

WEBVTT

NOTE duration:"01:02:29"

NOTE recognizability:0.829

NOTE language:en-us

NOTE Confidence: 0.657168135

00:00:03.990 --> 00:00:07.938 Start introducing your Natalia.

NOTE Confidence: 0.657168135

00:00:07.940 --> 00:00:10.612 Today's grand round speaker is

NOTE Confidence: 0.657168135

00:00:10.612 --> 00:00:14.718 Natalia Buza, our very own.

NOTE Confidence: 0.657168135

00:00:14.720 --> 00:00:17.879 Most of us know Natalia we work with her,

NOTE Confidence: 0.657168135

00:00:17.880 --> 00:00:20.304 we see her in the hallways

NOTE Confidence: 0.657168135

00:00:20.304 --> 00:00:24.630 and on the microscope Natalia.

NOTE Confidence: 0.657168135

00:00:24.630 --> 00:00:27.858 Did her medical schooling in Hungary

NOTE Confidence: 0.657168135

00:00:27.858 --> 00:00:31.318 from the University of PECS in 1999,

NOTE Confidence: 0.657168135

00:00:31.318 --> 00:00:34.208 and she joined the pathology

NOTE Confidence: 0.657168135

00:00:34.208 --> 00:00:37.127 residency program at the same

NOTE Confidence: 0.657168135

00:00:37.127 --> 00:00:39.657 place and after two years,

NOTE Confidence: 0.657168135

00:00:39.660 --> 00:00:42.918 not all year moved to complete

NOTE Confidence: 0.657168135

00:00:42.918 --> 00:00:46.462 the remaining two years of her

NOTE Confidence: 0.657168135

00:00:46.462 --> 00:00:48.998 pathology residency at National  
NOTE Confidence: 0.657168135

00:00:48.998 --> 00:00:52.540 Institute of Oncology in Budapest.  
NOTE Confidence: 0.657168135

00:00:52.540 --> 00:00:56.536 After her training in pathology,  
NOTE Confidence: 0.657168135

00:00:56.536 --> 00:00:59.560 Natalia spent a year at Tulane  
NOTE Confidence: 0.657168135

00:00:59.656 --> 00:01:01.603 University Pathology Department  
NOTE Confidence: 0.657168135

00:01:01.603 --> 00:01:05.497 as visiting physician so early on,  
NOTE Confidence: 0.657168135

00:01:05.500 --> 00:01:08.240 Natalia had established her  
NOTE Confidence: 0.657168135

00:01:08.240 --> 00:01:10.980 career path in pathology.  
NOTE Confidence: 0.657168135

00:01:10.980 --> 00:01:15.495 We were lucky to recruit Natalia to  
NOTE Confidence: 0.657168135

00:01:15.495 --> 00:01:19.068 yell pathology residency program in 2006  
NOTE Confidence: 0.657168135

00:01:19.068 --> 00:01:22.344 and Natalia finished her residency.  
NOTE Confidence: 0.657168135

00:01:22.344 --> 00:01:24.417 Became chief resident,  
NOTE Confidence: 0.657168135

00:01:24.420 --> 00:01:28.984 became a GY and and press fellow with  
NOTE Confidence: 0.657168135

00:01:28.984 --> 00:01:33.540 Doctor Tavassoli and then in 2010  
NOTE Confidence: 0.657168135

00:01:33.540 --> 00:01:36.890 Natalia became an assistant professor  
NOTE Confidence: 0.657168135

00:01:36.890 --> 00:01:41.253 with US and in 2016 very quickly.

NOTE Confidence: 0.657168135

00:01:41.253 --> 00:01:44.619 She was promoted to be an

NOTE Confidence: 0.657168135

00:01:44.619 --> 00:01:46.330 associate professor.

NOTE Confidence: 0.657168135

00:01:46.330 --> 00:01:50.646 I first met Natalia in 2009 when

NOTE Confidence: 0.657168135

00:01:50.646 --> 00:01:54.684 Natalia was a hot seat resident.

NOTE Confidence: 0.657168135

00:01:54.690 --> 00:01:57.108 And she was freaking out because

NOTE Confidence: 0.657168135

00:01:57.110 --> 00:01:59.168 someone had just asked her 15

NOTE Confidence: 0.657168135

00:01:59.168 --> 00:02:02.025 minutes ago to go to the head and

NOTE Confidence: 0.657168135

00:02:02.025 --> 00:02:04.131 neck tumor board and present the

NOTE Confidence: 0.657168135

00:02:04.206 --> 00:02:06.396 hair and act him aboard cases.

NOTE Confidence: 0.657168135

00:02:06.400 --> 00:02:08.040 Uhm?

NOTE Confidence: 0.657168135

00:02:08.040 --> 00:02:08.760 Anyway.

NOTE Confidence: 0.691064093478261

00:02:11.290 --> 00:02:14.181 Natalia is in addition also the associate

NOTE Confidence: 0.691064093478261

00:02:14.181 --> 00:02:17.003 director of the GY and Fellowship program

NOTE Confidence: 0.691064093478261

00:02:17.003 --> 00:02:20.570 and the Director of the GY and Journal Club,

NOTE Confidence: 0.691064093478261

00:02:20.570 --> 00:02:24.834 which is one of the best run Journal

NOTE Confidence: 0.691064093478261

00:02:24.834 --> 00:02:29.483 club in our department. Altogether,  
NOTE Confidence: 0.691064093478261

00:02:29.483 --> 00:02:33.596 Natalia has a total of 150 publications.  
NOTE Confidence: 0.691064093478261

00:02:33.596 --> 00:02:37.784 87 of these are original peer  
NOTE Confidence: 0.691064093478261

00:02:37.784 --> 00:02:41.890 reviewed papers. These include.  
NOTE Confidence: 0.691064093478261

00:02:41.890 --> 00:02:46.104 These do not include 25 book chapters.  
NOTE Confidence: 0.691064093478261

00:02:46.110 --> 00:02:49.410 Is book chapters do not include  
NOTE Confidence: 0.691064093478261

00:02:49.410 --> 00:02:54.799 18 chapters in the Blue Book on.  
NOTE Confidence: 0.691064093478261

00:02:54.800 --> 00:02:59.256 Tumors of the female genital tract and one  
NOTE Confidence: 0.691064093478261

00:02:59.256 --> 00:03:03.626 chapter in the pediatric tumor blue book.  
NOTE Confidence: 0.691064093478261

00:03:03.630 --> 00:03:07.725 In addition, she has 17 case reports,  
NOTE Confidence: 0.691064093478261

00:03:07.730 --> 00:03:11.140 three chapters in pathology outlines,  
NOTE Confidence: 0.691064093478261

00:03:11.140 --> 00:03:15.445 and she has contributed to or written  
NOTE Confidence: 0.691064093478261

00:03:15.445 --> 00:03:19.380 the CAP guidelines on GY and receptions  
NOTE Confidence: 0.691064093478261

00:03:19.380 --> 00:03:23.130 and all of this in the last 12 years.  
NOTE Confidence: 0.691064093478261

00:03:23.130 --> 00:03:26.298 Because I noticed that Natalia's first  
NOTE Confidence: 0.691064093478261

00:03:26.298 --> 00:03:29.478 paper was in 2009 with Doctor Tavassoli,

NOTE Confidence: 0.691064093478261  
00:03:29.478 --> 00:03:32.687 so I would give a shout out not  
NOTE Confidence: 0.691064093478261  
00:03:32.687 --> 00:03:34.423 just to Natalia, but.  
NOTE Confidence: 0.691064093478261  
00:03:34.423 --> 00:03:37.488 Also to our department for.  
NOTE Confidence: 0.691064093478261  
00:03:37.490 --> 00:03:41.836 Making it conducive to this  
NOTE Confidence: 0.691064093478261  
00:03:41.836 --> 00:03:44.860 phenomenal body of achievements.  
NOTE Confidence: 0.691064093478261  
00:03:44.860 --> 00:03:45.724 In addition,  
NOTE Confidence: 0.691064093478261  
00:03:45.724 --> 00:03:48.748 Natalia is on the editorial Board of  
NOTE Confidence: 0.691064093478261  
00:03:48.748 --> 00:03:51.886 Human Pathology and the International  
NOTE Confidence: 0.691064093478261  
00:03:51.886 --> 00:03:54.514 Journal of Gynecological Pathology,  
NOTE Confidence: 0.691064093478261  
00:03:54.520 --> 00:03:57.888 and she is also an ad hoc reviewer  
NOTE Confidence: 0.691064093478261  
00:03:57.890 --> 00:04:01.430 in on major.  
NOTE Confidence: 0.691064093478261  
00:04:01.430 --> 00:04:05.274 Journals of pathology Natalia  
NOTE Confidence: 0.691064093478261  
00:04:05.274 --> 00:04:07.970 is prominent in Uscap.  
NOTE Confidence: 0.691064093478261  
00:04:07.970 --> 00:04:10.518 She is a member of the abstract.  
NOTE Confidence: 0.691064093478261  
00:04:10.520 --> 00:04:13.584 She has served on the Abstract Review Board.  
NOTE Confidence: 0.691064093478261

00:04:13.590 --> 00:04:16.010 She has served as ambassadors.  
NOTE Confidence: 0.691064093478261

00:04:16.010 --> 00:04:18.680 She is moderated platform sessions.  
NOTE Confidence: 0.691064093478261

00:04:18.680 --> 00:04:19.799 In the past.  
NOTE Confidence: 0.691064093478261

00:04:19.799 --> 00:04:22.410 She is also a faculty mentor of  
NOTE Confidence: 0.691064093478261

00:04:22.502 --> 00:04:24.877 the men to escape mentoring.  
NOTE Confidence: 0.691064093478261

00:04:24.880 --> 00:04:27.930 Academy earlier has had several  
NOTE Confidence: 0.691064093478261

00:04:27.930 --> 00:04:32.430 short courses at a scab running for.  
NOTE Confidence: 0.691064093478261

00:04:32.430 --> 00:04:35.550 I believe for four consecutive years  
NOTE Confidence: 0.691064093478261

00:04:35.550 --> 00:04:40.184 and two of her short courses and and  
NOTE Confidence: 0.691064093478261

00:04:40.184 --> 00:04:43.176 an interactive microscope session  
NOTE Confidence: 0.691064093478261

00:04:43.176 --> 00:04:48.452 has been approved from 2022 onwards.  
NOTE Confidence: 0.691064093478261

00:04:48.452 --> 00:04:54.549 So Natalia Natalia's eminence in US Capiz.  
NOTE Confidence: 0.691064093478261

00:04:54.550 --> 00:05:00.540 Very laudable. She is.  
NOTE Confidence: 0.691064093478261

00:05:00.540 --> 00:05:04.170 A favored invited speaker both  
NOTE Confidence: 0.691064093478261

00:05:04.170 --> 00:05:06.348 nationally and internationally.  
NOTE Confidence: 0.691064093478261

00:05:06.350 --> 00:05:10.502 She has spoken in Canada and two

NOTE Confidence: 0.691064093478261  
00:05:10.502 --> 00:05:14.108 British societies and also in China.  
NOTE Confidence: 0.691064093478261  
00:05:14.110 --> 00:05:17.098 Natalia has been invited to give  
NOTE Confidence: 0.691064093478261  
00:05:17.098 --> 00:05:20.070 grand Rounds at MD Anderson.  
NOTE Confidence: 0.691064093478261  
00:05:20.070 --> 00:05:23.022 She has been a speaker at  
NOTE Confidence: 0.691064093478261  
00:05:23.022 --> 00:05:24.006 Princeton Symposium,  
NOTE Confidence: 0.691064093478261  
00:05:24.010 --> 00:05:27.280 one of the books that Natalia  
NOTE Confidence: 0.691064093478261  
00:05:27.280 --> 00:05:29.806 coauthored frozen sections in GY  
NOTE Confidence: 0.691064093478261  
00:05:29.806 --> 00:05:32.276 and pathology is actually in.  
NOTE Confidence: 0.691064093478261  
00:05:32.280 --> 00:05:33.873 Smilow frozen section.  
NOTE Confidence: 0.691064093478261  
00:05:33.873 --> 00:05:38.129 Sweet and it's I find it extremely helpful  
NOTE Confidence: 0.691064093478261  
00:05:38.129 --> 00:05:41.689 when I get a GY and broken section.  
NOTE Confidence: 0.691064093478261  
00:05:41.690 --> 00:05:45.550 And today's grand round is.  
NOTE Confidence: 0.691064093478261  
00:05:45.550 --> 00:05:47.790 Natalia is going to talk about it.  
NOTE Confidence: 0.691064093478261  
00:05:47.790 --> 00:05:51.560 This is her exemplary long-term  
NOTE Confidence: 0.691064093478261  
00:05:51.560 --> 00:05:56.020 work on bringing her to new.  
NOTE Confidence: 0.691064093478261

00:05:56.020 --> 00:06:00.604 Therapy in GGY and oncology and  
NOTE Confidence: 0.691064093478261

00:06:00.604 --> 00:06:04.010 with no further ado, I'm going to.  
NOTE Confidence: 0.680150086

00:06:06.160 --> 00:06:07.960 Give the floor to Natalia.  
NOTE Confidence: 0.903966018

00:06:09.900 --> 00:06:11.060 Thank you so much man.  
NOTE Confidence: 0.903966018

00:06:11.060 --> 00:06:13.559 Due for the very kind introduction and  
NOTE Confidence: 0.903966018

00:06:13.559 --> 00:06:16.240 and for this wonderful opportunity,  
NOTE Confidence: 0.903966018

00:06:16.240 --> 00:06:18.704 it is really a special a pleasure  
NOTE Confidence: 0.903966018

00:06:18.704 --> 00:06:21.550 for me to to speak in front  
NOTE Confidence: 0.903966018

00:06:21.550 --> 00:06:23.685 of my colleagues and friends,  
NOTE Confidence: 0.903966018

00:06:23.690 --> 00:06:25.298 even even though from my office.  
NOTE Confidence: 0.903966018

00:06:25.300 --> 00:06:26.578 But I I feel like I,  
NOTE Confidence: 0.903966018

00:06:26.580 --> 00:06:28.476 I'm I see all of you.  
NOTE Confidence: 0.903966018

00:06:28.480 --> 00:06:30.620 So I'm going to start  
NOTE Confidence: 0.903966018

00:06:30.620 --> 00:06:32.290 sharing my screen. Come.  
NOTE Confidence: 0.55535537

00:06:34.610 --> 00:06:37.498 OK. Can you see it?  
NOTE Confidence: 0.847580505

00:06:39.840 --> 00:06:43.746 Yep alright so as mentioned mentioned,

NOTE Confidence: 0.847580505

00:06:43.750 --> 00:06:47.166 this has been really a long term work.

NOTE Confidence: 0.847580505

00:06:47.170 --> 00:06:50.190 I've been working on.

NOTE Confidence: 0.847580505

00:06:50.190 --> 00:06:52.350 Or two in under meteor cancer

NOTE Confidence: 0.847580505

00:06:52.350 --> 00:06:54.749 for the past twelve years or so,

NOTE Confidence: 0.847580505

00:06:54.750 --> 00:06:57.822 and today, I'm going to give you an

NOTE Confidence: 0.847580505

00:06:57.822 --> 00:07:00.679 overview of the current status and

NOTE Confidence: 0.847580505

00:07:00.679 --> 00:07:03.179 future directions on this topic.

NOTE Confidence: 0.847580505

00:07:03.180 --> 00:07:06.048 First I'll start with.

NOTE Confidence: 0.847580505

00:07:06.050 --> 00:07:08.660 Brief overview of the Congo

NOTE Confidence: 0.847580505

00:07:08.660 --> 00:07:10.748 pathologic features of endometrial

NOTE Confidence: 0.847580505

00:07:10.748 --> 00:07:13.243 serous carcinoma for those of you

NOTE Confidence: 0.847580505

00:07:13.243 --> 00:07:16.288 not in GY and pathology and then

NOTE Confidence: 0.847580505

00:07:16.288 --> 00:07:19.732 give a historical overview of prior

NOTE Confidence: 0.847580505

00:07:19.732 --> 00:07:23.610 studies and trials and and her to

NOTE Confidence: 0.847580505

00:07:23.610 --> 00:07:26.945 anonymity of cancer and compare the

NOTE Confidence: 0.847580505

00:07:26.945 --> 00:07:30.455 features of her two expression and  
NOTE Confidence: 0.847580505

00:07:30.455 --> 00:07:33.232 amplification with the with those that  
NOTE Confidence: 0.847580505

00:07:33.232 --> 00:07:36.799 we know of breast and gastric cancer.  
NOTE Confidence: 0.847580505

00:07:36.800 --> 00:07:37.934 And finally,  
NOTE Confidence: 0.847580505

00:07:37.934 --> 00:07:40.202 I'll give practical recommendations  
NOTE Confidence: 0.847580505

00:07:40.202 --> 00:07:43.450 and talk about future directions.  
NOTE Confidence: 0.847580505

00:07:43.450 --> 00:07:47.142 So to start off, going back to the 1980s,  
NOTE Confidence: 0.847580505

00:07:47.142 --> 00:07:49.602 two Seminole papers were published  
NOTE Confidence: 0.847580505

00:07:49.602 --> 00:07:51.570 about the same time,  
NOTE Confidence: 0.847580505

00:07:51.570 --> 00:07:54.030 one from a pathology group.  
NOTE Confidence: 0.847580505

00:07:54.030 --> 00:07:55.850 Doctors Kempson and Hendrickson  
NOTE Confidence: 0.847580505

00:07:55.850 --> 00:07:58.125 described for the first time.  
NOTE Confidence: 0.847580505

00:07:58.130 --> 00:08:00.685 This tumor type uterine papillary  
NOTE Confidence: 0.847580505

00:08:00.685 --> 00:08:01.707 serous carcinoma,  
NOTE Confidence: 0.847580505

00:08:01.710 --> 00:08:04.920 which they recognized as a highly  
NOTE Confidence: 0.847580505

00:08:04.920 --> 00:08:08.430 malignant form of endometrial adenocarcinoma.

NOTE Confidence: 0.847580505

00:08:08.430 --> 00:08:11.430 At the same time, Jan Bachman,

NOTE Confidence: 0.847580505

00:08:11.430 --> 00:08:14.320 a physician.

NOTE Confidence: 0.847580505

00:08:14.320 --> 00:08:17.800 From gynecologist from the Soviet Union,

NOTE Confidence: 0.847580505

00:08:17.800 --> 00:08:20.275 published the clinical features that

NOTE Confidence: 0.847580505

00:08:20.275 --> 00:08:23.230 he noticed that and meteor cancer

NOTE Confidence: 0.847580505

00:08:23.230 --> 00:08:27.570 really has to drastically different.

NOTE Confidence: 0.847580505

00:08:27.570 --> 00:08:29.340 Uniquely different that the genetic

NOTE Confidence: 0.847580505

00:08:29.340 --> 00:08:31.426 types and he called them type

NOTE Confidence: 0.847580505

00:08:31.426 --> 00:08:34.744 one and type two type 1 being the

NOTE Confidence: 0.847580505

00:08:34.744 --> 00:08:37.068 more indolent form associated

NOTE Confidence: 0.847580505

00:08:37.068 --> 00:08:38.918 with estrogen access.

NOTE Confidence: 0.847580505

00:08:38.918 --> 00:08:41.670 Compared with Type 2,

NOTE Confidence: 0.847580505

00:08:41.670 --> 00:08:43.915 which would include uterine serous

NOTE Confidence: 0.847580505

00:08:43.915 --> 00:08:46.736 carcinomas that had a much more

NOTE Confidence: 0.847580505

00:08:46.736 --> 00:08:49.231 aggressive behavior and had no

NOTE Confidence: 0.847580505

00:08:49.231 --> 00:08:53.448 association with estrogen access in patients.

NOTE Confidence: 0.847580505

00:08:53.450 --> 00:08:54.292 Later on,

NOTE Confidence: 0.847580505

00:08:54.292 --> 00:08:57.268 it was recognized that these tumors actually

NOTE Confidence: 0.847580505

00:08:57.268 --> 00:08:59.508 can have other architectural patterns,

NOTE Confidence: 0.847580505

00:08:59.510 --> 00:09:01.406 not just the capillary,

NOTE Confidence: 0.847580505

00:09:01.406 --> 00:09:03.776 although it's commonly seen here,

NOTE Confidence: 0.847580505

00:09:03.780 --> 00:09:06.138 you can see in the upper

NOTE Confidence: 0.847580505

00:09:06.138 --> 00:09:07.317 left corner papillary,

NOTE Confidence: 0.847580505

00:09:07.320 --> 00:09:09.553 but they can also have a glandular

NOTE Confidence: 0.847580505

00:09:09.553 --> 00:09:11.080 pattern or solid pattern,

NOTE Confidence: 0.847580505

00:09:11.080 --> 00:09:12.910 and so the terminology changed

NOTE Confidence: 0.847580505

00:09:12.910 --> 00:09:15.729 over the years and now we are

NOTE Confidence: 0.847580505

00:09:15.729 --> 00:09:17.097 the preferred terminology.

NOTE Confidence: 0.847580505

00:09:17.100 --> 00:09:19.364 Is endometrial serous carcinoma

NOTE Confidence: 0.847580505

00:09:19.364 --> 00:09:21.628 or uterine serous carcinoma?

NOTE Confidence: 0.847580505

00:09:21.630 --> 00:09:23.410 I also put a higher.

NOTE Confidence: 0.847580505

00:09:23.410 --> 00:09:24.601 Image higher magnification.

NOTE Confidence: 0.847580505

00:09:24.601 --> 00:09:27.380 Image here for you to see the

NOTE Confidence: 0.847580505

00:09:27.451 --> 00:09:29.846 nuclear features which are very

NOTE Confidence: 0.847580505

00:09:29.846 --> 00:09:31.762 important and a characteristic

NOTE Confidence: 0.847580505

00:09:31.770 --> 00:09:33.725 finding that helps recognize this

NOTE Confidence: 0.847580505

00:09:33.725 --> 00:09:36.715 tumor type as a very high nuclear

NOTE Confidence: 0.847580505

00:09:36.715 --> 00:09:39.105 to cytoplasmic ratio mark nuclear

NOTE Confidence: 0.847580505

00:09:39.105 --> 00:09:41.779 tipiya and frequent mitotic figures.

NOTE Confidence: 0.799709588888889

00:09:43.870 --> 00:09:46.990 These tumors can only can also

NOTE Confidence: 0.799709588888889

00:09:46.990 --> 00:09:50.238 be a very subtle and and present

NOTE Confidence: 0.799709588888889

00:09:50.238 --> 00:09:54.902 in a in a an early form of 10

NOTE Confidence: 0.799709588888889

00:09:54.902 --> 00:09:57.606 associated with endometrial polyps.

NOTE Confidence: 0.799709588888889

00:09:57.610 --> 00:09:59.955 Sometimes just signing the surface

NOTE Confidence: 0.799709588888889

00:09:59.955 --> 00:10:02.932 of the endometrium or lining the

NOTE Confidence: 0.799709588888889

00:10:02.932 --> 00:10:05.136 pre-existing and demetria glands,

NOTE Confidence: 0.799709588888889

00:10:05.140 --> 00:10:08.409 and this has been termed a somewhat  
NOTE Confidence: 0.799709588888889

00:10:08.410 --> 00:10:10.990 miss miss leading or potentially  
NOTE Confidence: 0.799709588888889

00:10:10.990 --> 00:10:13.054 misleading term of serious.  
NOTE Confidence: 0.799709588888889

00:10:13.060 --> 00:10:15.745 Intrepid serial carcinoma or serious  
NOTE Confidence: 0.799709588888889

00:10:15.745 --> 00:10:17.893 endometrial intrepid serial carcinoma,  
NOTE Confidence: 0.799709588888889

00:10:17.900 --> 00:10:20.684 which is not really an insight to lesion.  
NOTE Confidence: 0.799709588888889

00:10:20.690 --> 00:10:23.091 It has already the same capacity for  
NOTE Confidence: 0.799709588888889

00:10:23.091 --> 00:10:26.200 spread as a full blown serous carcinoma,  
NOTE Confidence: 0.799709588888889

00:10:26.200 --> 00:10:29.055 so that's another interesting feature  
NOTE Confidence: 0.799709588888889

00:10:29.055 --> 00:10:33.210 about this tumor and another characteristic  
NOTE Confidence: 0.799709588888889

00:10:33.210 --> 00:10:36.826 finding is that very often more than  
NOTE Confidence: 0.799709588888889

00:10:36.826 --> 00:10:39.874 95% of tumors are associated with  
NOTE Confidence: 0.799709588888889

00:10:39.880 --> 00:10:42.490 P53 mutations which can be used.  
NOTE Confidence: 0.8550654755

00:10:44.580 --> 00:10:46.520 With the immunohistochemical work up  
NOTE Confidence: 0.8550654755

00:10:46.520 --> 00:10:49.616 and here is an example of showing an  
NOTE Confidence: 0.8550654755

00:10:49.616 --> 00:10:52.150 apparent staining in one of these tumors.

NOTE Confidence: 0.746053631818182  
00:10:54.650 --> 00:10:56.639 So clinically, again,  
NOTE Confidence: 0.746053631818182  
00:10:56.639 --> 00:11:01.820 often these women are post menopausal in the.  
NOTE Confidence: 0.746053631818182  
00:11:01.820 --> 00:11:05.260 Older post menopausal age.  
NOTE Confidence: 0.746053631818182  
00:11:05.260 --> 00:11:08.760 Designing with post menopausal bleeding.  
NOTE Confidence: 0.746053631818182  
00:11:08.760 --> 00:11:10.902 Most importantly, they have a poor  
NOTE Confidence: 0.746053631818182  
00:11:10.902 --> 00:11:13.180 prognosis and a five and 10 year.  
NOTE Confidence: 0.746053631818182  
00:11:13.180 --> 00:11:16.100 Overall survival is only 36%  
NOTE Confidence: 0.746053631818182  
00:11:16.100 --> 00:11:18.560 and 18% for these tumors,  
NOTE Confidence: 0.746053631818182  
00:11:18.560 --> 00:11:21.014 and that's mostly due to poor  
NOTE Confidence: 0.746053631818182  
00:11:21.014 --> 00:11:22.650 response to traditional chemotherapy.  
NOTE Confidence: 0.78360741375  
00:11:24.980 --> 00:11:26.732 Despite the advances in  
NOTE Confidence: 0.78360741375  
00:11:26.732 --> 00:11:28.484 cancer treatment and many,  
NOTE Confidence: 0.78360741375  
00:11:28.490 --> 00:11:30.278 many other tumor types,  
NOTE Confidence: 0.78360741375  
00:11:30.278 --> 00:11:34.142 there hasn't really been a lot of changes,  
NOTE Confidence: 0.78360741375  
00:11:34.142 --> 00:11:36.602 and the chronicle of Behavior,  
NOTE Confidence: 0.78360741375

00:11:36.602 --> 00:11:38.972 clinical outcome of these tumors  
NOTE Confidence: 0.78360741375

00:11:38.972 --> 00:11:42.060 looking back into a study in 2006,  
NOTE Confidence: 0.78360741375

00:11:42.060 --> 00:11:44.951 you can see that they have a  
NOTE Confidence: 0.78360741375

00:11:44.951 --> 00:11:46.600 disproportionately high mortality rate.  
NOTE Confidence: 0.78360741375

00:11:46.600 --> 00:11:49.869 Only 10% of tumors are serious carcinomas,  
NOTE Confidence: 0.78360741375

00:11:49.870 --> 00:11:54.064 and yet almost 40% of the cancer deaths are.  
NOTE Confidence: 0.78360741375

00:11:54.070 --> 00:11:56.760 Related to this tumor type.  
NOTE Confidence: 0.78360741375

00:11:56.760 --> 00:11:59.896 And even compared to other high grade tumors,  
NOTE Confidence: 0.78360741375

00:11:59.900 --> 00:12:02.000 agreed, three endometrioid or clear cell,  
NOTE Confidence: 0.78360741375

00:12:02.000 --> 00:12:04.140 they still do worse.  
NOTE Confidence: 0.78360741375

00:12:04.140 --> 00:12:07.350 And Fast forward to 2015 again,  
NOTE Confidence: 0.78360741375

00:12:07.350 --> 00:12:09.030 compared to other tumor types,  
NOTE Confidence: 0.78360741375

00:12:09.030 --> 00:12:11.770 serous carcinomas have diverse recurrence  
NOTE Confidence: 0.78360741375

00:12:11.770 --> 00:12:15.250 free and distant metastasis free survival.  
NOTE Confidence: 0.78360741375

00:12:15.250 --> 00:12:17.861 And even the most recent studies from  
NOTE Confidence: 0.78360741375

00:12:17.861 --> 00:12:20.913 the PORTEK 3 and from the Memorial

NOTE Confidence: 0.78360741375

00:12:20.913 --> 00:12:23.691 Sloan Kettering showed that these tumors

NOTE Confidence: 0.78360741375

00:12:23.769 --> 00:12:26.309 have the most aggressive behavior,

NOTE Confidence: 0.78360741375

00:12:26.310 --> 00:12:28.921 even compared to other P53 mutant tumors

NOTE Confidence: 0.78360741375

00:12:28.921 --> 00:12:31.739 or compared to other high grade tumors.

NOTE Confidence: 0.753757874545455

00:12:34.500 --> 00:12:37.685 Some we learned a lot about the

NOTE Confidence: 0.753757874545455

00:12:37.685 --> 00:12:39.960 molecular characteristics of endometrial

NOTE Confidence: 0.753757874545455

00:12:39.960 --> 00:12:43.360 carcinoma's over the past decade.

NOTE Confidence: 0.753757874545455

00:12:43.360 --> 00:12:46.558 The seminal paper from the TCA

NOTE Confidence: 0.753757874545455

00:12:46.560 --> 00:12:50.500 identified 4 molecular subgroups and

NOTE Confidence: 0.753757874545455

00:12:50.500 --> 00:12:52.810 the one that series carcinomas belong

NOTE Confidence: 0.753757874545455

00:12:52.810 --> 00:12:55.079 to as the so called copy number,

NOTE Confidence: 0.753757874545455

00:12:55.080 --> 00:12:58.720 high or serious like group which is which

NOTE Confidence: 0.753757874545455

00:12:58.720 --> 00:13:01.498 contains most of the serous carcinomas

NOTE Confidence: 0.753757874545455

00:13:01.498 --> 00:13:04.490 and is enriched in P53 mutations.

NOTE Confidence: 0.753757874545455

00:13:04.490 --> 00:13:05.700 Also interestingly,

NOTE Confidence: 0.753757874545455

00:13:05.700 --> 00:13:10.770 you can see that many of these tumors,  
NOTE Confidence: 0.753757874545455

00:13:10.770 --> 00:13:12.898 actually, I think on my next slide,  
NOTE Confidence: 0.753757874545455

00:13:12.900 --> 00:13:18.116 is that 25% of them also showed herb  
NOTE Confidence: 0.753757874545455

00:13:18.116 --> 00:13:21.240 two amplification by sequencing.  
NOTE Confidence: 0.753757874545455

00:13:21.240 --> 00:13:23.630 Abandoned at the same time,  
NOTE Confidence: 0.753757874545455

00:13:23.630 --> 00:13:27.630 Doctor Santini's group also published.  
NOTE Confidence: 0.753757874545455

00:13:27.630 --> 00:13:30.190 Study on.  
NOTE Confidence: 0.753757874545455

00:13:30.190 --> 00:13:32.738 Sequencing of serous carcinomas  
NOTE Confidence: 0.753757874545455

00:13:32.738 --> 00:13:36.453 and found that 44% of them  
NOTE Confidence: 0.753757874545455

00:13:36.453 --> 00:13:38.256 showed Erbitux amplification.  
NOTE Confidence: 0.87041821

00:13:40.390 --> 00:13:42.945 Soum this is really a  
NOTE Confidence: 0.87041821

00:13:42.945 --> 00:13:44.478 wonderful therapeutic target.  
NOTE Confidence: 0.87041821

00:13:44.480 --> 00:13:47.308 It's been recognized in other tumor types,  
NOTE Confidence: 0.87041821

00:13:47.310 --> 00:13:49.662 and there are so many potential drugs  
NOTE Confidence: 0.87041821

00:13:49.662 --> 00:13:52.659 that can be used to target this pathway,  
NOTE Confidence: 0.87041821

00:13:52.660 --> 00:13:55.066 and this cartoon is not even

NOTE Confidence: 0.87041821

00:13:55.066 --> 00:13:57.180 that recent is from 2018,

NOTE Confidence: 0.87041821

00:13:57.180 --> 00:13:59.420 but you can see the variety of drugs

NOTE Confidence: 0.87041821

00:13:59.420 --> 00:14:02.370 that are available in addition to the

NOTE Confidence: 0.87041821

00:14:02.370 --> 00:14:05.414 earliest ones that blocked the \*\*\*\*

NOTE Confidence: 0.87041821

00:14:05.414 --> 00:14:07.037 dimerization or heterodimerization,

NOTE Confidence: 0.87041821

00:14:07.040 --> 00:14:09.036 trastuzumab, pertuzumab there are

NOTE Confidence: 0.87041821

00:14:09.036 --> 00:14:12.030 now other drugs targeting the tires.

NOTE Confidence: 0.87041821

00:14:12.030 --> 00:14:14.826 And kinase domain of the receptor.

NOTE Confidence: 0.87041821

00:14:14.830 --> 00:14:20.150 There are other therapeutic approaches.

NOTE Confidence: 0.87041821

00:14:20.150 --> 00:14:21.536 To use antibody,

NOTE Confidence: 0.87041821

00:14:21.536 --> 00:14:23.846 drug conjugates and then even

NOTE Confidence: 0.87041821

00:14:23.846 --> 00:14:25.890 more recent developments,

NOTE Confidence: 0.87041821

00:14:25.890 --> 00:14:27.186 using bispecific antibodies

NOTE Confidence: 0.87041821

00:14:27.186 --> 00:14:29.346 or vaccines and so on.

NOTE Confidence: 0.87041821

00:14:29.350 --> 00:14:33.734 So there is really a variety of of.

NOTE Confidence: 0.87041821

00:14:33.740 --> 00:14:39.508 Drugs available to to be taken advantage of.

NOTE Confidence: 0.87041821

00:14:39.510 --> 00:14:41.766 So let's look at what happened

NOTE Confidence: 0.87041821

00:14:41.766 --> 00:14:44.200 in other tumor types and targeted

NOTE Confidence: 0.87041821

00:14:44.200 --> 00:14:46.744 her two treatment over the years.

NOTE Confidence: 0.87041821

00:14:46.750 --> 00:14:48.970 It's been a long, long history,

NOTE Confidence: 0.87041821

00:14:48.970 --> 00:14:51.698 so going back to 1998 I was still

NOTE Confidence: 0.87041821

00:14:51.698 --> 00:14:53.834 in medical school, went resume,

NOTE Confidence: 0.87041821

00:14:53.834 --> 00:14:56.306 it was first approved by the

NOTE Confidence: 0.87041821

00:14:56.306 --> 00:14:58.399 FDA for breast cancer.

NOTE Confidence: 0.87041821

00:14:58.400 --> 00:15:00.730 Dan, with a little gap, other drugs,

NOTE Confidence: 0.87041821

00:15:00.730 --> 00:15:04.490 or have also been approved for breast cancer,

NOTE Confidence: 0.87041821

00:15:04.490 --> 00:15:06.126 and in 2010 trust.

NOTE Confidence: 0.87041821

00:15:06.126 --> 00:15:08.171 Susan Webb was also approved

NOTE Confidence: 0.87041821

00:15:08.171 --> 00:15:09.870 for gastric cancer.

NOTE Confidence: 0.87041821

00:15:09.870 --> 00:15:11.634 So then since then,

NOTE Confidence: 0.87041821

00:15:11.634 --> 00:15:12.952 many other antibody,

NOTE Confidence: 0.87041821

00:15:12.952 --> 00:15:15.112 drug conjugates and other drugs

NOTE Confidence: 0.87041821

00:15:15.112 --> 00:15:17.190 have been approved as well

NOTE Confidence: 0.87041821

00:15:17.190 --> 00:15:19.536 on the bottom of the diagram.

NOTE Confidence: 0.87041821

00:15:19.540 --> 00:15:22.180 This is what happened in under media cancer.

NOTE Confidence: 0.87041821

00:15:22.180 --> 00:15:25.108 There was one trial that I

NOTE Confidence: 0.87041821

00:15:25.108 --> 00:15:27.720 will talk a little more.

NOTE Confidence: 0.87041821

00:15:27.720 --> 00:15:30.710 And a little bit about,

NOTE Confidence: 0.87041821

00:15:30.710 --> 00:15:33.176 as is the JIOJI trial that

NOTE Confidence: 0.87041821

00:15:33.176 --> 00:15:36.920 was published in 2010 and.

NOTE Confidence: 0.87041821

00:15:36.920 --> 00:15:39.020 After that it took so many years.

NOTE Confidence: 0.87041821

00:15:39.020 --> 00:15:39.445 Finally,

NOTE Confidence: 0.87041821

00:15:39.445 --> 00:15:42.845 in 2018 went resume AB was found to

NOTE Confidence: 0.87041821

00:15:42.845 --> 00:15:45.187 improve progression free survival

NOTE Confidence: 0.87041821

00:15:45.187 --> 00:15:48.247 and overall survival in endometrial

NOTE Confidence: 0.87041821

00:15:48.247 --> 00:15:51.347 carcinoma and that discovery was

NOTE Confidence: 0.87041821

00:15:51.347 --> 00:15:53.727 quickly followed by endorsement.

NOTE Confidence: 0.87041821

00:15:53.730 --> 00:15:55.858 From the NCCN guidelines,

NOTE Confidence: 0.87041821

00:15:55.858 --> 00:15:59.050 and also from the Society of

NOTE Confidence: 0.87041821

00:15:59.149 --> 00:16:01.709 Gynecological Oncologists.

NOTE Confidence: 0.87041821

00:16:01.710 --> 00:16:02.988 So what what?

NOTE Confidence: 0.87041821

00:16:02.988 --> 00:16:06.290 Why did it take so long to to

NOTE Confidence: 0.87041821

00:16:06.290 --> 00:16:09.580 these targeted therapies to be

NOTE Confidence: 0.87041821

00:16:09.580 --> 00:16:11.852 recognized for endometrial cancer?

NOTE Confidence: 0.87041821

00:16:11.852 --> 00:16:14.590 Well, the interest is not new.

NOTE Confidence: 0.87041821

00:16:14.590 --> 00:16:17.152 I took this statistics from PUB

NOTE Confidence: 0.87041821

00:16:17.152 --> 00:16:20.764 Med so if you do a search for

NOTE Confidence: 0.87041821

00:16:20.764 --> 00:16:22.568 her to an endometrial,

NOTE Confidence: 0.87041821

00:16:22.570 --> 00:16:23.938 there is this interesting.

NOTE Confidence: 0.812904934210526

00:16:26.420 --> 00:16:28.338 Double wave and you can see that

NOTE Confidence: 0.812904934210526

00:16:28.338 --> 00:16:30.709 we are in the second second wave

NOTE Confidence: 0.812904934210526

00:16:30.709 --> 00:16:32.559 of the her two publications,

NOTE Confidence: 0.812904934210526  
00:16:32.560 --> 00:16:35.485 so there was there was a lot of interest  
NOTE Confidence: 0.812904934210526  
00:16:35.485 --> 00:16:38.120 and then after the first trial publication  
NOTE Confidence: 0.812904934210526  
00:16:38.120 --> 00:16:40.745 the interest went down a little bit  
NOTE Confidence: 0.812904934210526  
00:16:40.745 --> 00:16:43.298 and now we're in this growing phase.  
NOTE Confidence: 0.812904934210526  
00:16:43.300 --> 00:16:45.710 We're not even done with 2021 yet,  
NOTE Confidence: 0.812904934210526  
00:16:45.710 --> 00:16:48.055 and there's there's a lot of papers  
NOTE Confidence: 0.812904934210526  
00:16:48.055 --> 00:16:50.409 that not all of them are from you.  
NOTE Confidence: 0.812904934210526  
00:16:50.410 --> 00:16:54.358 So this is a review I wrote in 2012 and  
NOTE Confidence: 0.812904934210526  
00:16:54.358 --> 00:16:57.750 it's not for you to read in detail,  
NOTE Confidence: 0.812904934210526  
00:16:57.750 --> 00:16:59.910 just to show that there were a lot of  
NOTE Confidence: 0.812904934210526  
00:16:59.910 --> 00:17:02.098 studies already published before 2012,  
NOTE Confidence: 0.812904934210526  
00:17:02.098 --> 00:17:05.062 and the rate of her two  
NOTE Confidence: 0.812904934210526  
00:17:05.062 --> 00:17:07.847 overexpression was all over the place.  
NOTE Confidence: 0.812904934210526  
00:17:07.850 --> 00:17:09.338 Different criteria,  
NOTE Confidence: 0.812904934210526  
00:17:09.338 --> 00:17:11.570 different scoring methods,  
NOTE Confidence: 0.812904934210526

00:17:11.570 --> 00:17:12.996 different antibodies,  
NOTE Confidence: 0.812904934210526

00:17:12.996 --> 00:17:15.848 different case inclusion criteria.  
NOTE Confidence: 0.812904934210526

00:17:15.850 --> 00:17:18.671 So the the rate of her two  
NOTE Confidence: 0.812904934210526

00:17:18.671 --> 00:17:20.560 overexpression was reported between.  
NOTE Confidence: 0.812904934210526

00:17:20.560 --> 00:17:23.864 14 and 80% and register same is  
NOTE Confidence: 0.812904934210526

00:17:23.864 --> 00:17:27.330 true for her two amplification.  
NOTE Confidence: 0.812904934210526

00:17:27.330 --> 00:17:31.170 The rates varied from 15 to 47%.  
NOTE Confidence: 0.844367594210526

00:17:34.220 --> 00:17:37.972 There were also a few case reports that  
NOTE Confidence: 0.844367594210526

00:17:37.972 --> 00:17:40.618 were encouraging showing response in  
NOTE Confidence: 0.844367594210526

00:17:40.618 --> 00:17:43.858 patients with her two positive tumors.  
NOTE Confidence: 0.844367594210526

00:17:43.860 --> 00:17:47.740 And then the GOG study that I mentioned.  
NOTE Confidence: 0.844367594210526

00:17:47.740 --> 00:17:51.060 So just also for context they kind of  
NOTE Confidence: 0.844367594210526

00:17:51.060 --> 00:17:53.059 collaged conchology group is really  
NOTE Confidence: 0.844367594210526

00:17:53.060 --> 00:17:55.900 the major gynecological oncology  
NOTE Confidence: 0.844367594210526

00:17:55.900 --> 00:17:59.250 clinical organization that runs large  
NOTE Confidence: 0.844367594210526

00:17:59.250 --> 00:18:02.310 number of clinical trials with with

NOTE Confidence: 0.844367594210526  
00:18:02.310 --> 00:18:03.840 several participating institutions.  
NOTE Confidence: 0.844367594210526  
00:18:03.840 --> 00:18:06.510 It's really the way that most.  
NOTE Confidence: 0.556626906666667  
00:18:09.540 --> 00:18:11.859 Oncology trials RR.  
NOTE Confidence: 0.70541961  
00:18:14.970 --> 00:18:17.050 Uhm conducted and and  
NOTE Confidence: 0.70541961  
00:18:17.050 --> 00:18:19.130 gynecological oncology so really.  
NOTE Confidence: 0.70541961  
00:18:19.130 --> 00:18:21.482 If if anyone could could could  
NOTE Confidence: 0.70541961  
00:18:21.482 --> 00:18:23.750 do and produce these numbers,  
NOTE Confidence: 0.70541961  
00:18:23.750 --> 00:18:26.006 that would be the jioji group.  
NOTE Confidence: 0.70541961  
00:18:26.010 --> 00:18:29.088 And despite of that they actually  
NOTE Confidence: 0.70541961  
00:18:29.090 --> 00:18:31.418 really had a hard time recruiting  
NOTE Confidence: 0.70541961  
00:18:31.418 --> 00:18:32.970 patients for this trial.  
NOTE Confidence: 0.70541961  
00:18:32.970 --> 00:18:34.050 It took them.  
NOTE Confidence: 0.70541961  
00:18:34.050 --> 00:18:36.210 It was running for seven years,  
NOTE Confidence: 0.70541961  
00:18:36.210 --> 00:18:39.266 took them seven years to recruit 33 patients.  
NOTE Confidence: 0.70541961  
00:18:39.270 --> 00:18:40.873 There was also a period of time  
NOTE Confidence: 0.70541961

00:18:40.873 --> 00:18:42.362 when the study was shut down  
NOTE Confidence: 0.70541961

00:18:42.362 --> 00:18:43.607 because of they called it.  
NOTE Confidence: 0.70541961

00:18:43.610 --> 00:18:45.898 Investigator fatigue and any.  
NOTE Confidence: 0.70541961

00:18:45.898 --> 00:18:48.758 Anyhow they the bottom line  
NOTE Confidence: 0.70541961

00:18:48.758 --> 00:18:51.148 is that it showed no.  
NOTE Confidence: 0.70541961

00:18:51.150 --> 00:18:53.124 Benefit from using Tris is a map,  
NOTE Confidence: 0.70541961

00:18:53.130 --> 00:18:56.455 although it was also criticised  
NOTE Confidence: 0.70541961

00:18:56.455 --> 00:18:59.265 for only using single agent resume  
NOTE Confidence: 0.70541961

00:18:59.265 --> 00:19:01.410 app and including other tumors  
NOTE Confidence: 0.70541961

00:19:01.487 --> 00:19:03.599 other than serious carcinomas.  
NOTE Confidence: 0.9148979483333333

00:19:05.730 --> 00:19:08.166 So so that seemed to be  
NOTE Confidence: 0.9148979483333333

00:19:08.170 --> 00:19:09.950 the that seemed to be.  
NOTE Confidence: 0.9148979483333333

00:19:09.950 --> 00:19:13.478 You know, that basically it's it's been.  
NOTE Confidence: 0.9148979483333333

00:19:13.480 --> 00:19:15.904 People have given up on on  
NOTE Confidence: 0.9148979483333333

00:19:15.904 --> 00:19:18.270 this on this potential targeted  
NOTE Confidence: 0.9148979483333333

00:19:18.270 --> 00:19:19.770 therapy for this tumor type.

NOTE Confidence: 0.914897948333333  
00:19:19.770 --> 00:19:22.874 After this, except Dr.  
NOTE Confidence: 0.914897948333333  
00:19:22.874 --> 00:19:25.630 Centene persisted and I think you know,  
NOTE Confidence: 0.914897948333333  
00:19:25.630 --> 00:19:27.754 I really have to give him a lot of  
NOTE Confidence: 0.914897948333333  
00:19:27.754 --> 00:19:29.607 credit for pursuing this and and  
NOTE Confidence: 0.914897948333333  
00:19:29.607 --> 00:19:31.499 he really believed that that there  
NOTE Confidence: 0.914897948333333  
00:19:31.499 --> 00:19:33.431 could be a better way of designing  
NOTE Confidence: 0.914897948333333  
00:19:33.431 --> 00:19:35.900 a study and showing that this this.  
NOTE Confidence: 0.914897948333333  
00:19:35.900 --> 00:19:38.665 Treatment can be really efficient  
NOTE Confidence: 0.914897948333333  
00:19:38.665 --> 00:19:41.095 and so dumb. Uhm?  
NOTE Confidence: 0.914897948333333  
00:19:41.095 --> 00:19:43.390 His persistently persistence  
NOTE Confidence: 0.914897948333333  
00:19:43.390 --> 00:19:47.232 led to publication of two major  
NOTE Confidence: 0.914897948333333  
00:19:47.232 --> 00:19:50.122 papers in 2018 and 2020,  
NOTE Confidence: 0.914897948333333  
00:19:50.130 --> 00:19:53.530 showing that trust is a map in combination  
NOTE Confidence: 0.914897948333333  
00:19:53.530 --> 00:19:56.774 with the traditional chemotherapy is  
NOTE Confidence: 0.914897948333333  
00:19:56.774 --> 00:19:59.260 actually improving progression free,  
NOTE Confidence: 0.914897948333333

00:19:59.260 --> 00:20:02.110 and overall survival in these tumors.  
NOTE Confidence: 0.9148979483333333

00:20:02.110 --> 00:20:05.598 So here is the diagram of this trial.  
NOTE Confidence: 0.9148979483333333

00:20:05.600 --> 00:20:08.720 There were a total of 61 patients enrolled  
NOTE Confidence: 0.9148979483333333

00:20:08.720 --> 00:20:12.536 in the treatment arm and in the control arm.  
NOTE Confidence: 0.9148979483333333

00:20:12.540 --> 00:20:17.115 And there was improvement of progression  
NOTE Confidence: 0.9148979483333333

00:20:17.115 --> 00:20:20.510 free survival with the best response  
NOTE Confidence: 0.9148979483333333

00:20:20.510 --> 00:20:23.538 in the advanced Stage Disease Group.  
NOTE Confidence: 0.9148979483333333

00:20:23.538 --> 00:20:25.414 Little less in patients  
NOTE Confidence: 0.9148979483333333

00:20:25.414 --> 00:20:27.290 who had recurrent disease.  
NOTE Confidence: 0.9148979483333333

00:20:27.290 --> 00:20:29.210 But still there was an improvement,  
NOTE Confidence: 0.9148979483333333

00:20:29.210 --> 00:20:32.026 and the same is true for overall survival.  
NOTE Confidence: 0.9148979483333333

00:20:32.030 --> 00:20:34.964 The patients who had advanced stage  
NOTE Confidence: 0.9148979483333333

00:20:34.964 --> 00:20:39.160 disease responded the best for treatment.  
NOTE Confidence: 0.9148979483333333

00:20:39.160 --> 00:20:42.232 So then there was a lot of publicity  
NOTE Confidence: 0.9148979483333333

00:20:42.232 --> 00:20:45.135 and Yale publications and also the  
NOTE Confidence: 0.9148979483333333

00:20:45.135 --> 00:20:48.585 ASKO named Justice and Map as one

NOTE Confidence: 0.914897948333333  
00:20:48.585 --> 00:20:52.740 of the advances of the year in 2019.  
NOTE Confidence: 0.914897948333333  
00:20:52.740 --> 00:20:55.939 So that was that was a major  
NOTE Confidence: 0.914897948333333  
00:20:55.939 --> 00:20:58.030 breakthrough for these really.  
NOTE Confidence: 0.914897948333333  
00:20:58.030 --> 00:21:00.210 Aggressive tumors with high mortality  
NOTE Confidence: 0.914897948333333  
00:21:00.210 --> 00:21:03.394 that really gave gave a lot of hope  
NOTE Confidence: 0.914897948333333  
00:21:03.394 --> 00:21:05.550 with a lot of hope for patients  
NOTE Confidence: 0.914897948333333  
00:21:05.550 --> 00:21:09.856 and so to recognize that in 2019,  
NOTE Confidence: 0.914897948333333  
00:21:09.856 --> 00:21:13.640 the NCCN guidelines included.  
NOTE Confidence: 0.914897948333333  
00:21:13.640 --> 00:21:14.945 Carboplatin, paclitaxel cluster  
NOTE Confidence: 0.914897948333333  
00:21:14.945 --> 00:21:17.120 Susan map for these tumors,  
NOTE Confidence: 0.914897948333333  
00:21:17.120 --> 00:21:17.586 and,  
NOTE Confidence: 0.914897948333333  
00:21:17.586 --> 00:21:18.984 as I mentioned,  
NOTE Confidence: 0.914897948333333  
00:21:18.984 --> 00:21:20.848 the Society of Gynecological  
NOTE Confidence: 0.914897948333333  
00:21:20.848 --> 00:21:23.478 Oncologists also recommends testing her.  
NOTE Confidence: 0.914897948333333  
00:21:23.480 --> 00:21:25.825 Two testing of serous carcinomas  
NOTE Confidence: 0.914897948333333

00:21:25.825 --> 00:21:28.738 and adding just zoom out and  
NOTE Confidence: 0.9148979483333333

00:21:28.738 --> 00:21:30.650 in the treatment regimen.  
NOTE Confidence: 0.9148979483333333

00:21:30.650 --> 00:21:33.492 So the question for us now in  
NOTE Confidence: 0.9148979483333333

00:21:33.492 --> 00:21:36.328 pathology is how to evaluate the  
NOTE Confidence: 0.9148979483333333

00:21:36.328 --> 00:21:38.868 hurdle status in these tumors.  
NOTE Confidence: 0.9148979483333333

00:21:38.870 --> 00:21:40.870 Come to answer that question,  
NOTE Confidence: 0.9148979483333333

00:21:40.870 --> 00:21:43.030 let's look at other tumor types.  
NOTE Confidence: 0.9148979483333333

00:21:43.030 --> 00:21:44.570 Again,  
NOTE Confidence: 0.9148979483333333

00:21:44.570 --> 00:21:46.718 here is the long evolution of  
NOTE Confidence: 0.9148979483333333

00:21:46.718 --> 00:21:48.150 the her two guidelines,  
NOTE Confidence: 0.9148979483333333

00:21:48.150 --> 00:21:51.105 and other tumor types and  
NOTE Confidence: 0.9148979483333333

00:21:51.105 --> 00:21:52.878 breast cancer starting.  
NOTE Confidence: 0.9148979483333333

00:21:52.880 --> 00:21:57.255 In 1998, with the FDA package insert,  
NOTE Confidence: 0.9148979483333333

00:21:57.260 --> 00:22:00.340 the first ASCO CAP guidelines came out in  
NOTE Confidence: 0.9148979483333333

00:22:00.340 --> 00:22:04.420 2007 and then another two set of guidelines.  
NOTE Confidence: 0.9148979483333333

00:22:04.420 --> 00:22:05.568 Finally, currently,

NOTE Confidence: 0.914897948333333  
00:22:05.568 --> 00:22:09.638 we use the 2018 ASCO CAP guidelines  
NOTE Confidence: 0.914897948333333  
00:22:09.638 --> 00:22:11.399 in gastric cancer.  
NOTE Confidence: 0.914897948333333  
00:22:11.400 --> 00:22:15.012 The tumor characteristics of her two  
NOTE Confidence: 0.914897948333333  
00:22:15.012 --> 00:22:17.420 expression and amplification were  
NOTE Confidence: 0.914897948333333  
00:22:17.513 --> 00:22:20.435 first described in the toga trial.  
NOTE Confidence: 0.914897948333333  
00:22:20.440 --> 00:22:23.650 Trastuzumab for gastric cancer trial.  
NOTE Confidence: 0.914897948333333  
00:22:23.650 --> 00:22:25.674 And based upon that,  
NOTE Confidence: 0.914897948333333  
00:22:25.674 --> 00:22:27.698 based upon the observations  
NOTE Confidence: 0.914897948333333  
00:22:27.698 --> 00:22:30.030 from that trial in 2016,  
NOTE Confidence: 0.914897948333333  
00:22:30.030 --> 00:22:32.364 they ask Cool CAP published the  
NOTE Confidence: 0.914897948333333  
00:22:32.364 --> 00:22:34.612 first official set of guidelines  
NOTE Confidence: 0.914897948333333  
00:22:34.612 --> 00:22:37.076 specific for gastric carcinoma,  
NOTE Confidence: 0.914897948333333  
00:22:37.080 --> 00:22:39.212 and most recently a.  
NOTE Confidence: 0.914897948333333  
00:22:39.212 --> 00:22:41.877 Clinical trial on colorectal cancer  
NOTE Confidence: 0.914897948333333  
00:22:41.877 --> 00:22:45.654 is using yet another set of criteria  
NOTE Confidence: 0.914897948333333

00:22:45.654 --> 00:22:48.930 different from the other two tumor types,  
NOTE Confidence: 0.914897948333333

00:22:48.930 --> 00:22:51.360 so it is recognized in other  
NOTE Confidence: 0.914897948333333

00:22:51.360 --> 00:22:53.780 tumor types that there is there  
NOTE Confidence: 0.914897948333333

00:22:53.780 --> 00:22:56.072 are differences in how the her  
NOTE Confidence: 0.914897948333333

00:22:56.155 --> 00:22:58.679 two expression and amplification.  
NOTE Confidence: 0.914897948333333

00:22:58.680 --> 00:23:02.854 Occurs and and how the treatment  
NOTE Confidence: 0.914897948333333

00:23:02.854 --> 00:23:05.998 response is associated with these features,  
NOTE Confidence: 0.914897948333333

00:23:06.000 --> 00:23:07.950 so that led to these  
NOTE Confidence: 0.8994679425

00:23:07.950 --> 00:23:11.398 development of different guidelines.  
NOTE Confidence: 0.8994679425

00:23:11.400 --> 00:23:13.770 And before I even go further,  
NOTE Confidence: 0.8994679425

00:23:13.770 --> 00:23:16.885 I want also wanted to emphasize that  
NOTE Confidence: 0.8994679425

00:23:16.885 --> 00:23:20.702 the clinical trial that I presented to  
NOTE Confidence: 0.8994679425

00:23:20.702 --> 00:23:25.880 you earlier started in 2011, when the.  
NOTE Confidence: 0.8994679425

00:23:25.880 --> 00:23:28.965 Guidelines the only guidelines existing  
NOTE Confidence: 0.8994679425

00:23:28.965 --> 00:23:32.959 for any hurt evaluation over the ones.  
NOTE Confidence: 0.8994679425

00:23:32.960 --> 00:23:35.756 Published by the ASCO CAP in 2007 that

NOTE Confidence: 0.8994679425

00:23:35.756 --> 00:23:38.390 I'll come back to that in a little bit.

NOTE Confidence: 0.841705185

00:23:40.820 --> 00:23:42.386 So let's look at the features

NOTE Confidence: 0.841705185

00:23:42.386 --> 00:23:44.329 of her two and breast cancer.

NOTE Confidence: 0.841705185

00:23:44.330 --> 00:23:47.730 Approximately 15 to 25% of the tumors are

NOTE Confidence: 0.841705185

00:23:47.730 --> 00:23:51.638 her two positive heterogeneity of her two

NOTE Confidence: 0.841705185

00:23:51.638 --> 00:23:54.473 expression and amplification is uncommon,

NOTE Confidence: 0.841705185

00:23:54.480 --> 00:23:57.819 although there is a little bit more

NOTE Confidence: 0.841705185

00:23:57.819 --> 00:24:01.980 variety and the reported rates and her

NOTE Confidence: 0.841705185

00:24:01.980 --> 00:24:05.280 two heterogeneity or gene amplification,

NOTE Confidence: 0.841705185

00:24:05.280 --> 00:24:07.513 and for those cases it's been reported

NOTE Confidence: 0.841705185

00:24:07.513 --> 00:24:09.768 that they can be either a cluster.

NOTE Confidence: 0.841705185

00:24:09.770 --> 00:24:12.610 Heterogeneity or mosaic pattern

NOTE Confidence: 0.841705185

00:24:12.610 --> 00:24:14.030 of heterogeneity.

NOTE Confidence: 0.841705185

00:24:14.030 --> 00:24:16.540 The basal basal lateral staining

NOTE Confidence: 0.841705185

00:24:16.540 --> 00:24:20.188 pattern is quite rare, mostly seen in

NOTE Confidence: 0.841705185

00:24:20.188 --> 00:24:21.826 invasive micropapillary carcinomas,  
NOTE Confidence: 0.841705185

00:24:21.830 --> 00:24:24.932 and in those cases that's considered  
NOTE Confidence: 0.841705185

00:24:24.932 --> 00:24:27.000 a two plus score.  
NOTE Confidence: 0.841705185

00:24:27.000 --> 00:24:29.856 And fish and I see are equally  
NOTE Confidence: 0.841705185

00:24:29.856 --> 00:24:31.840 predictive of treatment response.  
NOTE Confidence: 0.841705185

00:24:31.840 --> 00:24:33.724 So for that reason,  
NOTE Confidence: 0.841705185

00:24:33.724 --> 00:24:36.550 the herd to testing algorithm could  
NOTE Confidence: 0.841705185

00:24:36.642 --> 00:24:39.408 start either with IC or a fish.  
NOTE Confidence: 0.853787571428571

00:24:43.580 --> 00:24:47.297 In gastric cancer, as I mentioned the.  
NOTE Confidence: 0.853787571428571

00:24:47.300 --> 00:24:48.923 Guidelines were developed,  
NOTE Confidence: 0.853787571428571

00:24:48.923 --> 00:24:51.487 developed based on the information.  
NOTE Confidence: 0.853787571428571

00:24:51.487 --> 00:24:54.663 The data from the toga trial and there  
NOTE Confidence: 0.853787571428571

00:24:54.663 --> 00:24:57.156 were several nice papers are written  
NOTE Confidence: 0.853787571428571

00:24:57.156 --> 00:25:00.364 on on that in correlation with the OR  
NOTE Confidence: 0.853787571428571

00:25:00.364 --> 00:25:02.584 in conjunction with the toga trial.  
NOTE Confidence: 0.853787571428571

00:25:02.590 --> 00:25:05.047 And based on that we learned that

NOTE Confidence: 0.853787571428571  
00:25:05.050 --> 00:25:07.666 22% of gastric or GE junction  
NOTE Confidence: 0.853787571428571  
00:25:07.666 --> 00:25:10.320 tumors are her two positive.  
NOTE Confidence: 0.853787571428571  
00:25:10.320 --> 00:25:12.865 Although there is some variability  
NOTE Confidence: 0.853787571428571  
00:25:12.865 --> 00:25:15.410 depending on the histologic subtype,  
NOTE Confidence: 0.853787571428571  
00:25:15.410 --> 00:25:17.270 intestinal type tumors are more  
NOTE Confidence: 0.853787571428571  
00:25:17.270 --> 00:25:20.028 likely to be her two positive and  
NOTE Confidence: 0.853787571428571  
00:25:20.028 --> 00:25:22.494 also based on the tumor location.  
NOTE Confidence: 0.853787571428571  
00:25:22.500 --> 00:25:24.665 So GE Junction tumors are  
NOTE Confidence: 0.853787571428571  
00:25:24.665 --> 00:25:26.520 more often her two positive.  
NOTE Confidence: 0.79890442  
00:25:29.760 --> 00:25:32.450 Heterogeneity, unlike in breast cancer,  
NOTE Confidence: 0.79890442  
00:25:32.450 --> 00:25:34.304 is very common and it's present  
NOTE Confidence: 0.79890442  
00:25:34.304 --> 00:25:37.670 in up to 50% of tumors.  
NOTE Confidence: 0.79890442  
00:25:37.670 --> 00:25:39.945 The concordance between ISC and  
NOTE Confidence: 0.79890442  
00:25:39.945 --> 00:25:42.849 fresh has been reported to be high  
NOTE Confidence: 0.79890442  
00:25:42.850 --> 00:25:45.250 and another important difference  
NOTE Confidence: 0.79890442

00:25:45.250 --> 00:25:48.756 from breast cancer is that protein  
NOTE Confidence: 0.79890442

00:25:48.756 --> 00:25:50.780 expression shows the highest.  
NOTE Confidence: 0.79890442

00:25:50.780 --> 00:25:52.352 The strongest association  
NOTE Confidence: 0.79890442

00:25:52.352 --> 00:25:54.448 with the therapeutic response.  
NOTE Confidence: 0.79890442

00:25:54.450 --> 00:25:58.344 So the testing algorithm has to  
NOTE Confidence: 0.79890442

00:25:58.344 --> 00:26:00.291 start with immunohistochemistry  
NOTE Confidence: 0.79890442

00:26:00.291 --> 00:26:04.067 and only tumors with a two plus  
NOTE Confidence: 0.79890442

00:26:04.067 --> 00:26:06.822 immunostain will be reflex with.  
NOTE Confidence: 0.79890442

00:26:06.822 --> 00:26:09.894 Her two fish, although there's some  
NOTE Confidence: 0.79890442

00:26:09.894 --> 00:26:14.180 data and one of the trials that.  
NOTE Confidence: 0.79890442

00:26:14.180 --> 00:26:17.450 IC negative and fish positive tumors  
NOTE Confidence: 0.79890442

00:26:17.450 --> 00:26:20.670 may also benefit from treatment.  
NOTE Confidence: 0.79890442

00:26:20.670 --> 00:26:23.183 Come just to illustrate or what I  
NOTE Confidence: 0.79890442

00:26:23.183 --> 00:26:25.349 mentioned about the gastric tumors.  
NOTE Confidence: 0.79890442

00:26:25.350 --> 00:26:28.982 There is the characteristic  
NOTE Confidence: 0.79890442

00:26:28.982 --> 00:26:31.642 basolateral staining pattern,

NOTE Confidence: 0.79890442

00:26:31.642 --> 00:26:35.146 lack of epical staining.

NOTE Confidence: 0.79890442

00:26:35.150 --> 00:26:35.790 And so.

NOTE Confidence: 0.765255031666667

00:26:37.990 --> 00:26:40.558 And so at the beginning of the clinical

NOTE Confidence: 0.765255031666667

00:26:40.558 --> 00:26:42.710 trial for endometrial carcinoma,

NOTE Confidence: 0.765255031666667

00:26:42.710 --> 00:26:46.077 we decided to look at the characteristics

NOTE Confidence: 0.765255031666667

00:26:46.077 --> 00:26:48.787 of serious carcinomas to see if

NOTE Confidence: 0.765255031666667

00:26:48.787 --> 00:26:51.169 they also have unique features that

NOTE Confidence: 0.765255031666667

00:26:51.169 --> 00:26:53.778 should be taken into consideration.

NOTE Confidence: 0.765255031666667

00:26:53.780 --> 00:26:57.548 So we looked at 108 cases,

NOTE Confidence: 0.765255031666667

00:26:57.550 --> 00:27:00.504 most of which were pure serious carcinoma.

NOTE Confidence: 0.765255031666667

00:27:00.510 --> 00:27:04.128 Some of them are mixed tumors.

NOTE Confidence: 0.765255031666667

00:27:04.130 --> 00:27:07.220 And we performed a immunohistochemistry and

NOTE Confidence: 0.765255031666667

00:27:07.220 --> 00:27:11.638 her two fish on all of the two plus cases.

NOTE Confidence: 0.765255031666667

00:27:11.640 --> 00:27:14.360 And compared the scoring systems,

NOTE Confidence: 0.765255031666667

00:27:14.360 --> 00:27:17.720 the original FDA package insert score

NOTE Confidence: 0.765255031666667

00:27:17.720 --> 00:27:20.668 plus the 2007 ASCO CAP criteria.  
NOTE Confidence: 0.796174474285714

00:27:23.580 --> 00:27:27.094 I'm using the two different scoring criteria.  
NOTE Confidence: 0.796174474285714

00:27:27.100 --> 00:27:30.030 We found that there was of course  
NOTE Confidence: 0.796174474285714

00:27:30.030 --> 00:27:31.855 some differences in the her  
NOTE Confidence: 0.796174474285714

00:27:31.855 --> 00:27:34.540 two positive positive ITI rate,  
NOTE Confidence: 0.796174474285714

00:27:34.540 --> 00:27:38.157 about 30% of the tumors were her two positive  
NOTE Confidence: 0.796174474285714

00:27:38.157 --> 00:27:43.098 using the ASCO CAP 2007 criteria and.  
NOTE Confidence: 0.796174474285714

00:27:43.100 --> 00:27:45.860 More importantly, in terms of the  
NOTE Confidence: 0.796174474285714

00:27:45.860 --> 00:27:48.254 icy fish concordance to 2007,  
NOTE Confidence: 0.796174474285714

00:27:48.254 --> 00:27:51.578 breast criteria gave a higher concordance.  
NOTE Confidence: 0.796174474285714

00:27:51.580 --> 00:27:53.059 It was 86%.  
NOTE Confidence: 0.851113857272727

00:27:55.470 --> 00:27:58.242 Another very important finding from this  
NOTE Confidence: 0.851113857272727

00:27:58.242 --> 00:28:01.160 study was recognition of heterogeneity.  
NOTE Confidence: 0.851113857272727

00:28:01.160 --> 00:28:04.639 It is very common in these tumors.  
NOTE Confidence: 0.851113857272727

00:28:04.640 --> 00:28:08.048 More than 50% of the her two positive  
NOTE Confidence: 0.851113857272727

00:28:08.048 --> 00:28:10.718 cases and you can see some examples

NOTE Confidence: 0.851113857272727  
00:28:10.718 --> 00:28:13.135 here where there are several neoplastic  
NOTE Confidence: 0.851113857272727  
00:28:13.135 --> 00:28:16.110 glands on the right hand side and  
NOTE Confidence: 0.851113857272727  
00:28:16.110 --> 00:28:18.328 only a few of them are positive  
NOTE Confidence: 0.851113857272727  
00:28:18.328 --> 00:28:21.912 for her two on the left hand side.  
NOTE Confidence: 0.851113857272727  
00:28:21.920 --> 00:28:23.492 Same thing you know.  
NOTE Confidence: 0.851113857272727  
00:28:23.492 --> 00:28:26.296 You have several neoplastic areas  
NOTE Confidence: 0.851113857272727  
00:28:26.296 --> 00:28:29.968 that are her two positive in with an  
NOTE Confidence: 0.851113857272727  
00:28:29.968 --> 00:28:32.598 intense training and then in the upper  
NOTE Confidence: 0.851113857272727  
00:28:32.598 --> 00:28:34.735 right corner of the slide there is.  
NOTE Confidence: 0.851113857272727  
00:28:34.735 --> 00:28:35.530 There is no.  
NOTE Confidence: 0.907750445  
00:28:37.620 --> 00:28:40.030 Expression even within the same  
NOTE Confidence: 0.907750445  
00:28:40.030 --> 00:28:42.440 gland you can find different  
NOTE Confidence: 0.907750445  
00:28:42.440 --> 00:28:45.758 protein expression levels.  
NOTE Confidence: 0.907750445  
00:28:45.760 --> 00:28:47.740 And in addition to that,  
NOTE Confidence: 0.907750445  
00:28:47.740 --> 00:28:49.520 similar to gastric cancer,  
NOTE Confidence: 0.907750445

00:28:49.520 --> 00:28:52.190 these tumors also frequently lack the  
NOTE Confidence: 0.907750445

00:28:52.266 --> 00:28:55.714 ethical staining resulting in this  
NOTE Confidence: 0.907750445

00:28:55.714 --> 00:28:58.826 lateral basolateral staining pattern.  
NOTE Confidence: 0.907750445

00:28:58.830 --> 00:29:01.245 We also looked at a smaller number  
NOTE Confidence: 0.907750445

00:29:01.245 --> 00:29:04.352 of cases by fish to see if the  
NOTE Confidence: 0.907750445

00:29:04.352 --> 00:29:06.342 heterogeneity can also be observed  
NOTE Confidence: 0.907750445

00:29:06.419 --> 00:29:09.276 at the gene amplification level,  
NOTE Confidence: 0.907750445

00:29:09.276 --> 00:29:14.890 and we found two patterns of amplification  
NOTE Confidence: 0.907750445

00:29:14.890 --> 00:29:17.858 and named them similar to what the  
NOTE Confidence: 0.907750445

00:29:17.858 --> 00:29:19.570 breast cancer literature used.  
NOTE Confidence: 0.907750445

00:29:19.570 --> 00:29:20.468 Cluster amplification,  
NOTE Confidence: 0.907750445

00:29:20.468 --> 00:29:24.060 which is where you have a large cluster  
NOTE Confidence: 0.907750445

00:29:24.136 --> 00:29:26.271 of tumor cells showing amplification  
NOTE Confidence: 0.907750445

00:29:26.271 --> 00:29:28.920 and in next to another class.  
NOTE Confidence: 0.907750445

00:29:28.920 --> 00:29:32.406 Clustered at that has no amplification.  
NOTE Confidence: 0.907750445

00:29:32.410 --> 00:29:35.398 And another case where we found

NOTE Confidence: 0.907750445

00:29:35.398 --> 00:29:38.434 a strong correlation between the

NOTE Confidence: 0.907750445

00:29:38.434 --> 00:29:40.204 immunohistochemical expression of

NOTE Confidence: 0.907750445

00:29:40.204 --> 00:29:42.646 the protein and the gene application.

NOTE Confidence: 0.907750445

00:29:42.650 --> 00:29:45.788 You can see that the the.

NOTE Confidence: 0.907750445

00:29:45.790 --> 00:29:48.455 Her two positive areas corresponded

NOTE Confidence: 0.907750445

00:29:48.455 --> 00:29:50.587 to the amplified area.

NOTE Confidence: 0.907750445

00:29:50.590 --> 00:29:53.752 Her two week expression corresponded to

NOTE Confidence: 0.907750445

00:29:53.752 --> 00:29:58.160 the her two non amplified area on fish.

NOTE Confidence: 0.907750445

00:29:58.160 --> 00:30:00.888 And then we also saw some cases with

NOTE Confidence: 0.907750445

00:30:00.888 --> 00:30:03.424 a mosaic amplification pattern where

NOTE Confidence: 0.907750445

00:30:03.424 --> 00:30:06.964 there were individual tumor cells showing.

NOTE Confidence: 0.907750445

00:30:06.970 --> 00:30:08.944 Her two gene amplification in the

NOTE Confidence: 0.907750445

00:30:08.944 --> 00:30:10.640 background of non amplified cells.

NOTE Confidence: 0.8458429075

00:30:13.770 --> 00:30:16.731 So based on our. Observations

NOTE Confidence: 0.8458429075

00:30:16.731 --> 00:30:19.617 at the beginning of the trial,

NOTE Confidence: 0.8458429075

00:30:19.620 --> 00:30:23.475 we decided to use the existing  
NOTE Confidence: 0.8458429075

00:30:23.475 --> 00:30:28.080 2007 ASCO CAP scoring system at the  
NOTE Confidence: 0.8458429075

00:30:28.080 --> 00:30:30.000 time with specific modifications,  
NOTE Confidence: 0.8458429075

00:30:30.000 --> 00:30:33.759 namely that CIRCUMFERENTIALLY.  
NOTE Confidence: 0.8458429075

00:30:33.760 --> 00:30:35.508 Staining was not required.  
NOTE Confidence: 0.8458429075

00:30:35.508 --> 00:30:38.130 U shaped or based on lateral.  
NOTE Confidence: 0.8458429075

00:30:38.130 --> 00:30:40.490 Lateral pattern was also accepted  
NOTE Confidence: 0.8458429075

00:30:40.490 --> 00:30:43.302 for the her 2/3 plus score.  
NOTE Confidence: 0.8458429075

00:30:43.302 --> 00:30:44.230 In addition,  
NOTE Confidence: 0.8458429075

00:30:44.230 --> 00:30:48.206 due to the heterogeneity we decided  
NOTE Confidence: 0.8458429075

00:30:48.206 --> 00:30:51.554 to do the immunohistochemistry on the  
NOTE Confidence: 0.8458429075

00:30:51.554 --> 00:30:54.350 hysterectomy specimen to identify a large,  
NOTE Confidence: 0.8458429075

00:30:54.350 --> 00:30:56.742 larger amount of tumor.  
NOTE Confidence: 0.8458429075

00:30:56.742 --> 00:30:59.839 Uhm, for testing and also to do the  
NOTE Confidence: 0.8458429075

00:30:59.839 --> 00:31:02.805 fish on two plus cases in correlation  
NOTE Confidence: 0.8458429075

00:31:02.805 --> 00:31:05.965 with the IC stain slides so that

NOTE Confidence: 0.8458429075

00:31:05.965 --> 00:31:08.527 we look at the area with most

NOTE Confidence: 0.8458429075

00:31:08.527 --> 00:31:10.946 with the most protein expression.

NOTE Confidence: 0.8458429075

00:31:10.946 --> 00:31:14.318 Also, we typically selected a large,

NOTE Confidence: 0.8458429075

00:31:14.320 --> 00:31:16.492 larger area for fish,

NOTE Confidence: 0.8458429075

00:31:16.492 --> 00:31:19.750 unlike in breast cancer and her

NOTE Confidence: 0.8458429075

00:31:19.862 --> 00:31:22.802 to 17 ratio of two or greater

NOTE Confidence: 0.8458429075

00:31:22.802 --> 00:31:26.017 was used as a cutoff for fish.

NOTE Confidence: 0.8458429075

00:31:26.020 --> 00:31:29.852 So I would stop here for just a minute

NOTE Confidence: 0.8458429075

00:31:29.852 --> 00:31:34.599 to say that. Well, it would seem.

NOTE Confidence: 0.8458429075

00:31:34.600 --> 00:31:36.470 Uhm?

NOTE Confidence: 0.8458429075

00:31:36.470 --> 00:31:40.134 It would seem logical to at this point

NOTE Confidence: 0.8458429075

00:31:40.134 --> 00:31:43.819 use these clinical trial criteria too.

NOTE Confidence: 0.90248156

00:31:45.870 --> 00:31:49.458 2. Ident to come.

NOTE Confidence: 0.90248156

00:31:49.458 --> 00:31:52.790 Evaluate or two staining moving on in

NOTE Confidence: 0.90248156

00:31:52.884 --> 00:31:56.027 these tumor types at the same time.

NOTE Confidence: 0.90248156

00:31:56.030 --> 00:31:58.664 Since then, two different sets of  
NOTE Confidence: 0.90248156

00:31:58.664 --> 00:32:01.073 criteria have been proposed for or  
NOTE Confidence: 0.90248156

00:32:01.073 --> 00:32:03.646 have been published for breast cancer,  
NOTE Confidence: 0.90248156

00:32:03.646 --> 00:32:07.263 and there are some authors who would  
NOTE Confidence: 0.90248156

00:32:07.263 --> 00:32:10.966 advocate for using the 2018 breast criteria,  
NOTE Confidence: 0.90248156

00:32:10.970 --> 00:32:12.610 saying that, well, you know,  
NOTE Confidence: 0.90248156

00:32:12.610 --> 00:32:14.250 just for simplicity sake,  
NOTE Confidence: 0.90248156

00:32:14.250 --> 00:32:17.705 why don't we use the criteria that everybody  
NOTE Confidence: 0.90248156

00:32:17.705 --> 00:32:20.447 is already familiar with and this?  
NOTE Confidence: 0.90248156

00:32:20.450 --> 00:32:22.160 This is my my cartoon.  
NOTE Confidence: 0.90248156

00:32:22.160 --> 00:32:24.848 Just to show that I think one of  
NOTE Confidence: 0.90248156

00:32:24.848 --> 00:32:26.609 the arguments in addition just  
NOTE Confidence: 0.90248156

00:32:26.609 --> 00:32:28.635 to to the fact that, well,  
NOTE Confidence: 0.90248156

00:32:28.635 --> 00:32:31.315 this is the the criteria I just mentioned  
NOTE Confidence: 0.90248156

00:32:31.315 --> 00:32:33.896 are the ones that were shown to  
NOTE Confidence: 0.90248156

00:32:33.896 --> 00:32:36.530 correlate with response and the covert trial.

NOTE Confidence: 0.90248156

00:32:36.530 --> 00:32:39.250 In addition to that, if we use the

NOTE Confidence: 0.90248156

00:32:39.250 --> 00:32:41.279 criteria from another tour type,

NOTE Confidence: 0.90248156

00:32:41.280 --> 00:32:44.017 then we'll have a moving finish line.

NOTE Confidence: 0.90248156

00:32:44.020 --> 00:32:46.180 You know it's not over and breast cancer.

NOTE Confidence: 0.90248156

00:32:46.180 --> 00:32:49.890 I'm sure that or I'm I'm I'm.

NOTE Confidence: 0.90248156

00:32:49.890 --> 00:32:51.682 I, I suspect that there will be no

NOTE Confidence: 0.90248156

00:32:51.682 --> 00:32:53.403 as data accumulate and new studies

NOTE Confidence: 0.90248156

00:32:53.403 --> 00:32:54.918 come out and pressed it.

NOTE Confidence: 0.90248156

00:32:54.920 --> 00:32:58.148 It's entirely possible that they will

NOTE Confidence: 0.90248156

00:32:58.150 --> 00:32:59.238 adjust the guidelines accordingly,

NOTE Confidence: 0.90248156

00:32:59.238 --> 00:33:01.191 and there will be a new set

NOTE Confidence: 0.90248156

00:33:01.191 --> 00:33:02.279 of guidelines for breast.

NOTE Confidence: 0.90248156

00:33:02.280 --> 00:33:05.220 So are we going to change our

NOTE Confidence: 0.90248156

00:33:05.220 --> 00:33:06.897 interpretation criteria every time

NOTE Confidence: 0.90248156

00:33:06.897 --> 00:33:09.291 based on another tumor type on breast

NOTE Confidence: 0.90248156

00:33:09.291 --> 00:33:11.966 or or on gastric for that matter?

NOTE Confidence: 0.90248156

00:33:11.970 --> 00:33:14.952 So I really think that it's

NOTE Confidence: 0.90248156

00:33:14.952 --> 00:33:16.940 important to establish endometrial

NOTE Confidence: 0.90248156

00:33:17.030 --> 00:33:19.678 carcinoma specific guidelines on.

NOTE Confidence: 0.90248156

00:33:19.680 --> 00:33:23.694 At this point and and for that reason,

NOTE Confidence: 0.90248156

00:33:23.694 --> 00:33:25.018 based on our experience,

NOTE Confidence: 0.90248156

00:33:25.020 --> 00:33:28.870 I proposed her testing algorithm

NOTE Confidence: 0.90248156

00:33:28.870 --> 00:33:32.648 and and scoring criteria for

NOTE Confidence: 0.90248156

00:33:32.648 --> 00:33:35.656 an Demetria serious carcinoma,

NOTE Confidence: 0.90248156

00:33:35.660 --> 00:33:38.556 and this is of course just the first

NOTE Confidence: 0.90248156

00:33:38.556 --> 00:33:41.452 step and there will be many more

NOTE Confidence: 0.90248156

00:33:41.452 --> 00:33:44.030 steps to really identify the best.

NOTE Confidence: 0.90248156

00:33:44.030 --> 00:33:46.315 Testing algorithm and and there

NOTE Confidence: 0.90248156

00:33:46.315 --> 00:33:49.159 is already currently a lot of

NOTE Confidence: 0.90248156

00:33:49.159 --> 00:33:50.578 groups interested in.

NOTE Confidence: 0.725949411428572

00:33:53.070 --> 00:33:57.074 In studying these tumors and and uh.

NOTE Confidence: 0.725949411428572  
00:33:57.080 --> 00:33:59.912 There is many more publications that  
NOTE Confidence: 0.725949411428572  
00:33:59.912 --> 00:34:03.499 I expect to come out on this topic.  
NOTE Confidence: 0.725949411428572  
00:34:03.500 --> 00:34:06.116 We also performed an interobserver study  
NOTE Confidence: 0.725949411428572  
00:34:06.116 --> 00:34:09.514 to look at the reproducibility of this  
NOTE Confidence: 0.725949411428572  
00:34:09.514 --> 00:34:15.188 scoring system and found that it had a good.  
NOTE Confidence: 0.725949411428572  
00:34:15.190 --> 00:34:18.608 Interobserver uh agreement.  
NOTE Confidence: 0.725949411428572  
00:34:18.608 --> 00:34:22.661 Kappa, which is comparable to what's being  
NOTE Confidence: 0.725949411428572  
00:34:22.661 --> 00:34:25.878 published in breast and gastric tumors.  
NOTE Confidence: 0.8764338933333333  
00:34:28.620 --> 00:34:32.346 There are several remaining practical issues.  
NOTE Confidence: 0.8764338933333333  
00:34:32.350 --> 00:34:36.949 On this topic, we still have to.  
NOTE Confidence: 0.8764338933333333  
00:34:36.950 --> 00:34:39.799 Do more investigations to find out what  
NOTE Confidence: 0.8764338933333333  
00:34:39.799 --> 00:34:42.579 correlates best with the clinical response,  
NOTE Confidence: 0.8764338933333333  
00:34:42.580 --> 00:34:43.876 immunohistochemistry or fish.  
NOTE Confidence: 0.8764338933333333  
00:34:43.876 --> 00:34:47.830 We have not done fish on all of the  
NOTE Confidence: 0.8764338933333333  
00:34:47.830 --> 00:34:49.955 tumors and potentially there could  
NOTE Confidence: 0.8764338933333333

00:34:49.955 --> 00:34:52.745 be icy negative fish positive tumors  
NOTE Confidence: 0.8764338933333333

00:34:52.745 --> 00:34:55.625 that may also benefit from treatment.  
NOTE Confidence: 0.8764338933333333

00:34:55.630 --> 00:34:58.402 We don't know the full clinical  
NOTE Confidence: 0.8764338933333333

00:34:58.402 --> 00:35:00.250 impact of intratumoral heterogeneity  
NOTE Confidence: 0.8764338933333333

00:35:00.327 --> 00:35:01.619 in this tumor type.  
NOTE Confidence: 0.8764338933333333

00:35:01.620 --> 00:35:04.248 Also another question is sample selection.  
NOTE Confidence: 0.8764338933333333

00:35:04.250 --> 00:35:07.015 Should we do testing on the biopsy  
NOTE Confidence: 0.8764338933333333

00:35:07.015 --> 00:35:09.570 or grading versus the hysterectomy?  
NOTE Confidence: 0.8764338933333333

00:35:09.570 --> 00:35:12.888 Should we test primary versus metastasis  
NOTE Confidence: 0.8764338933333333

00:35:12.890 --> 00:35:16.982 and finally specimen handling and fixation  
NOTE Confidence: 0.8764338933333333

00:35:16.982 --> 00:35:21.540 time and and the issue of control?  
NOTE Confidence: 0.8764338933333333

00:35:21.540 --> 00:35:24.732 Slides on the on the topic of  
NOTE Confidence: 0.8764338933333333

00:35:24.732 --> 00:35:26.710 heterogeneity data from breast  
NOTE Confidence: 0.8764338933333333

00:35:26.710 --> 00:35:29.854 and gastric cancer have shown that  
NOTE Confidence: 0.8764338933333333

00:35:29.854 --> 00:35:32.810 homogeneous her two overexpression.  
NOTE Confidence: 0.8764338933333333

00:35:32.810 --> 00:35:36.128 Has more benefit from targeted therapy

NOTE Confidence: 0.876433893333333  
00:35:36.128 --> 00:35:39.649 compared to heterogeneous her two expression.  
NOTE Confidence: 0.876433893333333  
00:35:39.650 --> 00:35:43.496 On the topic of sample selection,  
NOTE Confidence: 0.876433893333333  
00:35:43.500 --> 00:35:44.848 there are several considerations  
NOTE Confidence: 0.876433893333333  
00:35:44.848 --> 00:35:46.533 and this is an interesting.  
NOTE Confidence: 0.92376738  
00:35:48.610 --> 00:35:52.676 Topic for that reason because first of all.  
NOTE Confidence: 0.92376738  
00:35:52.676 --> 00:35:54.924 Comparing biopsies versus hysterectomy  
NOTE Confidence: 0.92376738  
00:35:54.924 --> 00:35:58.090 of course fixation is probably better  
NOTE Confidence: 0.92376738  
00:35:58.090 --> 00:36:01.359 and and a better controlled and biopsies  
NOTE Confidence: 0.92376738  
00:36:01.439 --> 00:36:04.127 gradings compared to hysterectomy,  
NOTE Confidence: 0.92376738  
00:36:04.130 --> 00:36:06.965 especially if they're not open right away.  
NOTE Confidence: 0.92376738  
00:36:06.970 --> 00:36:09.910 Also we have to take the  
NOTE Confidence: 0.92376738  
00:36:09.910 --> 00:36:11.380 heterogeneity into consideration.  
NOTE Confidence: 0.92376738  
00:36:11.380 --> 00:36:13.780 What will give us a better  
NOTE Confidence: 0.92376738  
00:36:13.780 --> 00:36:15.380 sampling of the tumor?  
NOTE Confidence: 0.92376738  
00:36:15.380 --> 00:36:19.088 Is it if we select one block from the  
NOTE Confidence: 0.92376738

00:36:19.088 --> 00:36:21.075 hysterectomy or is it potentially

NOTE Confidence: 0.92376738

00:36:21.075 --> 00:36:22.774 a more spatially?

NOTE Confidence: 0.92376738

00:36:22.774 --> 00:36:26.590 Heterogeneous sampling, and inoculating.

NOTE Confidence: 0.92376738

00:36:26.590 --> 00:36:30.490 Also, the timing of the sample.

NOTE Confidence: 0.92376738

00:36:30.490 --> 00:36:33.646 In breast cancer? UM, it's a.

NOTE Confidence: 0.92376738

00:36:33.650 --> 00:36:37.202 It's a very important to have the her

NOTE Confidence: 0.92376738

00:36:37.202 --> 00:36:42.250 two status information before the.

NOTE Confidence: 0.92376738

00:36:42.250 --> 00:36:43.519 Definitive surgery because

NOTE Confidence: 0.92376738

00:36:43.519 --> 00:36:45.634 oftentimes based on that result,

NOTE Confidence: 0.92376738

00:36:45.640 --> 00:36:48.165 the patient will be offered

NOTE Confidence: 0.92376738

00:36:48.165 --> 00:36:49.175 neoadjuvant chemotherapy.

NOTE Confidence: 0.92376738

00:36:49.180 --> 00:36:51.287 So that's why I think it's a.

NOTE Confidence: 0.92376738

00:36:51.290 --> 00:36:53.342 It's a straightforward to do the

NOTE Confidence: 0.92376738

00:36:53.342 --> 00:36:55.530 started testing on the core biopsy.

NOTE Confidence: 0.92376738

00:36:55.530 --> 00:36:57.918 There is no such consideration or

NOTE Confidence: 0.92376738

00:36:57.918 --> 00:37:00.729 it's much less common in dimitriou

NOTE Confidence: 0.92376738

00:37:00.729 --> 00:37:03.013 cancer patients don't typically

NOTE Confidence: 0.92376738

00:37:03.013 --> 00:37:04.726 get neoadjuvant treatment,

NOTE Confidence: 0.92376738

00:37:04.730 --> 00:37:06.430 so for that reason,

NOTE Confidence: 0.92376738

00:37:06.430 --> 00:37:09.506 the the testing could wait until the

NOTE Confidence: 0.92376738

00:37:09.506 --> 00:37:12.164 hysterectomy in most of the cases.

NOTE Confidence: 0.92376738

00:37:12.170 --> 00:37:13.529 The question also,

NOTE Confidence: 0.92376738

00:37:13.529 --> 00:37:15.794 should we test multiple blocks?

NOTE Confidence: 0.92376738

00:37:15.800 --> 00:37:19.979 Should we test the metastasis if the?

NOTE Confidence: 0.92376738

00:37:19.980 --> 00:37:21.345 Primary was negative,

NOTE Confidence: 0.92376738

00:37:21.345 --> 00:37:24.075 so so to answer these questions,

NOTE Confidence: 0.92376738

00:37:24.080 --> 00:37:28.049 we can again take a look at the gastric

NOTE Confidence: 0.92376738

00:37:28.049 --> 00:37:30.697 literature and and learn from what.

NOTE Confidence: 0.92376738

00:37:30.700 --> 00:37:34.263 They found in gastric carcinomas a

NOTE Confidence: 0.92376738

00:37:34.263 --> 00:37:37.881 nice study from University of Rochester

NOTE Confidence: 0.92376738

00:37:37.881 --> 00:37:41.400 showed that the more specimens you test,

NOTE Confidence: 0.92376738

00:37:41.400 --> 00:37:43.295 the higher the likelihood that  
NOTE Confidence: 0.92376738

00:37:43.295 --> 00:37:45.720 you'll get her two positive result.  
NOTE Confidence: 0.92376738

00:37:45.720 --> 00:37:49.650 So comparing patients with only one  
NOTE Confidence: 0.92376738

00:37:49.650 --> 00:37:53.180 specimen from 12% positive ITI rate,  
NOTE Confidence: 0.92376738

00:37:53.180 --> 00:37:56.640 you go up to 24% of positive  
NOTE Confidence: 0.92376738

00:37:56.640 --> 00:37:58.940 ITI rate if patients have.  
NOTE Confidence: 0.92376738

00:37:58.940 --> 00:38:01.229 More than more than one specimen so.  
NOTE Confidence: 0.813491637333333

00:38:03.360 --> 00:38:06.104 Based on that, we designed a study  
NOTE Confidence: 0.813491637333333

00:38:06.104 --> 00:38:08.987 that Douglas was working on and and  
NOTE Confidence: 0.813491637333333

00:38:08.987 --> 00:38:11.429 published last year to compare the  
NOTE Confidence: 0.813491637333333

00:38:11.512 --> 00:38:14.844 her two status in paired biopsy and  
NOTE Confidence: 0.813491637333333

00:38:14.844 --> 00:38:17.356 hysterectomy specimens and showed that  
NOTE Confidence: 0.813491637333333

00:38:17.356 --> 00:38:21.255 the concordance was a lower than what  
NOTE Confidence: 0.813491637333333

00:38:21.255 --> 00:38:25.245 was reported in breast tumor literature,  
NOTE Confidence: 0.813491637333333

00:38:25.250 --> 00:38:26.982 so only 84% concordance,  
NOTE Confidence: 0.813491637333333

00:38:26.982 --> 00:38:30.608 and so if we only tested the endometrial

NOTE Confidence: 0.813491637333333  
00:38:30.608 --> 00:38:34.717 passes or grading the we would have a 15%.  
NOTE Confidence: 0.813491637333333  
00:38:34.717 --> 00:38:35.788 False negative rate,  
NOTE Confidence: 0.813491637333333  
00:38:35.788 --> 00:38:37.930 and if we only tested the  
NOTE Confidence: 0.813491637333333  
00:38:38.006 --> 00:38:40.006 hysterectomy you would have almost  
NOTE Confidence: 0.813491637333333  
00:38:40.006 --> 00:38:43.362 a 30% of false negative rates.  
NOTE Confidence: 0.813491637333333  
00:38:43.362 --> 00:38:46.136 So it really is true also for  
NOTE Confidence: 0.813491637333333  
00:38:46.136 --> 00:38:48.376 endometrial cancer that if we test  
NOTE Confidence: 0.813491637333333  
00:38:48.376 --> 00:38:50.226 multiple specimens then we increase  
NOTE Confidence: 0.813491637333333  
00:38:50.226 --> 00:38:52.818 the rate of her two positive ITI.  
NOTE Confidence: 0.813491637333333  
00:38:52.820 --> 00:38:55.389 Here are the six cases from this  
NOTE Confidence: 0.813491637333333  
00:38:55.389 --> 00:38:58.071 study that had a discrepant result  
NOTE Confidence: 0.813491637333333  
00:38:58.071 --> 00:39:00.571 between the biopsy and hysterectomy  
NOTE Confidence: 0.813491637333333  
00:39:00.571 --> 00:39:03.382 and most of the cases the change  
NOTE Confidence: 0.813491637333333  
00:39:03.382 --> 00:39:06.274 went from positive in the biopsy  
NOTE Confidence: 0.813491637333333  
00:39:06.274 --> 00:39:09.300 to negative and the hysterectomy.  
NOTE Confidence: 0.813491637333333

00:39:09.300 --> 00:39:12.164 Here is one of the examples where the  
NOTE Confidence: 0.8134916373333333

00:39:12.164 --> 00:39:14.692 biopsy was strongly positive or three  
NOTE Confidence: 0.8134916373333333

00:39:14.692 --> 00:39:17.740 plus and hysterectomy was a one plus.  
NOTE Confidence: 0.769834814

00:39:20.500 --> 00:39:22.710 Nice study from the Netherlands.  
NOTE Confidence: 0.769834814

00:39:22.710 --> 00:39:25.258 Looked at paired primary  
NOTE Confidence: 0.769834814

00:39:25.258 --> 00:39:27.169 and metastatic tumors,  
NOTE Confidence: 0.769834814

00:39:27.170 --> 00:39:29.750 metastatic and amietiel or carcinomas,  
NOTE Confidence: 0.769834814

00:39:29.750 --> 00:39:31.490 including serious carcinoma,  
NOTE Confidence: 0.769834814

00:39:31.490 --> 00:39:34.390 and they found that overall  
NOTE Confidence: 0.769834814

00:39:34.390 --> 00:39:37.356 there is a 23% discordance rate  
NOTE Confidence: 0.769834814

00:39:37.356 --> 00:39:40.066 between these tumors and again  
NOTE Confidence: 0.769834814

00:39:40.066 --> 00:39:42.910 the change could go both ways.  
NOTE Confidence: 0.769834814

00:39:42.910 --> 00:39:44.572 It could go from a positive  
NOTE Confidence: 0.769834814

00:39:44.572 --> 00:39:46.601 to negative or from a her two  
NOTE Confidence: 0.769834814

00:39:46.601 --> 00:39:48.036 negative to her two positive.  
NOTE Confidence: 0.9245777666666667

00:39:50.300 --> 00:39:52.898 For specimen handling.

NOTE Confidence: 0.924577766666667  
00:39:52.900 --> 00:39:55.942 The current recommendations for best breast  
NOTE Confidence: 0.924577766666667  
00:39:55.942 --> 00:39:59.220 and gastric cancer is cold ischaemia.  
NOTE Confidence: 0.924577766666667  
00:39:59.220 --> 00:40:02.444 Time of 1 hour or less and at  
NOTE Confidence: 0.924577766666667  
00:40:02.444 --> 00:40:07.190 least six hours of fixation. Uhm?  
NOTE Confidence: 0.924577766666667  
00:40:07.190 --> 00:40:11.022 So in terms of future on directions. Uhm?  
NOTE Confidence: 0.924577766666667  
00:40:11.022 --> 00:40:16.800 We still need to work on identifying the  
NOTE Confidence: 0.924577766666667  
00:40:16.800 --> 00:40:20.700 the correlation between clinical response  
NOTE Confidence: 0.924577766666667  
00:40:20.700 --> 00:40:24.396 and her two IC and fish characteristics,  
NOTE Confidence: 0.924577766666667  
00:40:24.400 --> 00:40:25.960 and in addition to that,  
NOTE Confidence: 0.924577766666667  
00:40:25.960 --> 00:40:27.927 there are new her two testing methods,  
NOTE Confidence: 0.924577766666667  
00:40:27.930 --> 00:40:32.424 namely sequencing, that may also be  
NOTE Confidence: 0.924577766666667  
00:40:32.424 --> 00:40:37.490 used for evaluation of her two status.  
NOTE Confidence: 0.924577766666667  
00:40:37.490 --> 00:40:40.577 In addition, there is a question about  
NOTE Confidence: 0.924577766666667  
00:40:40.577 --> 00:40:44.484 should we test the for the extracellular or  
NOTE Confidence: 0.924577766666667  
00:40:44.484 --> 00:40:47.820 the intracellular domain of the receptor?  
NOTE Confidence: 0.924577766666667

00:40:47.820 --> 00:40:49.824 And also, what about her too  
NOTE Confidence: 0.924577766666667

00:40:49.824 --> 00:40:51.160 and other gynecological tumors?  
NOTE Confidence: 0.924577766666667

00:40:51.160 --> 00:40:54.120 High grade endometrial carcinomas,  
NOTE Confidence: 0.924577766666667

00:40:54.120 --> 00:40:55.600 or carcinosarcoma?  
NOTE Confidence: 0.924577766666667

00:40:55.600 --> 00:40:58.666 There is also a lot of history  
NOTE Confidence: 0.924577766666667

00:40:58.666 --> 00:41:00.526 type agnostic clinical trials.  
NOTE Confidence: 0.924577766666667

00:41:00.526 --> 00:41:04.126 What should we use for those trials?  
NOTE Confidence: 0.924577766666667

00:41:04.126 --> 00:41:05.458 Scoring criteria?  
NOTE Confidence: 0.924577766666667

00:41:05.458 --> 00:41:08.007 And then finally what?  
NOTE Confidence: 0.924577766666667

00:41:08.007 --> 00:41:10.742 Is there any correlation between  
NOTE Confidence: 0.924577766666667

00:41:10.742 --> 00:41:14.370 the her two status and prognosis?  
NOTE Confidence: 0.924577766666667

00:41:14.370 --> 00:41:17.226 In terms of the next generation sequencing,  
NOTE Confidence: 0.924577766666667

00:41:17.230 --> 00:41:21.236 there is a study from a MSK a couple  
NOTE Confidence: 0.924577766666667

00:41:21.236 --> 00:41:24.330 years ago showing very nice very high  
NOTE Confidence: 0.924577766666667

00:41:24.426 --> 00:41:28.382 concordance between the her two IC and  
NOTE Confidence: 0.924577766666667

00:41:28.382 --> 00:41:33.608 fish and the MSK impact sequencing platform.

NOTE Confidence: 0.924577766666667  
00:41:33.610 --> 00:41:34.370 And similarly,  
NOTE Confidence: 0.924577766666667  
00:41:34.370 --> 00:41:35.510 just this year,  
NOTE Confidence: 0.924577766666667  
00:41:35.510 --> 00:41:38.882 published from Brigham UM,  
NOTE Confidence: 0.924577766666667  
00:41:38.882 --> 00:41:41.654 they identified 100% concordance  
NOTE Confidence: 0.924577766666667  
00:41:41.654 --> 00:41:43.822 between next generation sequencing  
NOTE Confidence: 0.924577766666667  
00:41:43.822 --> 00:41:45.990 results and the combined.  
NOTE Confidence: 0.924577766666667  
00:41:45.990 --> 00:41:48.355 I see fish interpretation and  
NOTE Confidence: 0.924577766666667  
00:41:48.355 --> 00:41:50.247 under meteor serious carcinoma.  
NOTE Confidence: 0.924577766666667  
00:41:50.250 --> 00:41:52.080 So this this almost sounds  
NOTE Confidence: 0.924577766666667  
00:41:52.080 --> 00:41:53.910 too good to be true,  
NOTE Confidence: 0.924577766666667  
00:41:53.910 --> 00:41:56.934 and I think one of the issues with  
NOTE Confidence: 0.924577766666667  
00:41:56.934 --> 00:41:59.226 this study was that almost very  
NOTE Confidence: 0.924577766666667  
00:41:59.226 --> 00:42:02.132 high percent of the cases 75% of  
NOTE Confidence: 0.924577766666667  
00:42:02.132 --> 00:42:05.018 the tumors were her two negative.  
NOTE Confidence: 0.924577766666667  
00:42:05.020 --> 00:42:08.075 So it's it's it's easier  
NOTE Confidence: 0.924577766666667

00:42:08.075 --> 00:42:09.908 to achieve concordant.  
NOTE Confidence: 0.924577766666667

00:42:09.910 --> 00:42:10.404 Uhm,  
NOTE Confidence: 0.924577766666667

00:42:10.404 --> 00:42:13.368 result when when the tumors her  
NOTE Confidence: 0.924577766666667

00:42:13.368 --> 00:42:15.981 two negative only 20% were two  
NOTE Confidence: 0.924577766666667

00:42:15.981 --> 00:42:19.107 plus and only 4% were three plus.  
NOTE Confidence: 0.924577766666667

00:42:19.107 --> 00:42:22.341 And also fish was only performed  
NOTE Confidence: 0.924577766666667

00:42:22.341 --> 00:42:25.789 on a smaller number of tumors.  
NOTE Confidence: 0.924577766666667

00:42:25.790 --> 00:42:26.226 Uhm,  
NOTE Confidence: 0.924577766666667

00:42:26.226 --> 00:42:29.278 a couple of years ago we also  
NOTE Confidence: 0.924577766666667

00:42:29.278 --> 00:42:31.817 presented our data on the  
NOTE Confidence: 0.924577766666667

00:42:31.817 --> 00:42:35.310 correlation between icy fish and next  
NOTE Confidence: 0.924577766666667

00:42:35.310 --> 00:42:37.686 generation sequencing or sequencing.  
NOTE Confidence: 0.924577766666667

00:42:37.690 --> 00:42:42.240 Results were from mostly just.  
NOTE Confidence: 0.924577766666667

00:42:42.240 --> 00:42:44.665 Retrieved from the foundation medicine  
NOTE Confidence: 0.924577766666667

00:42:44.665 --> 00:42:47.542 or the tumor profiling lab results  
NOTE Confidence: 0.924577766666667

00:42:47.542 --> 00:42:50.526 and we found that indeed we have 100%

NOTE Confidence: 0.924577766666667  
00:42:50.530 --> 00:42:53.380 concordance among the negative cases,  
NOTE Confidence: 0.924577766666667  
00:42:53.380 --> 00:42:56.075 but the concordance is much lower when  
NOTE Confidence: 0.924577766666667  
00:42:56.075 --> 00:43:00.960 we look at the positive cases only 43%.  
NOTE Confidence: 0.924577766666667  
00:43:00.960 --> 00:43:01.732 Concordance rate,  
NOTE Confidence: 0.924577766666667  
00:43:01.732 --> 00:43:04.048 but that still gives an overall  
NOTE Confidence: 0.924577766666667  
00:43:04.050 --> 00:43:06.980 87% concordance for these tumors.  
NOTE Confidence: 0.782352527692308  
00:43:11.130 --> 00:43:14.119 An enemy to our cancer is also  
NOTE Confidence: 0.782352527692308  
00:43:14.119 --> 00:43:16.320 different from other tumor types  
NOTE Confidence: 0.782352527692308  
00:43:16.320 --> 00:43:19.770 and with with regards to the.  
NOTE Confidence: 0.782352527692308  
00:43:19.770 --> 00:43:21.854 So cellular and extracellular  
NOTE Confidence: 0.782352527692308  
00:43:21.854 --> 00:43:23.938 domain of the receptor.  
NOTE Confidence: 0.782352527692308  
00:43:23.940 --> 00:43:25.640 Several studies have shown,  
NOTE Confidence: 0.782352527692308  
00:43:25.640 --> 00:43:27.340 including David Dream slap,  
NOTE Confidence: 0.782352527692308  
00:43:27.340 --> 00:43:29.360 that on these tumors often  
NOTE Confidence: 0.782352527692308  
00:43:29.360 --> 00:43:30.976 shut the extracellular domain,  
NOTE Confidence: 0.782352527692308

00:43:30.980 --> 00:43:34.722 which is the the drug binding domain,  
NOTE Confidence: 0.782352527692308

00:43:34.722 --> 00:43:36.782 to Susan Medwed binds to  
NOTE Confidence: 0.782352527692308

00:43:36.782 --> 00:43:38.018 the extracellular domain.  
NOTE Confidence: 0.782352527692308

00:43:38.020 --> 00:43:39.180 So once you lose that,  
NOTE Confidence: 0.782352527692308

00:43:39.180 --> 00:43:41.040 you lose the therapeutic target.  
NOTE Confidence: 0.782352527692308

00:43:41.040 --> 00:43:43.074 Yet most of the antibodies were  
NOTE Confidence: 0.782352527692308

00:43:43.074 --> 00:43:45.399 used in technical lab to detect her.  
NOTE Confidence: 0.782352527692308

00:43:45.400 --> 00:43:47.232 Two expression is actually  
NOTE Confidence: 0.782352527692308

00:43:47.232 --> 00:43:49.064 against the intracellular domain.  
NOTE Confidence: 0.782352527692308

00:43:49.070 --> 00:43:49.834 So are her two.  
NOTE Confidence: 0.782352527692308

00:43:49.834 --> 00:43:50.407 Let me know.  
NOTE Confidence: 0.782352527692308

00:43:50.410 --> 00:43:52.290 Staying may still be positive,  
NOTE Confidence: 0.782352527692308

00:43:52.290 --> 00:43:55.991 and yet the tumor may not responded  
NOTE Confidence: 0.782352527692308

00:43:55.991 --> 00:43:58.046 to treatment for that reason,  
NOTE Confidence: 0.782352527692308

00:43:58.050 --> 00:44:00.790 so that's another important consideration,  
NOTE Confidence: 0.782352527692308

00:44:00.790 --> 00:44:05.638 and here are some nice images from doctors,

NOTE Confidence: 0.782352527692308  
00:44:05.640 --> 00:44:09.948 rim rim slab showing the differences.  
NOTE Confidence: 0.782352527692308  
00:44:09.950 --> 00:44:12.130 I intracellular domain was  
NOTE Confidence: 0.782352527692308  
00:44:12.130 --> 00:44:14.670 labeled with the CB11 antibody,  
NOTE Confidence: 0.782352527692308  
00:44:14.670 --> 00:44:16.830 which we use for awhile now.  
NOTE Confidence: 0.782352527692308  
00:44:16.830 --> 00:44:18.480 We we use EP3 currently which  
NOTE Confidence: 0.782352527692308  
00:44:18.480 --> 00:44:20.200 is also against the interests.  
NOTE Confidence: 0.782352527692308  
00:44:20.200 --> 00:44:23.552 The domain and the only antibody  
NOTE Confidence: 0.782352527692308  
00:44:23.552 --> 00:44:25.662 clone that targets the extracellular  
NOTE Confidence: 0.782352527692308  
00:44:25.662 --> 00:44:27.909 domain that at least I'm aware  
NOTE Confidence: 0.782352527692308  
00:44:27.909 --> 00:44:32.308 of is the SP3 antibody and so.  
NOTE Confidence: 0.782352527692308  
00:44:32.310 --> 00:44:35.285 88% of the tumors with a high  
NOTE Confidence: 0.782352527692308  
00:44:35.285 --> 00:44:37.286 intracellular domain had low  
NOTE Confidence: 0.782352527692308  
00:44:37.286 --> 00:44:39.866 extracellular domain labeling levels.  
NOTE Confidence: 0.686973425714286  
00:44:42.950 --> 00:44:46.102 Her two testing could also be expanded to  
NOTE Confidence: 0.686973425714286  
00:44:46.102 --> 00:44:49.400 other high grade under material carcinomas.  
NOTE Confidence: 0.686973425714286

00:44:49.400 --> 00:44:51.512 There are several studies that just  
NOTE Confidence: 0.686973425714286

00:44:51.512 --> 00:44:54.143 came out this year showing that her  
NOTE Confidence: 0.686973425714286

00:44:54.143 --> 00:44:56.381 two positive ITI is highly associated  
NOTE Confidence: 0.686973425714286

00:44:56.381 --> 00:44:59.662 with a P53 apparent Geno type,  
NOTE Confidence: 0.686973425714286

00:44:59.662 --> 00:45:02.194 regardless of histologic classification.  
NOTE Confidence: 0.686973425714286

00:45:02.200 --> 00:45:06.399 As many of you know, there is some.  
NOTE Confidence: 0.686973425714286

00:45:06.400 --> 00:45:10.176 Uhm, interobserver variability and  
NOTE Confidence: 0.686973425714286

00:45:10.176 --> 00:45:14.896 how these tumors are classified.  
NOTE Confidence: 0.686973425714286

00:45:14.900 --> 00:45:17.766 So basically you could have a P53 aberrant  
NOTE Confidence: 0.686973425714286

00:45:17.766 --> 00:45:19.794 tumor that based on other features  
NOTE Confidence: 0.686973425714286

00:45:19.794 --> 00:45:22.222 may be called a clear cell carcinoma  
NOTE Confidence: 0.686973425714286

00:45:22.222 --> 00:45:24.600 or a grade 3 endometrial carcinoma,  
NOTE Confidence: 0.686973425714286

00:45:24.600 --> 00:45:28.513 and that would potentially make the patients  
NOTE Confidence: 0.686973425714286

00:45:28.513 --> 00:45:31.709 ineligible for ineligible for the treatment.  
NOTE Confidence: 0.686973425714286

00:45:31.710 --> 00:45:34.475 So there is there is a potential  
NOTE Confidence: 0.686973425714286

00:45:34.475 --> 00:45:37.230 to expand the treatment for to

NOTE Confidence: 0.686973425714286  
00:45:37.230 --> 00:45:39.700 include these tumors as well.  
NOTE Confidence: 0.686973425714286  
00:45:39.700 --> 00:45:42.204 And one of the studies showed that the  
NOTE Confidence: 0.686973425714286  
00:45:42.204 --> 00:45:43.820 correlation was even stronger between  
NOTE Confidence: 0.686973425714286  
00:45:43.820 --> 00:45:46.666 the her two status and the P53 mutation.  
NOTE Confidence: 0.686973425714286  
00:45:46.666 --> 00:45:50.610 Then her two status and serious sister type.  
NOTE Confidence: 0.686973425714286  
00:45:50.610 --> 00:45:54.570 And this was a one of our studies in  
NOTE Confidence: 0.686973425714286  
00:45:54.570 --> 00:45:56.194 collaboration with the University  
NOTE Confidence: 0.686973425714286  
00:45:56.194 --> 00:45:56.962 of Wisconsin,  
NOTE Confidence: 0.686973425714286  
00:45:56.962 --> 00:45:59.266 showing her two positive ITI in  
NOTE Confidence: 0.686973425714286  
00:45:59.266 --> 00:46:01.039 a clear soccer Sonoma.  
NOTE Confidence: 0.878378875  
00:46:03.630 --> 00:46:06.481 Similarly, in Carcinosarcoma's there are  
NOTE Confidence: 0.878378875  
00:46:06.481 --> 00:46:08.420 in vitro and in vivo studies showing.  
NOTE Confidence: 0.668924677142857  
00:46:11.020 --> 00:46:15.458 UMD at the targeted treatment may work.  
NOTE Confidence: 0.668924677142857  
00:46:15.460 --> 00:46:19.460 And in our study, we found that 12%  
NOTE Confidence: 0.668924677142857  
00:46:19.460 --> 00:46:22.952 of course in sarcomas are positive  
NOTE Confidence: 0.668924677142857

00:46:22.952 --> 00:46:26.344 if you use the 2007 criteria,  
NOTE Confidence: 0.668924677142857

00:46:26.344 --> 00:46:29.610 most of them are uterine her two  
NOTE Confidence: 0.668924677142857

00:46:29.610 --> 00:46:31.710 positive ITI is much less common and  
NOTE Confidence: 0.668924677142857

00:46:31.710 --> 00:46:34.037 high grade ovarian serous carcinomas,  
NOTE Confidence: 0.668924677142857

00:46:34.040 --> 00:46:35.688 so 14% versus 7%.  
NOTE Confidence: 0.668924677142857

00:46:35.688 --> 00:46:38.668 And most of the tumors that were  
NOTE Confidence: 0.668924677142857

00:46:38.668 --> 00:46:41.140 hurt a positive had a serious  
NOTE Confidence: 0.668924677142857

00:46:41.140 --> 00:46:45.440 or a mixed epithelial component.  
NOTE Confidence: 0.668924677142857

00:46:45.440 --> 00:46:48.560 Heterogeneity similar to an immediate,  
NOTE Confidence: 0.668924677142857

00:46:48.560 --> 00:46:50.260 serious carcinomas was also  
NOTE Confidence: 0.668924677142857

00:46:50.260 --> 00:46:52.385 commonly seen in these tumors,  
NOTE Confidence: 0.668924677142857

00:46:52.390 --> 00:46:54.322 and most of them had a positive  
NOTE Confidence: 0.668924677142857

00:46:54.322 --> 00:46:56.539 ITI in the carcinoma component.  
NOTE Confidence: 0.668924677142857

00:46:56.540 --> 00:46:58.591 Only one case had a two plus  
NOTE Confidence: 0.668924677142857

00:46:58.591 --> 00:47:00.810 staining in the circular component,  
NOTE Confidence: 0.668924677142857

00:47:00.810 --> 00:47:03.666 which is shown here on the upper right.

NOTE Confidence: 0.744379424705882  
00:47:05.970 --> 00:47:08.760 So there is currently a clinical  
NOTE Confidence: 0.744379424705882  
00:47:08.760 --> 00:47:11.894 trial in Japan and the Japanese  
NOTE Confidence: 0.744379424705882  
00:47:11.894 --> 00:47:14.829 group already published data on.  
NOTE Confidence: 0.744379424705882  
00:47:14.830 --> 00:47:17.567 Compared to status and they found they  
NOTE Confidence: 0.744379424705882  
00:47:17.567 --> 00:47:19.646 actually compared the gastric criteria  
NOTE Confidence: 0.744379424705882  
00:47:19.646 --> 00:47:22.148 with the current breast criteria and  
NOTE Confidence: 0.744379424705882  
00:47:22.148 --> 00:47:24.574 they found 70% concordance between  
NOTE Confidence: 0.744379424705882  
00:47:24.574 --> 00:47:27.214 the two different scoring criteria,  
NOTE Confidence: 0.744379424705882  
00:47:27.220 --> 00:47:31.888 mostly due to the differences in lateral  
NOTE Confidence: 0.744379424705882  
00:47:31.888 --> 00:47:34.120 based, lateral membranous pattern.  
NOTE Confidence: 0.94928628  
00:47:37.350 --> 00:47:40.029 There are many.  
NOTE Confidence: 0.94928628  
00:47:40.030 --> 00:47:42.898 Tissue agnostic or tumor type agnostic  
NOTE Confidence: 0.94928628  
00:47:42.898 --> 00:47:44.810 clinical trials are available.  
NOTE Confidence: 0.94928628  
00:47:44.810 --> 00:47:47.701 Basket trials that may include all solid  
NOTE Confidence: 0.94928628  
00:47:47.701 --> 00:47:50.768 tumors with her two positive positive status.  
NOTE Confidence: 0.94928628

00:47:50.768 --> 00:47:53.372 So what scoring criteria should we  
NOTE Confidence: 0.94928628

00:47:53.372 --> 00:47:56.159 use for for these trials or what?  
NOTE Confidence: 0.94928628

00:47:56.160 --> 00:47:58.872 What are those trials using one of  
NOTE Confidence: 0.94928628

00:47:58.872 --> 00:48:02.070 them was recently published, so I.  
NOTE Confidence: 0.94928628

00:48:02.070 --> 00:48:04.639 Went into the details and into the  
NOTE Confidence: 0.94928628

00:48:04.639 --> 00:48:06.769 supplementary material to find out how  
NOTE Confidence: 0.94928628

00:48:06.769 --> 00:48:08.689 was the her two status determined.  
NOTE Confidence: 0.94928628

00:48:08.690 --> 00:48:11.198 This particular trial included  
NOTE Confidence: 0.94928628

00:48:11.198 --> 00:48:13.079 two endometrial cancer.  
NOTE Confidence: 0.94928628

00:48:13.080 --> 00:48:14.746 Is one of them was not tested,  
NOTE Confidence: 0.94928628

00:48:14.750 --> 00:48:17.918 the other one was her 2/3 plus positive  
NOTE Confidence: 0.94928628

00:48:17.920 --> 00:48:21.960 and the only comment they made on how  
NOTE Confidence: 0.94928628

00:48:21.960 --> 00:48:24.880 the status was determined was that  
NOTE Confidence: 0.94928628

00:48:24.880 --> 00:48:27.491 the heritage status was defined on  
NOTE Confidence: 0.94928628

00:48:27.491 --> 00:48:30.200 the basis of local lab testing data  
NOTE Confidence: 0.94928628

00:48:30.284 --> 00:48:32.918 and no further detail is provided.

NOTE Confidence: 0.94928628

00:48:32.920 --> 00:48:35.975 These are the currently ongoing

NOTE Confidence: 0.94928628

00:48:35.975 --> 00:48:38.419 trials for endometrial serous

NOTE Confidence: 0.94928628

00:48:38.419 --> 00:48:41.158 carcinomas and coarseness sarcomas.

NOTE Confidence: 0.94928628

00:48:41.160 --> 00:48:44.104 And I expect there will be many more.

NOTE Confidence: 0.94928628

00:48:44.110 --> 00:48:47.060 There are many more in the works and

NOTE Confidence: 0.94928628

00:48:47.060 --> 00:48:49.700 I think lastly, on the prognostic,

NOTE Confidence: 0.94928628

00:48:49.700 --> 00:48:50.820 prognostic,

NOTE Confidence: 0.94928628

00:48:50.820 --> 00:48:54.820 and predictive significance of her two

NOTE Confidence: 0.94928628

00:48:54.820 --> 00:48:58.060 status in breast cancer and gastric cancer.

NOTE Confidence: 0.94928628

00:48:58.060 --> 00:49:01.600 It's a known negative prognostic marker,

NOTE Confidence: 0.94928628

00:49:01.600 --> 00:49:04.792 and in breast cancer also her two

NOTE Confidence: 0.94928628

00:49:04.792 --> 00:49:07.994 positive ITI predicts a good response

NOTE Confidence: 0.94928628

00:49:07.994 --> 00:49:10.318 to other chemotherapeutic agents.

NOTE Confidence: 0.94928628

00:49:10.320 --> 00:49:13.850 Soum a large, collaborative study,

NOTE Confidence: 0.94928628

00:49:13.850 --> 00:49:16.875 also looked at the correlation

NOTE Confidence: 0.94928628

00:49:16.875 --> 00:49:19.485 between prognosis and her two  
NOTE Confidence: 0.94928628

00:49:19.485 --> 00:49:21.345 status in endometrial cancer,  
NOTE Confidence: 0.94928628

00:49:21.350 --> 00:49:23.910 and found that that is also true and,  
NOTE Confidence: 0.94928628

00:49:23.910 --> 00:49:25.935 and the meteor serous carcinomas  
NOTE Confidence: 0.94928628

00:49:25.935 --> 00:49:28.521 her two positive tumors have worse  
NOTE Confidence: 0.94928628

00:49:28.521 --> 00:49:30.956 progression free and overall survival.  
NOTE Confidence: 0.931616652857143

00:49:32.970 --> 00:49:36.936 So in summary, about 25 to 30% of  
NOTE Confidence: 0.931616652857143

00:49:36.936 --> 00:49:39.732 endometrial serous carcinomas are her two  
NOTE Confidence: 0.931616652857143

00:49:39.732 --> 00:49:42.896 positive to Tsumeb improves progression  
NOTE Confidence: 0.931616652857143

00:49:42.896 --> 00:49:46.940 free and overall survival if added  
NOTE Confidence: 0.931616652857143

00:49:47.050 --> 00:49:50.890 to the standard chemotherapy regimen.  
NOTE Confidence: 0.931616652857143

00:49:50.890 --> 00:49:53.554 There are unique features of Hurtigruten  
NOTE Confidence: 0.931616652857143

00:49:53.554 --> 00:49:55.330 expression and gene amplification,  
NOTE Confidence: 0.931616652857143

00:49:55.330 --> 00:49:59.560 and the because of that.  
NOTE Confidence: 0.931616652857143

00:49:59.560 --> 00:50:02.440 Speaker two testing and scoring  
NOTE Confidence: 0.931616652857143

00:50:02.440 --> 00:50:05.506 algorithm was proposed based on the

NOTE Confidence: 0.931616652857143

00:50:05.510 --> 00:50:09.080 2018 clinical trial enrollment data.

NOTE Confidence: 0.931616652857143

00:50:09.080 --> 00:50:11.880 There's also prognostic significance of

NOTE Confidence: 0.931616652857143

00:50:11.880 --> 00:50:15.459 her two status and potentially weakening.

NOTE Confidence: 0.78061792

00:50:17.540 --> 00:50:20.810 We can expand this a targeted therapy

NOTE Confidence: 0.78061792

00:50:20.810 --> 00:50:24.578 to other tumor types and also to early

NOTE Confidence: 0.78061792

00:50:24.578 --> 00:50:27.350 stage and a meteor service carcinoma.

NOTE Confidence: 0.78061792

00:50:27.350 --> 00:50:31.222 And I would like to acknowledge my colleagues

NOTE Confidence: 0.78061792

00:50:31.222 --> 00:50:34.848 and many of them helping me in pathology,

NOTE Confidence: 0.78061792

00:50:34.850 --> 00:50:37.935 especially pay hue and also

NOTE Confidence: 0.78061792

00:50:37.935 --> 00:50:40.153 in gynecological oncology, Dr.

NOTE Confidence: 0.78061792

00:50:40.153 --> 00:50:43.057 Santina and his lab and all the other

NOTE Confidence: 0.78061792

00:50:43.057 --> 00:50:44.676 wonderful gynecological oncologist

NOTE Confidence: 0.78061792

00:50:44.676 --> 00:50:47.626 gynecologist center in our group.

NOTE Confidence: 0.78061792

00:50:47.630 --> 00:50:49.350 So thank you very much.

NOTE Confidence: 0.78061792

00:50:49.350 --> 00:50:50.160 Period attention.

NOTE Confidence: 0.68609166

00:50:54.450 --> 00:50:58.012 That was wonderful and I don't see  
NOTE Confidence: 0.68609166

00:50:58.012 --> 00:51:01.059 any questions in the chat yet.  
NOTE Confidence: 0.791896709090909

00:51:01.060 --> 00:51:04.724 But I do have a couple of companies  
NOTE Confidence: 0.791896709090909

00:51:04.724 --> 00:51:10.012 since her Tonio has is now embracing  
NOTE Confidence: 0.791896709090909

00:51:10.012 --> 00:51:12.826 adenocarcinomas in multiple.  
NOTE Confidence: 0.791896709090909

00:51:12.830 --> 00:51:17.846 Organ systems. Breast GY and ovary  
NOTE Confidence: 0.791896709090909

00:51:17.846 --> 00:51:22.990 and Dmitry AM gastric colorectal.  
NOTE Confidence: 0.791896709090909

00:51:22.990 --> 00:51:27.412 Uhm, why is it not used  
NOTE Confidence: 0.791896709090909

00:51:27.412 --> 00:51:29.623 for lung adenocarcinomas?  
NOTE Confidence: 0.791896709090909

00:51:29.630 --> 00:51:32.210 That's question number one and  
NOTE Confidence: 0.791896709090909

00:51:32.210 --> 00:51:35.486 the question #2 is what about  
NOTE Confidence: 0.791896709090909

00:51:35.486 --> 00:51:37.874 squamous cell carcinomas and  
NOTE Confidence: 0.791896709090909

00:51:37.874 --> 00:51:40.742 number of those RP53 positive?  
NOTE Confidence: 0.791896709090909

00:51:40.742 --> 00:51:42.886 The high grade ones  
NOTE Confidence: 0.782180664

00:51:43.460 --> 00:51:46.100 you mean high grade serous  
NOTE Confidence: 0.782180664

00:51:46.100 --> 00:51:47.408 carcinomas over the ovary.

NOTE Confidence: 0.80118766875

00:51:48.120 --> 00:51:50.585 No, actually. My question is

NOTE Confidence: 0.80118766875

00:51:50.585 --> 00:51:52.760 outside of that. You yeah.

NOTE Confidence: 0.812015182857143

00:51:52.770 --> 00:51:54.128 No I said no I I got.

NOTE Confidence: 0.812015182857143

00:51:54.130 --> 00:51:55.762 I got lost because I at the same

NOTE Confidence: 0.812015182857143

00:51:55.762 --> 00:51:57.530 time I was reading David Ramsey.

NOTE Confidence: 0.812015182857143

00:51:57.530 --> 00:52:02.262 Comments here he yeah I think for

NOTE Confidence: 0.812015182857143

00:52:02.262 --> 00:52:04.354 long I mean what I could tell you

NOTE Confidence: 0.812015182857143

00:52:04.354 --> 00:52:06.058 is probably, you know there's.

NOTE Confidence: 0.812015182857143

00:52:06.058 --> 00:52:08.556 I'm sure there's so many large

NOTE Confidence: 0.812015182857143

00:52:08.556 --> 00:52:11.420 studies on the molecular.

NOTE Confidence: 0.812015182857143

00:52:11.420 --> 00:52:13.012 Characteristics of lung cancers,

NOTE Confidence: 0.812015182857143

00:52:13.012 --> 00:52:15.002 and it's probably that that

NOTE Confidence: 0.812015182857143

00:52:15.010 --> 00:52:16.640 her two amplification is just

NOTE Confidence: 0.812015182857143

00:52:16.640 --> 00:52:18.640 not common among I don't know.

NOTE Confidence: 0.812015182857143

00:52:18.640 --> 00:52:21.152 I mean I that would be my guess

NOTE Confidence: 0.812015182857143

00:52:21.152 --> 00:52:22.874 that similar to other high  
NOTE Confidence: 0.812015182857143

00:52:22.874 --> 00:52:24.920 grade tumors in the GI tract,  
NOTE Confidence: 0.812015182857143

00:52:24.920 --> 00:52:26.078 I can speak for, you know,  
NOTE Confidence: 0.812015182857143

00:52:26.080 --> 00:52:28.010 like a high grade serous  
NOTE Confidence: 0.812015182857143

00:52:28.010 --> 00:52:29.554 carcinomas of the ovaries.  
NOTE Confidence: 0.812015182857143

00:52:29.560 --> 00:52:32.409 As much as they are similar to  
NOTE Confidence: 0.812015182857143

00:52:32.409 --> 00:52:33.630 endometrial serous carcinomas,  
NOTE Confidence: 0.812015182857143

00:52:33.630 --> 00:52:35.985 the amplification hurt amplification and  
NOTE Confidence: 0.812015182857143

00:52:35.985 --> 00:52:38.800 overexpression rate is much much lower,  
NOTE Confidence: 0.812015182857143

00:52:38.800 --> 00:52:40.676 so it's really not a good good  
NOTE Confidence: 0.812015182857143

00:52:40.676 --> 00:52:42.190 therapeutic target for those tumors.  
NOTE Confidence: 0.960545

00:52:44.220 --> 00:52:46.712 I can comment on that in long.  
NOTE Confidence: 0.960545

00:52:46.712 --> 00:52:48.516 There's hardly any amplification.  
NOTE Confidence: 0.960545

00:52:48.520 --> 00:52:50.560 There's some mutation for her too,  
NOTE Confidence: 0.960545

00:52:50.560 --> 00:52:52.360 but hardly any information.  
NOTE Confidence: 0.960545

00:52:52.360 --> 00:52:53.680 But in Italian that was

NOTE Confidence: 0.960545

00:52:53.680 --> 00:52:54.700 just a terrific lecture.

NOTE Confidence: 0.960545

00:52:54.700 --> 00:52:55.796 Thank you very much.

NOTE Confidence: 0.960545

00:52:55.796 --> 00:52:56.618 Thank you David,

NOTE Confidence: 0.960545

00:52:56.620 --> 00:52:58.104 but I do have a couple questions.

NOTE Confidence: 0.944742234

00:52:58.830 --> 00:53:00.050 The first one is about

NOTE Confidence: 0.900553714666667

00:53:00.530 --> 00:53:02.602 the more you look, the more you find

NOTE Confidence: 0.900553714666667

00:53:02.602 --> 00:53:05.166 that is that the more specimens that you

NOTE Confidence: 0.900553714666667

00:53:05.166 --> 00:53:07.487 looked at suggests that there are some

NOTE Confidence: 0.900553714666667

00:53:07.487 --> 00:53:09.860 input of heterogeneity that is and and we

NOTE Confidence: 0.900553714666667

00:53:09.860 --> 00:53:11.120 see there's some breast cancer as well.

NOTE Confidence: 0.900553714666667

00:53:11.120 --> 00:53:12.520 That is that if you look at more,

NOTE Confidence: 0.900553714666667

00:53:12.520 --> 00:53:13.820 there's some some breast cancers.

NOTE Confidence: 0.900553714666667

00:53:13.820 --> 00:53:16.328 Or someone had a genius heterogeneous,

NOTE Confidence: 0.900553714666667

00:53:16.330 --> 00:53:18.180 but the question is, does it affect outcome?

NOTE Confidence: 0.900553714666667

00:53:18.180 --> 00:53:20.895 That is, have you looked to see if

NOTE Confidence: 0.900553714666667

00:53:20.895 --> 00:53:23.190 when you find an increase in 10%  
NOTE Confidence: 0.900553714666667

00:53:23.190 --> 00:53:24.900 because you look at more specimens,  
NOTE Confidence: 0.900553714666667

00:53:24.900 --> 00:53:25.940 those patients actually respond  
NOTE Confidence: 0.900553714666667

00:53:25.940 --> 00:53:27.601 to trust as a madman? Chemo?  
NOTE Confidence: 0.900553714666667

00:53:27.601 --> 00:53:29.767 Yeah, that's that's one of the  
NOTE Confidence: 0.900553714666667

00:53:29.767 --> 00:53:31.419 unanswered questions and and I  
NOTE Confidence: 0.900553714666667

00:53:31.419 --> 00:53:32.943 don't have an answer to that.  
NOTE Confidence: 0.900553714666667

00:53:32.950 --> 00:53:35.600 I all I can say is that it's been looked  
NOTE Confidence: 0.900553714666667

00:53:35.668 --> 00:53:38.314 at in gastric cancer and apparently not.  
NOTE Confidence: 0.900553714666667

00:53:38.320 --> 00:53:39.130 Too surprisingly,  
NOTE Confidence: 0.900553714666667

00:53:39.130 --> 00:53:41.155 they don't respond that well.  
NOTE Confidence: 0.900553714666667

00:53:41.160 --> 00:53:43.575 If every rate of her two positive,  
NOTE Confidence: 0.900553714666667

00:53:43.580 --> 00:53:44.540 you know if they.  
NOTE Confidence: 0.900553714666667

00:53:44.540 --> 00:53:45.980 Percent of tumor cells that are  
NOTE Confidence: 0.900553714666667

00:53:46.034 --> 00:53:47.309 her two positive is lower.  
NOTE Confidence: 0.900553714666667

00:53:47.310 --> 00:53:49.062 On the other hand.

NOTE Confidence: 0.900553714666667  
00:53:49.062 --> 00:53:51.955 I'm, I know you're aware there is the  
NOTE Confidence: 0.900553714666667  
00:53:51.955 --> 00:53:54.130 antibody drug conjugates that actually  
NOTE Confidence: 0.900553714666667  
00:53:54.130 --> 00:53:56.480 may help overcome this problem,  
NOTE Confidence: 0.900553714666667  
00:53:56.480 --> 00:53:58.699 because once you know if you have,  
NOTE Confidence: 0.900553714666667  
00:53:58.700 --> 00:54:00.975 let's say a her two positive tumor  
NOTE Confidence: 0.900553714666667  
00:54:00.975 --> 00:54:02.568 cell cluster surrounded by all  
NOTE Confidence: 0.900553714666667  
00:54:02.568 --> 00:54:04.248 the her two negative tumor cells,  
NOTE Confidence: 0.900553714666667  
00:54:04.250 --> 00:54:06.452 but you're able to deliver that  
NOTE Confidence: 0.900553714666667  
00:54:06.452 --> 00:54:07.553 chemotherapeutic drug within  
NOTE Confidence: 0.900553714666667  
00:54:07.553 --> 00:54:09.359 the within the neighborhood,  
NOTE Confidence: 0.900553714666667  
00:54:09.360 --> 00:54:11.584 you know and and just bind to the  
NOTE Confidence: 0.900553714666667  
00:54:11.584 --> 00:54:13.784 receptor on the positive cells and then  
NOTE Confidence: 0.900553714666667  
00:54:13.784 --> 00:54:16.419 release the drug in the in the vicinity.  
NOTE Confidence: 0.900553714666667  
00:54:16.420 --> 00:54:19.150 That would also have this bystander.  
NOTE Confidence: 0.900553714666667  
00:54:19.150 --> 00:54:19.964 Chilling effect,  
NOTE Confidence: 0.900553714666667

00:54:19.964 --> 00:54:22.813 so I think that that is potentially  
NOTE Confidence: 0.900553714666667

00:54:22.813 --> 00:54:25.628 one way to to overcome this problem.  
NOTE Confidence: 0.900553714666667

00:54:25.630 --> 00:54:27.535 For these tumors,  
NOTE Confidence: 0.900553714666667

00:54:27.535 --> 00:54:28.170 yeah,  
NOTE Confidence: 0.900553714666667

00:54:28.170 --> 00:54:29.778 and just in follow up related to  
NOTE Confidence: 0.900553714666667

00:54:29.778 --> 00:54:31.779 that I was going to ask you about  
NOTE Confidence: 0.900553714666667

00:54:31.779 --> 00:54:33.753 in her two or trustees map drugs  
NOTE Confidence: 0.900553714666667

00:54:33.753 --> 00:54:36.084 taken and I I saw that there have  
NOTE Confidence: 0.900553714666667

00:54:36.084 --> 00:54:37.601 been some beginning trials in  
NOTE Confidence: 0.900553714666667

00:54:37.601 --> 00:54:39.323 and Dmitry AM in Destiny 3,  
NOTE Confidence: 0.900553714666667

00:54:39.330 --> 00:54:41.229 which is a breast cancer trial of that drug.  
NOTE Confidence: 0.900553714666667

00:54:41.230 --> 00:54:42.790 For the three plus breast cancer  
NOTE Confidence: 0.900553714666667

00:54:42.790 --> 00:54:44.330 just reported on as positive.  
NOTE Confidence: 0.900553714666667

00:54:44.330 --> 00:54:47.050 So some oncologists are saying that now we  
NOTE Confidence: 0.900553714666667

00:54:47.050 --> 00:54:48.910 won't need fish anymore because anyone,  
NOTE Confidence: 0.900553714666667

00:54:48.910 --> 00:54:49.445 that's.

NOTE Confidence: 0.900553714666667  
00:54:49.445 --> 00:54:51.340 Even plus one positive or  
NOTE Confidence: 0.900553714666667  
00:54:51.340 --> 00:54:52.790 higher will get transcribed.  
NOTE Confidence: 0.900553714666667  
00:54:52.790 --> 00:54:53.956 Rusty can,  
NOTE Confidence: 0.900553714666667  
00:54:53.956 --> 00:54:56.742 and we probably will just test biopsy  
NOTE Confidence: 0.900553714666667  
00:54:56.742 --> 00:54:59.234 or some similar tests to have because  
NOTE Confidence: 0.900553714666667  
00:54:59.234 --> 00:55:01.880 you only need a low level to benefit.  
NOTE Confidence: 0.900553714666667  
00:55:01.880 --> 00:55:03.145 Are you seeing the same  
NOTE Confidence: 0.900553714666667  
00:55:03.145 --> 00:55:03.904 thing and endometrium?  
NOTE Confidence: 0.900553714666667  
00:55:03.910 --> 00:55:05.278 That is where the low levels  
NOTE Confidence: 0.900553714666667  
00:55:05.278 --> 00:55:06.948 benefit or did in the trials that  
NOTE Confidence: 0.900553714666667  
00:55:06.948 --> 00:55:08.123 have been done so far,  
NOTE Confidence: 0.900553714666667  
00:55:08.130 --> 00:55:10.440 I've only high levels been looked at.  
NOTE Confidence: 0.900553714666667  
00:55:10.440 --> 00:55:10.773 Uhm,  
NOTE Confidence: 0.900553714666667  
00:55:10.773 --> 00:55:13.104 the that the only trial that so  
NOTE Confidence: 0.900553714666667  
00:55:13.104 --> 00:55:15.513 far has been published is the one  
NOTE Confidence: 0.900553714666667

00:55:15.513 --> 00:55:18.100 one I showed and I think there  
NOTE Confidence: 0.900553714666667

00:55:18.100 --> 00:55:20.608 is others on ongoing trials that  
NOTE Confidence: 0.900553714666667

00:55:20.608 --> 00:55:22.598 will include and her two,  
NOTE Confidence: 0.900553714666667

00:55:22.600 --> 00:55:25.869 but I'm not entirely sure what the  
NOTE Confidence: 0.900553714666667

00:55:25.869 --> 00:55:28.034 criteria for enrollment will be  
NOTE Confidence: 0.900553714666667

00:55:28.034 --> 00:55:30.738 for those so so there there are no  
NOTE Confidence: 0.900553714666667

00:55:30.826 --> 00:55:33.270 more data on that yet other than  
NOTE Confidence: 0.900553714666667

00:55:33.270 --> 00:55:35.895 maybe you know some of those basket  
NOTE Confidence: 0.900553714666667

00:55:35.895 --> 00:55:38.109 trials may have included tumors.  
NOTE Confidence: 0.900553714666667

00:55:38.110 --> 00:55:40.600 That would fit into that category.  
NOTE Confidence: 0.770553114444445

00:55:41.890 --> 00:55:47.651 So. So I have a question from Mary Robair UM.  
NOTE Confidence: 0.770553114444445

00:55:47.651 --> 00:55:50.656 You attribute the difference between  
NOTE Confidence: 0.770553114444445

00:55:50.656 --> 00:55:54.264 biopsy more like positive and resection  
NOTE Confidence: 0.770553114444445

00:55:54.264 --> 00:55:57.594 to fixation alone or other factors  
NOTE Confidence: 0.770553114444445

00:55:57.594 --> 00:56:01.533 and question number two is does the  
NOTE Confidence: 0.770553114444445

00:56:01.533 --> 00:56:04.263 internal versus external domain issue

NOTE Confidence: 0.770553114444445

00:56:04.270 --> 00:56:06.818 apply to gastric and breast as well?

NOTE Confidence: 0.873291762727273

00:56:08.570 --> 00:56:11.909 First question, yes, that one of the

NOTE Confidence: 0.873291762727273

00:56:11.909 --> 00:56:14.130 possible explanations is fixation,

NOTE Confidence: 0.873291762727273

00:56:14.130 --> 00:56:16.776 as so there would be one argument

NOTE Confidence: 0.873291762727273

00:56:16.776 --> 00:56:20.340 to to do the testing on the biopsy.

NOTE Confidence: 0.873291762727273

00:56:20.340 --> 00:56:22.260 And just like in breast cancer,

NOTE Confidence: 0.873291762727273

00:56:22.260 --> 00:56:23.994 basically we could start the and

NOTE Confidence: 0.873291762727273

00:56:23.994 --> 00:56:26.009 that that's what I started doing.

NOTE Confidence: 0.873291762727273

00:56:26.010 --> 00:56:28.810 Starting the testing on the biopsy or

NOTE Confidence: 0.873291762727273

00:56:28.810 --> 00:56:31.499 creating and if it's negative then

NOTE Confidence: 0.873291762727273

00:56:31.499 --> 00:56:34.319 repeat the tests on the hysterectomy.

NOTE Confidence: 0.873291762727273

00:56:34.320 --> 00:56:35.900 The other potential explanation,

NOTE Confidence: 0.873291762727273

00:56:35.900 --> 00:56:39.373 in addition to fixation, could be a.

NOTE Confidence: 0.873291762727273

00:56:39.373 --> 00:56:41.897 More spatially heterogeneous sampling

NOTE Confidence: 0.873291762727273

00:56:41.897 --> 00:56:44.748 you know, like unlike breast cancer,

NOTE Confidence: 0.873291762727273

00:56:44.748 --> 00:56:46.336 where it's a directive,  
NOTE Confidence: 0.873291762727273

00:56:46.340 --> 00:56:48.500 core biopsy or a gastric cancer,  
NOTE Confidence: 0.873291762727273

00:56:48.500 --> 00:56:51.258 it's so directed. And the scopic biopsy.  
NOTE Confidence: 0.873291762727273

00:56:51.260 --> 00:56:53.696 This is completely like a blinded biopsy,  
NOTE Confidence: 0.873291762727273

00:56:53.700 --> 00:56:54.346 right?  
NOTE Confidence: 0.873291762727273

00:56:54.346 --> 00:56:57.576 The gynecologist collects tissue from  
NOTE Confidence: 0.873291762727273

00:56:57.576 --> 00:57:00.867 all potentially all parts of the,  
NOTE Confidence: 0.873291762727273

00:57:00.867 --> 00:57:03.429 especially if it's a great time.  
NOTE Confidence: 0.873291762727273

00:57:03.430 --> 00:57:05.782 It samples the very large areas  
NOTE Confidence: 0.873291762727273

00:57:05.782 --> 00:57:07.350 of the endometrial lining,  
NOTE Confidence: 0.873291762727273

00:57:07.350 --> 00:57:10.430 as opposed to if I select a.  
NOTE Confidence: 0.873291762727273

00:57:10.430 --> 00:57:12.404 Block from this wreck to me that  
NOTE Confidence: 0.873291762727273

00:57:12.404 --> 00:57:14.411 that is just that one spot in  
NOTE Confidence: 0.873291762727273

00:57:14.411 --> 00:57:17.338 the on the heaters and exceller  
NOTE Confidence: 0.873291762727273

00:57:17.338 --> 00:57:20.080 versus intracellular domain.  
NOTE Confidence: 0.873291762727273

00:57:20.080 --> 00:57:23.834 From what I know, I think it's not that, uh?

NOTE Confidence: 0.873291762727273  
00:57:23.834 --> 00:57:27.578 There is not such a large discrepancy  
NOTE Confidence: 0.873291762727273  
00:57:27.578 --> 00:57:29.968 in breast and gastric cancer.  
NOTE Confidence: 0.873291762727273  
00:57:29.970 --> 00:57:33.190 I think that's a more.  
NOTE Confidence: 0.873291762727273  
00:57:33.190 --> 00:57:36.706 Specific problem for for endometrial cancer.  
NOTE Confidence: 0.873291762727273  
00:57:36.710 --> 00:57:38.865 This extracellular domain shedding occurs  
NOTE Confidence: 0.873291762727273  
00:57:38.865 --> 00:57:41.020 more frequently in dimitriou cancer.  
NOTE Confidence: 0.64835981875  
00:57:43.050 --> 00:57:46.760 And there is another question from Uma  
NOTE Confidence: 0.64835981875  
00:57:46.760 --> 00:57:48.757 Krishnamoorthy. In your experience,  
NOTE Confidence: 0.64835981875  
00:57:48.757 --> 00:57:51.202 what is the approximate percentage  
NOTE Confidence: 0.64835981875  
00:57:51.202 --> 00:57:54.120 of caser with with heterogeneity?  
NOTE Confidence: 0.8827684233333333  
00:57:54.820 --> 00:57:57.538 So in this study that we  
NOTE Confidence: 0.8827684233333333  
00:57:57.540 --> 00:57:59.775 performed 30% overall.  
NOTE Confidence: 0.8827684233333333  
00:57:59.775 --> 00:58:05.610 And among the positive cases more than 50%.  
NOTE Confidence: 0.8827684233333333  
00:58:05.610 --> 00:58:08.210 Had heterogeneity and since then  
NOTE Confidence: 0.8827684233333333  
00:58:08.210 --> 00:58:11.246 there there are other studies as  
NOTE Confidence: 0.8827684233333333

00:58:11.246 --> 00:58:13.686 well that confirmed a similarly  
NOTE Confidence: 0.8827684233333333

00:58:13.686 --> 00:58:15.698 high rate of heterogeneity.  
NOTE Confidence: 0.8827684233333333

00:58:15.700 --> 00:58:18.479 So that's I think in that regard  
NOTE Confidence: 0.8827684233333333

00:58:18.479 --> 00:58:21.270 it's more similar to gastric cancers.  
NOTE Confidence: 0.877986928

00:58:22.780 --> 00:58:24.290 Then there is another question,  
NOTE Confidence: 0.718220555

00:58:26.500 --> 00:58:30.316 MH446. It says what percentage of  
NOTE Confidence: 0.718220555

00:58:30.316 --> 00:58:32.860 endometrial serous carcinomas are.  
NOTE Confidence: 0.718220555

00:58:32.860 --> 00:58:35.810 I'd seen negative and fish  
NOTE Confidence: 0.718220555

00:58:35.810 --> 00:58:38.610 positive and what is the mechanism  
NOTE Confidence: 0.832882843666667

00:58:39.100 --> 00:58:41.932 so that would also be a good question  
NOTE Confidence: 0.832882843666667

00:58:41.932 --> 00:58:44.937 and that's that's also one of the  
NOTE Confidence: 0.832882843666667

00:58:44.937 --> 00:58:46.709 unanswered questions because based  
NOTE Confidence: 0.832882843666667

00:58:46.709 --> 00:58:49.356 on the current algorithm we only do  
NOTE Confidence: 0.832882843666667

00:58:49.356 --> 00:58:52.604 her two fish on the two plus is.  
NOTE Confidence: 0.832882843666667

00:58:52.604 --> 00:58:56.965 We we don't do her two fish routinely on  
NOTE Confidence: 0.832882843666667

00:58:56.965 --> 00:59:01.420 a 0 or one plus and and and on A3 plus.

NOTE Confidence: 0.832882843666667  
00:59:01.420 --> 00:59:04.508 There are a few cases that we we  
NOTE Confidence: 0.832882843666667  
00:59:04.510 --> 00:59:06.484 subjected to fish that were part  
NOTE Confidence: 0.832882843666667  
00:59:06.484 --> 00:59:09.018 of a study and and we looked at  
NOTE Confidence: 0.832882843666667  
00:59:09.018 --> 00:59:11.570 those and and it it does occur I  
NOTE Confidence: 0.832882843666667  
00:59:11.570 --> 00:59:13.470 I can't remember a percentage.  
NOTE Confidence: 0.832882843666667  
00:59:13.470 --> 00:59:15.675 We didn't test a lot of cases  
NOTE Confidence: 0.832882843666667  
00:59:15.675 --> 00:59:19.310 but once nobody it happens and.  
NOTE Confidence: 0.832882843666667  
00:59:19.310 --> 00:59:20.378 I don't know.  
NOTE Confidence: 0.832882843666667  
00:59:20.378 --> 00:59:22.870 What the what the potential mechanism you  
NOTE Confidence: 0.832882843666667  
00:59:22.939 --> 00:59:25.655 know probably similar to to breast cancer?  
NOTE Confidence: 0.832882843666667  
00:59:25.660 --> 00:59:26.899 I mean, I think these are not,  
NOTE Confidence: 0.832882843666667  
00:59:26.900 --> 00:59:28.960 you know, tumor type specific.  
NOTE Confidence: 0.832882843666667  
00:59:28.960 --> 00:59:31.742 It may be that that they,  
NOTE Confidence: 0.832882843666667  
00:59:31.742 --> 00:59:34.298 they they protein is not expressed,  
NOTE Confidence: 0.832882843666667  
00:59:34.300 --> 00:59:34.872 you know.  
NOTE Confidence: 0.832882843666667

00:59:34.872 --> 00:59:36.588 But but there is a there  
NOTE Confidence: 0.832882843666667

00:59:36.588 --> 00:59:38.570 could be still amplification.  
NOTE Confidence: 0.804575021

00:59:40.640 --> 00:59:43.160 OK, there is another one  
NOTE Confidence: 0.804575021

00:59:43.160 --> 00:59:45.680 from Karen Finberg by fish.  
NOTE Confidence: 0.804575021

00:59:45.680 --> 00:59:49.562 We assessed the her two gene nor  
NOTE Confidence: 0.804575021

00:59:49.562 --> 00:59:53.294 other nearby gene on chromosome 17.  
NOTE Confidence: 0.804575021

00:59:53.300 --> 00:59:54.820 And that's the question.  
NOTE Confidence: 0.804575021

00:59:54.820 --> 00:59:55.960 Is it known?  
NOTE Confidence: 0.804575021

00:59:55.960 --> 01:00:00.314 How much of chromosome 17 maybe Co  
NOTE Confidence: 0.804575021

01:00:00.314 --> 01:00:04.340 amplified with her to a mutual carcinomas?  
NOTE Confidence: 0.804575021

01:00:04.340 --> 01:00:07.340 And could this contribute to  
NOTE Confidence: 0.804575021

01:00:07.340 --> 01:00:09.622 tumor aggressiveness and or  
NOTE Confidence: 0.804575021

01:00:09.622 --> 01:00:11.786 response to targeted therapy?  
NOTE Confidence: 0.88474754826087

01:00:12.560 --> 01:00:14.864 Yeah, I think this this has been raised  
NOTE Confidence: 0.88474754826087

01:00:14.864 --> 01:00:17.703 also in breast cancer because there's a lot  
NOTE Confidence: 0.88474754826087

01:00:17.703 --> 01:00:20.279 of other important genes on chromosome 17.

NOTE Confidence: 0.88474754826087  
01:00:20.280 --> 01:00:25.296 Top 2P53 those all have been implicated  
NOTE Confidence: 0.88474754826087  
01:00:25.296 --> 01:00:30.870 in and cases where there is a.  
NOTE Confidence: 0.88474754826087  
01:00:30.870 --> 01:00:33.430 Chromosome 17 polysomy or gain  
NOTE Confidence: 0.88474754826087  
01:00:33.430 --> 01:00:35.291 of chromosome 17. Actually,  
NOTE Confidence: 0.88474754826087  
01:00:35.291 --> 01:00:37.859 I'm working on a paper right now on  
NOTE Confidence: 0.88474754826087  
01:00:37.859 --> 01:00:40.618 her two fish and related to, you know,  
NOTE Confidence: 0.88474754826087  
01:00:40.618 --> 01:00:43.012 to look at the specific characteristics  
NOTE Confidence: 0.88474754826087  
01:00:43.012 --> 01:00:45.309 of her two fish and and Co.  
NOTE Confidence: 0.88474754826087  
01:00:45.310 --> 01:00:47.550 Amplification is not that common.  
NOTE Confidence: 0.88474754826087  
01:00:47.550 --> 01:00:50.440 We had in our archives.  
NOTE Confidence: 0.88474754826087  
01:00:50.440 --> 01:00:54.234 We found about 15% rate of chromosome  
NOTE Confidence: 0.88474754826087  
01:00:54.234 --> 01:00:57.638 17 or polysomy in these tumors,  
NOTE Confidence: 0.88474754826087  
01:00:57.640 --> 01:01:00.115 or at least the chromosome  
NOTE Confidence: 0.88474754826087  
01:01:00.115 --> 01:01:02.045 17 centromeric gain. Uhm?  
NOTE Confidence: 0.88474754826087  
01:01:02.045 --> 01:01:04.270 But but clarification is actually  
NOTE Confidence: 0.88474754826087

01:01:04.270 --> 01:01:06.050 not not that common.  
NOTE Confidence: 0.88474754826087

01:01:06.050 --> 01:01:07.786 I think we had one case in  
NOTE Confidence: 0.88474754826087

01:01:07.786 --> 01:01:09.309 which that that was present.  
NOTE Confidence: 0.742643981

01:01:11.090 --> 01:01:13.856 And then finally, I'll recap where  
NOTE Confidence: 0.742643981

01:01:13.856 --> 01:01:15.700 Doctor Morrow's comments Natalia.  
NOTE Confidence: 0.742643981

01:01:15.700 --> 01:01:18.070 Thanks for the terrific review.  
NOTE Confidence: 0.742643981

01:01:18.070 --> 01:01:21.134 As you know, Yale may have been the  
NOTE Confidence: 0.742643981

01:01:21.134 --> 01:01:24.214 situation to have treated a patient  
NOTE Confidence: 0.742643981

01:01:24.214 --> 01:01:27.004 with Herceptin for endometrial serous  
NOTE Confidence: 0.742643981

01:01:27.004 --> 01:01:29.994 carcinoma Bay and Peter Schwartz.  
NOTE Confidence: 0.742643981

01:01:29.994 --> 01:01:32.855 Her two positive year 2002  
NOTE Confidence: 0.742643981

01:01:32.855 --> 01:01:35.030 bad win never reported it.  
NOTE Confidence: 0.742643981

01:01:35.030 --> 01:01:36.542 Really interesting to see  
NOTE Confidence: 0.742643981

01:01:36.542 --> 01:01:38.054 how this has evolved.  
NOTE Confidence: 0.302451706666667

01:01:38.920 --> 01:01:43.039 Yeah, I think. I remember you  
NOTE Confidence: 0.302451706666667

01:01:43.039 --> 01:01:44.904 told me that story before.

NOTE Confidence: 0.302451706666667  
01:01:44.910 --> 01:01:47.017 I think this this is one of  
NOTE Confidence: 0.302451706666667  
01:01:47.017 --> 01:01:48.574 the important lessons from this  
NOTE Confidence: 0.302451706666667  
01:01:48.574 --> 01:01:51.825 from this work is that when we  
NOTE Confidence: 0.302451706666667  
01:01:51.825 --> 01:01:53.640 started I was still a resident.  
NOTE Confidence: 0.302451706666667  
01:01:53.640 --> 01:01:55.115 Actually when I started working  
NOTE Confidence: 0.302451706666667  
01:01:55.115 --> 01:01:57.313 on this and and I just didn't  
NOTE Confidence: 0.302451706666667  
01:01:57.313 --> 01:01:59.299 know which direction it will go.  
NOTE Confidence: 0.302451706666667  
01:01:59.300 --> 01:02:02.908 It took many many years for this to  
NOTE Confidence: 0.302451706666667  
01:02:02.908 --> 01:02:06.614 to come to fruition and and it was  
NOTE Confidence: 0.302451706666667  
01:02:06.614 --> 01:02:09.043 just really wonderful to see how this  
NOTE Confidence: 0.302451706666667  
01:02:09.043 --> 01:02:11.499 became a successful treatment option.  
NOTE Confidence: 0.302451706666667  
01:02:11.500 --> 01:02:13.936 Again, thanks to Doctor 17 and.  
NOTE Confidence: 0.302451706666667  
01:02:13.940 --> 01:02:15.509 They seem so.  
NOTE Confidence: 0.761569752  
01:02:17.640 --> 01:02:19.020 OK, it's a long journey.  
NOTE Confidence: 0.820664886666667  
01:02:19.640 --> 01:02:23.348 Yeah, excellent so.  
NOTE Confidence: 0.820664886666667

01:02:23.350 --> 01:02:25.090 We can wrap it up now.

NOTE Confidence: 0.820664886666667

01:02:25.090 --> 01:02:26.770 Thank you so much Natalia.

NOTE Confidence: 0.820664886666667

01:02:26.770 --> 01:02:29.000 Thank you man bye bye.