

WEBVTT

NOTE duration:"00:59:41"

NOTE recognizability:0.826

NOTE language:en-us

NOTE Confidence: 0.614335107777778

00:00:00.000 --> 00:00:02.512 1. Today's Grand Ronde

NOTE Confidence: 0.614335107777778

00:00:02.512 --> 00:00:05.652 speaker is doctor Lisa ruper.

NOTE Confidence: 0.614335107777778

00:00:05.660 --> 00:00:09.956 Dr Rupert graduated summa \*\*\* laude from

NOTE Confidence: 0.614335107777778

00:00:09.956 --> 00:00:12.268 Northwestern University in Illinois

NOTE Confidence: 0.614335107777778

00:00:12.268 --> 00:00:16.080 with a major in communications.

NOTE Confidence: 0.614335107777778

00:00:16.080 --> 00:00:19.250 She completed MD from University

NOTE Confidence: 0.614335107777778

00:00:19.250 --> 00:00:21.786 of Illinois in Chicago,

NOTE Confidence: 0.614335107777778

00:00:21.790 --> 00:00:24.720 where she won many awards,

NOTE Confidence: 0.614335107777778

00:00:24.720 --> 00:00:28.032 including the Alpha Omega

NOTE Confidence: 0.614335107777778

00:00:28.032 --> 00:00:30.516 Alpha Honor Society.

NOTE Confidence: 0.614335107777778

00:00:30.520 --> 00:00:31.720 Subsequently, Dr.

NOTE Confidence: 0.614335107777778

00:00:31.720 --> 00:00:35.320 Rupert moved to Baltimore to train

NOTE Confidence: 0.614335107777778

00:00:35.320 --> 00:00:38.518 in pathology at Johns Hopkins.

NOTE Confidence: 0.614335107777778

00:00:38.518 --> 00:00:41.848 Where her winning streak continued

NOTE Confidence: 0.614335107777778

00:00:41.848 --> 00:00:45.542 and she collected several awards

NOTE Confidence: 0.614335107777778

00:00:45.542 --> 00:00:48.672 for excellence at the institutional

NOTE Confidence: 0.614335107777778

00:00:48.672 --> 00:00:52.139 level and at national level.

NOTE Confidence: 0.614335107777778

00:00:52.140 --> 00:00:55.745 Rewards for excellence and research

NOTE Confidence: 0.614335107777778

00:00:55.745 --> 00:00:59.350 and posters and platform sessions

NOTE Confidence: 0.614335107777778

00:00:59.350 --> 00:01:01.666 at the end of her training,

NOTE Confidence: 0.614335107777778

00:01:01.670 --> 00:01:04.928 doctor Rupert chose to do a

NOTE Confidence: 0.614335107777778

00:01:04.928 --> 00:01:07.100 one year advanced speciality

NOTE Confidence: 0.614335107777778

00:01:07.202 --> 00:01:10.210 training in surgical pathology.

NOTE Confidence: 0.614335107777778

00:01:10.210 --> 00:01:13.470 Instead of a formal fellowship.

NOTE Confidence: 0.614335107777778

00:01:13.470 --> 00:01:14.166 There,

NOTE Confidence: 0.614335107777778

00:01:14.166 --> 00:01:17.646 after Doctor Ruper was recruited

NOTE Confidence: 0.614335107777778

00:01:17.646 --> 00:01:22.590 as assistant professor in 2017.

NOTE Confidence: 0.614335107777778

00:01:22.590 --> 00:01:25.110 And as circumstances called

NOTE Confidence: 0.614335107777778

00:01:25.110 --> 00:01:27.246 for within three months,

NOTE Confidence: 0.614335107777778  
00:01:27.246 --> 00:01:29.254 she was appointed director  
NOTE Confidence: 0.614335107777778  
00:01:29.254 --> 00:01:32.130 of head and neck pathology.  
NOTE Confidence: 0.614335107777778  
00:01:32.130 --> 00:01:34.650 Dr Rupert rose to the challenge.  
NOTE Confidence: 0.614335107777778  
00:01:34.650 --> 00:01:37.680 Despite the departure of her  
NOTE Confidence: 0.614335107777778  
00:01:37.680 --> 00:01:40.630 mentors in head and neck pathology  
NOTE Confidence: 0.614335107777778  
00:01:40.630 --> 00:01:42.826 and in less than five years,  
NOTE Confidence: 0.614335107777778  
00:01:42.830 --> 00:01:46.424 Doctor Rupert has emerged as a  
NOTE Confidence: 0.614335107777778  
00:01:46.424 --> 00:01:49.570 star in this subspecialty field.  
NOTE Confidence: 0.614335107777778  
00:01:49.570 --> 00:01:52.705 Her research interest is in  
NOTE Confidence: 0.614335107777778  
00:01:52.705 --> 00:01:55.213 salivary and sinonasal tumors.  
NOTE Confidence: 0.614335107777778  
00:01:55.220 --> 00:01:58.620 She has published 80 original  
NOTE Confidence: 0.614335107777778  
00:01:58.620 --> 00:02:00.768 research articles, maybe more,  
NOTE Confidence: 0.614335107777778  
00:02:00.768 --> 00:02:02.738 but Eddie has a flask.  
NOTE Confidence: 0.763637673333333  
00:02:04.800 --> 00:02:06.160 I'm counting.  
NOTE Confidence: 0.763637673333333  
00:02:06.160 --> 00:02:09.560 Many of these articles describe  
NOTE Confidence: 0.763637673333333

00:02:09.560 --> 00:02:13.440 new entities such as Biphenotypic,  
NOTE Confidence: 0.7636376733333333

00:02:13.440 --> 00:02:16.992 sinonasal, sarcoma deck,  
NOTE Confidence: 0.7636376733333333

00:02:16.992 --> 00:02:22.960 F2 carcinomas, AKT 1 E, 17 K,  
NOTE Confidence: 0.7636376733333333

00:02:22.960 --> 00:02:25.585 mutated, mucinous adenocarcinomas.  
NOTE Confidence: 0.7636376733333333

00:02:25.585 --> 00:02:30.835 She has worked tirelessly to redefine,  
NOTE Confidence: 0.7636376733333333

00:02:30.840 --> 00:02:35.670 characterize, and to lay down the  
NOTE Confidence: 0.7636376733333333

00:02:35.670 --> 00:02:38.890 guidelines for salivary adenocarcinomas.  
NOTE Confidence: 0.7636376733333333

00:02:38.890 --> 00:02:41.745 I find Doctor Rupert's articles  
NOTE Confidence: 0.7636376733333333

00:02:41.745 --> 00:02:44.990 very helpful in my practical in,  
NOTE Confidence: 0.7636376733333333

00:02:44.990 --> 00:02:46.643 in my practice,  
NOTE Confidence: 0.7636376733333333

00:02:46.643 --> 00:02:49.949 and I often find myself quoting  
NOTE Confidence: 0.7636376733333333

00:02:49.949 --> 00:02:53.309 her or following up my cases,  
NOTE Confidence: 0.7636376733333333

00:02:53.310 --> 00:02:56.560 working them up with Doctor  
NOTE Confidence: 0.7636376733333333

00:02:56.560 --> 00:03:00.010 Rupert's recommendations.  
NOTE Confidence: 0.7636376733333333

00:03:00.010 --> 00:03:04.082 Lisa has a knack for laying out diagnostic  
NOTE Confidence: 0.7636376733333333

00:03:04.082 --> 00:03:06.919 and differential diagnostic criteria.

NOTE Confidence: 0.7636376733333333

00:03:06.920 --> 00:03:08.160 Not surprisingly,

NOTE Confidence: 0.7636376733333333

00:03:08.160 --> 00:03:11.260 she has written several invited

NOTE Confidence: 0.7636376733333333

00:03:11.260 --> 00:03:15.069 reviews and is on the editorial

NOTE Confidence: 0.7636376733333333

00:03:15.069 --> 00:03:18.154 board of seven pathology journals,

NOTE Confidence: 0.7636376733333333

00:03:18.160 --> 00:03:21.310 including the two top notch

NOTE Confidence: 0.7636376733333333

00:03:21.310 --> 00:03:23.200 surgical pathology journals,

NOTE Confidence: 0.7636376733333333

00:03:23.200 --> 00:03:26.420 American Journal of Surgical Pathology,

NOTE Confidence: 0.7636376733333333

00:03:26.420 --> 00:03:29.720 and modern pathology.

NOTE Confidence: 0.7636376733333333

00:03:29.720 --> 00:03:33.026 Doctor Rupert is often sought sought

NOTE Confidence: 0.7636376733333333

00:03:33.026 --> 00:03:35.961 after for speaking engagements at

NOTE Confidence: 0.7636376733333333

00:03:35.961 --> 00:03:38.529 national and international meetings.

NOTE Confidence: 0.7636376733333333

00:03:38.530 --> 00:03:43.165 She has written 14 chapters in the 5th.

NOTE Confidence: 0.7636376733333333

00:03:43.165 --> 00:03:46.325 WHO blue book on head and neck pathology,

NOTE Confidence: 0.7636376733333333

00:03:46.330 --> 00:03:50.325 not to mention contributing to

NOTE Confidence: 0.7636376733333333

00:03:50.325 --> 00:03:53.521 pathology outlines and receiving an

NOTE Confidence: 0.7636376733333333

00:03:53.521 --> 00:03:57.380 award for Path outlined contributions.  
NOTE Confidence: 0.7636376733333333

00:03:57.380 --> 00:04:01.730 Despite this phenomenal publishing portfolio,  
NOTE Confidence: 0.7636376733333333

00:04:01.730 --> 00:04:05.405 she maintains a demanding surgical  
NOTE Confidence: 0.7636376733333333

00:04:05.405 --> 00:04:08.345 pathology and counsel practice,  
NOTE Confidence: 0.7636376733333333

00:04:08.350 --> 00:04:12.532 a busy medical student and resident  
NOTE Confidence: 0.7636376733333333

00:04:12.532 --> 00:04:15.898 teaching program and and again,  
NOTE Confidence: 0.7636376733333333

00:04:15.898 --> 00:04:17.210 not surprisingly,  
NOTE Confidence: 0.7636376733333333

00:04:17.210 --> 00:04:20.410 she has won several best  
NOTE Confidence: 0.7636376733333333

00:04:20.410 --> 00:04:22.970 teaching awards in pathology.  
NOTE Confidence: 0.7636376733333333

00:04:22.970 --> 00:04:26.260 So with that brief introduction,  
NOTE Confidence: 0.7636376733333333

00:04:26.260 --> 00:04:27.704 I'll hand the floor.  
NOTE Confidence: 0.7636376733333333

00:04:27.704 --> 00:04:28.787 Over to Lisa.  
NOTE Confidence: 0.939273134545455

00:04:30.740 --> 00:04:32.342 Alright, thank you. Thank you so  
NOTE Confidence: 0.939273134545455

00:04:32.342 --> 00:04:34.140 much for the lovely introduction.  
NOTE Confidence: 0.939273134545455

00:04:34.140 --> 00:04:36.820 I am so delighted to be here today and and  
NOTE Confidence: 0.939273134545455

00:04:36.886 --> 00:04:39.438 and be giving grand rounds for you guys.

NOTE Confidence: 0.939273134545455

00:04:39.440 --> 00:04:41.720 You know I just want to say we've at Hopkins

NOTE Confidence: 0.939273134545455

00:04:41.773 --> 00:04:43.805 have had the pleasure of working with two

NOTE Confidence: 0.939273134545455

00:04:43.805 --> 00:04:45.919 of your excellent residency graduates.

NOTE Confidence: 0.939273134545455

00:04:45.920 --> 00:04:48.998 First, Sarah Rudder and and then Ben Mazer in

NOTE Confidence: 0.939273134545455

00:04:48.998 --> 00:04:52.279 our surgical pathology assistantship program.

NOTE Confidence: 0.939273134545455

00:04:52.280 --> 00:04:54.520 Currently wait to have Ben back next year,

NOTE Confidence: 0.939273134545455

00:04:54.520 --> 00:04:57.280 and you know, it's just been a delight.

NOTE Confidence: 0.939273134545455

00:04:57.280 --> 00:04:58.996 And and I, just, you know,

NOTE Confidence: 0.939273134545455

00:04:59.000 --> 00:05:00.981 have the utmost respect for for your

NOTE Confidence: 0.939273134545455

00:05:00.981 --> 00:05:02.509 department after after working with.

NOTE Confidence: 0.939273134545455

00:05:02.510 --> 00:05:04.750 With such excellent, excellent people.

NOTE Confidence: 0.939273134545455

00:05:04.750 --> 00:05:07.350 So, so today I'm going to talk about

NOTE Confidence: 0.939273134545455

00:05:07.350 --> 00:05:09.034 some sinonasal evolving concepts

NOTE Confidence: 0.939273134545455

00:05:09.034 --> 00:05:10.486 in sinonasal tumors,

NOTE Confidence: 0.939273134545455

00:05:10.490 --> 00:05:12.444 which is one of my favorite

NOTE Confidence: 0.939273134545455

00:05:12.444 --> 00:05:15.528 topics in head and neck pathology.  
NOTE Confidence: 0.939273134545455

00:05:15.530 --> 00:05:18.308 Nothing to disclose.  
NOTE Confidence: 0.939273134545455

00:05:18.310 --> 00:05:21.028 And just gonna start with a  
NOTE Confidence: 0.939273134545455

00:05:21.028 --> 00:05:21.934 little background.  
NOTE Confidence: 0.939273134545455

00:05:21.940 --> 00:05:24.103 Of course there has been a lot  
NOTE Confidence: 0.939273134545455

00:05:24.103 --> 00:05:26.675 that has changed in the last few  
NOTE Confidence: 0.939273134545455

00:05:26.675 --> 00:05:28.645 years in sinonasal pathology with  
NOTE Confidence: 0.939273134545455

00:05:28.645 --> 00:05:31.248 definition of new entities and better  
NOTE Confidence: 0.939273134545455

00:05:31.248 --> 00:05:33.383 understanding of existing tumor types.  
NOTE Confidence: 0.939273134545455

00:05:33.390 --> 00:05:35.230 But I would be lying if I weren't  
NOTE Confidence: 0.939273134545455

00:05:35.230 --> 00:05:36.819 pretending that this were all you know,  
NOTE Confidence: 0.939273134545455

00:05:36.820 --> 00:05:38.044 this were ever easy.  
NOTE Confidence: 0.939273134545455

00:05:38.044 --> 00:05:39.574 The sender nasal tract has  
NOTE Confidence: 0.939273134545455

00:05:39.574 --> 00:05:40.620 always been a very,  
NOTE Confidence: 0.939273134545455

00:05:40.620 --> 00:05:42.528 very challenging diagnostic area.  
NOTE Confidence: 0.939273134545455

00:05:42.528 --> 00:05:45.390 And that's true for several reasons.



NOTE Confidence: 0.939273134545455  
00:05:45.390 --> 00:05:46.083 First of all,  
NOTE Confidence: 0.939273134545455  
00:05:46.083 --> 00:05:47.700 we often get samples that are small,  
NOTE Confidence: 0.939273134545455  
00:05:47.700 --> 00:05:48.768 crushed and necrotic.  
NOTE Confidence: 0.939273134545455  
00:05:48.768 --> 00:05:51.260 They try to bite off a little  
NOTE Confidence: 0.939273134545455  
00:05:51.335 --> 00:05:53.261 tissue in clinic and give us  
NOTE Confidence: 0.939273134545455  
00:05:53.261 --> 00:05:55.250 the sad pieces to diagnose.  
NOTE Confidence: 0.939273134545455  
00:05:55.250 --> 00:05:55.508 Frequently,  
NOTE Confidence: 0.939273134545455  
00:05:55.508 --> 00:05:57.314 the tumor has a small round blue  
NOTE Confidence: 0.939273134545455  
00:05:57.314 --> 00:05:59.270 cell or undifferentiated morphology,  
NOTE Confidence: 0.939273134545455  
00:05:59.270 --> 00:06:02.686 so a lot of different entities have very  
NOTE Confidence: 0.939273134545455  
00:06:02.686 --> 00:06:05.120 much overlapping histologic features.  
NOTE Confidence: 0.939273134545455  
00:06:05.120 --> 00:06:07.882 There's also a range of tumors  
NOTE Confidence: 0.939273134545455  
00:06:07.882 --> 00:06:09.160 you can have diverse tumors of  
NOTE Confidence: 0.939273134545455  
00:06:09.209 --> 00:06:10.409 multiple lineages you know,  
NOTE Confidence: 0.939273134545455  
00:06:10.410 --> 00:06:11.810 including some tumors that occur.  
NOTE Confidence: 0.939273134545455

00:06:11.810 --> 00:06:13.218 Multiple sites that do  
NOTE Confidence: 0.939273134545455

00:06:13.218 --> 00:06:14.626 involve the sinonasal tract,  
NOTE Confidence: 0.939273134545455

00:06:14.630 --> 00:06:16.058 but there's obvious sinonasal  
NOTE Confidence: 0.939273134545455

00:06:16.058 --> 00:06:18.200 specific entities as well that really  
NOTE Confidence: 0.939273134545455

00:06:18.261 --> 00:06:19.966 don't don't occur anywhere else,  
NOTE Confidence: 0.939273134545455

00:06:19.970 --> 00:06:22.472 and then that we need to keep up on.  
NOTE Confidence: 0.939273134545455

00:06:22.480 --> 00:06:25.180 So in the last few years.  
NOTE Confidence: 0.939273134545455

00:06:25.180 --> 00:06:27.406 There's really been a molecular revolution  
NOTE Confidence: 0.939273134545455

00:06:27.406 --> 00:06:29.300 in classification of sinonasal tumors,  
NOTE Confidence: 0.939273134545455

00:06:29.300 --> 00:06:31.694 as molecular testing has been applied to  
NOTE Confidence: 0.939273134545455

00:06:31.694 --> 00:06:34.180 more and more entities as a result of that,  
NOTE Confidence: 0.939273134545455

00:06:34.180 --> 00:06:36.448 I think several things have happened.  
NOTE Confidence: 0.939273134545455

00:06:36.450 --> 00:06:37.533 First of all,  
NOTE Confidence: 0.939273134545455

00:06:37.533 --> 00:06:39.338 we've recognized some molecularly defined  
NOTE Confidence: 0.939273134545455

00:06:39.338 --> 00:06:41.324 entities that are known in other sites  
NOTE Confidence: 0.939273134545455

00:06:41.324 --> 00:06:43.629 for the first time in the sinonasal tract,

NOTE Confidence: 0.939273134545455  
00:06:43.630 --> 00:06:44.971 so that's great.  
NOTE Confidence: 0.939273134545455  
00:06:44.971 --> 00:06:47.653 We have to find new Sinonasal  
NOTE Confidence: 0.939273134545455  
00:06:47.653 --> 00:06:49.944 specific tumor types that you know.  
NOTE Confidence: 0.939273134545455  
00:06:49.944 --> 00:06:52.440 A lot of them that you hear about,  
NOTE Confidence: 0.939273134545455  
00:06:52.440 --> 00:06:53.990 and then we've also identified  
NOTE Confidence: 0.939273134545455  
00:06:53.990 --> 00:06:55.230 molecular drivers and existing  
NOTE Confidence: 0.939273134545455  
00:06:55.230 --> 00:06:56.427 tumor types and kind of.  
NOTE Confidence: 0.939273134545455  
00:06:56.430 --> 00:06:59.560 Contributed to understanding of those.  
NOTE Confidence: 0.939273134545455  
00:06:59.560 --> 00:07:02.872 Now today I'm going to go through a  
NOTE Confidence: 0.939273134545455  
00:07:02.872 --> 00:07:04.661 few of the areas in insider nasal  
NOTE Confidence: 0.939273134545455  
00:07:04.661 --> 00:07:06.696 pathology that I think are the most  
NOTE Confidence: 0.939273134545455  
00:07:06.696 --> 00:07:08.766 interesting and important areas of change,  
NOTE Confidence: 0.939273134545455  
00:07:08.770 --> 00:07:10.072 but I just want to start with  
NOTE Confidence: 0.939273134545455  
00:07:10.072 --> 00:07:11.449 a word of word of warning.  
NOTE Confidence: 0.939273134545455  
00:07:11.450 --> 00:07:13.442 I'm focusing all these cool new  
NOTE Confidence: 0.939273134545455

00:07:13.442 --> 00:07:14.770 changes in sinonasal carcinoma  
NOTE Confidence: 0.939273134545455

00:07:14.828 --> 00:07:16.488 is all this new classification,  
NOTE Confidence: 0.939273134545455

00:07:16.490 --> 00:07:18.380 which I think is very interesting  
NOTE Confidence: 0.939273134545455

00:07:18.380 --> 00:07:19.640 and really intellectually fulfilling  
NOTE Confidence: 0.939273134545455

00:07:19.689 --> 00:07:20.677 to us as pathologists,  
NOTE Confidence: 0.939273134545455

00:07:20.680 --> 00:07:22.444 especially as we try to figure  
NOTE Confidence: 0.939273134545455

00:07:22.444 --> 00:07:23.620 out why the tumor  
NOTE Confidence: 0.896688741111111

00:07:23.683 --> 00:07:25.368 on our microscope stage looks  
NOTE Confidence: 0.896688741111111

00:07:25.368 --> 00:07:27.550 a little funny and there are  
NOTE Confidence: 0.896688741111111

00:07:27.550 --> 00:07:28.720 large prognostic implications.  
NOTE Confidence: 0.896688741111111

00:07:28.720 --> 00:07:30.533 Which is why I do think it's  
NOTE Confidence: 0.896688741111111

00:07:30.533 --> 00:07:32.009 important to classify some of  
NOTE Confidence: 0.896688741111111

00:07:32.009 --> 00:07:33.289 these new entities correctly.  
NOTE Confidence: 0.896688741111111

00:07:33.290 --> 00:07:34.748 But the treatment utility of these  
NOTE Confidence: 0.896688741111111

00:07:34.748 --> 00:07:35.970 carcinomas are are still emerging  
NOTE Confidence: 0.896688741111111

00:07:35.970 --> 00:07:37.412 and a lot of these are still

NOTE Confidence: 0.8966887411111111  
00:07:37.412 --> 00:07:38.647 treated kind of in the same way,  
NOTE Confidence: 0.8966887411111111  
00:07:38.650 --> 00:07:39.980 with the standard solid tumor,  
NOTE Confidence: 0.8966887411111111  
00:07:39.980 --> 00:07:42.550 chemotherapy regimen and radiation therapy,  
NOTE Confidence: 0.8966887411111111  
00:07:42.550 --> 00:07:43.232 surgery, etc.  
NOTE Confidence: 0.8966887411111111  
00:07:43.232 --> 00:07:45.278 The most important thing for trainees  
NOTE Confidence: 0.8966887411111111  
00:07:45.278 --> 00:07:47.488 to know in in Sinonasal pathology is  
NOTE Confidence: 0.8966887411111111  
00:07:47.488 --> 00:07:49.889 the big thing you want to distinguish.  
NOTE Confidence: 0.8966887411111111  
00:07:49.890 --> 00:07:51.490 Are tumors of different lineages,  
NOTE Confidence: 0.8966887411111111  
00:07:51.490 --> 00:07:52.438 melanomas, sarcomas, lymphomas,  
NOTE Confidence: 0.8966887411111111  
00:07:52.438 --> 00:07:54.334 those kind of things I'm not  
NOTE Confidence: 0.8966887411111111  
00:07:54.334 --> 00:07:56.105 going to spend a lot of time  
NOTE Confidence: 0.8966887411111111  
00:07:56.105 --> 00:07:57.041 talking about those today,  
NOTE Confidence: 0.8966887411111111  
00:07:57.050 --> 00:07:59.162 but those are actually the things that will  
NOTE Confidence: 0.8966887411111111  
00:07:59.162 --> 00:08:01.388 drive the massive differences in treatment.  
NOTE Confidence: 0.8966887411111111  
00:08:01.390 --> 00:08:04.350 So if you're working up a sinonasal tumor,  
NOTE Confidence: 0.8966887411111111

00:08:04.350 --> 00:08:05.600 really the most important thing  
NOTE Confidence: 0.8966887411111111

00:08:05.600 --> 00:08:07.764 to do is make sure you have it  
NOTE Confidence: 0.8966887411111111

00:08:07.764 --> 00:08:08.908 in the appropriate language.  
NOTE Confidence: 0.8966887411111111

00:08:08.910 --> 00:08:09.175 Alright,  
NOTE Confidence: 0.8966887411111111

00:08:09.175 --> 00:08:11.030 so we could do go about this.  
NOTE Confidence: 0.8966887411111111

00:08:11.030 --> 00:08:11.970 A bunch of different ways.  
NOTE Confidence: 0.8966887411111111

00:08:11.970 --> 00:08:14.609 I've chosen chosen to focus on three  
NOTE Confidence: 0.8966887411111111

00:08:14.609 --> 00:08:17.276 key areas that really are transitioning  
NOTE Confidence: 0.8966887411111111

00:08:17.276 --> 00:08:20.186 as a result of molecular analysis,  
NOTE Confidence: 0.8966887411111111

00:08:20.190 --> 00:08:21.814 tumors with squamous differentiation.  
NOTE Confidence: 0.8966887411111111

00:08:21.814 --> 00:08:22.626 Swiss sniff,  
NOTE Confidence: 0.8966887411111111

00:08:22.630 --> 00:08:25.450 complex deficient tumors and IDH  
NOTE Confidence: 0.8966887411111111

00:08:25.450 --> 00:08:26.858 2 mutant sinonasal carcinoma.  
NOTE Confidence: 0.8966887411111111

00:08:26.858 --> 00:08:29.562 So I'm gonna start out by talking  
NOTE Confidence: 0.8966887411111111

00:08:29.562 --> 00:08:32.167 about sinonasal tumors that have  
NOTE Confidence: 0.8966887411111111

00:08:32.167 --> 00:08:34.062 squamous differentiation and it is

NOTE Confidence: 0.8966887411111111

00:08:34.062 --> 00:08:35.766 really kind of amazing that I'm

NOTE Confidence: 0.8966887411111111

00:08:35.766 --> 00:08:37.463 sitting here talking about squamous

NOTE Confidence: 0.8966887411111111

00:08:37.463 --> 00:08:39.863 cell carcinoma in the head and neck

NOTE Confidence: 0.8966887411111111

00:08:39.863 --> 00:08:42.096 of being an area of great molecular

NOTE Confidence: 0.8966887411111111

00:08:42.096 --> 00:08:44.380 change because in most headed next

NOTE Confidence: 0.8966887411111111

00:08:44.380 --> 00:08:46.735 sites it's been considered that there's

NOTE Confidence: 0.8966887411111111

00:08:46.735 --> 00:08:48.680 very limited pathways for squamous

NOTE Confidence: 0.8966887411111111

00:08:48.737 --> 00:08:50.652 carcinogenesis that are that are

NOTE Confidence: 0.8966887411111111

00:08:50.652 --> 00:08:52.567 pretty similar in different areas.

NOTE Confidence: 0.8966887411111111

00:08:52.570 --> 00:08:54.070 But historically the Center Newsletter

NOTE Confidence: 0.8966887411111111

00:08:54.070 --> 00:08:56.340 Act was sort of an enigma with

NOTE Confidence: 0.8966887411111111

00:08:56.340 --> 00:08:58.340 regard to squamous cell carcinoma.

NOTE Confidence: 0.8966887411111111

00:08:58.340 --> 00:09:00.095 With risk factors that were

NOTE Confidence: 0.8966887411111111

00:09:00.095 --> 00:09:01.148 really poorly understood,

NOTE Confidence: 0.8966887411111111

00:09:01.150 --> 00:09:02.944 it didn't have nearly as strong

NOTE Confidence: 0.8966887411111111

00:09:02.944 --> 00:09:04.510 of an association with cigarette  
NOTE Confidence: 0.8966887411111111

00:09:04.510 --> 00:09:06.370 smoking as other headed neck sites  
NOTE Confidence: 0.8966887411111111

00:09:06.370 --> 00:09:08.580 such as the oral cavity or lyrics,  
NOTE Confidence: 0.8966887411111111

00:09:08.580 --> 00:09:10.716 and it also was not associated  
NOTE Confidence: 0.8966887411111111

00:09:10.716 --> 00:09:12.140 with occupational exposures like  
NOTE Confidence: 0.8966887411111111

00:09:12.200 --> 00:09:14.305 other sinonasal tumor types like  
NOTE Confidence: 0.8966887411111111

00:09:14.305 --> 00:09:15.989 an intestinal type adenocarcinoma,  
NOTE Confidence: 0.8966887411111111

00:09:15.990 --> 00:09:17.440 sinonasal papillomas were known to  
NOTE Confidence: 0.8966887411111111

00:09:17.440 --> 00:09:19.810 be a precursor in a subset of cases,  
NOTE Confidence: 0.8966887411111111

00:09:19.810 --> 00:09:22.330 but the mechanism was unclear  
NOTE Confidence: 0.8966887411111111

00:09:22.330 --> 00:09:24.990 and etiology for a lot of cases  
NOTE Confidence: 0.8966887411111111

00:09:24.990 --> 00:09:26.130 was really unknown.  
NOTE Confidence: 0.8966887411111111

00:09:26.130 --> 00:09:28.326 Now that has changed because of  
NOTE Confidence: 0.8966887411111111

00:09:28.326 --> 00:09:29.424 emerging molecular understanding.  
NOTE Confidence: 0.8966887411111111

00:09:29.430 --> 00:09:31.290 Kind of in three areas.  
NOTE Confidence: 0.8966887411111111

00:09:31.290 --> 00:09:32.103 First of all,



NOTE Confidence: 0.8966887411111111  
00:09:32.103 --> 00:09:33.458 the role of human sinonasal  
NOTE Confidence: 0.8966887411111111  
00:09:33.458 --> 00:09:34.550 squamous cell carcinoma.  
NOTE Confidence: 0.8966887411111111  
00:09:34.550 --> 00:09:35.034 Second,  
NOTE Confidence: 0.8966887411111111  
00:09:35.034 --> 00:09:37.454 for mutations in Santa Nasal  
NOTE Confidence: 0.8966887411111111  
00:09:37.454 --> 00:09:39.798 Papillomas and finally the emergence  
NOTE Confidence: 0.8966887411111111  
00:09:39.798 --> 00:09:42.018 of fusion driven carcinomas that  
NOTE Confidence: 0.8966887411111111  
00:09:42.018 --> 00:09:43.350 have squamous differentiation.  
NOTE Confidence: 0.8966887411111111  
00:09:43.350 --> 00:09:45.126 So I'm going to start talking about HPV,  
NOTE Confidence: 0.8966887411111111  
00:09:45.130 --> 00:09:46.831 and of course we're all very familiar  
NOTE Confidence: 0.8966887411111111  
00:09:46.831 --> 00:09:49.107 with HPV as an oncogenic driver and head  
NOTE Confidence: 0.8966887411111111  
00:09:49.107 --> 00:09:51.050 neck squamous cell carcinoma in general,  
NOTE Confidence: 0.8966887411111111  
00:09:51.050 --> 00:09:53.325 but traditionally it was recognized in the  
NOTE Confidence: 0.8966887411111111  
00:09:53.325 --> 00:09:55.268 oropharynx and tonsillar and base of tongue,  
NOTE Confidence: 0.8966887411111111  
00:09:55.270 --> 00:09:56.053 squamous cell carcinomas,  
NOTE Confidence: 0.8966887411111111  
00:09:56.053 --> 00:09:57.619 and it's been thought of as  
NOTE Confidence: 0.8966887411111111

00:09:57.619 --> 00:09:59.050 sort of specific to that site.  
NOTE Confidence: 0.8966887411111111

00:09:59.050 --> 00:10:01.987 It does drive up to 80% of  
NOTE Confidence: 0.8966887411111111

00:10:01.987 --> 00:10:03.335 oropharyngeal squamous cell carcinoma  
NOTE Confidence: 0.8966887411111111

00:10:03.335 --> 00:10:05.445 in the United States with increasing  
NOTE Confidence: 0.8966887411111111

00:10:05.445 --> 00:10:07.275 incidents in the recent decades,  
NOTE Confidence: 0.8966887411111111

00:10:07.280 --> 00:10:08.617 but outside of that for a long  
NOTE Confidence: 0.8966887411111111

00:10:08.617 --> 00:10:09.911 time it was really thought to  
NOTE Confidence: 0.8966887411111111

00:10:09.911 --> 00:10:11.472 not play a role in other headed  
NOTE Confidence: 0.912479429285714

00:10:11.524 --> 00:10:13.436 next sites and even still the oral cavity.  
NOTE Confidence: 0.912479429285714

00:10:13.440 --> 00:10:15.666 Lyrics really, HPV is not a major  
NOTE Confidence: 0.912479429285714

00:10:15.666 --> 00:10:18.019 player and as such we are only  
NOTE Confidence: 0.912479429285714

00:10:18.019 --> 00:10:20.455 recommended to do HPV testing in the  
NOTE Confidence: 0.912479429285714

00:10:20.455 --> 00:10:22.717 oropharynx and in neck lymph nodes.  
NOTE Confidence: 0.912479429285714

00:10:22.720 --> 00:10:24.542 In the last few years, however,  
NOTE Confidence: 0.912479429285714

00:10:24.542 --> 00:10:27.278 HPV has really emerged as a driver of  
NOTE Confidence: 0.912479429285714

00:10:27.278 --> 00:10:29.650 sinonasal squamous cell carcinoma as well.

NOTE Confidence: 0.912479429285714

00:10:29.650 --> 00:10:31.842 And if not really regarded as a second

NOTE Confidence: 0.912479429285714

00:10:31.842 --> 00:10:33.580 hotspot for HPV involvement in the

NOTE Confidence: 0.912479429285714

00:10:33.580 --> 00:10:36.290 head and neck in most recent studies,

NOTE Confidence: 0.912479429285714

00:10:36.290 --> 00:10:38.850 about 20 to 25% of squamous cell

NOTE Confidence: 0.912479429285714

00:10:38.850 --> 00:10:40.300 carcinoma in the sinonasal tract

NOTE Confidence: 0.912479429285714

00:10:40.300 --> 00:10:42.146 is thought to be HPV associated,

NOTE Confidence: 0.912479429285714

00:10:42.150 --> 00:10:43.998 although there is a very large range

NOTE Confidence: 0.912479429285714

00:10:43.998 --> 00:10:46.078 in the literature and this is the

NOTE Confidence: 0.912479429285714

00:10:46.078 --> 00:10:47.486 highest prevalence of involvement

NOTE Confidence: 0.912479429285714

00:10:47.486 --> 00:10:49.963 in any non oropharyngeal site and

NOTE Confidence: 0.912479429285714

00:10:49.963 --> 00:10:52.014 it is now actually regarded as the

NOTE Confidence: 0.912479429285714

00:10:52.014 --> 00:10:54.364 most common defined risk factor for

NOTE Confidence: 0.912479429285714

00:10:54.364 --> 00:10:56.064 sinonasal squamous cell carcinoma.

NOTE Confidence: 0.912479429285714

00:10:56.070 --> 00:10:57.740 The pathogenesis of HPV driving

NOTE Confidence: 0.912479429285714

00:10:57.740 --> 00:10:59.833 tumors in the sinonasal tract is

NOTE Confidence: 0.912479429285714

00:10:59.833 --> 00:11:02.367 similar to the oropharynx and that its  
NOTE Confidence: 0.912479429285714

00:11:02.367 --> 00:11:03.969 transcriptionally active virus you know,  
NOTE Confidence: 0.912479429285714

00:11:03.970 --> 00:11:06.022 can be identified within the tumor  
NOTE Confidence: 0.912479429285714

00:11:06.022 --> 00:11:08.866 cells by by RNA inside 2 hybridization  
NOTE Confidence: 0.912479429285714

00:11:08.866 --> 00:11:10.270 or RNA sequencing,  
NOTE Confidence: 0.912479429285714

00:11:10.270 --> 00:11:12.976 and it drives viral on proteins  
NOTE Confidence: 0.912479429285714

00:11:12.976 --> 00:11:16.200 to push the cell proliferation.  
NOTE Confidence: 0.912479429285714

00:11:16.200 --> 00:11:16.438 Now,  
NOTE Confidence: 0.912479429285714

00:11:16.438 --> 00:11:17.628 one thing that's interesting that  
NOTE Confidence: 0.912479429285714

00:11:17.628 --> 00:11:19.370 we've noticed in the last in the last  
NOTE Confidence: 0.912479429285714

00:11:19.370 --> 00:11:20.752 couple years that the rate of HPV  
NOTE Confidence: 0.912479429285714

00:11:20.752 --> 00:11:22.108 involved in the center nasal tract  
NOTE Confidence: 0.912479429285714

00:11:22.108 --> 00:11:24.170 may actually have gone up over time.  
NOTE Confidence: 0.912479429285714

00:11:24.170 --> 00:11:25.915 I say 20 to 25%.  
NOTE Confidence: 0.912479429285714

00:11:25.915 --> 00:11:28.470 As as the the the prevalence overall,  
NOTE Confidence: 0.912479429285714

00:11:28.470 --> 00:11:30.174 but most of those studies are

NOTE Confidence: 0.912479429285714  
00:11:30.174 --> 00:11:31.646 actually dealing with the decades,  
NOTE Confidence: 0.912479429285714  
00:11:31.646 --> 00:11:33.494 the 90s and the early 2000s,  
NOTE Confidence: 0.912479429285714  
00:11:33.500 --> 00:11:35.342 and we noticed that there were  
NOTE Confidence: 0.912479429285714  
00:11:35.342 --> 00:11:37.718 a few recent papers that had a  
NOTE Confidence: 0.912479429285714  
00:11:37.718 --> 00:11:39.158 higher estimate of prevalence,  
NOTE Confidence: 0.912479429285714  
00:11:39.160 --> 00:11:41.518 and so we looked back at our own cases  
NOTE Confidence: 0.912479429285714  
00:11:41.518 --> 00:11:44.233 at Hopkins and actually parsed it out  
NOTE Confidence: 0.912479429285714  
00:11:44.233 --> 00:11:46.709 overtime and the prevalence of HPV  
NOTE Confidence: 0.912479429285714  
00:11:46.709 --> 00:11:48.764 and SINONASAL squamous cell carcinoma.  
NOTE Confidence: 0.912479429285714  
00:11:48.770 --> 00:11:51.500 We stained all of the.  
NOTE Confidence: 0.912479429285714  
00:11:51.500 --> 00:11:53.705 All of our cases on on tissue  
NOTE Confidence: 0.912479429285714  
00:11:53.705 --> 00:11:55.546 microarrays it went up from about  
NOTE Confidence: 0.912479429285714  
00:11:55.546 --> 00:11:57.697 10% in the 90s to about 50% now,  
NOTE Confidence: 0.912479429285714  
00:11:57.697 --> 00:11:59.359 so almost half of the squamous  
NOTE Confidence: 0.912479429285714  
00:11:59.359 --> 00:12:01.170 cell carcinomas we're seeing in the  
NOTE Confidence: 0.912479429285714

00:12:01.170 --> 00:12:02.720 sinonasal tractor now HPV associated.  
NOTE Confidence: 0.912479429285714

00:12:02.720 --> 00:12:03.710 So it seems to parallel.  
NOTE Confidence: 0.912479429285714

00:12:03.710 --> 00:12:05.822 But we'll pharynx in that the  
NOTE Confidence: 0.912479429285714

00:12:05.822 --> 00:12:07.250 involvement is increasing now.  
NOTE Confidence: 0.912479429285714

00:12:07.250 --> 00:12:09.100 Also parallel to the oropharynx,  
NOTE Confidence: 0.912479429285714

00:12:09.100 --> 00:12:10.400 that looks very similar,  
NOTE Confidence: 0.912479429285714

00:12:10.400 --> 00:12:12.025 HP associated squamous cell carcinoma  
NOTE Confidence: 0.912479429285714

00:12:12.025 --> 00:12:14.050 in the center nasal tract is non  
NOTE Confidence: 0.912479429285714

00:12:14.050 --> 00:12:16.100 keratinizing and it tends to have this  
NOTE Confidence: 0.912479429285714

00:12:16.100 --> 00:12:17.900 very pushing lobulated pattern of growth,  
NOTE Confidence: 0.912479429285714

00:12:17.900 --> 00:12:19.880 often very popular as well.  
NOTE Confidence: 0.912479429285714

00:12:19.880 --> 00:12:21.735 And these are these are very characteristic.  
NOTE Confidence: 0.912479429285714

00:12:21.740 --> 00:12:25.328 Appearances and very recognizable.  
NOTE Confidence: 0.912479429285714

00:12:25.330 --> 00:12:29.554 Now of course, is leads to upregulation  
NOTE Confidence: 0.912479429285714

00:12:29.554 --> 00:12:31.809 of P-16 and P-16 overexpression,  
NOTE Confidence: 0.912479429285714

00:12:31.810 --> 00:12:32.854 so that's consistently positive.

NOTE Confidence: 0.912479429285714  
00:12:32.854 --> 00:12:34.809 If you do want to test for it.  
NOTE Confidence: 0.912479429285714  
00:12:34.810 --> 00:12:35.068 However,  
NOTE Confidence: 0.912479429285714  
00:12:35.068 --> 00:12:36.874 it's not as specific in the sinonasal  
NOTE Confidence: 0.912479429285714  
00:12:36.874 --> 00:12:38.670 tract as it is in the oral pharynx,  
NOTE Confidence: 0.912479429285714  
00:12:38.670 --> 00:12:41.253 because there are a lot of different  
NOTE Confidence: 0.912479429285714  
00:12:41.253 --> 00:12:43.499 sinonasal tumor types that can overexpress  
NOTE Confidence: 0.912479429285714  
00:12:43.499 --> 00:12:45.991 P 16 by non HPV related mechanisms.  
NOTE Confidence: 0.912479429285714  
00:12:46.000 --> 00:12:46.257 Therefore,  
NOTE Confidence: 0.912479429285714  
00:12:46.257 --> 00:12:48.313 if there is a reason to do HPV  
NOTE Confidence: 0.912479429285714  
00:12:48.313 --> 00:12:49.838 testing in the sinonasal tract,  
NOTE Confidence: 0.912479429285714  
00:12:49.840 --> 00:12:51.040 confirming it with specific  
NOTE Confidence: 0.912479429285714  
00:12:51.040 --> 00:12:53.010 testing such as RNA and site 2,  
NOTE Confidence: 0.912479429285714  
00:12:53.010 --> 00:12:54.720 hybridization visualized here is the  
NOTE Confidence: 0.912479429285714  
00:12:54.720 --> 00:12:57.278 way to go to confirm it really is.  
NOTE Confidence: 0.912479429285714  
00:12:57.280 --> 00:12:59.525 Involvement now the question is  
NOTE Confidence: 0.912479429285714

00:12:59.525 --> 00:13:01.770 whether we would actually need  
NOTE Confidence: 0.83264559325

00:13:01.847 --> 00:13:04.788 to confirm HPV involvement or whether you  
NOTE Confidence: 0.83264559325

00:13:04.788 --> 00:13:06.852 know whether this is more of an academic  
NOTE Confidence: 0.83264559325

00:13:06.852 --> 00:13:08.115 question that explains pathogenesis  
NOTE Confidence: 0.83264559325

00:13:08.115 --> 00:13:10.019 but is not yet clinically relevant.  
NOTE Confidence: 0.83264559325

00:13:10.019 --> 00:13:12.890 And actually it does seem that HPV does lead  
NOTE Confidence: 0.83264559325

00:13:12.950 --> 00:13:15.610 to better prognosis than the sinonasal tract.  
NOTE Confidence: 0.83264559325

00:13:15.610 --> 00:13:16.742 This has actually been  
NOTE Confidence: 0.83264559325

00:13:16.742 --> 00:13:17.874 controversial for a while.  
NOTE Confidence: 0.83264559325

00:13:17.880 --> 00:13:20.680 Several single institutional studies showed  
NOTE Confidence: 0.83264559325

00:13:20.680 --> 00:13:23.480 either borderline significant or not  
NOTE Confidence: 0.83264559325

00:13:23.557 --> 00:13:26.427 significant benefit with HPV involvement,  
NOTE Confidence: 0.83264559325

00:13:26.430 --> 00:13:28.255 but actually looking at large  
NOTE Confidence: 0.83264559325

00:13:28.255 --> 00:13:29.350 National Cancer database.  
NOTE Confidence: 0.83264559325

00:13:29.350 --> 00:13:32.717 Studies there does seem to be a  
NOTE Confidence: 0.83264559325

00:13:32.717 --> 00:13:35.388 statistically significant benefit to HPV



NOTE Confidence: 0.83264559325  
00:13:35.388 --> 00:13:38.458 involvement in squamous cell carcinoma.  
NOTE Confidence: 0.83264559325  
00:13:38.460 --> 00:13:40.508 I think the real question is still whether  
NOTE Confidence: 0.83264559325  
00:13:40.508 --> 00:13:42.759 that is a clinically significant benefit.  
NOTE Confidence: 0.83264559325  
00:13:42.760 --> 00:13:45.714 The overall survival in the sinonasal tract,  
NOTE Confidence: 0.83264559325  
00:13:45.720 --> 00:13:47.430 even if it's HPV associated,  
NOTE Confidence: 0.83264559325  
00:13:47.430 --> 00:13:49.098 is still inferior to oropharyngeal  
NOTE Confidence: 0.83264559325  
00:13:49.098 --> 00:13:50.754 squamous cell carcinoma and that will  
NOTE Confidence: 0.83264559325  
00:13:50.754 --> 00:13:52.242 preclude some of the treatment changes  
NOTE Confidence: 0.83264559325  
00:13:52.242 --> 00:13:54.196 that have been happening in the oropharynx,  
NOTE Confidence: 0.83264559325  
00:13:54.200 --> 00:13:56.168 such as D escalation of chemotherapy  
NOTE Confidence: 0.83264559325  
00:13:56.168 --> 00:13:57.480 or radiation from happening.  
NOTE Confidence: 0.83264559325  
00:13:57.480 --> 00:13:58.974 And these are still tumors that  
NOTE Confidence: 0.83264559325  
00:13:58.974 --> 00:14:00.670 need to be treated aggressively.  
NOTE Confidence: 0.83264559325  
00:14:00.670 --> 00:14:01.156 So really,  
NOTE Confidence: 0.83264559325  
00:14:01.156 --> 00:14:02.857 the clinical utility of this is unclear.  
NOTE Confidence: 0.83264559325

00:14:02.860 --> 00:14:04.650 We're not recommended that we  
NOTE Confidence: 0.83264559325

00:14:04.650 --> 00:14:06.750 routinely test yet one thing that  
NOTE Confidence: 0.83264559325

00:14:06.750 --> 00:14:08.450 might change that is emerging.  
NOTE Confidence: 0.83264559325

00:14:08.450 --> 00:14:10.564 Serum markers, the ability to track tumors,  
NOTE Confidence: 0.83264559325

00:14:10.570 --> 00:14:13.846 overtime and and track for recurrence  
NOTE Confidence: 0.83264559325

00:14:13.846 --> 00:14:16.315 by by using circulating, hpde,  
NOTE Confidence: 0.83264559325

00:14:16.315 --> 00:14:18.025 and this is something our clinicians  
NOTE Confidence: 0.83264559325

00:14:18.025 --> 00:14:19.630 have been very interested in,  
NOTE Confidence: 0.83264559325

00:14:19.630 --> 00:14:21.658 and we have increasingly been doing  
NOTE Confidence: 0.83264559325

00:14:21.660 --> 00:14:26.777 testing on tumors for that that end.  
NOTE Confidence: 0.83264559325

00:14:26.780 --> 00:14:27.584 It will also,  
NOTE Confidence: 0.83264559325

00:14:27.584 --> 00:14:29.192 as as more trials go forward  
NOTE Confidence: 0.83264559325

00:14:29.192 --> 00:14:30.898 with more targeted therapies.  
NOTE Confidence: 0.83264559325

00:14:30.900 --> 00:14:32.836 This this may become relevant in the future,  
NOTE Confidence: 0.83264559325

00:14:32.840 --> 00:14:34.770 but routine testing is not  
NOTE Confidence: 0.83264559325

00:14:34.770 --> 00:14:35.928 not yet recommended.

NOTE Confidence: 0.83264559325

00:14:35.930 --> 00:14:38.072 Now of course I wouldn't be complete

NOTE Confidence: 0.83264559325

00:14:38.072 --> 00:14:40.340 talking about HPV and the sinonasal tract

NOTE Confidence: 0.83264559325

00:14:40.340 --> 00:14:42.716 without touching on the fact that it

NOTE Confidence: 0.83264559325

00:14:42.716 --> 00:14:44.996 doesn't just cause squamous cell carcinomas.

NOTE Confidence: 0.83264559325

00:14:45.000 --> 00:14:47.676 There's a very unique new entity

NOTE Confidence: 0.83264559325

00:14:47.680 --> 00:14:49.364 related multi phenotypic sinonasal

NOTE Confidence: 0.83264559325

00:14:49.364 --> 00:14:52.446 carcinoma that actually shows a mix of

NOTE Confidence: 0.83264559325

00:14:52.446 --> 00:14:54.418 squamous and salivary differentiation,

NOTE Confidence: 0.83264559325

00:14:54.420 --> 00:14:56.760 either myoepithelial or ductal combination.

NOTE Confidence: 0.83264559325

00:14:56.760 --> 00:14:59.244 Care of it was originally described

NOTE Confidence: 0.83264559325

00:14:59.244 --> 00:15:01.910 as HPV related carcinoma with adenoid

NOTE Confidence: 0.83264559325

00:15:01.910 --> 00:15:03.317 cystic like features,

NOTE Confidence: 0.83264559325

00:15:03.320 --> 00:15:05.329 but it's not an adenoid cystic carcinoma,

NOTE Confidence: 0.83264559325

00:15:05.330 --> 00:15:06.989 and sometimes it doesn't look like much,

NOTE Confidence: 0.83264559325

00:15:06.990 --> 00:15:09.222 much like one, they lack the

NOTE Confidence: 0.83264559325

00:15:09.222 --> 00:15:11.200 characteristic fusions of adenoid cystic,  
NOTE Confidence: 0.83264559325

00:15:11.200 --> 00:15:12.853 and instead harbor  
NOTE Confidence: 0.83264559325

00:15:12.853 --> 00:15:14.506 transcriptionally active HPV.  
NOTE Confidence: 0.83264559325

00:15:14.510 --> 00:15:16.250 Uniquely HPV type 33,  
NOTE Confidence: 0.83264559325

00:15:16.250 --> 00:15:19.365 which is which is not seen a  
NOTE Confidence: 0.83264559325

00:15:19.365 --> 00:15:21.890 lot in squamous cell carcinoma.  
NOTE Confidence: 0.83264559325

00:15:21.890 --> 00:15:24.426 So this tumor you can see its resemblance  
NOTE Confidence: 0.83264559325

00:15:24.426 --> 00:15:26.226 stagnant cystic carcinoma here with  
NOTE Confidence: 0.83264559325

00:15:26.226 --> 00:15:27.856 cribriform architecture and and and  
NOTE Confidence: 0.83264559325

00:15:27.856 --> 00:15:30.660 ductal in my web ethereal differentiation.  
NOTE Confidence: 0.83264559325

00:15:30.660 --> 00:15:32.670 But other areas look more basaloid  
NOTE Confidence: 0.83264559325

00:15:32.670 --> 00:15:35.081 look more squamous and it even is  
NOTE Confidence: 0.83264559325

00:15:35.081 --> 00:15:36.756 associated with some squamous dysplasia  
NOTE Confidence: 0.83264559325

00:15:36.756 --> 00:15:39.168 on the surface in a large proportion  
NOTE Confidence: 0.83264559325

00:15:39.168 --> 00:15:41.424 of cases which really point to it  
NOTE Confidence: 0.83264559325

00:15:41.424 --> 00:15:43.146 probably being a tumor of surface

NOTE Confidence: 0.83264559325  
00:15:43.146 --> 00:15:45.784 origin that just happens to be showing  
NOTE Confidence: 0.83264559325  
00:15:45.784 --> 00:15:46.987 some salivary differentiation.  
NOTE Confidence: 0.83264559325  
00:15:46.990 --> 00:15:48.379 Now on stains.  
NOTE Confidence: 0.83264559325  
00:15:48.379 --> 00:15:50.694 P40 highlights the squamous component,  
NOTE Confidence: 0.83264559325  
00:15:50.700 --> 00:15:52.272 but it also highlights the myoepithelial  
NOTE Confidence: 0.83264559325  
00:15:52.272 --> 00:15:53.709 component and you can see the.  
NOTE Confidence: 0.83264559325  
00:15:53.710 --> 00:15:55.460 Septal component is negative here,  
NOTE Confidence: 0.83264559325  
00:15:55.460 --> 00:15:57.748 which is is what you want for this.  
NOTE Confidence: 0.83264559325  
00:15:57.750 --> 00:15:59.661 For this diagnosis to prove that it  
NOTE Confidence: 0.83264559325  
00:15:59.661 --> 00:16:02.502 it has a biphasic differentiation or  
NOTE Confidence: 0.83264559325  
00:16:02.502 --> 00:16:04.458 true myoepithelial differentiation.  
NOTE Confidence: 0.83264559325  
00:16:04.460 --> 00:16:06.986 And here's our Nancy 2 hybridization  
NOTE Confidence: 0.83264559325  
00:16:06.986 --> 00:16:08.670 we happen to have  
NOTE Confidence: 0.687099516923077  
00:16:08.757 --> 00:16:11.230 a a probe that is specific for type 33  
NOTE Confidence: 0.687099516923077  
00:16:11.230 --> 00:16:13.406 and that allows us to recognize that  
NOTE Confidence: 0.687099516923077

00:16:13.406 --> 00:16:16.069 and in this tumor which is kind of fun.

NOTE Confidence: 0.687099516923077

00:16:16.070 --> 00:16:18.023 Now, this is a tumor HPV related

NOTE Confidence: 0.687099516923077

00:16:18.023 --> 00:16:19.219 multi phenotypic sinonasal carcinoma

NOTE Confidence: 0.687099516923077

00:16:19.219 --> 00:16:20.734 that's important to recognize 'cause

NOTE Confidence: 0.687099516923077

00:16:20.734 --> 00:16:22.709 it actually has a good prognosis,

NOTE Confidence: 0.687099516923077

00:16:22.710 --> 00:16:24.470 which is refreshingly different from

NOTE Confidence: 0.687099516923077

00:16:24.470 --> 00:16:26.660 many other center nasal tract tumors.

NOTE Confidence: 0.687099516923077

00:16:26.660 --> 00:16:28.596 It looks really bad, it looks high grade,

NOTE Confidence: 0.687099516923077

00:16:28.600 --> 00:16:31.225 but only about a third recur locally

NOTE Confidence: 0.687099516923077

00:16:31.230 --> 00:16:33.070 and distant metastasis, lymph node,

NOTE Confidence: 0.687099516923077

00:16:33.070 --> 00:16:34.575 metastasis and death from disease

NOTE Confidence: 0.687099516923077

00:16:34.575 --> 00:16:35.779 are all very rare,

NOTE Confidence: 0.687099516923077

00:16:35.780 --> 00:16:37.708 so this is 1 where HPV testing is

NOTE Confidence: 0.687099516923077

00:16:37.708 --> 00:16:39.188 important to make the diagnosis

NOTE Confidence: 0.687099516923077

00:16:39.190 --> 00:16:41.894 and helps helps point or it out to

NOTE Confidence: 0.687099516923077

00:16:41.894 --> 00:16:43.718 better outcomes for the patient.

NOTE Confidence: 0.687099516923077  
00:16:43.720 --> 00:16:44.880 Alright, moving it slightly  
NOTE Confidence: 0.687099516923077  
00:16:44.880 --> 00:16:46.040 outside the HPV realm,  
NOTE Confidence: 0.687099516923077  
00:16:46.040 --> 00:16:47.870 although will return briefly as  
NOTE Confidence: 0.687099516923077  
00:16:47.870 --> 00:16:49.700 the issue of Sinonasal papillomas.  
NOTE Confidence: 0.687099516923077  
00:16:49.700 --> 00:16:52.115 Now this is another pathway of Carcino  
NOTE Confidence: 0.687099516923077  
00:16:52.115 --> 00:16:54.260 Genesis in the Sinonasal tract,  
NOTE Confidence: 0.687099516923077  
00:16:54.260 --> 00:16:55.480 and as we all know,  
NOTE Confidence: 0.687099516923077  
00:16:55.480 --> 00:16:56.593 sinonasal papillomas used  
NOTE Confidence: 0.687099516923077  
00:16:56.593 --> 00:16:58.077 to be called schneiderian.  
NOTE Confidence: 0.687099516923077  
00:16:58.080 --> 00:16:59.942 They've taken Schneider out of out of  
NOTE Confidence: 0.687099516923077  
00:16:59.942 --> 00:17:01.897 the name just to remove the eponym.  
NOTE Confidence: 0.687099516923077  
00:17:01.900 --> 00:17:03.190 Nothing unsavory associated  
NOTE Confidence: 0.687099516923077  
00:17:03.190 --> 00:17:05.340 with him like other eponyms,  
NOTE Confidence: 0.687099516923077  
00:17:05.340 --> 00:17:07.722 but inverted papillomas are the most  
NOTE Confidence: 0.687099516923077  
00:17:07.722 --> 00:17:11.100 common exophytic and oncocytic also occur,  
NOTE Confidence: 0.687099516923077

00:17:11.100 --> 00:17:12.483 and carcinomatous transformation.  
NOTE Confidence: 0.687099516923077

00:17:12.483 --> 00:17:15.249 Is the thing that everyone worries  
NOTE Confidence: 0.687099516923077

00:17:15.249 --> 00:17:17.330 about with inverted papillomas.  
NOTE Confidence: 0.687099516923077

00:17:17.330 --> 00:17:19.152 This occurs in up to 15% of  
NOTE Confidence: 0.687099516923077

00:17:19.152 --> 00:17:19.636 inverted papillomas.  
NOTE Confidence: 0.687099516923077

00:17:19.636 --> 00:17:21.088 It's probably a little on the  
NOTE Confidence: 0.687099516923077

00:17:21.088 --> 00:17:22.468 higher end in terms of statistics,  
NOTE Confidence: 0.687099516923077

00:17:22.470 --> 00:17:24.606 probably a little lower these days.  
NOTE Confidence: 0.687099516923077

00:17:24.610 --> 00:17:26.770 5% of Oncocytic papillomas and it's  
NOTE Confidence: 0.687099516923077

00:17:26.770 --> 00:17:28.930 very rare with exophytic papillomas.  
NOTE Confidence: 0.687099516923077

00:17:28.930 --> 00:17:30.808 And really there's no reliable histologic  
NOTE Confidence: 0.687099516923077

00:17:30.808 --> 00:17:32.761 features to predict what will what  
NOTE Confidence: 0.687099516923077

00:17:32.761 --> 00:17:34.386 will lead to malignant transformation.  
NOTE Confidence: 0.687099516923077

00:17:34.390 --> 00:17:36.546 It's nothing that we can see histologically,  
NOTE Confidence: 0.687099516923077

00:17:36.550 --> 00:17:37.906 based on how the papilloma looks,  
NOTE Confidence: 0.687099516923077

00:17:37.910 --> 00:17:40.046 and even the number of recurrences



NOTE Confidence: 0.687099516923077  
00:17:40.050 --> 00:17:41.878 clinically doesn't predict the  
NOTE Confidence: 0.687099516923077  
00:17:41.878 --> 00:17:43.545 development of carcinoma most.  
NOTE Confidence: 0.687099516923077  
00:17:43.545 --> 00:17:45.905 Most times we can make the diagnosis of  
NOTE Confidence: 0.687099516923077  
00:17:45.905 --> 00:17:48.484 a carcinoma ex papilloma because we do  
NOTE Confidence: 0.687099516923077  
00:17:48.484 --> 00:17:50.868 see a benign papilloma underlying and  
NOTE Confidence: 0.687099516923077  
00:17:50.868 --> 00:17:53.794 and usually the carcinomas are squamous cell.  
NOTE Confidence: 0.687099516923077  
00:17:53.800 --> 00:17:56.117 So here's just a couple slides illustrating.  
NOTE Confidence: 0.687099516923077  
00:17:56.120 --> 00:17:58.550 Here's a nice benign inverted papilloma  
NOTE Confidence: 0.687099516923077  
00:17:58.550 --> 00:18:00.602 nice rounded nests extending downward  
NOTE Confidence: 0.687099516923077  
00:18:00.602 --> 00:18:03.157 into the stroma but no cytologic atypia,  
NOTE Confidence: 0.687099516923077  
00:18:03.160 --> 00:18:05.572 whereas the squamous cell carcinoma arising  
NOTE Confidence: 0.687099516923077  
00:18:05.572 --> 00:18:08.220 X inverted papilloma shows increased atypia,  
NOTE Confidence: 0.687099516923077  
00:18:08.220 --> 00:18:08.686 infiltrative,  
NOTE Confidence: 0.687099516923077  
00:18:08.686 --> 00:18:09.618 and expanse.  
NOTE Confidence: 0.687099516923077  
00:18:09.618 --> 00:18:15.060 I'll growth and a lot of.  
NOTE Confidence: 0.687099516923077

00:18:15.060 --> 00:18:16.512 Downward extension come on.  
NOTE Confidence: 0.687099516923077

00:18:16.512 --> 00:18:18.327 Civic Center nasal papillomas have  
NOTE Confidence: 0.687099516923077

00:18:18.327 --> 00:18:19.940 a different appearance.  
NOTE Confidence: 0.687099516923077

00:18:19.940 --> 00:18:21.312 They're more glandular looking.  
NOTE Confidence: 0.687099516923077

00:18:21.312 --> 00:18:23.860 Bilayer \*\*\*\*\* \*\*\*\* epithelium with  
NOTE Confidence: 0.687099516923077

00:18:23.860 --> 00:18:27.660 microcysts and microabscesses and then  
NOTE Confidence: 0.687099516923077

00:18:27.660 --> 00:18:29.840 carcinoma Exxon caustic papilloma we.  
NOTE Confidence: 0.687099516923077

00:18:29.840 --> 00:18:32.381 In this case we see colonization of  
NOTE Confidence: 0.687099516923077

00:18:32.381 --> 00:18:34.034 an atypical squamous proliferation  
NOTE Confidence: 0.687099516923077

00:18:34.034 --> 00:18:38.200 with that uncle cynic epithelial now.  
NOTE Confidence: 0.687099516923077

00:18:38.200 --> 00:18:39.640 Just to go back to the HPV issue  
NOTE Confidence: 0.687099516923077

00:18:39.640 --> 00:18:40.380 for a moment.  
NOTE Confidence: 0.687099516923077

00:18:40.380 --> 00:18:43.500 There has been historical controversy about  
NOTE Confidence: 0.687099516923077

00:18:43.500 --> 00:18:45.960 the role plays in Sinonasal Papillomas.  
NOTE Confidence: 0.687099516923077

00:18:45.960 --> 00:18:47.857 This is one of these annoying topics  
NOTE Confidence: 0.687099516923077

00:18:47.857 --> 00:18:49.359 in the literature that literally

NOTE Confidence: 0.687099516923077  
00:18:49.359 --> 00:18:50.939 the prevalence ranges from 0%  
NOTE Confidence: 0.687099516923077  
00:18:50.940 --> 00:18:53.320 to 100% in old literature.  
NOTE Confidence: 0.687099516923077  
00:18:53.320 --> 00:18:55.306 In any role you can imagine  
NOTE Confidence: 0.687099516923077  
00:18:55.306 --> 00:18:56.299 has been proposed,  
NOTE Confidence: 0.687099516923077  
00:18:56.300 --> 00:18:57.760 does it initiate the papilloma?  
NOTE Confidence: 0.687099516923077  
00:18:57.760 --> 00:18:58.800 Is it implicated in the  
NOTE Confidence: 0.687099516923077  
00:18:58.800 --> 00:18:59.632 growth as a papilloma,  
NOTE Confidence: 0.687099516923077  
00:18:59.640 --> 00:19:02.216 or does it play a role in  
NOTE Confidence: 0.687099516923077  
00:19:02.216 --> 00:19:02.952 malignant transformation?  
NOTE Confidence: 0.687099516923077  
00:19:02.960 --> 00:19:04.816 Now there's a lot of issues when you  
NOTE Confidence: 0.687099516923077  
00:19:04.816 --> 00:19:06.470 dig through this literature and try  
NOTE Confidence: 0.687099516923077  
00:19:06.470 --> 00:19:08.180 to figure out what's actually going  
NOTE Confidence: 0.924386175909091  
00:19:08.233 --> 00:19:10.104 on here. A lot of the older studies used  
NOTE Confidence: 0.924386175909091  
00:19:10.104 --> 00:19:11.860 on PCR based testing that was very,  
NOTE Confidence: 0.924386175909091  
00:19:11.860 --> 00:19:13.620 very sensitive and detected virus  
NOTE Confidence: 0.924386175909091

00:19:13.620 --> 00:19:16.018 at low levels. That was not  
NOTE Confidence: 0.924386175909091

00:19:16.018 --> 00:19:17.356 necessarily biologically relevant.  
NOTE Confidence: 0.924386175909091

00:19:17.360 --> 00:19:19.415 Some studies did not separate  
NOTE Confidence: 0.924386175909091

00:19:19.415 --> 00:19:22.350 low risk and high risk HPV types.  
NOTE Confidence: 0.924386175909091

00:19:22.350 --> 00:19:23.793 Some studies conflated  
NOTE Confidence: 0.924386175909091

00:19:23.793 --> 00:19:25.236 different papilloma types,  
NOTE Confidence: 0.924386175909091

00:19:25.240 --> 00:19:27.208 and many studies did not have  
NOTE Confidence: 0.924386175909091

00:19:27.208 --> 00:19:28.192 central pathology review,  
NOTE Confidence: 0.924386175909091

00:19:28.200 --> 00:19:29.964 which would particularly allow  
NOTE Confidence: 0.924386175909091

00:19:29.964 --> 00:19:31.728 separation of papillary squamous  
NOTE Confidence: 0.924386175909091

00:19:31.728 --> 00:19:33.724 cell carcinomas that don't truly  
NOTE Confidence: 0.924386175909091

00:19:33.724 --> 00:19:35.128 have a papilloma component.  
NOTE Confidence: 0.924386175909091

00:19:35.130 --> 00:19:39.930 From a true carcinoma X kapalama now.  
NOTE Confidence: 0.924386175909091

00:19:39.930 --> 00:19:40.896 In recent years,  
NOTE Confidence: 0.924386175909091

00:19:40.896 --> 00:19:43.150 use of of techniques like RNA and  
NOTE Confidence: 0.924386175909091

00:19:43.218 --> 00:19:45.498 site 2 hybridization have allowed for

NOTE Confidence: 0.924386175909091

00:19:45.498 --> 00:19:48.124 more consensus on the role of HP exited.

NOTE Confidence: 0.924386175909091

00:19:48.124 --> 00:19:50.488 Papilloma is at least 25 to

NOTE Confidence: 0.924386175909091

00:19:50.490 --> 00:19:52.730 55% of them have low risk HPV,

NOTE Confidence: 0.924386175909091

00:19:52.730 --> 00:19:54.000 kind of similar to papillomas.

NOTE Confidence: 0.924386175909091

00:19:54.000 --> 00:19:56.226 Another headed next site, so that's great.

NOTE Confidence: 0.924386175909091

00:19:56.230 --> 00:19:56.934 Inverted papillomas,

NOTE Confidence: 0.924386175909091

00:19:56.934 --> 00:19:59.398 about 10% of them do have low

NOTE Confidence: 0.924386175909091

00:19:59.398 --> 00:20:01.774 risk HPV and it is possible that

NOTE Confidence: 0.924386175909091

00:20:01.774 --> 00:20:04.045 that is associated with a higher

NOTE Confidence: 0.924386175909091

00:20:04.045 --> 00:20:05.837 risk of malignant transformation.

NOTE Confidence: 0.924386175909091

00:20:05.840 --> 00:20:06.410 Performance,

NOTE Confidence: 0.924386175909091

00:20:06.410 --> 00:20:08.690 absolutely no association with

NOTE Confidence: 0.924386175909091

00:20:08.690 --> 00:20:10.545 and multiple studies using RNA

NOTE Confidence: 0.924386175909091

00:20:10.545 --> 00:20:12.400 insight to hybridization have not

NOTE Confidence: 0.924386175909091

00:20:12.466 --> 00:20:14.322 found transcriptionally active high

NOTE Confidence: 0.924386175909091

00:20:14.322 --> 00:20:16.106 risk in any papilloma subtype,  
NOTE Confidence: 0.924386175909091

00:20:16.106 --> 00:20:18.080 so there really is not any  
NOTE Confidence: 0.924386175909091

00:20:18.144 --> 00:20:20.426 indication for testing at any type  
NOTE Confidence: 0.924386175909091

00:20:20.426 --> 00:20:22.520 of sinonasal papilloma at this point,  
NOTE Confidence: 0.924386175909091

00:20:22.520 --> 00:20:23.880 so if not HPV,  
NOTE Confidence: 0.924386175909091

00:20:23.880 --> 00:20:25.580 what's causing the sinonasal papilloma?  
NOTE Confidence: 0.924386175909091

00:20:25.580 --> 00:20:27.045 There's been this excellent series  
NOTE Confidence: 0.924386175909091

00:20:27.045 --> 00:20:29.122 of papers that have come out of  
NOTE Confidence: 0.924386175909091

00:20:29.122 --> 00:20:30.512 University of Michigan premiere in  
NOTE Confidence: 0.924386175909091

00:20:30.512 --> 00:20:32.314 Utica and Noah Brown that's really  
NOTE Confidence: 0.924386175909091

00:20:32.314 --> 00:20:33.834 parse this out really nicely.  
NOTE Confidence: 0.924386175909091

00:20:33.840 --> 00:20:35.560 In the past few years,  
NOTE Confidence: 0.924386175909091

00:20:35.560 --> 00:20:37.480 it most inverted papillomas.  
NOTE Confidence: 0.924386175909091

00:20:37.480 --> 00:20:38.440 For now.  
NOTE Confidence: 0.924386175909091

00:20:38.440 --> 00:20:41.518 Recognized to have activating EGFR mutations,  
NOTE Confidence: 0.924386175909091

00:20:41.520 --> 00:20:43.956 as do the associated squamous cell

NOTE Confidence: 0.924386175909091

00:20:43.956 --> 00:20:45.580 carcinomas and oncotic papillomas

NOTE Confidence: 0.924386175909091

00:20:45.647 --> 00:20:47.677 have consistent care as mutations,

NOTE Confidence: 0.924386175909091

00:20:47.680 --> 00:20:50.067 as do the carcinomas associated with them.

NOTE Confidence: 0.924386175909091

00:20:50.070 --> 00:20:52.310 So now we have a clear oncogenic

NOTE Confidence: 0.924386175909091

00:20:52.310 --> 00:20:53.948 driver associated with both of

NOTE Confidence: 0.924386175909091

00:20:53.948 --> 00:20:56.246 these types of papilloma that kind

NOTE Confidence: 0.924386175909091

00:20:56.246 --> 00:20:58.753 of explains their growth now.

NOTE Confidence: 0.924386175909091

00:20:58.753 --> 00:20:59.146 Interestingly,

NOTE Confidence: 0.924386175909091

00:20:59.146 --> 00:21:01.897 that is not those mutations are not

NOTE Confidence: 0.924386175909091

00:21:01.897 --> 00:21:04.138 enough for squamous cell carcinoma.

NOTE Confidence: 0.924386175909091

00:21:04.140 --> 00:21:05.014 Recently again,

NOTE Confidence: 0.924386175909091

00:21:05.014 --> 00:21:07.199 the same group for Michigan

NOTE Confidence: 0.924386175909091

00:21:07.199 --> 00:21:08.510 reported that transformation.

NOTE Confidence: 0.924386175909091

00:21:08.510 --> 00:21:10.506 Squamous cell carcinoma required.

NOTE Confidence: 0.924386175909091

00:21:10.506 --> 00:21:13.001 The accumulation of additional mutations

NOTE Confidence: 0.924386175909091

00:21:13.001 --> 00:21:15.645 so the squamous cell carcinoma does  
NOTE Confidence: 0.924386175909091

00:21:15.645 --> 00:21:18.370 harbor the underlying EGFR KRAS mutation,  
NOTE Confidence: 0.924386175909091

00:21:18.370 --> 00:21:20.280 but it gains additional TP  
NOTE Confidence: 0.924386175909091

00:21:20.280 --> 00:21:22.289 53 or CDKN 2A alterations.  
NOTE Confidence: 0.924386175909091

00:21:22.289 --> 00:21:24.595 In most cases when those additional  
NOTE Confidence: 0.924386175909091

00:21:24.595 --> 00:21:26.725 alterations are not seen in matched  
NOTE Confidence: 0.924386175909091

00:21:26.725 --> 00:21:28.210 Sinonasal papilloma and really,  
NOTE Confidence: 0.924386175909091

00:21:28.210 --> 00:21:29.980 this mutational profile is unique among  
NOTE Confidence: 0.924386175909091

00:21:29.980 --> 00:21:31.790 head neck squamous cell carcinoma,  
NOTE Confidence: 0.924386175909091

00:21:31.790 --> 00:21:34.250 so it's a very unique group.  
NOTE Confidence: 0.924386175909091

00:21:34.250 --> 00:21:35.785 Now there are some implications  
NOTE Confidence: 0.924386175909091

00:21:35.785 --> 00:21:36.399 for treatment,  
NOTE Confidence: 0.924386175909091

00:21:36.400 --> 00:21:38.500 although this is not yet fleshed  
NOTE Confidence: 0.924386175909091

00:21:38.500 --> 00:21:39.692 out yet either.  
NOTE Confidence: 0.924386175909091

00:21:39.692 --> 00:21:42.152 EGFR mutations of course broadly  
NOTE Confidence: 0.924386175909091

00:21:42.152 --> 00:21:43.628 are potentially actionable,



NOTE Confidence: 0.924386175909091

00:21:43.630 --> 00:21:45.772 similar to how they're they're very

NOTE Confidence: 0.924386175909091

00:21:45.772 --> 00:21:48.506 commonly targeted, and lung lung cancer.

NOTE Confidence: 0.924386175909091

00:21:48.506 --> 00:21:49.010 Unfortunately,

NOTE Confidence: 0.924386175909091

00:21:49.010 --> 00:21:51.056 most of the mutations in the

NOTE Confidence: 0.924386175909091

00:21:51.056 --> 00:21:52.660 sinonasal papillomas are exon 20,

NOTE Confidence: 0.924386175909091

00:21:52.660 --> 00:21:55.090 which are often resistant to the

NOTE Confidence: 0.924386175909091

00:21:55.090 --> 00:21:56.674 common EGFR inhibitors compared

NOTE Confidence: 0.924386175909091

00:21:56.674 --> 00:21:58.130 to exon 19 deletions,

NOTE Confidence: 0.924386175909091

00:21:58.130 --> 00:21:59.922 but there are newer drugs that may

NOTE Confidence: 0.924386175909091

00:21:59.922 --> 00:22:01.848 be more robust to these alterations,

NOTE Confidence: 0.924386175909091

00:22:01.850 --> 00:22:03.770 so it's definitely a promising

NOTE Confidence: 0.924386175909091

00:22:03.770 --> 00:22:06.250 Ave for treatment in the future.

NOTE Confidence: 0.924386175909091

00:22:06.250 --> 00:22:07.834 Have a last squamous thing I

NOTE Confidence: 0.924386175909091

00:22:07.834 --> 00:22:08.890 want to talk about.

NOTE Confidence: 0.924386175909091

00:22:08.890 --> 00:22:11.065 Our fusion driven tumors that

NOTE Confidence: 0.924386175909091

00:22:11.065 --> 00:22:12.370 show squamous differentiation  
NOTE Confidence: 0.924386175909091

00:22:12.370 --> 00:22:14.664 and this is something that has  
NOTE Confidence: 0.924386175909091

00:22:14.664 --> 00:22:16.698 really flowered in the last few  
NOTE Confidence: 0.910352593333334

00:22:16.766 --> 00:22:18.700 years. So first I'm going to  
NOTE Confidence: 0.910352593333334

00:22:18.700 --> 00:22:20.250 touch briefly on nut carcinoma.  
NOTE Confidence: 0.910352593333334

00:22:20.250 --> 00:22:21.355 This is something probably people  
NOTE Confidence: 0.910352593333334

00:22:21.355 --> 00:22:23.023 are a lot of people are familiar  
NOTE Confidence: 0.910352593333334

00:22:23.023 --> 00:22:24.318 with from different organ systems  
NOTE Confidence: 0.910352593333334

00:22:24.318 --> 00:22:26.020 because this is a tumor type that  
NOTE Confidence: 0.910352593333334

00:22:26.020 --> 00:22:27.346 arises kind of throughout the body.  
NOTE Confidence: 0.910352593333334

00:22:27.350 --> 00:22:29.744 It used to be called nut midline  
NOTE Confidence: 0.910352593333334

00:22:29.744 --> 00:22:31.488 carcinoma but midline of course  
NOTE Confidence: 0.910352593333334

00:22:31.488 --> 00:22:33.426 has been removed from the name  
NOTE Confidence: 0.910352593333334

00:22:33.426 --> 00:22:35.350 because it can occur anywhere.  
NOTE Confidence: 0.910352593333334

00:22:35.350 --> 00:22:37.840 Approximately 35% of cases are involved,  
NOTE Confidence: 0.910352593333334

00:22:37.840 --> 00:22:38.960 head and neck and.

NOTE Confidence: 0.910352593333334

00:22:38.960 --> 00:22:40.640 Most commonly in the sinonasal tract,

NOTE Confidence: 0.910352593333334

00:22:40.640 --> 00:22:43.140 so it really is a hot spot for this tumor

NOTE Confidence: 0.910352593333334

00:22:43.209 --> 00:22:45.834 to arise and defined by nut translocations,

NOTE Confidence: 0.910352593333334

00:22:45.840 --> 00:22:47.448 and this translation is not to

NOTE Confidence: 0.910352593333334

00:22:47.448 --> 00:22:49.957 play on to jenik role by blocking

NOTE Confidence: 0.910352593333334

00:22:49.957 --> 00:22:51.785 epithelial differentiation and meaning,

NOTE Confidence: 0.910352593333334

00:22:51.790 --> 00:22:54.658 maintaining the proliferation of tumor cells.

NOTE Confidence: 0.910352593333334

00:22:54.660 --> 00:22:56.365 Now here's a beautiful example

NOTE Confidence: 0.910352593333334

00:22:56.365 --> 00:22:57.729 of classic nut carcinoma.

NOTE Confidence: 0.910352593333334

00:22:57.730 --> 00:22:58.434 Very primitive,

NOTE Confidence: 0.910352593333334

00:22:58.434 --> 00:23:00.194 very high grade looking tumor.

NOTE Confidence: 0.910352593333334

00:23:00.200 --> 00:23:02.020 All the tumor cells are very monotonous.

NOTE Confidence: 0.910352593333334

00:23:02.020 --> 00:23:03.675 It is a translocation driven

NOTE Confidence: 0.910352593333334

00:23:03.675 --> 00:23:04.999 tumor but prominent nucleoli.

NOTE Confidence: 0.910352593333334

00:23:05.000 --> 00:23:06.550 Lots of necrosis in mitosis,

NOTE Confidence: 0.910352593333334

00:23:06.550 --> 00:23:08.097 very high grade, and often there's a  
NOTE Confidence: 0.910352593333334

00:23:08.097 --> 00:23:09.940 lot of tumor infiltrating neutrophils,  
NOTE Confidence: 0.910352593333334

00:23:09.940 --> 00:23:11.506 which we're seeing.  
NOTE Confidence: 0.910352593333334

00:23:11.506 --> 00:23:12.028 Account.  
NOTE Confidence: 0.910352593333334

00:23:12.030 --> 00:23:13.410 Here is what we classically  
NOTE Confidence: 0.910352593333334

00:23:13.410 --> 00:23:14.790 think of with nut carcinoma.  
NOTE Confidence: 0.910352593333334

00:23:14.790 --> 00:23:16.500 Unfortunately not there in every case,  
NOTE Confidence: 0.910352593333334

00:23:16.500 --> 00:23:17.628 but when it is,  
NOTE Confidence: 0.910352593333334

00:23:17.628 --> 00:23:19.320 it's super helpful in this abrupt  
NOTE Confidence: 0.910352593333334

00:23:19.381 --> 00:23:21.451 keratinization where you have the  
NOTE Confidence: 0.910352593333334

00:23:21.451 --> 00:23:23.521 primitive selves that crossover really  
NOTE Confidence: 0.910352593333334

00:23:23.530 --> 00:23:25.228 quickly to to form keratinized cells  
NOTE Confidence: 0.910352593333334

00:23:25.228 --> 00:23:27.484 and that can be a really helpful  
NOTE Confidence: 0.910352593333334

00:23:27.484 --> 00:23:29.254 clue to the differential diagnosis.  
NOTE Confidence: 0.910352593333334

00:23:29.260 --> 00:23:30.307 Now nut carcinoma.  
NOTE Confidence: 0.910352593333334

00:23:30.307 --> 00:23:32.750 You know not only has squamous pearls,

NOTE Confidence: 0.910352593333334

00:23:32.750 --> 00:23:34.860 most cases have expression of

NOTE Confidence: 0.910352593333334

00:23:34.860 --> 00:23:37.014 squamous markers such as P40I will

NOTE Confidence: 0.910352593333334

00:23:37.014 --> 00:23:38.870 add that a small subset of them don't,

NOTE Confidence: 0.910352593333334

00:23:38.870 --> 00:23:41.446 so it is reasonable to do a nut

NOTE Confidence: 0.910352593333334

00:23:41.450 --> 00:23:42.510 even if you don't have.

NOTE Confidence: 0.910352593333334

00:23:42.510 --> 00:23:44.730 Evidence of of overt squamous differentiation

NOTE Confidence: 0.910352593333334

00:23:44.730 --> 00:23:47.198 that does those do exist out there,

NOTE Confidence: 0.910352593333334

00:23:47.200 --> 00:23:49.330 but the real clincher is

NOTE Confidence: 0.910352593333334

00:23:49.330 --> 00:23:50.608 often the immunostain.

NOTE Confidence: 0.910352593333334

00:23:50.610 --> 00:23:53.599 The nut stain for that can help

NOTE Confidence: 0.910352593333334

00:23:53.599 --> 00:23:55.290 confirm the diagnosis now.

NOTE Confidence: 0.910352593333334

00:23:55.290 --> 00:23:57.162 A couple years ago I would have said

NOTE Confidence: 0.910352593333334

00:23:57.162 --> 00:23:59.170 that this stain was 100% specific for

NOTE Confidence: 0.910352593333334

00:23:59.170 --> 00:24:01.210 nut carcinoma and it's not anymore.

NOTE Confidence: 0.910352593333334

00:24:01.210 --> 00:24:03.136 There's a few hybrid sarcomas that

NOTE Confidence: 0.910352593333334

00:24:03.136 --> 00:24:05.122 are also driven by nut translocation  
NOTE Confidence: 0.910352593333334

00:24:05.122 --> 00:24:07.690 so that also picks up on the stage,  
NOTE Confidence: 0.910352593333334

00:24:07.690 --> 00:24:09.316 but a subset of poroid neoplasms  
NOTE Confidence: 0.910352593333334

00:24:09.316 --> 00:24:11.293 of the skin have also been found  
NOTE Confidence: 0.910352593333334

00:24:11.293 --> 00:24:12.678 to have not involved in.  
NOTE Confidence: 0.910352593333334

00:24:12.680 --> 00:24:13.964 In the translocation.  
NOTE Confidence: 0.910352593333334

00:24:13.964 --> 00:24:16.524 So it's not not 100% specific,  
NOTE Confidence: 0.910352593333334

00:24:16.524 --> 00:24:18.634 but in the sinonasal differential  
NOTE Confidence: 0.910352593333334

00:24:18.634 --> 00:24:20.760 diagnosis it is really good.  
NOTE Confidence: 0.910352593333334

00:24:20.760 --> 00:24:21.278 Now, not,  
NOTE Confidence: 0.910352593333334

00:24:21.278 --> 00:24:21.796 of course,  
NOTE Confidence: 0.910352593333334

00:24:21.796 --> 00:24:23.091 is important to recognize because  
NOTE Confidence: 0.910352593333334

00:24:23.091 --> 00:24:24.757 it's a highly aggressive malignancy,  
NOTE Confidence: 0.910352593333334

00:24:24.760 --> 00:24:26.839 median survival of less than a year.  
NOTE Confidence: 0.910352593333334

00:24:26.840 --> 00:24:29.444 There's been some temporary success with  
NOTE Confidence: 0.910352593333334

00:24:29.444 --> 00:24:31.650 BROMODOMAIN inhibitors in clinical trials,

NOTE Confidence: 0.910352593333334  
00:24:31.650 --> 00:24:33.582 but they don't seem to be improving  
NOTE Confidence: 0.910352593333334  
00:24:33.582 --> 00:24:34.870 outcomes that much overall,  
NOTE Confidence: 0.910352593333334  
00:24:34.870 --> 00:24:36.400 but it is definitely something  
NOTE Confidence: 0.910352593333334  
00:24:36.400 --> 00:24:38.914 if you come across a case to to  
NOTE Confidence: 0.910352593333334  
00:24:38.914 --> 00:24:40.492 point the patients toward now  
NOTE Confidence: 0.910352593333334  
00:24:40.492 --> 00:24:42.202 adamantinoma like Ewing sarcoma is  
NOTE Confidence: 0.910352593333334  
00:24:42.202 --> 00:24:44.396 another tumor that has recently been  
NOTE Confidence: 0.910352593333334  
00:24:44.396 --> 00:24:46.316 recognized in the sinonasal tract.  
NOTE Confidence: 0.910352593333334  
00:24:46.320 --> 00:24:47.736 This is a really weird tumor.  
NOTE Confidence: 0.910352593333334  
00:24:47.740 --> 00:24:50.158 It's a rare variant of Ewing  
NOTE Confidence: 0.910352593333334  
00:24:50.158 --> 00:24:51.770 sarcoma in most cases.  
NOTE Confidence: 0.910352593333334  
00:24:51.770 --> 00:24:52.458 To date,  
NOTE Confidence: 0.910352593333334  
00:24:52.458 --> 00:24:55.210 have been reported in the head and neck.  
NOTE Confidence: 0.910352593333334  
00:24:55.210 --> 00:24:56.561 We see we found that there they  
NOTE Confidence: 0.910352593333334  
00:24:56.561 --> 00:24:58.296 seem to be more common in the  
NOTE Confidence: 0.910352593333334

00:24:58.296 --> 00:24:59.676 salivary glands than anywhere else.

NOTE Confidence: 0.900053225833334

00:24:59.680 --> 00:25:01.227 But the sinonasal tract is is 1

NOTE Confidence: 0.900053225833334

00:25:01.227 --> 00:25:03.002 site where we do see them and it

NOTE Confidence: 0.900053225833334

00:25:03.002 --> 00:25:04.559 is another tumor that is defined

NOTE Confidence: 0.900053225833334

00:25:04.559 --> 00:25:05.888 by squamous differentiation.

NOTE Confidence: 0.900053225833334

00:25:05.890 --> 00:25:07.098 So it's really bizarre.

NOTE Confidence: 0.900053225833334

00:25:07.098 --> 00:25:08.910 It has the Ewing sarcoma fusion.

NOTE Confidence: 0.900053225833334

00:25:08.910 --> 00:25:11.792 It's positive for CD99 and NKX 2.2,

NOTE Confidence: 0.900053225833334

00:25:11.792 --> 00:25:13.759 but at the same time it shows

NOTE Confidence: 0.900053225833334

00:25:13.759 --> 00:25:15.238 diffuse cytokeratin expression

NOTE Confidence: 0.900053225833334

00:25:15.238 --> 00:25:17.934 positivity for P63 and P40 and

NOTE Confidence: 0.900053225833334

00:25:17.934 --> 00:25:19.889 actually forms overt keratin pearls.

NOTE Confidence: 0.900053225833334

00:25:19.890 --> 00:25:20.995 They're often abrupt pearls to

NOTE Confidence: 0.900053225833334

00:25:20.995 --> 00:25:22.578 sort of sort of like we see in.

NOTE Confidence: 0.900053225833334

00:25:22.580 --> 00:25:23.042 Not so.

NOTE Confidence: 0.900053225833334

00:25:23.042 --> 00:25:24.197 It's really weird that it's



NOTE Confidence: 0.900053225833334  
00:25:24.197 --> 00:25:25.650 doing all the viewing things,  
NOTE Confidence: 0.900053225833334  
00:25:25.650 --> 00:25:27.350 whereas the same time staining  
NOTE Confidence: 0.900053225833334  
00:25:27.350 --> 00:25:28.710 much like a carcinoma,  
NOTE Confidence: 0.900053225833334  
00:25:28.710 --> 00:25:29.925 and it's something that you  
NOTE Confidence: 0.900053225833334  
00:25:29.925 --> 00:25:31.310 really actively have to think of,  
NOTE Confidence: 0.900053225833334  
00:25:31.310 --> 00:25:33.434 because otherwise you might not even  
NOTE Confidence: 0.900053225833334  
00:25:33.434 --> 00:25:36.020 think of doing the Ewing doing markers.  
NOTE Confidence: 0.900053225833334  
00:25:36.020 --> 00:25:38.750 So here's a classic example of an  
NOTE Confidence: 0.900053225833334  
00:25:38.750 --> 00:25:41.186 adamantinoma like Ewing kind of small  
NOTE Confidence: 0.900053225833334  
00:25:41.186 --> 00:25:43.166 nest basaloid cells very infiltrative  
NOTE Confidence: 0.900053225833334  
00:25:43.237 --> 00:25:45.217 embedded in fibromyxoid stroma.  
NOTE Confidence: 0.900053225833334  
00:25:45.220 --> 00:25:47.516 These cells also tend to be very monotonous.  
NOTE Confidence: 0.900053225833334  
00:25:47.520 --> 00:25:48.570 They're a little bit lower  
NOTE Confidence: 0.900053225833334  
00:25:48.570 --> 00:25:49.410 grade looking than not.  
NOTE Confidence: 0.900053225833334  
00:25:49.410 --> 00:25:50.398 They don't really have  
NOTE Confidence: 0.900053225833334

00:25:50.398 --> 00:25:51.139 those prominent nucleoli,  
NOTE Confidence: 0.900053225833334

00:25:51.140 --> 00:25:53.024 and often there's not quite as  
NOTE Confidence: 0.900053225833334

00:25:53.024 --> 00:25:54.850 much necrosis and mitotic activity.  
NOTE Confidence: 0.900053225833334

00:25:54.850 --> 00:25:56.229 But you do see a little bit  
NOTE Confidence: 0.900053225833334

00:25:56.229 --> 00:25:57.570 of this abrupt keratinization.  
NOTE Confidence: 0.900053225833334

00:25:57.570 --> 00:26:01.035 I'll say the keratinization is pretty rare.  
NOTE Confidence: 0.900053225833334

00:26:01.040 --> 00:26:02.986 It's it's not a majority of the  
NOTE Confidence: 0.900053225833334

00:26:02.986 --> 00:26:05.029 cases that happen, so this is,  
NOTE Confidence: 0.900053225833334

00:26:05.029 --> 00:26:06.238 again, you know,  
NOTE Confidence: 0.900053225833334

00:26:06.240 --> 00:26:08.016 something to to keep in mind,  
NOTE Confidence: 0.900053225833334

00:26:08.020 --> 00:26:10.360 even if it's lacking bad feature.  
NOTE Confidence: 0.900053225833334

00:26:10.360 --> 00:26:12.132 And here's the stains.  
NOTE Confidence: 0.900053225833334

00:26:12.132 --> 00:26:13.018 Diffuse keratin,  
NOTE Confidence: 0.900053225833334

00:26:13.020 --> 00:26:15.099 positive it's more than kind of the  
NOTE Confidence: 0.900053225833334

00:26:15.099 --> 00:26:17.281 focal keratin that you can occasionally  
NOTE Confidence: 0.900053225833334

00:26:17.281 --> 00:26:18.917 encounter in regular viewings.

NOTE Confidence: 0.900053225833334  
00:26:18.920 --> 00:26:21.416 P40 really diffusely strongly  
NOTE Confidence: 0.900053225833334  
00:26:21.416 --> 00:26:23.420 positive CD 99 strongly positive,  
NOTE Confidence: 0.900053225833334  
00:26:23.420 --> 00:26:26.458 and again they have the WS R1 fly one  
NOTE Confidence: 0.900053225833334  
00:26:26.458 --> 00:26:29.130 fusion that we expect to see in doing  
NOTE Confidence: 0.900053225833334  
00:26:29.130 --> 00:26:31.450 so is this really a sarcoma when it's?  
NOTE Confidence: 0.900053225833334  
00:26:31.450 --> 00:26:33.268 Staining so much like a carcinoma,  
NOTE Confidence: 0.900053225833334  
00:26:33.270 --> 00:26:34.846 it's an excellent question,  
NOTE Confidence: 0.900053225833334  
00:26:34.846 --> 00:26:37.210 and it's controversial different there are.  
NOTE Confidence: 0.900053225833334  
00:26:37.210 --> 00:26:38.975 There are different opinions about  
NOTE Confidence: 0.900053225833334  
00:26:38.975 --> 00:26:40.705 this in the literature there  
NOTE Confidence: 0.900053225833334  
00:26:40.705 --> 00:26:42.280 have been some identical tumors  
NOTE Confidence: 0.900053225833334  
00:26:42.280 --> 00:26:44.175 that have been described as a  
NOTE Confidence: 0.900053225833334  
00:26:44.175 --> 00:26:45.625 carcinoma with doing like elements,  
NOTE Confidence: 0.900053225833334  
00:26:45.630 --> 00:26:47.302 and it used to be that one  
NOTE Confidence: 0.900053225833334  
00:26:47.302 --> 00:26:49.062 fly one fusion was considered  
NOTE Confidence: 0.900053225833334

00:26:49.062 --> 00:26:50.470 pathognomonic for Ewing diagnosis.  
NOTE Confidence: 0.900053225833334

00:26:50.470 --> 00:26:52.990 So clearly if the tumor had that fusion,  
NOTE Confidence: 0.900053225833334

00:26:52.990 --> 00:26:54.670 we considered a Ewing I think now  
NOTE Confidence: 0.900053225833334

00:26:54.670 --> 00:26:56.463 so many more fusions that occur  
NOTE Confidence: 0.900053225833334

00:26:56.463 --> 00:26:58.158 in different tumors of different  
NOTE Confidence: 0.900053225833334

00:26:58.158 --> 00:26:59.730 lineages have been recognized.  
NOTE Confidence: 0.900053225833334

00:26:59.730 --> 00:27:00.214 You know,  
NOTE Confidence: 0.900053225833334

00:27:00.214 --> 00:27:01.908 it might be time to question question.  
NOTE Confidence: 0.900053225833334

00:27:01.910 --> 00:27:02.878 However, uhm.  
NOTE Confidence: 0.900053225833334

00:27:02.878 --> 00:27:05.298 It's definitely a discrete entity,  
NOTE Confidence: 0.900053225833334

00:27:05.300 --> 00:27:06.304 whichever whichever group you  
NOTE Confidence: 0.900053225833334

00:27:06.304 --> 00:27:07.559 want to put it in.  
NOTE Confidence: 0.900053225833334

00:27:07.560 --> 00:27:09.450 I'll also add that you ain't  
NOTE Confidence: 0.900053225833334

00:27:09.450 --> 00:27:10.395 specific chemotherapy regimens,  
NOTE Confidence: 0.900053225833334

00:27:10.400 --> 00:27:11.540 which are a little different  
NOTE Confidence: 0.900053225833334

00:27:11.540 --> 00:27:12.224 than carcinoma regimens,

NOTE Confidence: 0.900053225833334  
00:27:12.230 --> 00:27:13.378 have led different responses  
NOTE Confidence: 0.900053225833334  
00:27:13.378 --> 00:27:14.239 with several patients,  
NOTE Confidence: 0.900053225833334  
00:27:14.240 --> 00:27:18.155 which might argue to keep it in the circle.  
NOTE Confidence: 0.900053225833334  
00:27:18.160 --> 00:27:20.056 Alright, so the left's Klamath entity.  
NOTE Confidence: 0.900053225833334  
00:27:20.060 --> 00:27:21.278 I want to talk about is  
NOTE Confidence: 0.900053225833334  
00:27:21.278 --> 00:27:22.340 really a brand new one,  
NOTE Confidence: 0.900053225833334  
00:27:22.340 --> 00:27:24.398 which is a new group of carcinomas  
NOTE Confidence: 0.900053225833334  
00:27:24.398 --> 00:27:26.500 that have a deck aft 2 fusion.  
NOTE Confidence: 0.900053225833334  
00:27:26.500 --> 00:27:27.728 Now it's really interesting  
NOTE Confidence: 0.900053225833334  
00:27:27.728 --> 00:27:28.956 how these tumors arose.  
NOTE Confidence: 0.900053225833334  
00:27:28.960 --> 00:27:31.767 They actually were described in a case  
NOTE Confidence: 0.900053225833334  
00:27:31.767 --> 00:27:34.223 report of a patient who had a really  
NOTE Confidence: 0.900053225833334  
00:27:34.223 --> 00:27:36.198 dramatic response to immunotherapy,  
NOTE Confidence: 0.900053225833334  
00:27:36.200 --> 00:27:37.670 and they did extensive sequencing  
NOTE Confidence: 0.900053225833334  
00:27:37.670 --> 00:27:39.655 other tumor and found that they happen  
NOTE Confidence: 0.900053225833334

00:27:39.655 --> 00:27:41.495 to have this decaf 2 fusion on that  
NOTE Confidence: 0.858372003181818

00:27:41.552 --> 00:27:42.190 they thought.  
NOTE Confidence: 0.858372003181818

00:27:42.190 --> 00:27:45.070 Was, you know, a neoadjuvant Neo  
NOTE Confidence: 0.858372003181818

00:27:45.070 --> 00:27:47.909 neo antigen against which the tumor?  
NOTE Confidence: 0.858372003181818

00:27:47.910 --> 00:27:50.256 Other that immune response was occurring,  
NOTE Confidence: 0.858372003181818

00:27:50.260 --> 00:27:51.670 a couple more cases, though,  
NOTE Confidence: 0.858372003181818

00:27:51.670 --> 00:27:53.320 were then reported in the pathology  
NOTE Confidence: 0.858372003181818

00:27:53.320 --> 00:27:54.681 literature and it seemed that  
NOTE Confidence: 0.858372003181818

00:27:54.681 --> 00:27:56.123 it was not just a random event,  
NOTE Confidence: 0.858372003181818

00:27:56.130 --> 00:27:58.818 it was actually a recurring thing.  
NOTE Confidence: 0.858372003181818

00:27:58.820 --> 00:27:59.996 Now, even weirder,  
NOTE Confidence: 0.858372003181818

00:27:59.996 --> 00:28:02.740 the two genes involved in this fusion  
NOTE Confidence: 0.858372003181818

00:28:02.810 --> 00:28:05.468 are not particularly common in Carson.  
NOTE Confidence: 0.858372003181818

00:28:05.470 --> 00:28:09.560 No ones deck has been upregulated.  
NOTE Confidence: 0.858372003181818

00:28:09.560 --> 00:28:11.792 It's been found to be upregulated  
NOTE Confidence: 0.858372003181818

00:28:11.792 --> 00:28:13.536 in various cancer types,

NOTE Confidence: 0.858372003181818

00:28:13.540 --> 00:28:16.172 and it is rearranged with NHP

NOTE Confidence: 0.858372003181818

00:28:16.172 --> 00:28:18.404 214 in a subset of leukemia,

NOTE Confidence: 0.858372003181818

00:28:18.410 --> 00:28:20.130 but really not reported in

NOTE Confidence: 0.858372003181818

00:28:20.130 --> 00:28:21.850 carcinomas before and after two

NOTE Confidence: 0.858372003181818

00:28:21.916 --> 00:28:23.636 actually has had not previously

NOTE Confidence: 0.858372003181818

00:28:23.636 --> 00:28:25.660 been reported in cancer at all,

NOTE Confidence: 0.858372003181818

00:28:25.660 --> 00:28:26.970 although it is closely related

NOTE Confidence: 0.858372003181818

00:28:26.970 --> 00:28:28.650 to a family of genes which.

NOTE Confidence: 0.858372003181818

00:28:28.650 --> 00:28:29.842 Are implicated in leukemia,

NOTE Confidence: 0.858372003181818

00:28:29.842 --> 00:28:32.012 so once these came in the literature

NOTE Confidence: 0.858372003181818

00:28:32.012 --> 00:28:34.294 we were really curious in terms of

NOTE Confidence: 0.858372003181818

00:28:34.294 --> 00:28:36.552 finding more of them and and kind of

NOTE Confidence: 0.858372003181818

00:28:36.552 --> 00:28:38.216 figuring out what they look like.

NOTE Confidence: 0.858372003181818

00:28:38.216 --> 00:28:40.407 There were only a couple pictures in

NOTE Confidence: 0.858372003181818

00:28:40.407 --> 00:28:42.758 the in the initial papers that that.

NOTE Confidence: 0.92830525

00:28:44.930 --> 00:28:46.238 You know, just kind of describe  
NOTE Confidence: 0.92830525

00:28:46.238 --> 00:28:47.440 them as as high grade,  
NOTE Confidence: 0.92830525

00:28:47.440 --> 00:28:48.481 extensively infiltrative tumors,  
NOTE Confidence: 0.92830525

00:28:48.481 --> 00:28:50.910 and so we were interested in finding  
NOTE Confidence: 0.92830525

00:28:50.961 --> 00:28:53.209 out if there was a way we could  
NOTE Confidence: 0.92830525

00:28:53.209 --> 00:28:54.080 histologically recognize them,  
NOTE Confidence: 0.92830525

00:28:54.080 --> 00:28:56.950 especially if there was potential.  
NOTE Confidence: 0.92830525

00:28:56.950 --> 00:28:59.450 Relevance to immunotherapy response.  
NOTE Confidence: 0.92830525

00:28:59.450 --> 00:29:03.200 So we found over 3 institutions,  
NOTE Confidence: 0.92830525

00:29:03.200 --> 00:29:05.390 a bunch of non criticizing sinonasal  
NOTE Confidence: 0.92830525

00:29:05.390 --> 00:29:07.257 install based squamous cell carcinomas  
NOTE Confidence: 0.92830525

00:29:07.257 --> 00:29:09.693 that were negative and EVV negative and  
NOTE Confidence: 0.92830525

00:29:09.693 --> 00:29:11.587 these were tumors that previously were  
NOTE Confidence: 0.92830525

00:29:11.587 --> 00:29:14.102 kind of put in the non keratinizing  
NOTE Confidence: 0.92830525

00:29:14.102 --> 00:29:17.310 squamous cell carcinoma category.  
NOTE Confidence: 0.92830525

00:29:17.310 --> 00:29:19.806 And when we ran RNA sequencing on these,



NOTE Confidence: 0.92830525

00:29:19.810 --> 00:29:20.683 13 of them,

NOTE Confidence: 0.92830525

00:29:20.683 --> 00:29:23.310 almost half had a deck Act 2 fusion.

NOTE Confidence: 0.92830525

00:29:23.310 --> 00:29:26.446 So among HPV indeed negative non keratinizing

NOTE Confidence: 0.92830525

00:29:26.446 --> 00:29:28.710 squamous cell carcinoma that are not,

NOTE Confidence: 0.92830525

00:29:28.710 --> 00:29:30.210 you know other fusion related.

NOTE Confidence: 0.92830525

00:29:30.210 --> 00:29:32.410 These are actually not that

NOTE Confidence: 0.92830525

00:29:32.410 --> 00:29:34.236 uncommon and we didn't do a full

NOTE Confidence: 0.92830525

00:29:34.236 --> 00:29:36.062 DNA sequencing as well on a few of

NOTE Confidence: 0.92830525

00:29:36.062 --> 00:29:37.768 the cases and they didn't have any

NOTE Confidence: 0.92830525

00:29:37.768 --> 00:29:39.300 other oxygenic driver alterations.

NOTE Confidence: 0.92830525

00:29:39.300 --> 00:29:40.638 So it really seems that even

NOTE Confidence: 0.92830525

00:29:40.638 --> 00:29:41.530 though they're weird jeans,

NOTE Confidence: 0.92830525

00:29:41.530 --> 00:29:44.272 Decap 2 seems to be driving

NOTE Confidence: 0.92830525

00:29:44.272 --> 00:29:46.720 the pathogenesis of this tumor.

NOTE Confidence: 0.92830525

00:29:46.720 --> 00:29:47.917 After looking at a bunch of them,

NOTE Confidence: 0.92830525

00:29:47.920 --> 00:29:50.128 we found that they really did have some  
NOTE Confidence: 0.92830525

00:29:50.128 --> 00:29:52.119 some recurrent pathologic characteristics.  
NOTE Confidence: 0.92830525

00:29:52.120 --> 00:29:55.366 They tend to grow in complex.  
NOTE Confidence: 0.92830525

00:29:55.370 --> 00:29:57.026 Actually should point out really quick.  
NOTE Confidence: 0.92830525

00:29:57.030 --> 00:29:58.745 A lot of them were called papilloma.  
NOTE Confidence: 0.92830525

00:29:58.750 --> 00:29:59.950 There were three of them  
NOTE Confidence: 0.92830525

00:29:59.950 --> 00:30:00.910 that were called benign,  
NOTE Confidence: 0.92830525

00:30:00.910 --> 00:30:01.297 sinonasal,  
NOTE Confidence: 0.92830525

00:30:01.297 --> 00:30:03.232 papillomas and three were called  
NOTE Confidence: 0.92830525

00:30:03.232 --> 00:30:05.390 squamous cell carcinoma ex papilloma,  
NOTE Confidence: 0.92830525

00:30:05.390 --> 00:30:08.099 so they actually in contrast with the  
NOTE Confidence: 0.92830525

00:30:08.099 --> 00:30:10.767 first couple examples which were high grade.  
NOTE Confidence: 0.92830525

00:30:10.770 --> 00:30:13.130 A lot of these had a more low  
NOTE Confidence: 0.92830525

00:30:13.130 --> 00:30:14.430 grade appearance and again,  
NOTE Confidence: 0.92830525

00:30:14.430 --> 00:30:15.838 as I as I'm getting too they seem  
NOTE Confidence: 0.92830525

00:30:15.838 --> 00:30:17.149 to be pretty recognizable,

NOTE Confidence: 0.92830525

00:30:17.150 --> 00:30:19.926 so a lot of them show kind of

NOTE Confidence: 0.92830525

00:30:19.926 --> 00:30:21.557 complex anastomosing lobules kind

NOTE Confidence: 0.92830525

00:30:21.557 --> 00:30:23.862 of downward growth tend to have a

NOTE Confidence: 0.92830525

00:30:23.862 --> 00:30:25.127 deep pushing pattern of invasion,

NOTE Confidence: 0.92830525

00:30:25.130 --> 00:30:26.480 but have a rounded border.

NOTE Confidence: 0.92830525

00:30:26.480 --> 00:30:30.470 Often that can mimic a benign process.

NOTE Confidence: 0.92830525

00:30:30.470 --> 00:30:32.114 They do show some more confluent

NOTE Confidence: 0.92830525

00:30:32.114 --> 00:30:34.173 growth and we expect to see in a

NOTE Confidence: 0.92830525

00:30:34.173 --> 00:30:35.535 papilloma as opposed to the Nice

NOTE Confidence: 0.92830525

00:30:35.593 --> 00:30:37.555 separated lobules we see in papilloma.

NOTE Confidence: 0.92830525

00:30:37.560 --> 00:30:39.786 And one thing that seems to be

NOTE Confidence: 0.92830525

00:30:39.786 --> 00:30:41.594 pretty helpful for for and pretty

NOTE Confidence: 0.92830525

00:30:41.594 --> 00:30:43.340 specific is that they have these

NOTE Confidence: 0.92830525

00:30:43.406 --> 00:30:45.176 central areas of this cohesion,

NOTE Confidence: 0.92830525

00:30:45.180 --> 00:30:46.100 whether they're tumor cells

NOTE Confidence: 0.92830525

00:30:46.100 --> 00:30:47.480 just fall apart from each other,  
NOTE Confidence: 0.92830525

00:30:47.480 --> 00:30:49.718 and that always makes me think  
NOTE Confidence: 0.92830525

00:30:49.718 --> 00:30:50.837 of the diagnosis.  
NOTE Confidence: 0.92830525

00:30:50.840 --> 00:30:53.440 They do tend to have very bland technology.  
NOTE Confidence: 0.92830525

00:30:53.440 --> 00:30:54.580 The first examples were on the  
NOTE Confidence: 0.92830525

00:30:54.580 --> 00:30:55.880 higher grade end of the spectrum,  
NOTE Confidence: 0.92830525

00:30:55.880 --> 00:30:58.267 but the vast majority that we found  
NOTE Confidence: 0.92830525

00:30:58.267 --> 00:31:00.216 actually were lower grade appearing  
NOTE Confidence: 0.92830525

00:31:00.216 --> 00:31:02.994 and kind of like not carcinoma.  
NOTE Confidence: 0.92830525

00:31:03.000 --> 00:31:04.602 They have a lot of tumor  
NOTE Confidence: 0.92830525

00:31:04.602 --> 00:31:05.136 infiltrating neutrophils,  
NOTE Confidence: 0.92830525

00:31:05.140 --> 00:31:06.650 and that also shows overlap  
NOTE Confidence: 0.92830525

00:31:06.650 --> 00:31:07.556 with sinonasal papillomas,  
NOTE Confidence: 0.92830525

00:31:07.560 --> 00:31:09.335 which can also have tumor  
NOTE Confidence: 0.92830525

00:31:09.335 --> 00:31:10.045 infiltrating neutrophils.  
NOTE Confidence: 0.92830525

00:31:10.050 --> 00:31:11.842 So lots of things kind of kind

NOTE Confidence: 0.92830525

00:31:11.842 --> 00:31:13.843 of leading to red herrings in

NOTE Confidence: 0.92830525

00:31:13.843 --> 00:31:15.010 terms of classification.

NOTE Confidence: 0.92830525

00:31:15.010 --> 00:31:17.140 Occasionally they have squamous pearls,

NOTE Confidence: 0.92830525

00:31:17.140 --> 00:31:19.240 but most of them are non keratinizing

NOTE Confidence: 0.92830525

00:31:19.240 --> 00:31:20.880 and they show immunohistochemical

NOTE Confidence: 0.92830525

00:31:20.880 --> 00:31:23.568 evidence of squamous differentiation.

NOTE Confidence: 0.92830525

00:31:23.570 --> 00:31:26.018 So interestingly as as we kind

NOTE Confidence: 0.92830525

00:31:26.018 --> 00:31:27.242 of characterize these,

NOTE Confidence: 0.92830525

00:31:27.250 --> 00:31:28.811 we notice that they looked a lot

NOTE Confidence: 0.92830525

00:31:28.811 --> 00:31:30.658 like a group of other tumors that

NOTE Confidence: 0.92830525

00:31:30.658 --> 00:31:32.350 had been described in the literature

NOTE Confidence: 0.92830525

00:31:32.406 --> 00:31:33.916 as low grade papillary schneiderian

NOTE Confidence: 0.92830525

00:31:33.916 --> 00:31:35.426 carcinoma about 14 in the

NOTE Confidence: 0.785181426666667

00:31:35.430 --> 00:31:37.600 literature also had complex papillary

NOTE Confidence: 0.785181426666667

00:31:37.600 --> 00:31:39.770 architecture and frequent low grade

NOTE Confidence: 0.785181426666667

00:31:39.832 --> 00:31:42.447 psychology also mimics sinonasal papillomas.  
NOTE Confidence: 0.785181426666667

00:31:42.450 --> 00:31:44.601 We suggested this when we wrote up our paper  
NOTE Confidence: 0.785181426666667

00:31:44.601 --> 00:31:46.690 and almost simultaneously another group.  
NOTE Confidence: 0.785181426666667

00:31:46.690 --> 00:31:49.007 Included some of the original tumors reported  
NOTE Confidence: 0.785181426666667

00:31:49.007 --> 00:31:51.108 under that other name and found that  
NOTE Confidence: 0.785181426666667

00:31:51.108 --> 00:31:53.269 they were also had deck asked to fusion,  
NOTE Confidence: 0.785181426666667

00:31:53.270 --> 00:31:55.511 so this is all thought to be part of  
NOTE Confidence: 0.785181426666667

00:31:55.511 --> 00:31:57.629 the deck aft 2 carcinoma special.  
NOTE Confidence: 0.785181426666667

00:31:57.630 --> 00:32:00.520 So do we care clinically?  
NOTE Confidence: 0.785181426666667

00:32:00.520 --> 00:32:02.150 Well, although they're low grade,  
NOTE Confidence: 0.785181426666667

00:32:02.150 --> 00:32:03.534 they can't actually behave  
NOTE Confidence: 0.785181426666667

00:32:03.534 --> 00:32:04.226 pretty aggressively.  
NOTE Confidence: 0.785181426666667

00:32:04.230 --> 00:32:05.330 A lot of them occur,  
NOTE Confidence: 0.785181426666667

00:32:05.330 --> 00:32:07.065 and a significant subset metastasized  
NOTE Confidence: 0.785181426666667

00:32:07.065 --> 00:32:09.610 and even lead to death from disease,  
NOTE Confidence: 0.785181426666667

00:32:09.610 --> 00:32:11.276 so it's something to recognize is not

NOTE Confidence: 0.785181426666667

00:32:11.276 --> 00:32:13.498 just a very, very low grade tumor,

NOTE Confidence: 0.785181426666667

00:32:13.498 --> 00:32:15.383 certainly not just a papilloma

NOTE Confidence: 0.785181426666667

00:32:15.390 --> 00:32:16.690 and the real question.

NOTE Confidence: 0.785181426666667

00:32:16.690 --> 00:32:19.200 Raised by the the first recognition of it is,

NOTE Confidence: 0.785181426666667

00:32:19.200 --> 00:32:21.797 is this a new target for immunotherapy?

NOTE Confidence: 0.785181426666667

00:32:21.800 --> 00:32:23.368 Of course there was one patient who

NOTE Confidence: 0.785181426666667

00:32:23.368 --> 00:32:24.839 did really well on immunotherapy.

NOTE Confidence: 0.785181426666667

00:32:24.840 --> 00:32:26.190 We actually had two in our

NOTE Confidence: 0.785181426666667

00:32:26.190 --> 00:32:27.713 series who happened to be treated

NOTE Confidence: 0.785181426666667

00:32:27.713 --> 00:32:28.849 for immunotherapy as well.

NOTE Confidence: 0.785181426666667

00:32:28.850 --> 00:32:30.282 One responded at first,

NOTE Confidence: 0.785181426666667

00:32:30.282 --> 00:32:32.072 although they later recurred and

NOTE Confidence: 0.785181426666667

00:32:32.072 --> 00:32:33.357 unfortunately died of a disease

NOTE Confidence: 0.785181426666667

00:32:33.360 --> 00:32:34.818 and one patient did not respond.

NOTE Confidence: 0.785181426666667

00:32:34.820 --> 00:32:37.484 So it doesn't seem to be a slam dunk.

NOTE Confidence: 0.785181426666667

00:32:37.490 --> 00:32:38.460 But overall,  
NOTE Confidence: 0.785181426666667

00:32:38.460 --> 00:32:41.370 it's an interesting addition to the  
NOTE Confidence: 0.785181426666667

00:32:41.370 --> 00:32:44.078 squamous neoplasia in the sinonasal tract,  
NOTE Confidence: 0.785181426666667

00:32:44.080 --> 00:32:46.423 so in the 5th Edition 8 WHO classification,  
NOTE Confidence: 0.785181426666667

00:32:46.423 --> 00:32:47.878 which hopefully should be coming  
NOTE Confidence: 0.785181426666667

00:32:47.878 --> 00:32:48.740 out this year,  
NOTE Confidence: 0.785181426666667

00:32:48.740 --> 00:32:51.440 several of these entities have been  
NOTE Confidence: 0.785181426666667

00:32:51.440 --> 00:32:52.790 recognized squamous cell carcinoma  
NOTE Confidence: 0.785181426666667

00:32:52.790 --> 00:32:54.590 in general is still split into  
NOTE Confidence: 0.785181426666667

00:32:54.590 --> 00:32:56.147 keratinizing and non keratinizing types,  
NOTE Confidence: 0.785181426666667

00:32:56.150 --> 00:32:58.320 but associated squamous cell carcinoma  
NOTE Confidence: 0.785181426666667

00:32:58.320 --> 00:33:00.490 and deck after carcinomas are  
NOTE Confidence: 0.785181426666667

00:33:00.555 --> 00:33:02.787 going to be recognized as subtypes.  
NOTE Confidence: 0.785181426666667

00:33:02.790 --> 00:33:04.374 With multi phenotypic carcinoma  
NOTE Confidence: 0.785181426666667

00:33:04.374 --> 00:33:06.750 and nut carcinoma are recognized as  
NOTE Confidence: 0.785181426666667

00:33:06.815 --> 00:33:08.471 separate entities and adamantinoma



NOTE Confidence: 0.785181426666667

00:33:08.471 --> 00:33:10.898 like Ewing sarcoma is you know,

NOTE Confidence: 0.785181426666667

00:33:10.898 --> 00:33:12.818 a subtype of Ewing sarcoma.

NOTE Confidence: 0.785181426666667

00:33:12.820 --> 00:33:14.512 There's no special recognition

NOTE Confidence: 0.785181426666667

00:33:14.512 --> 00:33:16.204 for carcinomas X kapalama,

NOTE Confidence: 0.785181426666667

00:33:16.210 --> 00:33:19.540 but that pathogenesis is also reflected.

NOTE Confidence: 0.785181426666667

00:33:19.540 --> 00:33:19.882 Alright,

NOTE Confidence: 0.785181426666667

00:33:19.882 --> 00:33:22.276 so going on to another interesting area

NOTE Confidence: 0.785181426666667

00:33:22.276 --> 00:33:24.880 of Swiss sniff complex deficient tumors.

NOTE Confidence: 0.785181426666667

00:33:24.880 --> 00:33:27.004 Now the sweets sniff complex met

NOTE Confidence: 0.785181426666667

00:33:27.004 --> 00:33:28.420 stands for switched sucrose,

NOTE Confidence: 0.785181426666667

00:33:28.420 --> 00:33:29.632 non fermenting belicza,

NOTE Confidence: 0.785181426666667

00:33:29.632 --> 00:33:30.440 chromatin remodeling,

NOTE Confidence: 0.785181426666667

00:33:30.440 --> 00:33:32.760 complex 15 protein subunits that

NOTE Confidence: 0.785181426666667

00:33:32.760 --> 00:33:36.248 are coded for by up to 29 jeans.

NOTE Confidence: 0.785181426666667

00:33:36.250 --> 00:33:37.918 And there's lots of these that

NOTE Confidence: 0.785181426666667

00:33:37.918 --> 00:33:38.752 are very important.  
NOTE Confidence: 0.785181426666667

00:33:38.760 --> 00:33:40.824 The ones we in pathology here about a  
NOTE Confidence: 0.785181426666667

00:33:40.824 --> 00:33:42.958 lot are smart be one hour I and I-1  
NOTE Confidence: 0.785181426666667

00:33:42.958 --> 00:33:45.100 on smarca 4 or BR G1 and these are  
NOTE Confidence: 0.785181426666667

00:33:45.100 --> 00:33:46.996 the ones that have become important  
NOTE Confidence: 0.785181426666667

00:33:46.996 --> 00:33:49.864 to pathogenesis in the sinonasal tract.  
NOTE Confidence: 0.785181426666667

00:33:49.870 --> 00:33:51.510 They play an important role  
NOTE Confidence: 0.785181426666667

00:33:51.510 --> 00:33:52.822 in remodeling nucleosomes and  
NOTE Confidence: 0.785181426666667

00:33:52.822 --> 00:33:54.407 regulating the accessibility of DNA,  
NOTE Confidence: 0.785181426666667

00:33:54.410 --> 00:33:55.126 which can,  
NOTE Confidence: 0.785181426666667

00:33:55.126 --> 00:33:58.213 you know have a huge role in cancer and  
NOTE Confidence: 0.785181426666667

00:33:58.213 --> 00:33:59.997 mutations in at least one of the subunits.  
NOTE Confidence: 0.785181426666667

00:34:00.000 --> 00:34:01.680 And of course there's a bunch of subunits,  
NOTE Confidence: 0.785181426666667

00:34:01.680 --> 00:34:03.941 so lots of opportunities but can be  
NOTE Confidence: 0.785181426666667

00:34:03.941 --> 00:34:06.194 seen in up to 25% of human cancer,  
NOTE Confidence: 0.785181426666667

00:34:06.194 --> 00:34:08.124 so they really seem to play a

NOTE Confidence: 0.785181426666667

00:34:08.124 --> 00:34:09.509 very important role arid 1A,

NOTE Confidence: 0.785181426666667

00:34:09.510 --> 00:34:11.030 which is of course seen in a lot

NOTE Confidence: 0.785181426666667

00:34:11.030 --> 00:34:12.959 of a lot of gynecological cancers,

NOTE Confidence: 0.785181426666667

00:34:12.960 --> 00:34:16.229 is the most common implicated in cancer.

NOTE Confidence: 0.785181426666667

00:34:16.230 --> 00:34:18.306 But it's really across the board

NOTE Confidence: 0.785181426666667

00:34:18.310 --> 00:34:19.218 and we have tumors,

NOTE Confidence: 0.785181426666667

00:34:19.218 --> 00:34:20.870 some of them that are defined by

NOTE Confidence: 0.785181426666667

00:34:20.870 --> 00:34:22.065 the presence of Swiss knife.

NOTE Confidence: 0.852038641428572

00:34:22.070 --> 00:34:23.930 Alterations some that frequently

NOTE Confidence: 0.852038641428572

00:34:23.930 --> 00:34:25.325 have these alterations,

NOTE Confidence: 0.852038641428572

00:34:25.330 --> 00:34:27.460 although they're not exclusive and and

NOTE Confidence: 0.852038641428572

00:34:27.460 --> 00:34:29.993 some tumors that kind of have these

NOTE Confidence: 0.852038641428572

00:34:29.993 --> 00:34:32.087 alterations at the secondary or tertiary

NOTE Confidence: 0.852038641428572

00:34:32.087 --> 00:34:34.277 that as part of of differentiation.

NOTE Confidence: 0.852038641428572

00:34:34.280 --> 00:34:36.761 So the tumors we want the complex

NOTE Confidence: 0.852038641428572

00:34:36.761 --> 00:34:38.728 numbers we want to talk about today  
NOTE Confidence: 0.852038641428572

00:34:38.728 --> 00:34:40.508 are smart B1 and Smart K4 smart,  
NOTE Confidence: 0.852038641428572

00:34:40.510 --> 00:34:41.470 B1 deficient tumors.  
NOTE Confidence: 0.852038641428572

00:34:41.470 --> 00:34:43.710 We're very familiar with many of these  
NOTE Confidence: 0.852038641428572

00:34:43.767 --> 00:34:46.023 that are defined by loss of smart V1  
NOTE Confidence: 0.852038641428572

00:34:46.023 --> 00:34:47.742 rhabdoid tumor, atypical teratoid,  
NOTE Confidence: 0.852038641428572

00:34:47.742 --> 00:34:50.046 rhabdoid tumor, epithelioid sarcoma,  
NOTE Confidence: 0.852038641428572

00:34:50.050 --> 00:34:52.690 renal medullary carcinoma, very common.  
NOTE Confidence: 0.852038641428572

00:34:52.690 --> 00:34:53.942 Smacking 4 deficient tumors,  
NOTE Confidence: 0.852038641428572

00:34:53.942 --> 00:34:56.203 the most common one defined by that  
NOTE Confidence: 0.852038641428572

00:34:56.203 --> 00:34:57.838 is ovarian small cell carcinoma,  
NOTE Confidence: 0.852038641428572

00:34:57.840 --> 00:34:58.860 hypercalcemic type,  
NOTE Confidence: 0.852038641428572

00:34:58.860 --> 00:35:01.920 but it's also seen in undifferentiated  
NOTE Confidence: 0.852038641428572

00:35:01.920 --> 00:35:05.155 uterine and thoracic Neoplan Now in the  
NOTE Confidence: 0.852038641428572

00:35:05.155 --> 00:35:07.914 past decade it has been recognized as an  
NOTE Confidence: 0.852038641428572

00:35:07.914 --> 00:35:10.410 important player in the sinonasal tract.

NOTE Confidence: 0.852038641428572

00:35:10.410 --> 00:35:12.555 Smarcb 1 deficient sinonasal carcinomas

NOTE Confidence: 0.852038641428572

00:35:12.555 --> 00:35:15.488 are a unique and newly recognized

NOTE Confidence: 0.852038641428572

00:35:15.488 --> 00:35:17.618 sinonasal specific malignancy.

NOTE Confidence: 0.852038641428572

00:35:17.620 --> 00:35:19.705 It is defined by recurrence

NOTE Confidence: 0.852038641428572

00:35:19.705 --> 00:35:20.956 Mark B1 inactivation,

NOTE Confidence: 0.852038641428572

00:35:20.960 --> 00:35:23.648 and they don't have any other

NOTE Confidence: 0.852038641428572

00:35:23.648 --> 00:35:24.992 recurrent oncogenic mutations,

NOTE Confidence: 0.852038641428572

00:35:25.000 --> 00:35:27.140 and they have a very

NOTE Confidence: 0.852038641428572

00:35:27.140 --> 00:35:27.996 variable immunophenotype,

NOTE Confidence: 0.852038641428572

00:35:28.000 --> 00:35:29.680 so they have lots of smart view

NOTE Confidence: 0.852038641428572

00:35:29.680 --> 00:35:31.700 on one by immunohistochemistry.

NOTE Confidence: 0.852038641428572

00:35:31.700 --> 00:35:33.700 Some of them are positive for P63 and

NOTE Confidence: 0.852038641428572

00:35:33.700 --> 00:35:35.804 P40 and have to be kind of considered in

NOTE Confidence: 0.852038641428572

00:35:35.804 --> 00:35:37.300 your squamous differential diagnosis.

NOTE Confidence: 0.852038641428572

00:35:37.300 --> 00:35:38.872 Some of them have synaptophysin positive

NOTE Confidence: 0.852038641428572

00:35:38.872 --> 00:35:40.755 ITI so it can be really heterogeneous  
NOTE Confidence: 0.852038641428572

00:35:40.755 --> 00:35:42.589 and it really is that smart B1  
NOTE Confidence: 0.852038641428572

00:35:42.590 --> 00:35:45.090 that is central to classification.  
NOTE Confidence: 0.852038641428572

00:35:45.090 --> 00:35:46.190 As a result of this,  
NOTE Confidence: 0.852038641428572

00:35:46.190 --> 00:35:48.486 they were initially reclassified  
NOTE Confidence: 0.852038641428572

00:35:48.486 --> 00:35:50.208 from several categories.  
NOTE Confidence: 0.852038641428572

00:35:50.210 --> 00:35:51.666 We think of these as being pulled  
NOTE Confidence: 0.852038641428572

00:35:51.666 --> 00:35:53.429 out of the sinonasal undifferentiated  
NOTE Confidence: 0.852038641428572

00:35:53.429 --> 00:35:55.820 carcinoma category, and most of them were,  
NOTE Confidence: 0.852038641428572

00:35:55.820 --> 00:35:57.506 but others were called squamous cell  
NOTE Confidence: 0.852038641428572

00:35:57.506 --> 00:35:58.660 carcinoma, myoepithelial carcinoma,  
NOTE Confidence: 0.852038641428572

00:35:58.660 --> 00:35:59.530 even adenocarcinoma.  
NOTE Confidence: 0.852038641428572

00:35:59.530 --> 00:36:02.140 So they came from different areas.  
NOTE Confidence: 0.852038641428572

00:36:02.140 --> 00:36:03.184 Here's a beautiful example,  
NOTE Confidence: 0.852038641428572

00:36:03.184 --> 00:36:05.124 most of them kind of show nests  
NOTE Confidence: 0.852038641428572

00:36:05.124 --> 00:36:06.714 and lobules of basaloid cells

NOTE Confidence: 0.852038641428572

00:36:06.714 --> 00:36:07.668 with intermixed cells.

NOTE Confidence: 0.852038641428572

00:36:07.670 --> 00:36:09.590 That sort of have a rhabdoid

NOTE Confidence: 0.852038641428572

00:36:09.590 --> 00:36:10.550 in plasmacytoid appearance,

NOTE Confidence: 0.852038641428572

00:36:10.550 --> 00:36:12.210 and that rhabdoid appearance can

NOTE Confidence: 0.852038641428572

00:36:12.210 --> 00:36:14.243 really make you think of this

NOTE Confidence: 0.852038641428572

00:36:14.243 --> 00:36:16.385 diagnosis if you happen to find them.

NOTE Confidence: 0.852038641428572

00:36:16.390 --> 00:36:18.540 I have seen cases unfortunately

NOTE Confidence: 0.852038641428572

00:36:18.540 --> 00:36:21.130 that don't have that helpful clue.

NOTE Confidence: 0.852038641428572

00:36:21.130 --> 00:36:23.315 Here is some cytoplasmic maculation

NOTE Confidence: 0.852038641428572

00:36:23.315 --> 00:36:26.420 which is a very frequent finding in

NOTE Confidence: 0.852038641428572

00:36:26.420 --> 00:36:28.845 these tumors and some some of the

NOTE Confidence: 0.852038641428572

00:36:28.845 --> 00:36:30.430 tumors are more uniformly composed

NOTE Confidence: 0.852038641428572

00:36:30.494 --> 00:36:33.970 of the plasmoid or rhabdoid cells.

NOTE Confidence: 0.852038641428572

00:36:33.970 --> 00:36:34.660 And this, again,

NOTE Confidence: 0.852038641428572

00:36:34.660 --> 00:36:36.270 is one of these tumors with a

NOTE Confidence: 0.852038641428572

00:36:36.320 --> 00:36:37.620 recurrent genetic abnormality that  
NOTE Confidence: 0.852038641428572

00:36:37.620 --> 00:36:39.570 even though it's high grade it  
NOTE Confidence: 0.852038641428572

00:36:39.620 --> 00:36:41.335 hasn't across in a lot of mitosis  
NOTE Confidence: 0.852038641428572

00:36:41.335 --> 00:36:42.950 the cells still seem to look pretty,  
NOTE Confidence: 0.852038641428572

00:36:42.950 --> 00:36:44.532 but not as they were all kind  
NOTE Confidence: 0.852038641428572

00:36:44.532 --> 00:36:45.988 of cut out of the same cloth.  
NOTE Confidence: 0.852038641428572

00:36:45.990 --> 00:36:48.195 And here is beautiful loss of smart  
NOTE Confidence: 0.852038641428572

00:36:48.195 --> 00:36:50.524 be one with retained staining in  
NOTE Confidence: 0.852038641428572

00:36:50.524 --> 00:36:52.704 endothelial cells as a control,  
NOTE Confidence: 0.852038641428572

00:36:52.710 --> 00:36:54.840 which again other than the other  
NOTE Confidence: 0.852038641428572

00:36:54.840 --> 00:36:56.180 immune profile, is heterogeneous.  
NOTE Confidence: 0.852038641428572

00:36:56.180 --> 00:36:58.700 But this is the key to the diagnosis.  
NOTE Confidence: 0.852038641428572

00:36:58.700 --> 00:37:01.164 Now smart B1 loss has also been  
NOTE Confidence: 0.852038641428572

00:37:01.164 --> 00:37:03.380 recently reported in adenocarcinomas.  
NOTE Confidence: 0.852038641428572

00:37:03.380 --> 00:37:05.039 These can actually mimic yolk SAC tumors,  
NOTE Confidence: 0.852038641428572

00:37:05.040 --> 00:37:06.768 and it's likely that things reported



NOTE Confidence: 0.852038641428572  
00:37:06.768 --> 00:37:08.842 as yolk SAC tumors in the sinonasal  
NOTE Confidence: 0.852038641428572  
00:37:08.842 --> 00:37:10.282 tractor also are all probably  
NOTE Confidence: 0.852038641428572  
00:37:10.282 --> 00:37:12.280 smart B1 deficient adenocarcinomas.  
NOTE Confidence: 0.852038641428572  
00:37:12.280 --> 00:37:14.800 They even have gotten 3 and sell  
NOTE Confidence: 0.852038641428572  
00:37:14.800 --> 00:37:15.520 for positivity,  
NOTE Confidence: 0.852038641428572  
00:37:15.520 --> 00:37:17.350 and it's not likely that they  
NOTE Confidence: 0.852038641428572  
00:37:17.350 --> 00:37:18.570 behave any different than  
NOTE Confidence: 0.789941586666667  
00:37:18.628 --> 00:37:20.458 other smart B1 deficient cancers,  
NOTE Confidence: 0.789941586666667  
00:37:20.460 --> 00:37:22.524 but they actually do make glands  
NOTE Confidence: 0.789941586666667  
00:37:22.524 --> 00:37:24.767 and they still do have loss of  
NOTE Confidence: 0.789941586666667  
00:37:24.767 --> 00:37:26.856 a smart V1 and then smarca 4,  
NOTE Confidence: 0.789941586666667  
00:37:26.856 --> 00:37:28.800 you know another switched across non  
NOTE Confidence: 0.789941586666667  
00:37:28.867 --> 00:37:31.453 fermentable complex member has also recently  
NOTE Confidence: 0.789941586666667  
00:37:31.453 --> 00:37:33.710 been implicated in sinonasal cancers.  
NOTE Confidence: 0.789941586666667  
00:37:33.710 --> 00:37:35.334 Now this seems to be rarer than  
NOTE Confidence: 0.789941586666667

00:37:35.334 --> 00:37:36.979 the smart B1 deficient tumors.  
NOTE Confidence: 0.789941586666667

00:37:36.980 --> 00:37:39.924 There's only about 20 cases reported to date,  
NOTE Confidence: 0.789941586666667

00:37:39.930 --> 00:37:42.506 and in contrast, they tend to have a  
NOTE Confidence: 0.789941586666667

00:37:42.506 --> 00:37:44.310 neuroendocrine phenotype kind of patchy  
NOTE Confidence: 0.789941586666667

00:37:44.310 --> 00:37:45.786 week positivity for synaptophysin,  
NOTE Confidence: 0.789941586666667

00:37:45.790 --> 00:37:48.410 less expression of P. 40.  
NOTE Confidence: 0.789941586666667

00:37:48.410 --> 00:37:51.494 Most of them were previously classified  
NOTE Confidence: 0.789941586666667

00:37:51.494 --> 00:37:53.036 as neuroendocrine carcinomas.  
NOTE Confidence: 0.789941586666667

00:37:53.040 --> 00:37:54.412 Here's a nice example.  
NOTE Confidence: 0.789941586666667

00:37:54.412 --> 00:37:57.045 Most of them have this very high  
NOTE Confidence: 0.789941586666667

00:37:57.045 --> 00:37:58.548 grade undifferentiated basaloid  
NOTE Confidence: 0.789941586666667

00:37:58.548 --> 00:38:01.554 small cell or large cell morphology,  
NOTE Confidence: 0.789941586666667

00:38:01.560 --> 00:38:03.506 but a few of them look substantially  
NOTE Confidence: 0.789941586666667

00:38:03.506 --> 00:38:04.062 more rhabdoid,  
NOTE Confidence: 0.789941586666667

00:38:04.070 --> 00:38:05.726 kind of similar to the smart  
NOTE Confidence: 0.789941586666667

00:38:05.726 --> 00:38:06.554 P1 deficient carcinoma.

NOTE Confidence: 0.716760741428571  
00:38:11.310 --> 00:38:14.635 And here is the smart Smarca 4,  
NOTE Confidence: 0.716760741428571  
00:38:14.640 --> 00:38:17.676 which is nicely lost with it  
NOTE Confidence: 0.716760741428571  
00:38:17.676 --> 00:38:19.194 retained internal control.  
NOTE Confidence: 0.716760741428571  
00:38:19.200 --> 00:38:21.040 So clinically, these are important  
NOTE Confidence: 0.716760741428571  
00:38:21.040 --> 00:38:22.880 to recognize because they're really  
NOTE Confidence: 0.716760741428571  
00:38:22.935 --> 00:38:24.510 aggressive tumors that really there's  
NOTE Confidence: 0.716760741428571  
00:38:24.510 --> 00:38:26.880 a few patients who had good outcomes,  
NOTE Confidence: 0.716760741428571  
00:38:26.880 --> 00:38:28.444 had aggressive multimodality therapy.  
NOTE Confidence: 0.716760741428571  
00:38:28.444 --> 00:38:30.399 But the five year disease  
NOTE Confidence: 0.716760741428571  
00:38:30.399 --> 00:38:32.117 free survival is very poor.  
NOTE Confidence: 0.716760741428571  
00:38:32.120 --> 00:38:33.424 Hopefully they'll eventually become  
NOTE Confidence: 0.716760741428571  
00:38:33.424 --> 00:38:35.054 relevant to treatment as well.  
NOTE Confidence: 0.716760741428571  
00:38:35.060 --> 00:38:36.260 There's various potential,  
NOTE Confidence: 0.716760741428571  
00:38:36.260 --> 00:38:38.150 like small molecule inhibitors, which.  
NOTE Confidence: 0.722714998571429  
00:38:40.910 --> 00:38:44.402 10 player role in various Swiss  
NOTE Confidence: 0.722714998571429

00:38:44.402 --> 00:38:46.960 sniff mutated tumors that are under  
NOTE Confidence: 0.722714998571429

00:38:46.960 --> 00:38:48.536 investigation and hopefully will  
NOTE Confidence: 0.722714998571429

00:38:48.536 --> 00:38:50.629 provide new directions in the future.  
NOTE Confidence: 0.722714998571429

00:38:50.630 --> 00:38:51.494 Now really quick.  
NOTE Confidence: 0.722714998571429

00:38:51.494 --> 00:38:54.213 I wanna touch base on an unexpected  
NOTE Confidence: 0.722714998571429

00:38:54.213 --> 00:38:57.620 addition to the Swiss Family Center  
NOTE Confidence: 0.722714998571429

00:38:57.620 --> 00:39:01.620 nasal treto carcinosarcoma excuse me.  
NOTE Confidence: 0.722714998571429

00:39:01.620 --> 00:39:03.710 Isn't aggressive neoplasm unique to  
NOTE Confidence: 0.722714998571429

00:39:03.710 --> 00:39:06.443 the sinonasal tract and it has been  
NOTE Confidence: 0.722714998571429

00:39:06.443 --> 00:39:08.707 kind of an enigma for years it is  
NOTE Confidence: 0.722714998571429

00:39:08.782 --> 00:39:11.347 defined by three intermixed components  
NOTE Confidence: 0.722714998571429

00:39:11.350 --> 00:39:13.574 and neuro epithelial, epithelial,  
NOTE Confidence: 0.722714998571429

00:39:13.574 --> 00:39:16.354 and mesenchymal all mixed together,  
NOTE Confidence: 0.722714998571429

00:39:16.360 --> 00:39:17.974 which we look at some pictures  
NOTE Confidence: 0.722714998571429

00:39:17.974 --> 00:39:19.380 of and despite its name,  
NOTE Confidence: 0.722714998571429

00:39:19.380 --> 00:39:20.920 it really doesn't have a

NOTE Confidence: 0.722714998571429  
00:39:20.920 --> 00:39:22.152 conventional germ cell component,  
NOTE Confidence: 0.722714998571429  
00:39:22.160 --> 00:39:24.120 but because it has such diverse Histology,  
NOTE Confidence: 0.722714998571429  
00:39:24.120 --> 00:39:25.970 it's very difficult to diagnose  
NOTE Confidence: 0.722714998571429  
00:39:25.970 --> 00:39:27.450 on small biopsy specimens.  
NOTE Confidence: 0.722714998571429  
00:39:27.450 --> 00:39:29.964 So here's a beautiful example of  
NOTE Confidence: 0.722714998571429  
00:39:29.964 --> 00:39:31.640 a classic torretto carcinosarcoma  
NOTE Confidence: 0.722714998571429  
00:39:31.712 --> 00:39:33.777 with all of these different  
NOTE Confidence: 0.722714998571429  
00:39:33.777 --> 00:39:35.016 elements mixed together.  
NOTE Confidence: 0.722714998571429  
00:39:35.020 --> 00:39:36.220 No no no no no.  
NOTE Confidence: 0.722714998571429  
00:39:36.220 --> 00:39:39.248 Let me just explain component that had  
NOTE Confidence: 0.722714998571429  
00:39:39.248 --> 00:39:42.920 kind of a fetal clear cell of appearance.  
NOTE Confidence: 0.722714998571429  
00:39:42.920 --> 00:39:45.368 So I'm more glandular looking area  
NOTE Confidence: 0.722714998571429  
00:39:45.368 --> 00:39:47.860 which kind of produces some music.  
NOTE Confidence: 0.8142966  
00:39:49.920 --> 00:39:52.230 Part of the epithelial elements  
NOTE Confidence: 0.8142966  
00:39:52.230 --> 00:39:54.174 here is a spindle component that  
NOTE Confidence: 0.8142966

00:39:54.174 --> 00:39:55.909 tends to be hypercellular kind  
NOTE Confidence: 0.8142966

00:39:55.909 --> 00:39:57.429 of nondescript spindle cells.  
NOTE Confidence: 0.8142966

00:39:57.430 --> 00:40:00.700 Sometimes it makes matrix either chondroid  
NOTE Confidence: 0.8142966

00:40:00.700 --> 00:40:03.483 or osteoid matrix here and then.  
NOTE Confidence: 0.8142966

00:40:03.483 --> 00:40:05.007 Here's a neuroectodermal component.  
NOTE Confidence: 0.8142966

00:40:05.010 --> 00:40:07.470 Primitive cells with some  
NOTE Confidence: 0.8142966

00:40:07.470 --> 00:40:09.930 neuropil formation and rosettes,  
NOTE Confidence: 0.8142966

00:40:09.930 --> 00:40:12.234 and all of these things are mixed together,  
NOTE Confidence: 0.8142966

00:40:12.240 --> 00:40:14.082 and because this is such a  
NOTE Confidence: 0.8142966

00:40:14.082 --> 00:40:15.003 histologically diverse tumor,  
NOTE Confidence: 0.8142966

00:40:15.010 --> 00:40:16.130 it's historically been controversial  
NOTE Confidence: 0.8142966

00:40:16.130 --> 00:40:18.198 as to how it should be classified  
NOTE Confidence: 0.8142966

00:40:18.198 --> 00:40:19.530 and where it originates.  
NOTE Confidence: 0.8142966

00:40:19.530 --> 00:40:21.217 Is it truly a germ cell tumor?  
NOTE Confidence: 0.8142966

00:40:21.220 --> 00:40:23.398 Does it originate from some sort  
NOTE Confidence: 0.8142966

00:40:23.398 --> 00:40:25.260 of a pluripotent stem cell,

NOTE Confidence: 0.8142966

00:40:25.260 --> 00:40:27.290 or is it some sort of divergent

NOTE Confidence: 0.8142966

00:40:27.290 --> 00:40:28.953 differentiation and it's historically not

NOTE Confidence: 0.8142966

00:40:28.953 --> 00:40:31.167 well characterized on a molecular level?

NOTE Confidence: 0.8142966

00:40:31.170 --> 00:40:33.234 Now we looked at this not because we

NOTE Confidence: 0.8142966

00:40:33.234 --> 00:40:35.420 thought it was going to have any sort

NOTE Confidence: 0.8142966

00:40:35.420 --> 00:40:37.100 of sweet sniff related mutations,

NOTE Confidence: 0.8142966

00:40:37.100 --> 00:40:39.416 but actually because we'd written another

NOTE Confidence: 0.8142966

00:40:39.416 --> 00:40:41.570 paper recently about thyroid teratomas,

NOTE Confidence: 0.8142966

00:40:41.570 --> 00:40:42.944 totally different tumor,

NOTE Confidence: 0.8142966

00:40:42.944 --> 00:40:45.234 but also had multilineage differentiation,

NOTE Confidence: 0.8142966

00:40:45.240 --> 00:40:46.635 and we'd found dyster mutations

NOTE Confidence: 0.8142966

00:40:46.635 --> 00:40:48.835 in those that was fun and we just

NOTE Confidence: 0.8142966

00:40:48.835 --> 00:40:50.323 wondered if they were there as

NOTE Confidence: 0.8142966

00:40:50.323 --> 00:40:52.050 well as enterado carcinosarcoma.

NOTE Confidence: 0.8142966

00:40:52.050 --> 00:40:53.996 And I only bring that up to

NOTE Confidence: 0.8142966

00:40:53.996 --> 00:40:54.830 highlight to trainees.  
NOTE Confidence: 0.8142966

00:40:54.830 --> 00:40:56.576 Sometimes the best research comes when  
NOTE Confidence: 0.8142966

00:40:56.576 --> 00:40:58.332 you're absolutely wrong and we were  
NOTE Confidence: 0.8142966

00:40:58.332 --> 00:40:59.687 totally wrong about our hypothesis.  
NOTE Confidence: 0.8142966

00:40:59.690 --> 00:41:02.805 But we found something else cool instead.  
NOTE Confidence: 0.8142966

00:41:02.810 --> 00:41:05.249 When we ran one case just to test it,  
NOTE Confidence: 0.8142966

00:41:05.250 --> 00:41:07.728 we found lots of smart 4.  
NOTE Confidence: 0.8142966

00:41:07.730 --> 00:41:09.998 And we expanded that ended up  
NOTE Confidence: 0.8142966

00:41:09.998 --> 00:41:12.982 staining 18 of them and found  
NOTE Confidence: 0.8142966

00:41:12.982 --> 00:41:15.880 immunohistochemical lost in 82% of  
NOTE Confidence: 0.8142966

00:41:15.880 --> 00:41:18.295 them and we did sequencing on three  
NOTE Confidence: 0.8142966

00:41:18.295 --> 00:41:21.300 of them to start out with and all of  
NOTE Confidence: 0.8142966

00:41:21.300 --> 00:41:24.408 them had biolex market for inactivation.  
NOTE Confidence: 0.8142966

00:41:24.410 --> 00:41:26.290 So it seems like Toretto  
NOTE Confidence: 0.8142966

00:41:26.290 --> 00:41:28.170 Carcinosarcoma does fit into this.  
NOTE Confidence: 0.8142966

00:41:28.170 --> 00:41:31.210 We sniff of deficient complex,



NOTE Confidence: 0.8142966

00:41:31.210 --> 00:41:32.359 and that's interesting,

NOTE Confidence: 0.8142966

00:41:32.359 --> 00:41:34.274 mostly in terms of classification

NOTE Confidence: 0.8142966

00:41:34.274 --> 00:41:35.510 of these tumors,

NOTE Confidence: 0.8142966

00:41:35.510 --> 00:41:36.800 because it suggests that they're on

NOTE Confidence: 0.8142966

00:41:36.800 --> 00:41:38.478 a spectrum with a smart K4 deficient.

NOTE Confidence: 0.8142966

00:41:38.480 --> 00:41:39.150 Sinonasal carcinoma,

NOTE Confidence: 0.8142966

00:41:39.150 --> 00:41:41.830 as opposed to being a germ cell tumor,

NOTE Confidence: 0.8142966

00:41:41.830 --> 00:41:44.326 and that it's a stool for

NOTE Confidence: 0.8142966

00:41:44.326 --> 00:41:45.574 for identifying them.

NOTE Confidence: 0.8142966

00:41:45.580 --> 00:41:46.576 Immunohistochemically when

NOTE Confidence: 0.8142966

00:41:46.576 --> 00:41:48.568 the diagnosis is difficult.

NOTE Confidence: 0.8142966

00:41:48.570 --> 00:41:50.554 Of course, that is not the entire story.

NOTE Confidence: 0.8142966

00:41:50.560 --> 00:41:51.478 With these tumors,

NOTE Confidence: 0.8142966

00:41:51.478 --> 00:41:53.008 there's another report in the

NOTE Confidence: 0.8142966

00:41:53.008 --> 00:41:54.817 literature of one with beta catenin

NOTE Confidence: 0.8142966

00:41:54.817 --> 00:41:56.247 mutation and and several other  
NOTE Confidence: 0.8142966

00:41:56.247 --> 00:41:57.773 cases in our series actually did  
NOTE Confidence: 0.8142966

00:41:57.773 --> 00:41:59.313 not have smart K four loss.  
NOTE Confidence: 0.8142966

00:41:59.313 --> 00:42:02.137 So since then we haven't published this yet,  
NOTE Confidence: 0.8142966

00:42:02.140 --> 00:42:04.716 but we've sequenced a bunch more of them.  
NOTE Confidence: 0.8142966

00:42:04.720 --> 00:42:06.816 14 cases of them,  
NOTE Confidence: 0.8142966

00:42:06.816 --> 00:42:08.804 and with known immunohistochemical  
NOTE Confidence: 0.8142966

00:42:08.804 --> 00:42:10.268 expression of smart.  
NOTE Confidence: 0.8142966

00:42:10.270 --> 00:42:11.128 Or or loss.  
NOTE Confidence: 0.8142966

00:42:11.128 --> 00:42:13.581 And we did find that most of them  
NOTE Confidence: 0.8142966

00:42:13.581 --> 00:42:15.849 had either smart K4 mutations or  
NOTE Confidence: 0.8142966

00:42:15.850 --> 00:42:18.470 ctne B1 beta catenin mutations,  
NOTE Confidence: 0.8142966

00:42:18.470 --> 00:42:21.710 although there were other genes implicated.  
NOTE Confidence: 0.8142966

00:42:21.710 --> 00:42:22.990 I'm in a cluster together,  
NOTE Confidence: 0.8142966

00:42:22.990 --> 00:42:24.988 tumors that had some market for  
NOTE Confidence: 0.8142966

00:42:24.988 --> 00:42:26.550 lost by amino Histochemistry had

NOTE Confidence: 0.8142966

00:42:26.550 --> 00:42:28.605 smart K4 inactivation or beta

NOTE Confidence: 0.8142966

00:42:28.605 --> 00:42:30.660 catenin mutations and then other

NOTE Confidence: 0.8142966

00:42:30.731 --> 00:42:32.956 molecular alterations were seen in

NOTE Confidence: 0.8142966

00:42:32.956 --> 00:42:35.058 other tumors and this actually kind

NOTE Confidence: 0.8142966

00:42:35.058 --> 00:42:36.870 of just expands the link between

NOTE Confidence: 0.8142966

00:42:36.929 --> 00:42:38.465 Toretto carcinosarcoma and and

NOTE Confidence: 0.8142966

00:42:38.465 --> 00:42:40.385 sinonasal carcinomas because all of

NOTE Confidence: 0.8142966

00:42:40.385 --> 00:42:42.917 the mutations seen here have been

NOTE Confidence: 0.8142966

00:42:42.917 --> 00:42:44.585 reported in sinonasal neuroendocrine

NOTE Confidence: 0.8142966

00:42:44.585 --> 00:42:47.460 neoplasms and it also beta catenin

NOTE Confidence: 0.8142966

00:42:47.460 --> 00:42:50.840 provides another helpful tool for diagnosis.

NOTE Confidence: 0.8142966

00:42:50.840 --> 00:42:51.126 However,

NOTE Confidence: 0.8142966

00:42:51.126 --> 00:42:52.270 it's important to emphasize.

NOTE Confidence: 0.6281852575

00:42:52.270 --> 00:42:53.770 Try to partner sarcoma is

NOTE Confidence: 0.6281852575

00:42:53.770 --> 00:42:54.670 a morphologic diagnosis.

NOTE Confidence: 0.6281852575

00:42:54.670 --> 00:42:56.840 You're looking out for all of these  
NOTE Confidence: 0.6281852575

00:42:56.840 --> 00:42:59.094 elements together and it is not yet  
NOTE Confidence: 0.6281852575

00:42:59.094 --> 00:43:00.669 defined by Swiss snapgene involvement.  
NOTE Confidence: 0.6281852575

00:43:00.670 --> 00:43:02.250 So in the next edition,  
NOTE Confidence: 0.6281852575

00:43:02.250 --> 00:43:03.228 WHO sinonasal carcinoma,  
NOTE Confidence: 0.6281852575

00:43:03.228 --> 00:43:05.510 there's a new category for Swiss sniff.  
NOTE Confidence: 0.6281852575

00:43:05.510 --> 00:43:07.530 Complex deficient sinonasal carcinomas that  
NOTE Confidence: 0.6281852575

00:43:07.530 --> 00:43:10.150 includes this mark B1 deficient carcinoma,  
NOTE Confidence: 0.6281852575

00:43:10.150 --> 00:43:10.874 and adenocarcinoma,  
NOTE Confidence: 0.6281852575

00:43:10.874 --> 00:43:13.408 as well as the smart K4 deficient  
NOTE Confidence: 0.6281852575

00:43:13.408 --> 00:43:14.910 carcinoma and Toretto carcinoma  
NOTE Confidence: 0.6281852575

00:43:14.910 --> 00:43:16.705 is lumped under the Toretto.  
NOTE Confidence: 0.6281852575

00:43:16.710 --> 00:43:18.394 Carcinosarcoma is lumped under  
NOTE Confidence: 0.6281852575

00:43:18.394 --> 00:43:20.078 the sinonasal carcinoma category.  
NOTE Confidence: 0.6281852575

00:43:20.080 --> 00:43:22.481 But it is not formally defined as  
NOTE Confidence: 0.6281852575

00:43:22.481 --> 00:43:24.546 a Swiss sniff deficient neoplasm.

NOTE Confidence: 0.6281852575

00:43:24.546 --> 00:43:27.654 Alright, just a few more minutes.

NOTE Confidence: 0.6281852575

00:43:27.660 --> 00:43:29.300 I really wanna hit something

NOTE Confidence: 0.6281852575

00:43:29.300 --> 00:43:30.612 quick at the end.

NOTE Confidence: 0.6281852575

00:43:30.620 --> 00:43:32.700 Definitely new and emerging

NOTE Confidence: 0.6281852575

00:43:32.700 --> 00:43:34.780 story in sinonasal carcinomas,

NOTE Confidence: 0.6281852575

00:43:34.780 --> 00:43:37.818 and that's tumors with IDH 2 mutations.

NOTE Confidence: 0.6281852575

00:43:37.820 --> 00:43:39.884 Now we've talked about a lot of tumor

NOTE Confidence: 0.6281852575

00:43:39.884 --> 00:43:41.700 types that have been reclassified,

NOTE Confidence: 0.6281852575

00:43:41.700 --> 00:43:43.310 and a lot of these have been

NOTE Confidence: 0.6281852575

00:43:43.310 --> 00:43:45.016 reclassified out of the sinonasal

NOTE Confidence: 0.6281852575

00:43:45.016 --> 00:43:46.456 undifferentiated carcinoma category.

NOTE Confidence: 0.6281852575

00:43:46.460 --> 00:43:47.730 It's been a shrinking category

NOTE Confidence: 0.6281852575

00:43:47.730 --> 00:43:49.000 in the last few years.

NOTE Confidence: 0.6281852575

00:43:49.000 --> 00:43:50.668 It's a hybrid carcinoma and has

NOTE Confidence: 0.6281852575

00:43:50.668 --> 00:43:52.176 always kind of been regarded

NOTE Confidence: 0.6281852575

00:43:52.176 --> 00:43:53.856 as a diagnosis of exclusion.  
NOTE Confidence: 0.6281852575

00:43:53.860 --> 00:43:55.849 No squamous differentiation,  
NOTE Confidence: 0.6281852575

00:43:55.849 --> 00:43:57.838 no glandular differentiation.  
NOTE Confidence: 0.6281852575

00:43:57.840 --> 00:43:58.868 Usually no neuroendocrine differentiation.  
NOTE Confidence: 0.6281852575

00:43:58.868 --> 00:44:00.640 I'm going to get back to that.  
NOTE Confidence: 0.6281852575

00:44:00.640 --> 00:44:02.520 It's been controversial, but formally,  
NOTE Confidence: 0.6281852575

00:44:02.520 --> 00:44:04.304 according to the guidelines,  
NOTE Confidence: 0.6281852575

00:44:04.304 --> 00:44:06.605 not and rule out all of these other  
NOTE Confidence: 0.6281852575

00:44:06.605 --> 00:44:07.836 tumor types. Smart one smart.  
NOTE Confidence: 0.6281852575

00:44:07.836 --> 00:44:09.460 Or not all of the good stuff  
NOTE Confidence: 0.6281852575

00:44:09.515 --> 00:44:10.997 once you rule everything out and  
NOTE Confidence: 0.6281852575

00:44:10.997 --> 00:44:12.870 you have a high grade carcinoma,  
NOTE Confidence: 0.6281852575

00:44:12.870 --> 00:44:15.426 you can call it a sinonasal  
NOTE Confidence: 0.6281852575

00:44:15.426 --> 00:44:16.278 undifferentiated carcinoma.  
NOTE Confidence: 0.6281852575

00:44:16.280 --> 00:44:18.098 And here's an example of 1  
NOTE Confidence: 0.6281852575

00:44:18.098 --> 00:44:19.770 sheets of high grade cells,

NOTE Confidence: 0.6281852575  
00:44:19.770 --> 00:44:20.742 lots of necrosis,  
NOTE Confidence: 0.6281852575  
00:44:20.742 --> 00:44:22.686 and these cells are a little  
NOTE Confidence: 0.6281852575  
00:44:22.686 --> 00:44:24.426 bit more polymorphic than the  
NOTE Confidence: 0.6281852575  
00:44:24.426 --> 00:44:26.448 ones that we see in other.  
NOTE Confidence: 0.6281852575  
00:44:26.450 --> 00:44:27.830 Some of the translocations  
NOTE Confidence: 0.6281852575  
00:44:27.830 --> 00:44:28.865 driven sinonasal tumors,  
NOTE Confidence: 0.6281852575  
00:44:28.870 --> 00:44:30.858 often very prominent nucleoli  
NOTE Confidence: 0.6281852575  
00:44:30.858 --> 00:44:33.343 kind of more nuclear atypia.  
NOTE Confidence: 0.6281852575  
00:44:33.350 --> 00:44:35.490 Now, interestingly,  
NOTE Confidence: 0.6281852575  
00:44:35.490 --> 00:44:37.632 a lot of the residual category of  
NOTE Confidence: 0.6281852575  
00:44:37.632 --> 00:44:39.649 snuck that has not been reclassified  
NOTE Confidence: 0.6281852575  
00:44:39.649 --> 00:44:42.057 was recently found to have IDH 2  
NOTE Confidence: 0.6281852575  
00:44:42.128 --> 00:44:44.535 mutation anywhere between 50 and 88%  
NOTE Confidence: 0.6281852575  
00:44:44.535 --> 00:44:46.725 of residual tumors in that category.  
NOTE Confidence: 0.6281852575  
00:44:46.730 --> 00:44:49.846 Had IDH 2 hot spot mutations and  
NOTE Confidence: 0.6281852575

00:44:49.846 --> 00:44:51.826 what's interesting is that it's  
NOTE Confidence: 0.6281852575

00:44:51.826 --> 00:44:53.410 actually recognizable via mutation  
NOTE Confidence: 0.6281852575

00:44:53.471 --> 00:44:55.169 specific immunohistochemistry,  
NOTE Confidence: 0.6281852575

00:44:55.170 --> 00:44:57.330 which provides a confirmatory marker,  
NOTE Confidence: 0.6281852575

00:44:57.330 --> 00:44:59.895 so it kind of moves snuck out of the  
NOTE Confidence: 0.6281852575

00:44:59.895 --> 00:45:02.027 category of a diagnosis of exclusion,  
NOTE Confidence: 0.6281852575

00:45:02.030 --> 00:45:03.630 and lets us actually actively  
NOTE Confidence: 0.6281852575

00:45:03.630 --> 00:45:04.910 prove what it is.  
NOTE Confidence: 0.6281852575

00:45:04.910 --> 00:45:07.326 So here's a beautiful example of the stain.  
NOTE Confidence: 0.6281852575

00:45:07.330 --> 00:45:08.818 It picks up the mutant protein,  
NOTE Confidence: 0.6281852575

00:45:08.820 --> 00:45:10.464 so you are looking for positive  
NOTE Confidence: 0.6281852575

00:45:10.464 --> 00:45:12.170 expression in the cytoplasm of the cell.  
NOTE Confidence: 0.6281852575

00:45:12.170 --> 00:45:13.678 So that's really cool.  
NOTE Confidence: 0.6281852575

00:45:13.678 --> 00:45:15.563 Now the question of neuroendocrine  
NOTE Confidence: 0.6281852575

00:45:15.563 --> 00:45:17.155 differentiation and stuck has  
NOTE Confidence: 0.6281852575

00:45:17.155 --> 00:45:18.316 minimal controversial overtime.



NOTE Confidence: 0.6281852575

00:45:18.320 --> 00:45:20.720 It actually originally was defined

NOTE Confidence: 0.6281852575

00:45:20.720 --> 00:45:22.640 as having some neuroendocrine

NOTE Confidence: 0.6281852575

00:45:22.640 --> 00:45:24.200 differentiation despite its name,

NOTE Confidence: 0.6281852575

00:45:24.200 --> 00:45:25.925 and although most pathologic guidelines

NOTE Confidence: 0.6281852575

00:45:25.925 --> 00:45:27.650 do not technically allow this,

NOTE Confidence: 0.6281852575

00:45:27.650 --> 00:45:30.191 it has been a source of persistent

NOTE Confidence: 0.6281852575

00:45:30.191 --> 00:45:31.472 confusion because of distinctions

NOTE Confidence: 0.6281852575

00:45:31.472 --> 00:45:33.296 with other high grade tumors that

NOTE Confidence: 0.6281852575

00:45:33.296 --> 00:45:35.170 have neuroendocrine differentiation.

NOTE Confidence: 0.6281852575

00:45:35.170 --> 00:45:37.400 Large cell neuron during carcinoma

NOTE Confidence: 0.6281852575

00:45:37.400 --> 00:45:39.184 has been particularly challenging,

NOTE Confidence: 0.6281852575

00:45:39.190 --> 00:45:41.450 mostly because it shows substantial

NOTE Confidence: 0.6281852575

00:45:41.450 --> 00:45:42.354 histologic overlap.

NOTE Confidence: 0.6281852575

00:45:42.360 --> 00:45:44.118 So here's a large cell neural

NOTE Confidence: 0.6281852575

00:45:44.118 --> 00:45:44.704 endocrine carcinoma.

NOTE Confidence: 0.6281852575

00:45:44.710 --> 00:45:48.010 Nest the cells pleomorphism prominent nuclei.

NOTE Confidence: 0.6281852575

00:45:48.010 --> 00:45:49.186 A lot of cytoplasm,

NOTE Confidence: 0.6281852575

00:45:49.186 --> 00:45:50.950 very similar to what we're seeing

NOTE Confidence: 0.6281852575

00:45:51.014 --> 00:45:51.958 in this knock up,

NOTE Confidence: 0.6281852575

00:45:51.960 --> 00:45:53.952 but it shows substantial

NOTE Confidence: 0.6281852575

00:45:53.952 --> 00:45:54.948 neuroendocrine differentiation.

NOTE Confidence: 0.810374003125

00:45:54.950 --> 00:45:56.595 Here's one nuclear positivity kind

NOTE Confidence: 0.810374003125

00:45:56.595 --> 00:45:59.114 of at a level that currently we

NOTE Confidence: 0.810374003125

00:45:59.114 --> 00:46:01.186 wouldn't accept and snack. Well.

NOTE Confidence: 0.810374003125

00:46:01.186 --> 00:46:03.466 Large scale Neurontin carcinomas have

NOTE Confidence: 0.810374003125

00:46:03.466 --> 00:46:06.475 also recently been found to have IDH 2

NOTE Confidence: 0.810374003125

00:46:06.475 --> 00:46:09.330 mutations up to 83% of them show mutation,

NOTE Confidence: 0.810374003125

00:46:09.330 --> 00:46:10.554 which suggests that,

NOTE Confidence: 0.810374003125

00:46:10.554 --> 00:46:12.186 as their morphology suggests,

NOTE Confidence: 0.810374003125

00:46:12.190 --> 00:46:13.615 they probably actually are on

NOTE Confidence: 0.810374003125

00:46:13.615 --> 00:46:15.790 us on a spectrum with sinonasal

NOTE Confidence: 0.810374003125

00:46:15.790 --> 00:46:17.170 undifferentiated carcinoma.

NOTE Confidence: 0.810374003125

00:46:17.170 --> 00:46:18.625 And here's an example of, again,

NOTE Confidence: 0.810374003125

00:46:18.625 --> 00:46:21.055 nice IDH 2 mutant immunohistochemistry in

NOTE Confidence: 0.810374003125

00:46:21.055 --> 00:46:23.828 the largest cell neuron during carcinoma.

NOTE Confidence: 0.810374003125

00:46:23.830 --> 00:46:25.018 Nicely positive,

NOTE Confidence: 0.810374003125

00:46:25.018 --> 00:46:27.394 now beyond morphology and

NOTE Confidence: 0.810374003125

00:46:27.394 --> 00:46:29.176 immunohistochemistry and molecular

NOTE Confidence: 0.810374003125

00:46:29.176 --> 00:46:31.600 methylation profiling is something that's

NOTE Confidence: 0.810374003125

00:46:31.600 --> 00:46:34.240 starting to emerge in the literature

NOTE Confidence: 0.810374003125

00:46:34.313 --> 00:46:36.449 to be used for sinonasal tumors,

NOTE Confidence: 0.810374003125

00:46:36.450 --> 00:46:38.454 and there's lots of different tumor

NOTE Confidence: 0.810374003125

00:46:38.454 --> 00:46:40.501 types that have very distinctive

NOTE Confidence: 0.810374003125

00:46:40.501 --> 00:46:42.427 clustered methylation profiles.

NOTE Confidence: 0.810374003125

00:46:42.430 --> 00:46:43.818 So regardless of Histology,

NOTE Confidence: 0.810374003125

00:46:43.818 --> 00:46:46.444 IDH 2 mutant snuck and large cell

NOTE Confidence: 0.810374003125

00:46:46.444 --> 00:46:48.372 neuroendocrine carcinoma do cluster  
NOTE Confidence: 0.810374003125

00:46:48.372 --> 00:46:50.300 together on this methylation.  
NOTE Confidence: 0.810374003125

00:46:50.300 --> 00:46:52.184 Profiling with a global  
NOTE Confidence: 0.810374003125

00:46:52.184 --> 00:46:53.126 hypermethylation pattern,  
NOTE Confidence: 0.810374003125

00:46:53.130 --> 00:46:54.540 which is actually very characteristic  
NOTE Confidence: 0.810374003125

00:46:54.540 --> 00:46:56.419 of multiple tumor types that have died.  
NOTE Confidence: 0.810374003125

00:46:56.420 --> 00:46:58.926 2 mutation and this kind of further  
NOTE Confidence: 0.810374003125

00:46:58.926 --> 00:47:01.148 validates that they are similar and  
NOTE Confidence: 0.810374003125

00:47:01.148 --> 00:47:03.314 probably belong in the same group.  
NOTE Confidence: 0.810374003125

00:47:03.320 --> 00:47:05.060 Now, does this matter clinically?  
NOTE Confidence: 0.810374003125

00:47:05.060 --> 00:47:07.440 This also has significant prognostic  
NOTE Confidence: 0.810374003125

00:47:07.440 --> 00:47:09.820 implications because regardless of Histology,  
NOTE Confidence: 0.810374003125

00:47:09.820 --> 00:47:11.520 either large cell neuroendocrine  
NOTE Confidence: 0.810374003125

00:47:11.520 --> 00:47:12.795 carcinoma or knock,  
NOTE Confidence: 0.810374003125

00:47:12.800 --> 00:47:14.642 they have better prognosis than snakes  
NOTE Confidence: 0.810374003125

00:47:14.642 --> 00:47:17.318 that don't have known mutations as well as

NOTE Confidence: 0.810374003125

00:47:17.318 --> 00:47:19.053 smart B1 deficient sinonasal carcinomas.

NOTE Confidence: 0.810374003125

00:47:19.060 --> 00:47:21.052 So it's helpful now.

NOTE Confidence: 0.810374003125

00:47:21.052 --> 00:47:22.614 Prognostically in terms of treatment.

NOTE Confidence: 0.810374003125

00:47:22.614 --> 00:47:23.146 Of course.

NOTE Confidence: 0.810374003125

00:47:23.150 --> 00:47:26.942 I DH two as well as one encodes

NOTE Confidence: 0.810374003125

00:47:26.942 --> 00:47:27.890 isocitrate dehydrogenase.

NOTE Confidence: 0.810374003125

00:47:27.890 --> 00:47:29.619 Which is the enzyme that plays an

NOTE Confidence: 0.810374003125

00:47:29.619 --> 00:47:31.188 important role in the Krebs cycle.

NOTE Confidence: 0.810374003125

00:47:31.190 --> 00:47:33.206 So we were actually seeing real

NOTE Confidence: 0.810374003125

00:47:33.206 --> 00:47:34.918 live significance of the Kreb

NOTE Confidence: 0.810374003125

00:47:34.918 --> 00:47:38.184 cycle here and mutations lead to

NOTE Confidence: 0.810374003125

00:47:38.184 --> 00:47:40.848 Uncle metabolites which cause.

NOTE Confidence: 0.810374003125

00:47:40.850 --> 00:47:42.455 Cancer and it's pretty common

NOTE Confidence: 0.810374003125

00:47:42.455 --> 00:47:43.739 in different tumor types.

NOTE Confidence: 0.810374003125

00:47:43.740 --> 00:47:45.064 Leukemia glioma chondrosarcoma are

NOTE Confidence: 0.810374003125

00:47:45.064 --> 00:47:47.310 all very well known for having IDH,  
NOTE Confidence: 0.810374003125

00:47:47.310 --> 00:47:49.718 one or two mutations.  
NOTE Confidence: 0.810374003125

00:47:49.718 --> 00:47:50.320 Fortunately,  
NOTE Confidence: 0.810374003125

00:47:50.320 --> 00:47:52.210 inhibitors have been developed that  
NOTE Confidence: 0.810374003125

00:47:52.210 --> 00:47:54.100 can kind of induce differentiation  
NOTE Confidence: 0.810374003125

00:47:54.155 --> 00:47:55.830 and lead to treatment response,  
NOTE Confidence: 0.810374003125

00:47:55.830 --> 00:47:57.570 and it's a potential target  
NOTE Confidence: 0.810374003125

00:47:57.570 --> 00:47:59.428 for treating these IDH mutant  
NOTE Confidence: 0.810374003125

00:47:59.428 --> 00:48:01.358 sinonasal tumors in the future.  
NOTE Confidence: 0.810374003125

00:48:01.360 --> 00:48:02.731 So 5th edition,  
NOTE Confidence: 0.810374003125

00:48:02.731 --> 00:48:04.102 WHO classification sinonasal  
NOTE Confidence: 0.810374003125

00:48:04.102 --> 00:48:05.473 undifferentiated carcinoma large  
NOTE Confidence: 0.810374003125

00:48:05.473 --> 00:48:07.257 cell neuron endocrine carcinoma  
NOTE Confidence: 0.810374003125

00:48:07.257 --> 00:48:08.949 are actually still separately  
NOTE Confidence: 0.810374003125

00:48:08.949 --> 00:48:10.840 classified and it's mentioned.  
NOTE Confidence: 0.810374003125

00:48:10.840 --> 00:48:13.311 Under in both disease chapters that IDH

NOTE Confidence: 0.810374003125

00:48:13.311 --> 00:48:16.092 2 mutations are seen but it's not yet.

NOTE Confidence: 0.810374003125

00:48:16.092 --> 00:48:17.832 The classification driver will see

NOTE Confidence: 0.810374003125

00:48:17.832 --> 00:48:20.176 how this holds forth in the future.

NOTE Confidence: 0.810374003125

00:48:20.180 --> 00:48:22.028 Alright, so just to finish up,

NOTE Confidence: 0.810374003125

00:48:22.030 --> 00:48:24.109 a molecular testing has had a huge

NOTE Confidence: 0.810374003125

00:48:24.109 --> 00:48:26.247 impact over the last decade in

NOTE Confidence: 0.810374003125

00:48:26.247 --> 00:48:28.212 sinonasal tumors with definition and

NOTE Confidence: 0.810374003125

00:48:28.212 --> 00:48:30.370 recognition of multiple new diagnosis

NOTE Confidence: 0.810374003125

00:48:30.370 --> 00:48:31.730 understanding the pathogenesis of

NOTE Confidence: 0.810374003125

00:48:31.730 --> 00:48:33.770 existing tumor types as well as

NOTE Confidence: 0.810374003125

00:48:33.832 --> 00:48:35.137 clarifying relationships between

NOTE Confidence: 0.810374003125

00:48:35.137 --> 00:48:36.877 entities that were previously

NOTE Confidence: 0.810374003125

00:48:36.877 --> 00:48:38.710 regarded as entirely separate.

NOTE Confidence: 0.810374003125

00:48:38.710 --> 00:48:38.992 Now,

NOTE Confidence: 0.810374003125

00:48:38.992 --> 00:48:40.966 right now the practical implications of this,

NOTE Confidence: 0.810374003125

00:48:40.970 --> 00:48:41.504 I think,  
NOTE Confidence: 0.810374003125

00:48:41.504 --> 00:48:44.118 are sort of at a precipice we like to learn.  
NOTE Confidence: 0.810374003125

00:48:44.118 --> 00:48:45.378 Data is sort of partially  
NOTE Confidence: 0.810374003125

00:48:45.378 --> 00:48:46.469 integrated into the new WHL.  
NOTE Confidence: 0.810374003125

00:48:46.470 --> 00:48:47.094 Of course,  
NOTE Confidence: 0.810374003125

00:48:47.094 --> 00:48:48.342 some of these molecularly  
NOTE Confidence: 0.810374003125

00:48:48.342 --> 00:48:49.590 defined categories are there.  
NOTE Confidence: 0.810374003125

00:48:49.590 --> 00:48:51.720 This, we sniff deficient tumors,  
NOTE Confidence: 0.810374003125

00:48:51.720 --> 00:48:52.912 nut carcinoma, etc, etc.  
NOTE Confidence: 0.810374003125

00:48:52.912 --> 00:48:55.370 So those are written into the literature,  
NOTE Confidence: 0.810374003125

00:48:55.370 --> 00:48:57.850 but not all of it has crossed over over yet.  
NOTE Confidence: 0.810374003125

00:48:57.850 --> 00:49:00.730 In terms of shaping the classification,  
NOTE Confidence: 0.810374003125

00:49:00.730 --> 00:49:02.295 what's fortunate at this point  
NOTE Confidence: 0.810374003125

00:49:02.295 --> 00:49:03.860 is that most relevant molecular  
NOTE Confidence: 0.82185596047619

00:49:03.915 --> 00:49:05.735 findings are identifiable through  
NOTE Confidence: 0.82185596047619

00:49:05.735 --> 00:49:07.100 surrogate immunohistochemical or



NOTE Confidence: 0.82185596047619  
00:49:07.100 --> 00:49:08.920 insight 2 hybridization markers.  
NOTE Confidence: 0.82185596047619  
00:49:08.920 --> 00:49:10.460 So we can do a nut immunostain.  
NOTE Confidence: 0.82185596047619  
00:49:10.460 --> 00:49:12.164 We can do an IDH 2 immunostain and  
NOTE Confidence: 0.82185596047619  
00:49:12.164 --> 00:49:14.201 we don't necessarily have to do  
NOTE Confidence: 0.82185596047619  
00:49:14.201 --> 00:49:15.860 comprehensive sequencing and therefore  
NOTE Confidence: 0.82185596047619  
00:49:15.860 --> 00:49:17.620 we don't usually comprehensive  
NOTE Confidence: 0.82185596047619  
00:49:17.620 --> 00:49:20.080 molecular analysis is not performed.  
NOTE Confidence: 0.82185596047619  
00:49:20.080 --> 00:49:22.530 A standard of care and usually it's  
NOTE Confidence: 0.82185596047619  
00:49:22.530 --> 00:49:24.910 only used around here when they're  
NOTE Confidence: 0.82185596047619  
00:49:24.910 --> 00:49:26.582 they're searching actively for  
NOTE Confidence: 0.82185596047619  
00:49:26.582 --> 00:49:29.120 for end stage treatment options.  
NOTE Confidence: 0.82185596047619  
00:49:29.120 --> 00:49:32.594 So you know it's not quite in the mainstream,  
NOTE Confidence: 0.82185596047619  
00:49:32.600 --> 00:49:34.570 and it's certainly not impacting  
NOTE Confidence: 0.82185596047619  
00:49:34.570 --> 00:49:36.860 on standard of care treatment yet.  
NOTE Confidence: 0.82185596047619  
00:49:36.860 --> 00:49:39.225 Now is further molecular classification  
NOTE Confidence: 0.82185596047619

00:49:39.225 --> 00:49:39.698 coming?  
NOTE Confidence: 0.82185596047619

00:49:39.700 --> 00:49:41.268 I mean, we kind of all watch  
NOTE Confidence: 0.82185596047619

00:49:41.268 --> 00:49:42.629 other other areas of pathology.  
NOTE Confidence: 0.82185596047619

00:49:42.630 --> 00:49:43.524 I think neuropathology,  
NOTE Confidence: 0.82185596047619

00:49:43.524 --> 00:49:45.610 right now is is the main one.  
NOTE Confidence: 0.82185596047619

00:49:45.610 --> 00:49:48.496 Switch over to an entirely molecular  
NOTE Confidence: 0.82185596047619

00:49:48.496 --> 00:49:49.939 driven classification system.  
NOTE Confidence: 0.82185596047619

00:49:49.940 --> 00:49:52.117 There's actually this very week in ABCP.  
NOTE Confidence: 0.82185596047619

00:49:52.120 --> 00:49:54.852 There was a proposal for a molecular  
NOTE Confidence: 0.82185596047619

00:49:54.852 --> 00:49:57.140 based subclassification of sinonasal  
NOTE Confidence: 0.82185596047619

00:49:57.140 --> 00:49:59.391 squamous cell carcinoma, and you know?  
NOTE Confidence: 0.82185596047619

00:49:59.391 --> 00:50:00.453 In some ways this is great.  
NOTE Confidence: 0.82185596047619

00:50:00.460 --> 00:50:01.660 If it gives us more information,  
NOTE Confidence: 0.82185596047619

00:50:01.660 --> 00:50:03.308 but in other ways we we risk making  
NOTE Confidence: 0.82185596047619

00:50:03.308 --> 00:50:05.134 what is already a challenging  
NOTE Confidence: 0.82185596047619

00:50:05.134 --> 00:50:06.499 classification really inaccessible.

NOTE Confidence: 0.82185596047619  
00:50:06.500 --> 00:50:07.313 For many pathologists,  
NOTE Confidence: 0.82185596047619  
00:50:07.313 --> 00:50:09.210 if it if it is driven only  
NOTE Confidence: 0.82185596047619  
00:50:09.275 --> 00:50:10.439 by molecular testing,  
NOTE Confidence: 0.82185596047619  
00:50:10.440 --> 00:50:12.526 and we also are struggling to get  
NOTE Confidence: 0.82185596047619  
00:50:12.526 --> 00:50:14.589 insurers and even Medicare to pay  
NOTE Confidence: 0.82185596047619  
00:50:14.589 --> 00:50:16.480 for molecular testing, so you know,  
NOTE Confidence: 0.82185596047619  
00:50:16.480 --> 00:50:18.300 do we really wanna hinge everything on  
NOTE Confidence: 0.82185596047619  
00:50:18.359 --> 00:50:20.655 on testing that we potentially can't even do?  
NOTE Confidence: 0.82185596047619  
00:50:20.660 --> 00:50:22.330 A can't even bill for,  
NOTE Confidence: 0.82185596047619  
00:50:22.330 --> 00:50:23.258 so it's a question.  
NOTE Confidence: 0.82185596047619  
00:50:23.258 --> 00:50:25.354 I think it's gonna need to be resolved  
NOTE Confidence: 0.82185596047619  
00:50:25.354 --> 00:50:26.974 on multiple levels going forward.  
NOTE Confidence: 0.82185596047619  
00:50:26.980 --> 00:50:28.462 And of course new categories still  
NOTE Confidence: 0.82185596047619  
00:50:28.462 --> 00:50:30.109 may be coming down the pipeline.  
NOTE Confidence: 0.82185596047619  
00:50:30.110 --> 00:50:31.926 So that still will be kind of evolving.  
NOTE Confidence: 0.82185596047619

00:50:31.930 --> 00:50:34.480 Evolving changes as we go forward.  
NOTE Confidence: 0.82185596047619

00:50:34.480 --> 00:50:36.460 Alright, thank you so much.  
NOTE Confidence: 0.82185596047619

00:50:36.460 --> 00:50:38.050 I'm happy to take any questions.  
NOTE Confidence: 0.905890574

00:50:40.200 --> 00:50:42.040 Thank you so much Lisa.  
NOTE Confidence: 0.905890574

00:50:42.040 --> 00:50:45.196 So if you have a question,  
NOTE Confidence: 0.905890574

00:50:45.200 --> 00:50:47.660 please unmute yourself and ask.  
NOTE Confidence: 0.905890574

00:50:47.660 --> 00:50:50.026 I don't see any questions in chat.  
NOTE Confidence: 0.914951585

00:50:56.920 --> 00:51:00.696 Hi Lisa. It's a really great talk,  
NOTE Confidence: 0.914951585

00:51:00.696 --> 00:51:02.472 so I have one question so I'm not.  
NOTE Confidence: 0.914951585

00:51:02.472 --> 00:51:03.699 I'm the molecular pathology.  
NOTE Confidence: 0.914951585

00:51:03.700 --> 00:51:06.769 So here we do the the UN command tests  
NOTE Confidence: 0.729071692

00:51:07.540 --> 00:51:10.560 for the for the oncologist and occasion.  
NOTE Confidence: 0.729071692

00:51:10.560 --> 00:51:12.160 As I understand that.  
NOTE Confidence: 0.729071692

00:51:12.160 --> 00:51:14.740 And the smart smart CP1,  
NOTE Confidence: 0.729071692

00:51:14.740 --> 00:51:17.748 smart safe for deficiency.  
NOTE Confidence: 0.729071692

00:51:17.750 --> 00:51:19.870 So carcinoma is measured based on the

NOTE Confidence: 0.729071692

00:51:19.870 --> 00:51:21.038 morphology and the immunostaining

NOTE Confidence: 0.648426692

00:51:21.050 --> 00:51:24.080 confirmation. Yeah, but occasionally we

NOTE Confidence: 0.6008665975

00:51:24.090 --> 00:51:25.478 see the molecular result,

NOTE Confidence: 0.6008665975

00:51:25.478 --> 00:51:27.656 which is a hint. There's some smart

NOTE Confidence: 0.6008665975

00:51:27.656 --> 00:51:30.108 CP one and smart C4 deficiency,

NOTE Confidence: 0.6008665975

00:51:30.110 --> 00:51:32.040 but morphology doesn't quite fit

NOTE Confidence: 0.727900485

00:51:32.070 --> 00:51:35.522 the the what describes how do we

NOTE Confidence: 0.727900485

00:51:35.522 --> 00:51:37.442 explain for this excellent question?

NOTE Confidence: 0.727900485

00:51:37.442 --> 00:51:39.409 I don't. I don't know if we've

NOTE Confidence: 0.727900485

00:51:39.409 --> 00:51:43.260 answered that question yet, I think.

NOTE Confidence: 0.727900485

00:51:43.260 --> 00:51:45.900 The way this tumor was defined, I you know,

NOTE Confidence: 0.727900485

00:51:45.900 --> 00:51:47.720 I'm saying I'm using molecular loosely as

NOTE Confidence: 0.727900485

00:51:47.773 --> 00:51:49.639 in kind of molecular related findings,

NOTE Confidence: 0.727900485

00:51:49.640 --> 00:51:52.320 but it really was defined based on the

NOTE Confidence: 0.727900485

00:51:52.320 --> 00:51:53.811 immunohistochemistry and kind of the

NOTE Confidence: 0.727900485

00:51:53.811 --> 00:51:56.080 functional like loss of that of that protein.

NOTE Confidence: 0.727900485

00:51:56.080 --> 00:51:58.243 So you know it's really a great

NOTE Confidence: 0.727900485

00:51:58.243 --> 00:52:00.084 question in terms of what to

NOTE Confidence: 0.727900485

00:52:00.084 --> 00:52:01.770 do with a tumor that doesn't.

NOTE Confidence: 0.727900485

00:52:01.770 --> 00:52:04.596 Doesn't fit into into that category,

NOTE Confidence: 0.727900485

00:52:04.600 --> 00:52:06.840 not apparently, but has has the loss.

NOTE Confidence: 0.727900485

00:52:06.840 --> 00:52:09.178 I've had a couple of those cases

NOTE Confidence: 0.727900485

00:52:09.180 --> 00:52:11.837 that I've had some some apparent.

NOTE Confidence: 0.727900485

00:52:11.837 --> 00:52:14.039 In you know Histochemical findings or

NOTE Confidence: 0.727900485

00:52:14.039 --> 00:52:16.329 molecular findings and end up end up

NOTE Confidence: 0.727900485

00:52:16.329 --> 00:52:18.132 signing it out descriptively, but I don't.

NOTE Confidence: 0.727900485

00:52:18.132 --> 00:52:19.028 I'm not certain yet.

NOTE Confidence: 0.727900485

00:52:19.030 --> 00:52:20.590 I think those are those.

NOTE Confidence: 0.727900485

00:52:20.590 --> 00:52:22.114 It's not entirely clear what to

NOTE Confidence: 0.727900485

00:52:22.114 --> 00:52:23.730 do with those and and probably

NOTE Confidence: 0.727900485

00:52:23.730 --> 00:52:25.627 won't be until we have more clear,

NOTE Confidence: 0.727900485

00:52:25.630 --> 00:52:26.356 you know,

NOTE Confidence: 0.727900485

00:52:26.356 --> 00:52:27.808 treatment implications for for

NOTE Confidence: 0.727900485

00:52:27.808 --> 00:52:29.650 what we do with them.

NOTE Confidence: 0.727900485

00:52:29.650 --> 00:52:30.160 So my

NOTE Confidence: 0.766309903333333

00:52:30.170 --> 00:52:31.385 second question is

NOTE Confidence: 0.766309903333333

00:52:31.385 --> 00:52:32.600 regarding your presentation

NOTE Confidence: 0.656145915714286

00:52:32.610 --> 00:52:35.196 and also there's some experts also

NOTE Confidence: 0.656145915714286

00:52:35.196 --> 00:52:37.954 speculate that the AI D18 losses

NOTE Confidence: 0.656145915714286

00:52:37.954 --> 00:52:40.782 also should be in that category,

NOTE Confidence: 0.656145915714286

00:52:40.782 --> 00:52:43.603 but so far nobody has discovered any

NOTE Confidence: 0.656145915714286

00:52:43.603 --> 00:52:45.842 case yet, at least in the literature.

NOTE Confidence: 0.656145915714286

00:52:45.842 --> 00:52:47.890 And So what do you think?

NOTE Confidence: 0.656145915714286

00:52:47.890 --> 00:52:48.889 So that's interesting,

NOTE Confidence: 0.656145915714286

00:52:48.889 --> 00:52:51.220 so I think there's a couple cases

NOTE Confidence: 0.656145915714286

00:52:51.283 --> 00:52:53.977 that have error 1A mutations in

NOTE Confidence: 0.656145915714286

00:52:53.977 --> 00:52:55.324 sinonasal neuroendocrine carcinomas.  
NOTE Confidence: 0.656145915714286

00:52:55.330 --> 00:52:57.733 I think there was a paper from out of  
NOTE Confidence: 0.656145915714286

00:52:57.733 --> 00:53:00.886 MSK a couple years ago that sequenced  
NOTE Confidence: 0.656145915714286

00:53:00.886 --> 00:53:02.296 some neuroendocrine carcinomas.  
NOTE Confidence: 0.656145915714286

00:53:02.300 --> 00:53:04.344 And I think there may have been  
NOTE Confidence: 0.656145915714286

00:53:04.344 --> 00:53:06.969 one or two mutations in that there.  
NOTE Confidence: 0.656145915714286

00:53:06.970 --> 00:53:08.930 I know we have some emerging data.  
NOTE Confidence: 0.656145915714286

00:53:08.930 --> 00:53:10.315 There's some weird neuro epithelial  
NOTE Confidence: 0.656145915714286

00:53:10.315 --> 00:53:12.356 tumors that I didn't get into here  
NOTE Confidence: 0.656145915714286

00:53:12.356 --> 00:53:14.180 that are kind of overlap between  
NOTE Confidence: 0.656145915714286

00:53:14.180 --> 00:53:15.489 olfactory neuroblastoma and carcinoma.  
NOTE Confidence: 0.656145915714286

00:53:15.490 --> 00:53:17.380 And we have at least one of those that have.  
NOTE Confidence: 0.656145915714286

00:53:17.380 --> 00:53:19.100 I have an error with 1A mutation 2,  
NOTE Confidence: 0.656145915714286

00:53:19.100 --> 00:53:20.765 so I think there's probably more more of a  
NOTE Confidence: 0.656145915714286

00:53:20.765 --> 00:53:22.498 role for the other partners coming forward.  
NOTE Confidence: 0.656145915714286

00:53:22.500 --> 00:53:24.300 I think. I think it's probably I mean,



NOTE Confidence: 0.656145915714286  
00:53:24.300 --> 00:53:24.954 for whatever reason,  
NOTE Confidence: 0.656145915714286  
00:53:24.954 --> 00:53:26.480 smart B1 is the most common here,  
NOTE Confidence: 0.656145915714286  
00:53:26.480 --> 00:53:27.915 so that's that's what we figured out,  
NOTE Confidence: 0.656145915714286  
00:53:27.920 --> 00:53:29.918 but I think I think there's going to be  
NOTE Confidence: 0.656145915714286  
00:53:29.918 --> 00:53:31.520 more kind of figured out going forward.  
NOTE Confidence: 0.656145915714286  
00:53:31.520 --> 00:53:33.380 I think it's it's definitely  
NOTE Confidence: 0.656145915714286  
00:53:33.380 --> 00:53:34.496 floating around there.  
NOTE Confidence: 0.656145915714286  
00:53:34.500 --> 00:53:35.250 OK, thank you.  
NOTE Confidence: 0.30511427  
00:53:37.210 --> 00:53:41.526 Oh Lisa, do you mind on sharing your  
NOTE Confidence: 0.30511427  
00:53:41.530 --> 00:53:44.230 screen so I can see if there are  
NOTE Confidence: 0.30511427  
00:53:44.230 --> 00:53:47.368 any hands that are OK? Thank you.  
NOTE Confidence: 0.30511427  
00:53:47.368 --> 00:53:51.466 I don't see any hands up right now,  
NOTE Confidence: 0.30511427  
00:53:51.466 --> 00:53:54.730 so I'll go ahead and ask my question.  
NOTE Confidence: 0.30511427  
00:53:54.730 --> 00:53:58.648 You said that 83% of Sinonasal  
NOTE Confidence: 0.30511427  
00:53:58.650 --> 00:54:00.106 Lascelles Newland, Ukraine,  
NOTE Confidence: 0.30511427

00:54:00.106 --> 00:54:02.254 cold snow Mars turned out  
NOTE Confidence: 0.30511427

00:54:02.254 --> 00:54:04.264 to have IDH 2 mutation.  
NOTE Confidence: 0.30511427

00:54:04.270 --> 00:54:06.686 What about the LC next of the lung?  
NOTE Confidence: 0.30511427

00:54:06.690 --> 00:54:07.800 Do they have the same?  
NOTE Confidence: 0.26466308425

00:54:08.290 --> 00:54:10.570 They don't. Come early.  
NOTE Confidence: 0.903194185714286

00:54:12.850 --> 00:54:14.250 Yeah, at least most of them don't.  
NOTE Confidence: 0.903194185714286

00:54:14.250 --> 00:54:15.058 I mean, largest owner,  
NOTE Confidence: 0.903194185714286

00:54:15.058 --> 00:54:16.068 different person over the lung.  
NOTE Confidence: 0.903194185714286

00:54:16.070 --> 00:54:17.984 To my you know somewhat novice  
NOTE Confidence: 0.903194185714286

00:54:17.984 --> 00:54:19.719 understanding of it is kind  
NOTE Confidence: 0.903194185714286

00:54:19.719 --> 00:54:21.307 of three different pathways,  
NOTE Confidence: 0.903194185714286

00:54:21.310 --> 00:54:22.126 and it's probably similar  
NOTE Confidence: 0.903194185714286

00:54:22.126 --> 00:54:23.146 in the head and neck.  
NOTE Confidence: 0.903194185714286

00:54:23.150 --> 00:54:24.625 Honestly, it's kind of an  
NOTE Confidence: 0.903194185714286

00:54:24.625 --> 00:54:25.805 amalgamation of different things.  
NOTE Confidence: 0.903194185714286

00:54:25.810 --> 00:54:27.834 Some of them are more like small cells

NOTE Confidence: 0.903194185714286

00:54:27.834 --> 00:54:29.554 and small cells than most most sites

NOTE Confidence: 0.903194185714286

00:54:29.554 --> 00:54:31.770 not in not in the center nasal tract.

NOTE Confidence: 0.903194185714286

00:54:31.770 --> 00:54:32.170 Interestingly,

NOTE Confidence: 0.903194185714286

00:54:32.170 --> 00:54:34.826 but most other sites have P53RB mutations,

NOTE Confidence: 0.903194185714286

00:54:34.826 --> 00:54:36.794 some of them some of large

NOTE Confidence: 0.903194185714286

00:54:36.794 --> 00:54:39.386 hereunder in the lung do have the

NOTE Confidence: 0.903194185714286

00:54:39.386 --> 00:54:40.508 same mutations adenocarcinoma,

NOTE Confidence: 0.903194185714286

00:54:40.510 --> 00:54:43.120 so you might actually find a few with with.

NOTE Confidence: 0.903194185714286

00:54:43.120 --> 00:54:45.448 Smarca 4 there because that's actually,

NOTE Confidence: 0.903194185714286

00:54:45.450 --> 00:54:46.120 you know,

NOTE Confidence: 0.903194185714286

00:54:46.120 --> 00:54:47.795 reasonably common in lung adenocarcinoma,

NOTE Confidence: 0.903194185714286

00:54:47.800 --> 00:54:49.900 Stew and then summer like carcinoids.

NOTE Confidence: 0.903194185714286

00:54:49.900 --> 00:54:52.238 So I think it's probably analogous in

NOTE Confidence: 0.903194185714286

00:54:52.238 --> 00:54:54.859 the head and neck that large scale

NOTE Confidence: 0.903194185714286

00:54:54.859 --> 00:54:56.794 neuroendocrine with some of them

NOTE Confidence: 0.903194185714286

00:54:56.794 --> 00:54:59.908 are kind of like snuck some of them.  
NOTE Confidence: 0.903194185714286

00:54:59.908 --> 00:55:02.680 I didn't get into that now.  
NOTE Confidence: 0.903194185714286

00:55:02.680 --> 00:55:04.857 Some of them also have HPV as  
NOTE Confidence: 0.903194185714286

00:55:04.857 --> 00:55:07.019 well as small cell carcinomas.  
NOTE Confidence: 0.903194185714286

00:55:07.020 --> 00:55:09.084 That's fairly commonly seen in sinonasal  
NOTE Confidence: 0.903194185714286

00:55:09.084 --> 00:55:10.460 neuroendocrine carcinomas as well,  
NOTE Confidence: 0.903194185714286

00:55:10.460 --> 00:55:11.940 so.  
NOTE Confidence: 0.903194185714286

00:55:11.940 --> 00:55:12.849 Probably mixed bag.  
NOTE Confidence: 0.8270769

00:55:14.470 --> 00:55:16.690 The other question I have is  
NOTE Confidence: 0.8270769

00:55:16.690 --> 00:55:19.990 as of today in your practice,  
NOTE Confidence: 0.8270769

00:55:19.990 --> 00:55:22.228 how do you pick this deck?  
NOTE Confidence: 0.8270769

00:55:22.230 --> 00:55:23.865 F2 carcinomas because  
NOTE Confidence: 0.8270769

00:55:23.865 --> 00:55:26.045 Histology is not enough.  
NOTE Confidence: 0.8270769

00:55:26.050 --> 00:55:28.970 You would suspect it based on the Histology.  
NOTE Confidence: 0.8270769

00:55:28.970 --> 00:55:31.834 Where do you send it out to confirm,  
NOTE Confidence: 0.8270769

00:55:31.840 --> 00:55:34.000 and what tests do you request?

NOTE Confidence: 0.95303745

00:55:34.740 --> 00:55:36.336 So it's it's super frustrating right

NOTE Confidence: 0.95303745

00:55:36.336 --> 00:55:38.239 now because it's not widely available.

NOTE Confidence: 0.95303745

00:55:38.240 --> 00:55:40.035 Testing it is not available

NOTE Confidence: 0.95303745

00:55:40.035 --> 00:55:42.180 on our fusion panel here yet.

NOTE Confidence: 0.95303745

00:55:42.180 --> 00:55:44.308 There is a fish that is now

NOTE Confidence: 0.95303745

00:55:44.308 --> 00:55:45.920 available at PROPATH in Dallas,

NOTE Confidence: 0.95303745

00:55:45.920 --> 00:55:48.824 TX and and that is is is one

NOTE Confidence: 0.95303745

00:55:48.824 --> 00:55:52.176 place I have have sent one thing.

NOTE Confidence: 0.95303745

00:55:52.180 --> 00:55:53.998 I have heard rumors that there

NOTE Confidence: 0.95303745

00:55:53.998 --> 00:55:55.818 is an immunostain and we might

NOTE Confidence: 0.95303745

00:55:55.818 --> 00:55:57.438 be hearing about it at uscap

NOTE Confidence: 0.95303745

00:55:57.440 --> 00:55:59.105 that that there's a forthcoming

NOTE Confidence: 0.95303745

00:55:59.105 --> 00:56:01.040 immunostain that picks up after two,

NOTE Confidence: 0.95303745

00:56:01.040 --> 00:56:03.752 and I think that that hopefully will help

NOTE Confidence: 0.95303745

00:56:03.752 --> 00:56:05.998 us recognize these more in the future

NOTE Confidence: 0.95303745

00:56:06.000 --> 00:56:07.746 since it doesn't have treatment implications.

NOTE Confidence: 0.95303745

00:56:07.750 --> 00:56:09.612 At this point I have been mostly

NOTE Confidence: 0.95303745

00:56:09.612 --> 00:56:11.220 signing these out descriptively,

NOTE Confidence: 0.95303745

00:56:11.220 --> 00:56:13.054 unless the clinicians really want to know,

NOTE Confidence: 0.95303745

00:56:13.060 --> 00:56:16.329 and kind of say it has morphologic

NOTE Confidence: 0.95303745

00:56:16.329 --> 00:56:18.639 features suggestive of decaf too.

NOTE Confidence: 0.95303745

00:56:18.640 --> 00:56:20.432 And and we can kind of pursue

NOTE Confidence: 0.95303745

00:56:20.432 --> 00:56:21.850 the testing if necessary,

NOTE Confidence: 0.95303745

00:56:21.850 --> 00:56:22.680 but I think we're a

NOTE Confidence: 0.95303745

00:56:22.680 --> 00:56:23.344 little ahead of ourselves.

NOTE Confidence: 0.95303745

00:56:23.350 --> 00:56:25.894 I think in terms of recognizing these these

NOTE Confidence: 0.95303745

00:56:25.894 --> 00:56:28.129 fusions on research based sequencing,

NOTE Confidence: 0.95303745

00:56:28.130 --> 00:56:29.760 but not necessarily being able

NOTE Confidence: 0.95303745

00:56:29.760 --> 00:56:31.390 to find them clinically yet.

NOTE Confidence: 0.95303745

00:56:31.390 --> 00:56:32.318 But hopefully they will.

NOTE Confidence: 0.95303745

00:56:32.318 --> 00:56:32.550 Again,

NOTE Confidence: 0.95303745

00:56:32.550 --> 00:56:34.558 there will be a stain coming coming shortly.

NOTE Confidence: 0.70837376

00:56:36.400 --> 00:56:39.595 The third question I have is do you order

NOTE Confidence: 0.70837376

00:56:39.600 --> 00:56:44.185 CD 99 on all non keratinizing carcinoma

NOTE Confidence: 0.70837376

00:56:44.185 --> 00:56:47.770 as I do no scared after your talks? Yes

NOTE Confidence: 0.821321155

00:56:48.490 --> 00:56:50.698 I'm always worried about missing adamantine

NOTE Confidence: 0.821321155

00:56:50.698 --> 00:56:53.275 oma like Ewing because that will be a

NOTE Confidence: 0.821321155

00:56:53.275 --> 00:56:55.125 big treatment change I I think they

NOTE Confidence: 0.821321155

00:56:55.125 --> 00:56:57.687 do tend to air here on on doing chemo.

NOTE Confidence: 0.821321155

00:56:57.690 --> 00:56:59.040 For that you know. Again,

NOTE Confidence: 0.821321155

00:56:59.040 --> 00:57:00.980 it's controversial whether that's right

NOTE Confidence: 0.821321155

00:57:00.980 --> 00:57:03.512 or that's wrong but but I at least

NOTE Confidence: 0.821321155

00:57:03.512 --> 00:57:05.760 want that to be in the discussion.

NOTE Confidence: 0.821321155

00:57:05.760 --> 00:57:08.890 So if I do have a non Karen Ising carcinoma

NOTE Confidence: 0.821321155

00:57:08.963 --> 00:57:11.803 that chose squamous differentiation I

NOTE Confidence: 0.821321155

00:57:11.803 --> 00:57:13.268 or another undifferentiated tumor that

NOTE Confidence: 0.821321155

00:57:13.268 --> 00:57:15.349 I'm having a hard time classifying,  
NOTE Confidence: 0.821321155

00:57:15.350 --> 00:57:19.870 I will do a CD 99 for trainees.  
NOTE Confidence: 0.821321155

00:57:19.870 --> 00:57:22.262 At the end, you know NKX 2.2 is  
NOTE Confidence: 0.821321155

00:57:22.262 --> 00:57:23.966 also a great great Ewing marker,  
NOTE Confidence: 0.821321155

00:57:23.970 --> 00:57:25.979 but there's a lot more overlap with  
NOTE Confidence: 0.821321155

00:57:25.979 --> 00:57:27.979 other entities in the sinonasal tract,  
NOTE Confidence: 0.821321155

00:57:27.980 --> 00:57:31.325 so NTX 2.2 tends to stain a lot of things  
NOTE Confidence: 0.821321155

00:57:31.325 --> 00:57:32.650 with neuroendocrine differentiation,  
NOTE Confidence: 0.821321155

00:57:32.650 --> 00:57:34.330 and you see it in a lot of  
NOTE Confidence: 0.821321155

00:57:34.330 --> 00:57:34.750 olfactory neuroblastomas,  
NOTE Confidence: 0.821321155

00:57:34.750 --> 00:57:37.000 so I tend to air on CD 99 for that reason.  
NOTE Confidence: 0.728688662

00:57:39.380 --> 00:57:43.800 It's a good good learning. Call message  
NOTE Confidence: 0.911978777142857

00:57:45.470 --> 00:57:47.405 is there another question in  
NOTE Confidence: 0.911978777142857

00:57:47.405 --> 00:57:50.530 the chat? Uh, something cropped  
NOTE Confidence: 0.719996628888889

00:57:50.540 --> 00:57:53.708 up, yeah? How do you assess  
NOTE Confidence: 0.719996628888889

00:57:53.708 --> 00:57:55.292 global DNA methylation?



NOTE Confidence: 0.719996628888889

00:57:55.300 --> 00:57:58.204 In your talk, there were a number of

NOTE Confidence: 0.719996628888889

00:57:58.204 --> 00:58:01.110 entities that seemed to show distinctive

NOTE Confidence: 0.719996628888889

00:58:01.110 --> 00:58:03.214 patterns of global methylation.

NOTE Confidence: 0.719996628888889

00:58:03.220 --> 00:58:06.030 How widely have you applied

NOTE Confidence: 0.719996628888889

00:58:06.030 --> 00:58:08.278 this test in tumors?

NOTE Confidence: 0.719996628888889

00:58:08.280 --> 00:58:11.196 Does it provide classification

NOTE Confidence: 0.719996628888889

00:58:11.196 --> 00:58:14.112 information that is substantially

NOTE Confidence: 0.719996628888889

00:58:14.112 --> 00:58:16.499 different than RNA seq?

NOTE Confidence: 0.913606012

00:58:17.190 --> 00:58:18.890 That is an excellent question.

NOTE Confidence: 0.913606012

00:58:18.890 --> 00:58:20.794 We have not used it widely widely at

NOTE Confidence: 0.913606012

00:58:20.794 --> 00:58:23.094 all at that point that that that chart

NOTE Confidence: 0.913606012

00:58:23.094 --> 00:58:24.855 that I was presenting was actually

NOTE Confidence: 0.913606012

00:58:24.855 --> 00:58:26.710 from from from MSK who did it.

NOTE Confidence: 0.913606012

00:58:26.710 --> 00:58:28.420 Some generally speaking,

NOTE Confidence: 0.913606012

00:58:28.420 --> 00:58:30.130 the methylation analysis.

NOTE Confidence: 0.913606012

00:58:30.130 --> 00:58:31.605 It's beginning to be used  
NOTE Confidence: 0.913606012

00:58:31.605 --> 00:58:32.490 widely in neuropathology,  
NOTE Confidence: 0.913606012

00:58:32.490 --> 00:58:33.930 but it's not widely available  
NOTE Confidence: 0.913606012

00:58:33.930 --> 00:58:36.330 as a test on my understanding,  
NOTE Confidence: 0.913606012

00:58:36.330 --> 00:58:38.325 in any neuropathologists can can chime in.  
NOTE Confidence: 0.913606012

00:58:38.330 --> 00:58:39.398 Here are neuropathologists,  
NOTE Confidence: 0.913606012

00:58:39.398 --> 00:58:42.169 as with I think multiple institutions in the  
NOTE Confidence: 0.913606012

00:58:42.169 --> 00:58:44.588 country send it all to the NIH to get done,  
NOTE Confidence: 0.913606012

00:58:44.588 --> 00:58:46.590 so it's not a test at all.  
NOTE Confidence: 0.913606012

00:58:46.590 --> 00:58:49.100 That is, is widely available.  
NOTE Confidence: 0.913606012

00:58:49.100 --> 00:58:50.060 And I think it's,  
NOTE Confidence: 0.913606012

00:58:50.060 --> 00:58:51.260 and I think it provides  
NOTE Confidence: 0.913606012

00:58:51.260 --> 00:58:52.090 interesting information.  
NOTE Confidence: 0.913606012

00:58:52.090 --> 00:58:53.428 You know it's an interesting Lee.  
NOTE Confidence: 0.913606012

00:58:53.430 --> 00:58:55.060 Different way to classify it,  
NOTE Confidence: 0.913606012

00:58:55.060 --> 00:58:56.580 and if we're able to do it more,

NOTE Confidence: 0.913606012

00:58:56.580 --> 00:58:57.675 I think it will definitely

NOTE Confidence: 0.913606012

00:58:57.675 --> 00:58:59.060 be great to see you know.

NOTE Confidence: 0.913606012

00:58:59.060 --> 00:59:01.223 Does it add benefits to to classification

NOTE Confidence: 0.913606012

00:59:01.223 --> 00:59:02.459 to answer answer challenging

NOTE Confidence: 0.913606012

00:59:02.459 --> 00:59:04.499 questions or or you know is is RNA

NOTE Confidence: 0.913606012

00:59:04.499 --> 00:59:06.360 C giving us everything we need?

NOTE Confidence: 0.913606012

00:59:06.360 --> 00:59:08.033 I think that's a that's a great

NOTE Confidence: 0.913606012

00:59:08.033 --> 00:59:09.843 question and still a very early in

NOTE Confidence: 0.913606012

00:59:09.843 --> 00:59:11.143 the emergence of that technology.

NOTE Confidence: 0.5603736

00:59:13.600 --> 00:59:16.420 OK, thank you so much Lisa.

NOTE Confidence: 0.890592248571428

00:59:16.420 --> 00:59:19.220 I don't see any other hands up.

NOTE Confidence: 0.890592248571428

00:59:19.220 --> 00:59:21.920 This was really very very educational

NOTE Confidence: 0.890592248571428

00:59:21.920 --> 00:59:25.260 for us head and neck with Ologist

NOTE Confidence: 0.890592248571428

00:59:25.260 --> 00:59:27.948 and I hope others also enjoyed it.

NOTE Confidence: 0.966849775714286

00:59:28.760 --> 00:59:31.780 Thank you so much for having me. Thank you.