 00:33:55.798 and so it'll be interesting to

NOTE Confidence: 0.82374823

00:33:55.798 --> 00:33:57.170 see in the end

NOTE Confidence: 0.8228799

00:33:57.250 --> 00:33:59.994 if that's the arm that really is the

NOTE Confidence: 0.8228799

00:33:59.994 --> 00:34:03.047 best one to move forward to within HCC,

NOTE Confidence: 0.8228799

00:34:03.050 --> 00:34:05.858 and this is to show you the group I

NOTE Confidence: 0.8228799

00:34:05.858 --> 00:34:08.087 mentioned from the Phase one study

NOTE Confidence: 0.8228799

00:34:08.087 --> 00:34:10.774 from the Checkmate 040 study of the

NOTE Confidence: 0.8228799

00:34:10.774 --> 00:34:12.709 combination of Nivolumab and IP,

NOTE Confidence: 0.8228799

00:34:12.710 --> 00:34:15.216 aluminum AB and so they used again.

NOTE Confidence: 0.8228799

00:34:15.220 --> 00:34:17.368 You know a few different dosing

NOTE Confidence: 0.8228799

00:34:17.368 --> 00:34:18.800 schemes for the patients,

NOTE Confidence: 0.8228799

00:34:18.800 --> 00:34:20.978 and it looks like you know

NOTE Confidence: 0.8228799

00:34:20.978 --> 00:34:23.400 for HCC the winner was really.

NOTE Confidence: 0.8228799

00:34:23.400 --> 00:34:26.072 Than evil one it be 3 arm that

NOTE Confidence: 0.8228799

00:34:26.072 --> 00:34:28.805 had the best overall survival and

NOTE Confidence: 0.8228799

00:34:28.805 --> 00:34:31.763 so that's sort of these colors

NOTE Confidence: 0.8228799

00:34:31.851 --> 00:34:34.575 came out different on this one,

NOTE Confidence: 0.8228799

00:34:34.580 --> 00:34:37.040 but basically it's it's this dosing

NOTE Confidence: 0.8228799

00:34:37.040 --> 00:34:40.526 here of the four doses and then they

NOTE Confidence: 0.8228799

00:34:40.526 --> 00:34:43.172 continue with just nuvola MAB alone.

NOTE Confidence: 0.8228799

00:34:43.180 --> 00:34:46.190 And you know, so lots of so.

NOTE Confidence: 0.8228799

00:34:46.190 --> 00:34:47.910 Lots of good questions.

NOTE Confidence: 0.8228799

00:34:47.910 --> 00:34:49.630 Kind of thinking about,

NOTE Confidence: 0.8228799

00:34:49.630 --> 00:34:52.210 you know the combination data and.

NOTE Confidence: 0.8559677

00:34:56.170 --> 00:34:58.198 I think the biggest ones you

NOTE Confidence: 0.8559677

00:34:58.198 --> 00:35:00.488 know right now, right eye for me.

NOTE Confidence: 0.8559677

00:35:00.488 --> 00:35:02.800 Two of the biggest questions to really

NOTE Confidence: 0.8559677

00:35:02.800 --> 00:35:05.201 think about our how do we sequence

NOTE Confidence: 0.8559677

00:35:05.201 --> 00:35:07.697 after tease Alisme Heaven Bevis is mad,

NOTE Confidence: 0.8559677

00:35:07.700 --> 00:35:10.122 so if that's the first line option

NOTE Confidence: 0.8559677

00:35:10.122 --> 00:35:12.779 then what do we do in second line?

NOTE Confidence: 0.8559677

00:35:12.780 --> 00:35:15.545 Do we restart with a tyrosine kinase

NOTE Confidence: 0.8559677

00:35:15.545 --> 00:35:17.568 inhibitor like Lynn Fat and if

NOTE Confidence: 0.8559677

00:35:17.568 --> 00:35:20.125 so go to a first line and kind of

NOTE Confidence: 0.8559677

00:35:20.125 --> 00:35:22.596 start through the you know the first

NOTE Confidence: 0.8559677

00:35:22.596 --> 00:35:24.650 slide into the second line again.

NOTE Confidence: 0.8559677

00:35:24.650 --> 00:35:26.678 Or do we think about going

NOTE Confidence: 0.8559677

00:35:26.678 --> 00:35:27.692 into combination immunotherapy?

NOTE Confidence: 0.8559677

00:35:27.700 --> 00:35:29.156 You know we have.

NOTE Confidence: 0.8559677

00:35:29.156 --> 00:35:30.248 It be anevo,

NOTE Confidence: 0.8559677

00:35:30.250 --> 00:35:32.798 now approved as a second line regimen,

NOTE Confidence: 0.8559677

00:35:32.800 --> 00:35:35.624 and then do we use another TKI and

NOTE Confidence: 0.8559677

00:35:35.624 --> 00:35:36.820 the third line?

NOTE Confidence: 0.8559677

00:35:36.820 --> 00:35:39.740 You know, I think about and I mean,

NOTE Confidence: 0.8559677

00:35:39.740 --> 00:35:42.288 obviously you know this is relatively new,

NOTE Confidence: 0.8559677

00:35:42.290 --> 00:35:44.480 'cause we've only had approval of

NOTE Confidence: 0.8559677

00:35:44.480 --> 00:35:45.940 the regimen since June,

NOTE Confidence: 0.8559677

00:35:45.940 --> 00:35:48.130 and so depending on how long

NOTE Confidence: 0.8559677

00:35:48.130 --> 00:35:49.590 someone's on the regimen,

NOTE Confidence: 0.8559677

00:35:49.590 --> 00:35:52.334 I think that could potentially help guide

NOTE Confidence: 0.8559677

00:35:52.334 --> 00:35:55.799 you know what what you would want to do next.

NOTE Confidence: 0.8559677

00:35:55.800 --> 00:35:57.236 So if someone really,

NOTE Confidence: 0.8559677

00:35:57.236 --> 00:35:59.810 I think progressives quickly through a tease.

NOTE Confidence: 0.8559677

00:35:59.810 --> 00:36:00.508 Oh, Bev.

NOTE Confidence: 0.8559677

00:36:00.508 --> 00:36:02.951 I don't know that going to a

NOTE Confidence: 0.8559677

00:36:02.951 --> 00:36:04.563 combination immune therapy you

NOTE Confidence: 0.8559677

00:36:04.563 --> 00:36:06.939 know regimen would be the best,

NOTE Confidence: 0.8559677

00:36:06.940 --> 00:36:08.740 but perhaps if someone responds

NOTE Confidence: 0.8559677

00:36:08.740 --> 00:36:10.180 and then eventually progresses,

NOTE Confidence: 0.8559677

00:36:10.180 --> 00:36:13.372 you may want to think about

NOTE Confidence: 0.8559677

00:36:13.372 --> 00:36:14.968 combination immune therapy.

NOTE Confidence: 0.8559677

00:36:14.970 --> 00:36:17.020 And.

NOTE Confidence: 0.8559677

00:36:17.020 --> 00:36:19.075 For the patients that tolerate

NOTE Confidence: 0.8559677

00:36:19.075 --> 00:36:21.130 a tyrosine kinase inhibitor and

NOTE Confidence: 0.8559677

00:36:21.202 --> 00:36:23.542 maybe have good control or decrease

NOTE Confidence: 0.8559677

00:36:23.542 --> 00:36:24.712 in AFP initially,

NOTE Confidence: 0.8559677

00:36:24.720 --> 00:36:27.268 I think it's very reasonable to go

NOTE Confidence: 0.8559677

00:36:27.268 --> 00:36:29.579 to another tyrosine kinase inhibitor.

NOTE Confidence: 0.8559677

00:36:29.580 --> 00:36:30.448 You know,

NOTE Confidence: 0.8559677

00:36:30.448 --> 00:36:32.618 maybe for patients that really

NOTE Confidence: 0.8559677

00:36:32.618 --> 00:36:34.838 did not tolerate a TKI well,

NOTE Confidence: 0.8559677

00:36:34.840 --> 00:36:36.456 even at reduced dose,

NOTE Confidence: 0.8559677

00:36:36.456 --> 00:36:39.389 and they have a high AFP that

NOTE Confidence: 0.8559677

00:36:39.389 --> 00:36:42.336 maybe a group that I would think

NOTE Confidence: 0.8559677

00:36:42.336 --> 00:36:44.590 more about ramucirumab in.

NOTE Confidence: 0.8559677

00:36:44.590 --> 00:36:47.406 I think another big question to think about,

NOTE Confidence: 0.8559677

00:36:47.410 --> 00:36:49.516 you know, for treating these patients,

NOTE Confidence: 0.8559677

00:36:49.520 --> 00:36:51.704 is that all of the clinical child

NOTE Confidence: 0.8559677

00:36:51.704 --> 00:36:54.232 data that you know that I presented

NOTE Confidence: 0.8559677

00:36:54.232 --> 00:36:56.910 here really only reflects the child Pugh,

NOTE Confidence: 0.8559677

00:36:56.910 --> 00:36:59.726 a population and maybe a couple of B7's.

NOTE Confidence: 0.8559677

00:36:59.730 --> 00:37:00.783 And you know,

NOTE Confidence: 0.8559677

00:37:00.783 --> 00:37:01.836 as we know,

NOTE Confidence: 0.8559677

00:37:01.840 --> 00:37:04.132 the majority of the patients that

NOTE Confidence: 0.8559677

00:37:04.132 --> 00:37:06.044 were actually treating in our

NOTE Confidence: 0.8559677

00:37:06.044 --> 00:37:07.946 practice have child Pugh B disease

NOTE Confidence: 0.8559677

00:37:07.946 --> 00:37:10.338 and so the question then is what

NOTE Confidence: 0.8559677

00:37:10.338 --> 00:37:12.396 is safe to give those patients?

NOTE Confidence: 0.8559677

00:37:12.400 --> 00:37:15.360 And as the data that we are seeing.

NOTE Confidence: 0.8559677

00:37:15.360 --> 00:37:16.672 From the trial really,

NOTE Confidence: 0.8559677

00:37:16.672 --> 00:37:19.240 is it really applicable to these patients?

NOTE Confidence: 0.8559677

00:37:19.240 --> 00:37:20.656 So as a tease?

NOTE Confidence: 0.8559677

00:37:20.656 --> 00:37:21.010 Oh,

NOTE Confidence: 0.8559677

00:37:21.010 --> 00:37:24.187 and Bev safe in the child Pugh B patients.

NOTE Confidence: 0.8559677

00:37:24.190 --> 00:37:24.519 Well,

NOTE Confidence: 0.8559677

00:37:24.519 --> 00:37:26.822 I think we're going to have a

NOTE Confidence: 0.8559677

00:37:26.822 --> 00:37:29.130 lot of data from that soon.

NOTE Confidence: 0.8559677

00:37:29.130 --> 00:37:29.766 You know,

NOTE Confidence: 0.8559677

00:37:29.766 --> 00:37:31.356 as patients are being treated

NOTE Confidence: 0.8559677

00:37:31.356 --> 00:37:33.010 out in the community,

NOTE Confidence: 0.8559677

00:37:33.010 --> 00:37:34.954 you know with approval now and

NOTE Confidence: 0.8559677

00:37:34.954 --> 00:37:37.084 you know patients with child PB

NOTE Confidence: 0.8559677

00:37:37.084 --> 00:37:39.004 disease or being treated regularly.

NOTE Confidence: 0.8559677

00:37:39.010 --> 00:37:41.418 My hope is that at least everyone's

NOTE Confidence: 0.8559677

00:37:41.418 --> 00:37:43.581 getting endoscopies so that we're not

NOTE Confidence: 0.8559677

00:37:43.581 --> 00:37:45.717 seeing higher incidence of GI bleeding.

NOTE Confidence: 0.8559677

00:37:45.720 --> 00:37:47.739 But that's certainly.

NOTE Confidence: 0.8559677

00:37:47.739 --> 00:37:51.104 A concern that I have.

NOTE Confidence: 0.8559677

00:37:51.110 --> 00:37:52.700 An you know which tyrosine

NOTE Confidence: 0.8559677

00:37:52.700 --> 00:37:53.972 kinase inhibitors you know.

NOTE Confidence: 0.8559677

00:37:53.980 --> 00:37:55.204 We're better to give.

NOTE Confidence: 0.8559677

00:37:55.204 --> 00:37:57.765 We have a lot of data for Saraf

NOTE Confidence: 0.8559677

00:37:57.765 --> 00:38:00.033 and if in Child Pugh B disease,

NOTE Confidence: 0.8559677

00:38:00.040 --> 00:38:01.726 so there was a Gideon registry

NOTE Confidence: 0.8559677

00:38:01.726 --> 00:38:02.850 that included a lot

NOTE Confidence: 0.8055654

00:38:02.911 --> 00:38:04.663 of data for patients with child

NOTE Confidence: 0.8055654

00:38:04.663 --> 00:38:06.637 PB and even somewhat see disease

NOTE Confidence: 0.8055654

00:38:06.637 --> 00:38:08.492 which basically showed that patients

NOTE Confidence: 0.8055654

00:38:08.492 --> 00:38:10.846 would see disease barely or on the

NOTE Confidence: 0.8055654

00:38:10.846 --> 00:38:13.063 drug for any length of time and

NOTE Confidence: 0.8055654

00:38:13.063 --> 00:38:15.367 don't seem to be on it long enough

NOTE Confidence: 0.8055654

00:38:15.367 --> 00:38:17.907 to really get any benefit from it.

NOTE Confidence: 0.8055654

00:38:17.910 --> 00:38:20.213 We do have some child Pugh B

NOTE Confidence: 0.8055654

00:38:20.213 --> 00:38:22.298 data now with Lynn VAT nib.

NOTE Confidence: 0.8055654

00:38:22.300 --> 00:38:24.804 Um, and we do have some data with

NOTE Confidence: 0.8055654

00:38:24.804 --> 00:38:26.690 with cabins antonym you know.

NOTE Confidence: 0.8055654

00:38:26.690 --> 00:38:28.685 Overall I would say it seems to

NOTE Confidence: 0.8055654

00:38:28.685 --> 00:38:30.400 me that these patients really

NOTE Confidence: 0.8055654

00:38:30.400 --> 00:38:32.776 wind up with more dose reductions,

NOTE Confidence: 0.8055654

00:38:32.780 --> 00:38:35.139 which is what the data suggests below.

NOTE Confidence: 0.8055654

00:38:35.140 --> 00:38:37.506 None of these were randomized studies right,

NOTE Confidence: 0.8055654

00:38:37.510 --> 00:38:39.538 but just you know more observation.

NOTE Confidence: 0.8055654

00:38:39.540 --> 00:38:41.948 ULL and I think the really when we

NOTE Confidence: 0.8055654

00:38:41.948 --> 00:38:43.738 think about the combination data

NOTE Confidence: 0.8055654

00:38:43.738 --> 00:38:45.976 from the slide I showed before

NOTE Confidence: 0.8055654

00:38:45.976 --> 00:38:47.988 right of thinking of you know,

NOTE Confidence: 0.8055654

00:38:47.990 --> 00:38:50.686 are we adding a see TL A4 antibody,

NOTE Confidence: 0.8055654

00:38:50.690 --> 00:38:53.168 a tyrosine kinase or Beves ISM AB?

NOTE Confidence: 0.8055654

00:38:53.170 --> 00:38:56.106 I think it's going to be really important

NOTE Confidence: 0.8055654

00:38:56.106 --> 00:38:58.900 to have data in those groups later

NOTE Confidence: 0.8055654

00:38:58.900 --> 00:39:01.372 with Child Pugh B patients because

NOTE Confidence: 0.8055654

00:39:01.372 --> 00:39:04.256 it may turn out that one combination

NOTE Confidence: 0.8055654

00:39:04.256 --> 00:39:06.668 is clearly better in that group,

NOTE Confidence: 0.8055654

00:39:06.668 --> 00:39:09.050 or at least you know safer.

NOTE Confidence: 0.8055654

00:39:09.050 --> 00:39:11.983 And so I think having that data

NOTE Confidence: 0.8055654

00:39:11.983 --> 00:39:15.392 after we have the initial trial data

NOTE Confidence: 0.8055654

00:39:15.392 --> 00:39:18.470 is going to be really important.

NOTE Confidence: 0.8055654

00:39:18.470 --> 00:39:20.878 So you know one thing that I

NOTE Confidence: 0.8055654

00:39:20.878 --> 00:39:22.270 haven't mentioned at all,

NOTE Confidence: 0.8055654

00:39:22.270 --> 00:39:24.405 which we usually spend a lot of

NOTE Confidence: 0.8055654

00:39:24.405 --> 00:39:26.410 time in other oncology talks.

NOTE Confidence: 0.8055654

00:39:26.410 --> 00:39:27.786 Thinking about right is

NOTE Confidence: 0.8055654

00:39:27.786 --> 00:39:28.818 molecular directed therapy.

NOTE Confidence: 0.8055654

00:39:28.820 --> 00:39:31.235 And so I just wanted to mention,

NOTE Confidence: 0.8055654

00:39:31.240 --> 00:39:31.916 you know,

NOTE Confidence: 0.8055654

00:39:31.916 --> 00:39:35.720 I think that this is a this is a big issue,

NOTE Confidence: 0.8055654

00:39:35.720 --> 00:39:36.073 right?

NOTE Confidence: 0.8055654

00:39:36.073 --> 00:39:38.544 So we're only talking about mostly tyrosine

NOTE Confidence: 0.8055654

00:39:38.544 --> 00:39:40.548 kinase inhibitors and then immune therapy.

NOTE Confidence: 0.8055654

00:39:40.550 --> 00:39:42.620 So we really have no biomarker.

NOTE Confidence: 0.8055654

00:39:42.620 --> 00:39:45.035 You know we have we have ramucirumab

NOTE Confidence: 0.8055654

00:39:45.035 --> 00:39:46.420 with a higher AFP,

NOTE Confidence: 0.8055654

00:39:46.420 --> 00:39:49.269 although I wouldn't necessarily call that a.

NOTE Confidence: 0.8055654

00:39:49.270 --> 00:39:50.806 No marker, you know,

NOTE Confidence: 0.8055654

00:39:50.806 --> 00:39:53.110 and even for the immune therapy

NOTE Confidence: 0.8055654

00:39:53.185 --> 00:39:55.177 responses in many diseases,

NOTE Confidence: 0.8055654

00:39:55.180 --> 00:39:57.682 you see that there is clear

NOTE Confidence: 0.8055654

00:39:57.682 --> 00:40:00.319 correlation with PDL one status and.

NOTE Confidence: 0.8055654

00:40:00.320 --> 00:40:03.470 So a lot of drug approvals are based on

NOTE Confidence: 0.8055654

00:40:03.470 --> 00:40:06.957 the CPS scores that we get from our path

NOTE Confidence: 0.8055654

00:40:06.957 --> 00:40:10.248 ologist an those multiple studies do not.

NOTE Confidence: 0.8055654

00:40:10.250 --> 00:40:12.632 There does not seem to be

NOTE Confidence: 0.8055654

00:40:12.632 --> 00:40:14.220 any correlation for HTC,

NOTE Confidence: 0.8055654

00:40:14.220 --> 00:40:17.292 which makes it harder for us to know

NOTE Confidence: 0.8055654

00:40:17.292 --> 00:40:20.166 which patients are more likely to respond.

NOTE Confidence: 0.8055654

00:40:20.170 --> 00:40:20.962 You know,

NOTE Confidence: 0.8055654

00:40:20.962 --> 00:40:22.942 there have been studies with

NOTE Confidence: 0.8055654

00:40:22.942 --> 00:40:23.734 met amplification.

NOTE Confidence: 0.8055654

00:40:23.740 --> 00:40:25.328 There's some studies looking

NOTE Confidence: 0.8055654

00:40:25.328 --> 00:40:26.519 at chromosome remodeling,

NOTE Confidence: 0.8055654

00:40:26.520 --> 00:40:29.299 which will be interesting to see right,

NOTE Confidence: 0.8055654

00:40:29.300 --> 00:40:31.350 but so far we have.

NOTE Confidence: 0.8055654

00:40:31.350 --> 00:40:32.714 No molecular directed therapy

NOTE Confidence: 0.8055654

00:40:32.714 --> 00:40:35.222 we are aware of course of the

NOTE Confidence: 0.8055654

00:40:35.222 --> 00:40:36.810 mutational landscape of HCC,

NOTE Confidence: 0.8055654

00:40:36.810 --> 00:40:37.516 you know,

NOTE Confidence: 0.8055654

00:40:37.516 --> 00:40:39.281 but unfortunately right the ones

NOTE Confidence: 0.8055654

00:40:39.281 --> 00:40:40.810 on the top there,

NOTE Confidence: 0.8055654

00:40:40.810 --> 00:40:43.358 we don't have any drugs for and

NOTE Confidence: 0.8055654

00:40:43.358 --> 00:40:46.242 the drugs that we do have for the

NOTE Confidence: 0.8055654

00:40:46.242 --> 00:40:48.819 targets at the bottom of the slide,

NOTE Confidence: 0.8055654

00:40:48.820 --> 00:40:52.168 right or very uncommon in HCC.

NOTE Confidence: 0.8055654

00:40:52.170 --> 00:40:54.956 I have sequence in patients this year,

NOTE Confidence: 0.8055654

00:40:54.960 --> 00:40:57.510 especially ones that had no underlying

NOTE Confidence: 0.8055654

00:40:57.510 --> 00:40:59.969 cirrhosis and this kind of confusing

NOTE Confidence: 0.8055654

00:40:59.969 --> 00:41:02.370 why they developed HCC and we found

NOTE Confidence: 0.8055654

00:41:02.370 --> 00:41:04.838 a couple of Baraka carriers which

NOTE Confidence: 0.8055654

00:41:04.838 --> 00:41:07.298 have not been well described in

NOTE Confidence: 0.8055654

00:41:07.298 --> 00:41:09.288 the literature as thinking about

NOTE Confidence: 0.8055654

00:41:09.288 --> 00:41:10.880 HCC's abraco related disease.

NOTE Confidence: 0.85235196

00:41:10.880 --> 00:41:13.659 And we've seen some back one mutations,

NOTE Confidence: 0.85235196

00:41:13.660 --> 00:41:16.476 so I think it's you know it's interesting

NOTE Confidence: 0.85235196

00:41:16.476 --> 00:41:18.838 to find these select patients,

NOTE Confidence: 0.85235196

00:41:18.840 --> 00:41:21.222 although it's not clear that they

NOTE Confidence: 0.85235196

00:41:21.222 --> 00:41:23.880 necessarily, you know, respond better to.

NOTE Confidence: 0.85235196

00:41:23.880 --> 00:41:26.040 PARP inhibitors or that there's really

NOTE Confidence: 0.85235196

00:41:26.040 --> 00:41:27.979 necessarily other targeted therapy for them,

NOTE Confidence: 0.85235196

00:41:27.980 --> 00:41:30.524 but I think you know the more patients

NOTE Confidence: 0.85235196

00:41:30.524 --> 00:41:33.108 that we sequence and do testing on.

NOTE Confidence: 0.85235196

00:41:33.110 --> 00:41:35.846 We may. You know, we may find more.

NOTE Confidence: 0.85235196

00:41:35.850 --> 00:41:38.048 And of course you know a lot

NOTE Confidence: 0.85235196

00:41:38.048 --> 00:41:40.159 of the patients with HCC get

NOTE Confidence: 0.85235196

00:41:40.159 --> 00:41:42.349 treated in the absence of biopsy,

NOTE Confidence: 0.85235196

00:41:42.350 --> 00:41:44.060 which is really unique to

NOTE Confidence: 0.85235196

00:41:44.060 --> 00:41:45.428 this to this disease.

NOTE Confidence: 0.85235196

00:41:45.430 --> 00:41:47.482 And so going back to the

NOTE Confidence: 0.85235196

00:41:47.482 --> 00:41:48.850 BC else staging system.

NOTE Confidence: 0.85235196

00:41:48.850 --> 00:41:51.847 So I think this is an important slide to

NOTE Confidence: 0.85235196

00:41:51.847 --> 00:41:54.767 kind of circle circle back to right so?

NOTE Confidence: 0.85235196

00:41:54.770 --> 00:41:57.318 You know, thinking of the narrow role

NOTE Confidence: 0.85235196

00:41:57.318 --> 00:41:59.395 where oncology could fall kind of

NOTE Confidence: 0.85235196

00:41:59.395 --> 00:42:01.544 just in this advanced stage C group,

NOTE Confidence: 0.85235196

00:42:01.550 --> 00:42:03.518 you know we've now accumulated rates

NOTE Confidence: 0.85235196

00:42:03.518 --> 00:42:05.619 several different drugs in this category,

NOTE Confidence: 0.85235196

00:42:05.620 --> 00:42:07.846 so adding into seref and if now

NOTE Confidence: 0.85235196

00:42:07.846 --> 00:42:09.350 we have a tease.

NOTE Confidence: 0.85235196

00:42:09.350 --> 00:42:12.054 Oh, and Bev approved in the first line.

NOTE Confidence: 0.85235196

00:42:12.060 --> 00:42:13.755 Also Lynn VAT and approved

NOTE Confidence: 0.85235196

00:42:13.755 --> 00:42:15.450 in the first line cabins,

NOTE Confidence: 0.85235196

00:42:15.450 --> 00:42:17.145 antonym burgraff and IMMA ramucirumab

NOTE Confidence: 0.85235196

00:42:17.145 --> 00:42:18.840 approved in the second line.

NOTE Confidence: 0.85235196

00:42:18.840 --> 00:42:21.032 Also it be niveau right and then we

NOTE Confidence: 0.85235196

00:42:21.032 --> 00:42:23.635 have pen Bruen Niveau still kind of

NOTE Confidence: 0.85235196

00:42:23.635 --> 00:42:26.070 conditionally approved a single agent drugs.

NOTE Confidence: 0.85235196

00:42:26.070 --> 00:42:28.275 But I think those will be largely

NOTE Confidence: 0.85235196

00:42:28.275 --> 00:42:30.446 replaced soon by the multiple combination

NOTE Confidence: 0.85235196

00:42:30.446 --> 00:42:33.460 studies of data that's going to come out,

NOTE Confidence: 0.85235196

00:42:33.460 --> 00:42:35.524 and so we've really added a

NOTE Confidence: 0.85235196

00:42:35.524 --> 00:42:37.330 lot in this category here,

NOTE Confidence: 0.85235196

00:42:37.330 --> 00:42:39.794 but I think that even more importantly,

NOTE Confidence: 0.85235196

00:42:39.800 --> 00:42:42.110 right now we need to kind of

NOTE Confidence: 0.85235196

00:42:42.110 --> 00:42:44.374 think of the whole, you know,

NOTE Confidence: 0.85235196

00:42:44.374 --> 00:42:46.486 the whole staging system he ran.

NOTE Confidence: 0.85235196

00:42:46.490 --> 00:42:48.602 Really say now that we finally

NOTE Confidence: 0.85235196

00:42:48.602 --> 00:42:50.010 have more effective therapies.

NOTE Confidence: 0.85235196

00:42:50.010 --> 00:42:51.770 You know, in my mind,

NOTE Confidence: 0.85235196

00:42:51.770 --> 00:42:53.174 combination doesn't just mean

NOTE Confidence: 0.85235196

00:42:53.174 --> 00:42:54.929 combination of two systemic therapies,

NOTE Confidence: 0.85235196

00:42:54.930 --> 00:42:56.840 but it's really combination of.

NOTE Confidence: 0.85235196

00:42:56.840 --> 00:42:58.940 All the modalities that we

NOTE Confidence: 0.85235196

00:42:58.940 --> 00:43:00.620 use in this disease,

NOTE Confidence: 0.85235196

00:43:00.620 --> 00:43:02.300 with potentially systemic therapy,

NOTE Confidence: 0.85235196

00:43:02.300 --> 00:43:03.980 and so you know,

NOTE Confidence: 0.85235196

00:43:03.980 --> 00:43:06.500 there's a lot of interest now.

NOTE Confidence: 0.85235196

00:43:06.500 --> 00:43:08.600 I'm thinking of Advent therapy,

NOTE Confidence: 0.85235196

00:43:08.600 --> 00:43:10.433 thinking of combination

NOTE Confidence: 0.85235196

00:43:10.433 --> 00:43:12.877 therapy with local therapy.

NOTE Confidence: 0.85235196

00:43:12.880 --> 00:43:15.196 This study is that it weren't

NOTE Confidence: 0.85235196

00:43:15.196 --> 00:43:16.740 done in the past.

NOTE Confidence: 0.85235196

00:43:16.740 --> 00:43:17.512 You know,

NOTE Confidence: 0.85235196

00:43:17.512 --> 00:43:18.670 looked at Saraf,

NOTE Confidence: 0.85235196

00:43:18.670 --> 00:43:21.640 and it's so there was an adjutant fit study

NOTE Confidence: 0.85235196

00:43:21.640 --> 00:43:24.457 that looked at Seraphim after reception.

NOTE Confidence: 0.85235196

00:43:24.460 --> 00:43:26.004 That study was negative,

NOTE Confidence: 0.85235196

00:43:26.004 --> 00:43:28.320 but as far as I know,

NOTE Confidence: 0.85235196

00:43:28.320 --> 00:43:30.438 I don't think there's a tyrosine

NOTE Confidence: 0.85235196

00:43:30.438 --> 00:43:32.350 kinase inhibitor approved in any

NOTE Confidence: 0.85235196

00:43:32.350 --> 00:43:34.110 diseases adjutant therapy because,

NOTE Confidence: 0.85235196

00:43:34.110 --> 00:43:34.882 you know,

NOTE Confidence: 0.85235196

00:43:34.882 --> 00:43:37.970 when you think of the mechanism of action.

NOTE Confidence: 0.85235196

00:43:37.970 --> 00:43:40.280 I don't think it's actually really

NOTE Confidence: 0.85235196

00:43:40.280 --> 00:43:41.435 illuminating microscopic disease,

NOTE Confidence: 0.85235196

00:43:41.440 --> 00:43:43.550 and so it's not surprising.

NOTE Confidence: 0.85235196

00:43:43.550 --> 00:43:45.345 I guess in retrospect that

NOTE Confidence: 0.85235196

00:43:45.345 --> 00:43:47.140 it wasn't a positive study.

NOTE Confidence: 0.85235196

00:43:47.140 --> 00:43:49.506 There was also the first study that

NOTE Confidence: 0.85235196

00:43:49.506 --> 00:43:52.252 I that I opened when I came here

NOTE Confidence: 0.85235196

00:43:52.252 --> 00:43:55.163 was the E Card 1208 study which was

NOTE Confidence: 0.85235196

00:43:55.163 --> 00:43:57.907 looking at the role of adding saraf

NOTE Confidence: 0.85235196

00:43:57.910 --> 00:43:59.710 number placebo to sequential tastes.

NOTE Confidence: 0.85235196

00:43:59.710 --> 00:44:00.787 And you know,

NOTE Confidence: 0.85235196

00:44:00.787 --> 00:44:03.300 I think it's interesting 'cause going back.

NOTE Confidence: 0.85235196

00:44:03.300 --> 00:44:03.964 You know,

NOTE Confidence: 0.85235196

00:44:03.964 --> 00:44:05.956 to almost 10 years ago now

NOTE Confidence: 0.85235196

00:44:05.956 --> 00:44:07.960 you know doing this study.

NOTE Confidence: 0.85235196

00:44:07.960 --> 00:44:10.480 It accrued really poorly across the country,

NOTE Confidence: 0.85235196

00:44:10.480 --> 00:44:12.628 and so the study never finished.

NOTE Confidence: 0.85235196

00:44:12.630 --> 00:44:13.746 Accrual and it,

NOTE Confidence: 0.85235196

00:44:13.746 --> 00:44:14.490 kind of.

NOTE Confidence: 0.88146096

00:44:14.490 --> 00:44:17.034 Ended halfway through the data somehow

NOTE Confidence: 0.88146096

00:44:17.034 --> 00:44:19.359 is still not published from it.

NOTE Confidence: 0.88146096

00:44:19.360 --> 00:44:22.083 There was another study in the UK

NOTE Confidence: 0.88146096

00:44:22.083 --> 00:44:24.589 that looked at a similar question

NOTE Confidence: 0.88146096

00:44:24.589 --> 00:44:27.343 in a smaller way, but you know,

NOTE Confidence: 0.88146096

00:44:27.343 --> 00:44:29.870 I think partially why it didn't accrue

NOTE Confidence: 0.88146096

00:44:29.940 --> 00:44:32.688 well was because there wasn't the

NOTE Confidence: 0.88146096

00:44:32.688 --> 00:44:34.968 kind of multidisciplinary groups that

NOTE Confidence: 0.88146096

00:44:34.968 --> 00:44:37.224 were able to do studies together.

NOTE Confidence: 0.88146096

00:44:37.230 --> 00:44:39.810 Because this study really required a

NOTE Confidence: 0.88146096

00:44:39.810 --> 00:44:41.530 relationship with interventional radiology

NOTE Confidence: 0.88146096

00:44:41.593 --> 00:44:43.717 that allowed everyone to work together,

NOTE Confidence: 0.88146096

00:44:43.720 --> 00:44:45.830 an really approach the patients.

NOTE Confidence: 0.88146096

00:44:45.830 --> 00:44:48.014 Before they moved on to systemic

NOTE Confidence: 0.88146096

00:44:48.014 --> 00:44:49.966 therapy to get them interested

NOTE Confidence: 0.88146096

00:44:49.966 --> 00:44:52.486 in the study and work together.

NOTE Confidence: 0.88146096

00:44:52.490 --> 00:44:55.618 Which is why I think we're in such

NOTE Confidence: 0.88146096

00:44:55.618 --> 00:44:58.274 a different place now in 2021 that

NOTE Confidence: 0.88146096

00:44:58.274 --> 00:45:01.510 I think we have the ability at Yale,

NOTE Confidence: 0.88146096

00:45:01.510 --> 00:45:04.247 as do other centers to really do

NOTE Confidence: 0.88146096

00:45:04.247 --> 00:45:05.420 multidisciplinary studies like

NOTE Confidence: 0.88146096

00:45:05.490 --> 00:45:06.609 the AGEMENT study,

NOTE Confidence: 0.88146096

00:45:06.610 --> 00:45:08.565 and like the combination with

NOTE Confidence: 0.88146096

00:45:08.565 --> 00:45:09.738 local therapy study.

NOTE Confidence: 0.88146096

00:45:09.740 --> 00:45:12.176 And so I'm excited to really think

NOTE Confidence: 0.88146096

00:45:12.176 --> 00:45:15.164 about what the role is for combination

NOTE Confidence: 0.88146096

00:45:15.164 --> 00:45:17.494 therapy in this intermediate stage.

NOTE Confidence: 0.88146096

00:45:17.500 --> 00:45:20.372 You know group and so I just wanted

NOTE Confidence: 0.88146096

00:45:20.372 --> 00:45:22.545 to mention a couple of studies

NOTE Confidence: 0.88146096

00:45:22.545 --> 00:45:25.080 that we have open now at Yale.

NOTE Confidence: 0.88146096

00:45:25.080 --> 00:45:28.329 So one of them is the Keynote 937 study.

NOTE Confidence: 0.88146096

00:45:28.330 --> 00:45:30.647 So this study is looking at Agilent

NOTE Confidence: 0.88146096

00:45:30.647 --> 00:45:32.659 Pember Lizum app versus placebo.

NOTE Confidence: 0.88146096

00:45:32.660 --> 00:45:35.468 So for patients that have had a complete

NOTE Confidence: 0.88146096

00:45:35.468 --> 00:45:36.964 radiologic response after surgical

NOTE Confidence: 0.88146096

00:45:36.964 --> 00:45:39.160 resection or local ablation of HCC,

NOTE Confidence: 0.88146096

00:45:39.160 --> 00:45:41.340 they're planning to enroll

NOTE Confidence: 0.88146096

00:45:41.340 --> 00:45:43.520 close to 1000 patients.

NOTE Confidence: 0.88146096

00:45:43.520 --> 00:45:46.268 In one to one randomization September,

NOTE Confidence: 0.88146096

00:45:46.270 --> 00:45:47.224 Liz, member,

NOTE Confidence: 0.88146096

00:45:47.224 --> 00:45:47.701 placebo,

NOTE Confidence: 0.88146096

00:45:47.701 --> 00:45:51.706 which would be for one year and then

NOTE Confidence: 0.88146096

00:45:51.706 --> 00:45:54.586 they'll be followed for survival

NOTE Confidence: 0.88146096

00:45:54.586 --> 00:45:57.250 with primary objectives of of.

NOTE Confidence: 0.88146096

00:45:57.250 --> 00:45:59.212 Re recurrence free survival in an

NOTE Confidence: 0.88146096

00:45:59.212 --> 00:46:01.348 overall survival and also safety and

NOTE Confidence: 0.88146096

00:46:01.348 --> 00:46:03.640 patient reported outcomes will be collected,

NOTE Confidence: 0.88146096

00:46:03.640 --> 00:46:06.480 so I think this is an interesting study.

NOTE Confidence: 0.88146096

00:46:06.480 --> 00:46:08.965 This is not the only adjutant study,

NOTE Confidence: 0.88146096

00:46:08.970 --> 00:46:09.632 you know.

NOTE Confidence: 0.88146096

00:46:09.632 --> 00:46:11.287 There's other companies that are

NOTE Confidence: 0.88146096

00:46:11.287 --> 00:46:13.230 doing kind of similar design.

NOTE Confidence: 0.88146096

00:46:13.230 --> 00:46:14.295 Similar design studies,

NOTE Confidence: 0.88146096

00:46:14.295 --> 00:46:16.780 so I think this will be interesting.

NOTE Confidence: 0.88146096

00:46:16.780 --> 00:46:19.223 And then I wanted to mention that

NOTE Confidence: 0.88146096

00:46:19.223 --> 00:46:22.138 we also have a study open of the

NOTE Confidence: 0.88146096

00:46:22.138 --> 00:46:24.339 safety and efficacy of live at

NOTE Confidence: 0.88146096

00:46:24.339 --> 00:46:26.355 and it was Pember Lizum app.

NOTE Confidence: 0.88146096

00:46:26.360 --> 00:46:27.828 So one of the.

NOTE Confidence: 0.88146096

00:46:27.828 --> 00:46:29.296 Doublet regimens that's being

NOTE Confidence: 0.88146096

00:46:29.296 --> 00:46:31.738 looked at in the advanced setting.

NOTE Confidence: 0.88146096

00:46:31.740 --> 00:46:34.068 That's a typo there versus placebo

NOTE Confidence: 0.88146096

00:46:34.068 --> 00:46:35.620 in combination with tastes

NOTE Confidence: 0.88146096

00:46:35.689 --> 00:46:37.089 and David Mann office.

NOTE Confidence: 0.88146096

00:46:37.090 --> 00:46:40.138 The Pi of this study here at Yale,

NOTE Confidence: 0.88146096

00:46:40.140 --> 00:46:42.050 and we have the primary

NOTE Confidence: 0.88146096

00:46:42.050 --> 00:46:43.196 outcomes of progression,

NOTE Confidence: 0.88146096

00:46:43.200 --> 00:46:45.110 free survival and overall survival,

NOTE Confidence: 0.88146096

00:46:45.110 --> 00:46:47.115 and then multiple secondary outcomes

NOTE Confidence: 0.88146096

00:46:47.115 --> 00:46:49.895 that will be looked at by resist

NOTE Confidence: 0.88146096

00:46:49.895 --> 00:46:51.989 1.1 and by the modified resist.

NOTE Confidence: 0.88146096

00:46:51.990 --> 00:46:54.276 And so I think you know,

NOTE Confidence: 0.88146096

00:46:54.280 --> 00:46:56.770 and again, there's other studies in

NOTE Confidence: 0.88146096

00:46:56.770 --> 00:46:58.959 combination with tastes and why 90.

NOTE Confidence: 0.88146096

00:46:58.960 --> 00:47:02.570 That are in development or, you know,

NOTE Confidence: 0.88146096

00:47:02.570 --> 00:47:05.145 recently started in the country.

NOTE Confidence: 0.88146096

00:47:05.150 --> 00:47:09.654 And I think this will give us really

NOTE Confidence: 0.88146096

00:47:09.654 --> 00:47:12.378 interesting information to see you know,

NOTE Confidence: 0.88146096

00:47:12.380 --> 00:47:15.350 are these patients kind of better

NOTE Confidence: 0.88146096

00:47:15.350 --> 00:47:17.952 off by getting systemic therapy

NOTE Confidence: 0.88146096

00:47:17.952 --> 00:47:20.627 earlier in the algorithm and.

NOTE Confidence: 0.831055

00:47:22.710 --> 00:47:25.671 We also are planning to open the

NOTE Confidence: 0.831055

00:47:25.671 --> 00:47:27.939 Morpheus HCC study so this is,

NOTE Confidence: 0.831055

00:47:27.940 --> 00:47:30.508 uh, so Genentech has this platform

NOTE Confidence: 0.831055

00:47:30.508 --> 00:47:33.026 called Morpheus where it allows them

NOTE Confidence: 0.831055

00:47:33.026 --> 00:47:35.567 to do a bunch of small protocols.

NOTE Confidence: 0.831055

00:47:35.570 --> 00:47:37.733 Kind of that can cycle into the

NOTE Confidence: 0.831055

00:47:37.733 --> 00:47:39.820 trial as there's new combinations

NOTE Confidence: 0.831055

00:47:39.820 --> 00:47:42.008 that look potentially interesting.

NOTE Confidence: 0.831055

00:47:42.010 --> 00:47:44.768 So the competitor the comparator arm in

NOTE Confidence: 0.831055

00:47:44.768 --> 00:47:48.040 this study is the combination of a tease.

NOTE Confidence: 0.831055

00:47:48.040 --> 00:47:49.177 Oh and Bev.

NOTE Confidence: 0.831055

00:47:49.177 --> 00:47:51.830 So all patients get that and then

NOTE Confidence: 0.831055

00:47:51.920 --> 00:47:55.040 right now the experimental stage one.

NOTE Confidence: 0.831055

00:47:55.040 --> 00:47:57.539 Looks at a drug added called to

NOTE Confidence: 0.831055

00:47:57.539 --> 00:48:00.329 Raghuram AB and then the other one

NOTE Confidence: 0.831055

00:48:00.329 --> 00:48:02.789 is totalism AB and there's actually

NOTE Confidence: 0.831055

00:48:02.871 --> 00:48:05.479 going to be 2 new arms opening soon

NOTE Confidence: 0.831055

00:48:05.479 --> 00:48:07.990 which I can tell you more about.

NOTE Confidence: 0.831055

00:48:07.990 --> 00:48:10.552 Once once we have those open this

NOTE Confidence: 0.831055

00:48:10.552 --> 00:48:12.799 study we don't have open yet,

NOTE Confidence: 0.831055

00:48:12.800 --> 00:48:15.131 but once the two new arms open

NOTE Confidence: 0.831055

00:48:15.131 --> 00:48:17.609 will will be opening the study.

NOTE Confidence: 0.831055

00:48:17.610 --> 00:48:20.200 Hopefully in the next couple of months.

NOTE Confidence: 0.831055

00:48:20.200 --> 00:48:23.644 So this will be a good first

NOTE Confidence: 0.831055

00:48:23.644 --> 00:48:25.120 line systemic therapy.

NOTE Confidence: 0.831055

00:48:25.120 --> 00:48:29.240 Option for our patients.

NOTE Confidence: 0.831055

00:48:29.240 --> 00:48:30.780 And so you know,

NOTE Confidence: 0.831055

00:48:30.780 --> 00:48:32.705 I just wanted to mention,

NOTE Confidence: 0.831055

00:48:32.710 --> 00:48:33.360 as Mario,

NOTE Confidence: 0.831055

00:48:33.360 --> 00:48:34.010 you know,

NOTE Confidence: 0.831055

00:48:34.010 --> 00:48:35.635 was discussing in the introduction

NOTE Confidence: 0.831055

00:48:35.635 --> 00:48:37.933 that this disease really requires

NOTE Confidence: 0.831055

00:48:37.933 --> 00:48:38.889 multidisciplinary care.

NOTE Confidence: 0.831055

00:48:38.890 --> 00:48:41.344 I really enjoy meeting with my

NOTE Confidence: 0.831055

00:48:41.344 --> 00:48:42.980 colleagues every Thursday at

NOTE Confidence: 0.831055

00:48:43.056 --> 00:48:45.066 our at our liver tumor board.

NOTE Confidence: 0.831055

00:48:45.070 --> 00:48:46.069 And, you know,

NOTE Confidence: 0.831055

00:48:46.069 --> 00:48:48.067 I think we have great discussions

NOTE Confidence: 0.831055

00:48:48.067 --> 00:48:50.239 on the patients because even

NOTE Confidence: 0.831055

00:48:50.239 --> 00:48:52.003 though there are guidelines,

NOTE Confidence: 0.831055

00:48:52.010 --> 00:48:54.038 they really are just guidelines and

NOTE Confidence: 0.831055

00:48:54.038 --> 00:48:56.346 and there never a replacement for

NOTE Confidence: 0.831055

00:48:56.346 --> 00:48:58.576 the real discussion that happens,

NOTE Confidence: 0.831055

00:48:58.580 --> 00:48:59.849 you know, centered.

NOTE Confidence: 0.831055

00:48:59.849 --> 00:49:02.360 For each patient, and so you know,

NOTE Confidence: 0.831055

00:49:02.360 --> 00:49:04.954 I think as we have more systemic

NOTE Confidence: 0.831055

00:49:04.954 --> 00:49:08.230 therapy options, we have to think about,

NOTE Confidence: 0.831055

00:49:08.230 --> 00:49:10.926 you know the role for that and how

NOTE Confidence: 0.831055

00:49:10.926 --> 00:49:12.946 that affects the other modalities

NOTE Confidence: 0.831055

00:49:12.946 --> 00:49:15.061 of treatment that we're giving

NOTE Confidence: 0.831055

00:49:15.061 --> 00:49:17.710 and how best to sequence things.

NOTE Confidence: 0.831055

00:49:17.710 --> 00:49:20.545 And it's been really great for me

NOTE Confidence: 0.831055

00:49:20.545 --> 00:49:23.303 over the last 10 years to have

NOTE Confidence: 0.831055

00:49:23.303 --> 00:49:26.000 such a great team to work with,

NOTE Confidence: 0.831055

00:49:26.000 --> 00:49:28.779 and also to see so much growth

NOTE Confidence: 0.831055

00:49:28.779 --> 00:49:30.720 and new treatment options.

NOTE Confidence: 0.831055

00:49:30.720 --> 00:49:32.073 For our patients,

NOTE Confidence: 0.831055

00:49:32.073 --> 00:49:35.230 so with that I'll end in leave

NOTE Confidence: 0.831055

00:49:35.325 --> 00:49:37.577 some room for questions.

NOTE Confidence: 0.831055

00:49:37.580 --> 00:49:38.560 Thank you.

NOTE Confidence: 0.72237843

00:49:43.720 --> 00:49:46.620 Fuller's courses then at Andrew.

NOTE Confidence: 0.72237843

00:49:46.620 --> 00:49:50.622 Very successful 10 years in which

NOTE Confidence: 0.72237843

00:49:50.622 --> 00:49:54.493 we saw everything changing so we

NOTE Confidence: 0.72237843

00:49:54.493 --> 00:49:57.745 have already a few questions one.

NOTE Confidence: 0.72237843

00:49:57.750 --> 00:50:01.684 Is a. From Doctor Rohit Gupta and

NOTE Confidence: 0.72237843

00:50:01.684 --> 00:50:05.697 the question is would you stop at

NOTE Confidence: 0.72237843

00:50:05.697 --> 00:50:09.727 ease or Bev completely if they do

NOTE Confidence: 0.72237843

00:50:09.727 --> 00:50:13.369 have very cell bleed on treatment?

NOTE Confidence: 0.85653335

00:50:14.830 --> 00:50:17.310 Yeah, you know that's that's a good question.

NOTE Confidence: 0.85653335

00:50:17.310 --> 00:50:19.782 I mean, so I guess the question then

NOTE Confidence: 0.85653335

00:50:19.782 --> 00:50:22.267 is you know if they could be so.

NOTE Confidence: 0.85653335

00:50:22.270 --> 00:50:24.750 I mean, hopefully the risk is very low.

NOTE Confidence: 0.85653335

00:50:24.750 --> 00:50:26.920 'cause if we're selecting the right patients,

NOTE Confidence: 0.85653335

00:50:26.920 --> 00:50:29.090 then hopefully they shouldn't have a bleed.

NOTE Confidence: 0.85653335

00:50:29.090 --> 00:50:31.146 And so I guess the question then you

NOTE Confidence: 0.85653335

00:50:31.146 --> 00:50:33.477 know if someone bleeds where they on

NOTE Confidence: 0.85653335

00:50:33.477 --> 00:50:35.910 anticoagulation do they need to be on

NOTE Confidence: 0.85653335

00:50:35.910 --> 00:50:37.770 an anticoagulation and could they be

NOTE Confidence: 0.85653335

00:50:37.770 --> 00:50:39.494 banded and then be considered back?

NOTE Confidence: 0.85653335

00:50:39.494 --> 00:50:42.420 Kind of in a low risk population you know.

NOTE Confidence: 0.85653335

00:50:42.420 --> 00:50:44.948 I will mention that there was another arm

NOTE Confidence: 0.85653335

00:50:44.948 --> 00:50:47.895 on the study from the Phase one study so.

NOTE Confidence: 0.85653335

00:50:47.900 --> 00:50:49.868 After the arm A was positive,

NOTE Confidence: 0.85653335

00:50:49.870 --> 00:50:52.425 the combination the FDA asked for data

NOTE Confidence: 0.85653335

00:50:52.425 --> 00:50:54.788 for single agent at Easel is a map,

NOTE Confidence: 0.85653335

00:50:54.790 --> 00:50:57.206 so there was another arm on the Phase

NOTE Confidence: 0.85653335

00:50:57.206 --> 00:50:59.612 one study that looked at the combination

NOTE Confidence: 0.85653335

00:50:59.612 --> 00:51:02.377 versus a tease oh alone and you really

NOTE Confidence: 0.85653335

00:51:02.377 --> 00:51:04.933 don't get the same responses with a tease.

NOTE Confidence: 0.85653335

00:51:04.933 --> 00:51:05.539 Oh alone.

NOTE Confidence: 0.85653335

00:51:05.539 --> 00:51:08.096 So I think if you could you would

NOTE Confidence: 0.85653335

00:51:08.096 --> 00:51:10.651 try to continue the you know the

NOTE Confidence: 0.85653335

00:51:10.651 --> 00:51:12.827 combination if if you were able to,

NOTE Confidence: 0.85653335

00:51:12.830 --> 00:51:15.414 you know bans them or you know put

NOTE Confidence: 0.85653335

00:51:15.414 --> 00:51:17.969 them back in a lower risk category.

NOTE Confidence: 0.85653335

00:51:17.970 --> 00:51:19.014 I haven't had that.

NOTE Confidence: 0.85653335

00:51:19.014 --> 00:51:20.840 I haven't been in that situation yet,

NOTE Confidence: 0.85653335

00:51:20.840 --> 00:51:22.667 but I think I think it's something

NOTE Confidence: 0.85653335

00:51:22.667 --> 00:51:24.760 that you know. If we could, we would.

NOTE Confidence: 0.85653335

00:51:24.760 --> 00:51:27.622 We would try to get them back on systemic

NOTE Confidence: 0.85653335

00:51:27.622 --> 00:51:29.570 therapy if they were responding.

NOTE Confidence: 0.85653335

00:51:29.570 --> 00:51:29.960 So

NOTE Confidence: 0.8166275

00:51:29.960 --> 00:51:33.810 let let me ask you a question in this regard,

NOTE Confidence: 0.8166275

00:51:33.810 --> 00:51:36.120 but so outside of a try,

NOTE Confidence: 0.8166275

00:51:36.120 --> 00:51:38.406 we're probably you will have to

NOTE Confidence: 0.8166275

00:51:38.406 --> 00:51:40.739 have a certain month of leeway.

NOTE Confidence: 0.8166275

00:51:40.740 --> 00:51:42.665 You know you probably need

NOTE Confidence: 0.8166275

00:51:42.665 --> 00:51:44.590 to have a recent endoscopy,

NOTE Confidence: 0.8166275

00:51:44.590 --> 00:51:47.670 but we we do have a very well

NOTE Confidence: 0.8166275

00:51:47.670 --> 00:51:49.876 detailed guidelines, so you know what,

NOTE Confidence: 0.8166275

00:51:49.876 --> 00:51:52.670 how many times the patient should undergo,

NOTE Confidence: 0.8166275

00:51:52.670 --> 00:51:55.750 but it's still in the Earth in the

NOTE Confidence: 0.8166275

00:51:55.750 --> 00:51:57.909 Oscar people, very sick screening,

NOTE Confidence: 0.8166275

00:51:57.909 --> 00:52:00.687 you know where they are in.

NOTE Confidence: 0.8166275

00:52:00.690 --> 00:52:02.370 A beta blocker there.

NOTE Confidence: 0.8166275

00:52:02.370 --> 00:52:05.310 Nothing but the blocker, so it's it's

NOTE Confidence: 0.8166275

00:52:05.310 --> 00:52:07.830 a pretty well a detailed protocol.

NOTE Confidence: 0.8166275

00:52:07.830 --> 00:52:11.406 In order for you to put the patient

NOTE Confidence: 0.8166275

00:52:11.406 --> 00:52:15.436 in a in one of such a treatment.

NOTE Confidence: 0.8166275

00:52:15.440 --> 00:52:16.744 What do you need?

NOTE Confidence: 0.8166275

00:52:16.744 --> 00:52:18.855 I mean, do you need somebody who

NOTE Confidence: 0.8166275

00:52:18.855 --> 00:52:21.000 has already done at an endoscopy?

NOTE Confidence: 0.8166275

00:52:21.000 --> 00:52:22.185 Azie anhyzer prophylaxis?

NOTE Confidence: 0.8166275

00:52:22.185 --> 00:52:24.950 Or do you need to have something?

NOTE Confidence: 0.8166275

00:52:24.950 --> 00:52:27.253 A more recent and what are the

NOTE Confidence: 0.8166275

00:52:27.253 --> 00:52:29.110 mechanism of breathing in that case?

NOTE Confidence: 0.8341714

00:52:30.020 --> 00:52:32.830 Yeah, so I mean you know the truth is right.

NOTE Confidence: 0.8341714

00:52:32.830 --> 00:52:34.664 So we treat a lot of other

NOTE Confidence: 0.8341714

00:52:34.664 --> 00:52:35.920 cancers like colon cancer.

NOTE Confidence: 0.8341714

00:52:35.920 --> 00:52:38.172 Bevacizumab is a staple of therapy, you know.

NOTE Confidence: 0.8341714

00:52:38.172 --> 00:52:39.858 Unfortunately we just see bleeding sometimes.

NOTE Confidence: 0.8341714

00:52:39.860 --> 00:52:41.701 You know we see bleeding from the

NOTE Confidence: 0.8341714

00:52:41.701 --> 00:52:44.013 tumor or we just see you know we

NOTE Confidence: 0.8341714

00:52:44.013 --> 00:52:45.473 see other causes of bleeding.

NOTE Confidence: 0.8341714

00:52:45.480 --> 00:52:47.160 So it's not only variceal bleed,

NOTE Confidence: 0.8341714

00:52:47.160 --> 00:52:49.374 you know there was a patient on the study

NOTE Confidence: 0.8341714

00:52:49.374 --> 00:52:51.658 that just had like a abdominal hemorrhage.

NOTE Confidence: 0.8341714

00:52:51.660 --> 00:52:52.431 So you know.

NOTE Confidence: 0.8341714

00:52:52.431 --> 00:52:54.230 So there's always a risk with Bevis

NOTE Confidence: 0.8341714

00:52:54.288 --> 00:52:56.176 ISM AB and let you know when patients

NOTE Confidence: 0.8341714

00:52:56.176 --> 00:52:57.805 are on anticoagulation, right?

NOTE Confidence: 0.8341714

00:52:57.805 --> 00:52:59.520 You have to think about that too

NOTE Confidence: 0.8341714

00:52:59.520 --> 00:53:01.658 if you think they might be having

NOTE Confidence: 0.8341714

00:53:01.658 --> 00:53:03.276 a surgical procedure, right? So?

NOTE Confidence: 0.8341714

00:53:03.276 --> 00:53:05.572 You know there's more thought around that,

NOTE Confidence: 0.8341714

00:53:05.580 --> 00:53:07.638 but but overall you know if they've

NOTE Confidence: 0.8341714

00:53:07.638 --> 00:53:08.520 had an endoscopy.

NOTE Confidence: 0.8341714

00:53:08.520 --> 00:53:10.648 Even if it was a little bit out

NOTE Confidence: 0.8341714

00:53:10.648 --> 00:53:12.338 of six months, but I,

NOTE Confidence: 0.8341714

00:53:12.338 --> 00:53:14.396 but they have a hepatologist following them,

NOTE Confidence: 0.8341714

00:53:14.400 --> 00:53:16.458 who thinks that their risk is low.

NOTE Confidence: 0.8341714

00:53:16.460 --> 00:53:18.356 You know, I think right whenever

NOTE Confidence: 0.8341714

00:53:18.356 --> 00:53:20.280 whenever patients are not on a trial,

NOTE Confidence: 0.8341714

00:53:20.280 --> 00:53:22.198 I think there's always a little bit

NOTE Confidence: 0.8341714

00:53:22.198 --> 00:53:23.810 more leeway kind of discussion,

NOTE Confidence: 0.8341714

00:53:23.810 --> 00:53:24.394 you know,

NOTE Confidence: 0.8341714

00:53:24.394 --> 00:53:25.854 and thinking about each patient,

NOTE Confidence: 0.8341714

00:53:25.860 --> 00:53:27.972 I just think that you know it would

NOTE Confidence: 0.8341714

00:53:27.972 --> 00:53:29.100 be a mistake.

NOTE Confidence: 0.8341714

00:53:29.100 --> 00:53:31.512 I think for an oncologist to treat a patient

NOTE Confidence: 0.8341714

00:53:31.512 --> 00:53:33.709 like this without any hepatology input.

NOTE Confidence: 0.8341714

00:53:33.710 --> 00:53:34.164 You know,

NOTE Confidence: 0.8341714

00:53:34.164 --> 00:53:36.728 and so I think if you at least have the

NOTE Confidence: 0.8341714

00:53:36.728 --> 00:53:38.433 hepatology input of someone familiar

NOTE Confidence: 0.8341714

00:53:38.433 --> 00:53:40.887 with this with this data to really say,

NOTE Confidence: 0.8341714

00:53:40.890 --> 00:53:42.922 I think this patient is low risk even

NOTE Confidence: 0.8341714

00:53:42.922 --> 00:53:45.403 if you didn't do it exactly in the

NOTE Confidence: 0.8341714

00:53:45.403 --> 00:53:47.490 timeframe that was required on the child.

NOTE Confidence: 0.8341714

00:53:47.490 --> 00:53:48.920 I think that's that's fine,

NOTE Confidence: 0.8341714

00:53:48.920 --> 00:53:49.500 you know.

NOTE Confidence: 0.81392854

00:53:50.710 --> 00:53:51.386 Another question,

NOTE Confidence: 0.81392854

00:53:51.386 --> 00:53:53.076 thank you for your answer,

NOTE Confidence: 0.81392854

00:53:53.080 --> 00:53:54.504 and there's another question

NOTE Confidence: 0.81392854

00:53:54.504 --> 00:53:56.640 from Leshan why Japan is excluded

NOTE Confidence: 0.81392854

00:53:56.699 --> 00:53:58.475 and food Japan and US together.

NOTE Confidence: 0.81392854

00:53:58.480 --> 00:53:59.494 Any specific missing?

NOTE Confidence: 0.81392854

00:53:59.494 --> 00:54:00.846 Yeah, I don't know.

NOTE Confidence: 0.81392854

00:54:00.850 --> 00:54:03.546 You know I have a feeling that was

NOTE Confidence: 0.81392854

00:54:03.550 --> 00:54:05.578 more based on how the company

NOTE Confidence: 0.81392854

00:54:05.578 --> 00:54:06.930 was opening the study.

NOTE Confidence: 0.81392854

00:54:06.930 --> 00:54:08.076 Because you're right,

NOTE Confidence: 0.81392854

00:54:08.076 --> 00:54:10.750 I'm not really sure I saw that

NOTE Confidence: 0.81392854

00:54:10.824 --> 00:54:12.931 I saw that also in the trial

NOTE Confidence: 0.81392854

00:54:12.931 --> 00:54:15.380 design and I I don't have a good.

NOTE Confidence: 0.81392854

00:54:15.380 --> 00:54:18.084 I don't have a good answer for that,

NOTE Confidence: 0.81392854

00:54:18.090 --> 00:54:20.106 but I think it probably has

NOTE Confidence: 0.81392854

00:54:20.106 --> 00:54:22.295 to do with where the company

NOTE Confidence: 0.81392854

00:54:22.295 --> 00:54:24.587 is located and how they set.

NOTE Confidence: 0.81392854

00:54:24.590 --> 00:54:26.326 We set up the child because I

NOTE Confidence: 0.81392854

00:54:26.326 --> 00:54:27.796 don't think that there really

NOTE Confidence: 0.81392854

00:54:27.796 --> 00:54:29.128 is a separate signature.

NOTE Confidence: 0.778359

00:54:30.140 --> 00:54:33.216 OK, more questions so.