WEBVTT

NOTE duration:"01:06:12"

NOTE recognizability:0.928

NOTE language:en-us

NOTE Confidence: 0.896323206

00:00:00.000 --> 00:00:03.192 It's my great pleasure to introduce

NOTE Confidence: 0.896323206

00:00:03.192 --> 00:00:05.585 Doctor Fadari for today's Who's

NOTE Confidence: 0.896323206

00:00:05.585 --> 00:00:07.440 going to Give us the grand Rounds?

NOTE Confidence: 0.896323206

00:00:07.440 --> 00:00:10.320 He's Professor of Pathology and Chief

NOTE Confidence: 0.896323206

00:00:10.320 --> 00:00:13.515 of Anatomic Pathology at University of

NOTE Confidence: 0.896323206

00:00:13.515 --> 00:00:16.440 California San Diego Health System,

NOTE Confidence: 0.896323206

00:00:16.440 --> 00:00:19.177 and he received his MD degree from

NOTE Confidence: 0.896323206

00:00:19.177 --> 00:00:21.124 Harvard University, Washington, DC,

NOTE Confidence: 0.896323206

00:00:21.124 --> 00:00:24.616 followed by residency in anatomic and

NOTE Confidence: 0.896323206

00:00:24.616 --> 00:00:27.399 clinical pathology at Yale University.

NOTE Confidence: 0.896323206

00:00:27.400 --> 00:00:29.416 He then completed his fellowship in

NOTE Confidence: 0.896323206

00:00:29.416 --> 00:00:31.498 breast and. Gynecologic pathology,

NOTE Confidence: 0.896323206

00:00:31.498 --> 00:00:35.798 also at Yale and his clinical and

NOTE Confidence: 0.896323206

00:00:35.798 --> 00:00:37.986 Consultation practice is focused

NOTE Confidence: 0.896323206

00:00:37.986 --> 00:00:40.688 on gynecologic and breast cancers.

NOTE Confidence: 0.896323206

00:00:40.690 --> 00:00:44.128 He is lectured widely on these

NOTE Confidence: 0.896323206

00:00:44.128 --> 00:00:45.847 and related topics.

NOTE Confidence: 0.896323206

00:00:45.850 --> 00:00:47.822 He has authored, coauthored,

NOTE Confidence: 0.896323206

00:00:47.822 --> 00:00:52.770 and edited over 230 papers and five books,

NOTE Confidence: 0.896323206

00:00:52.770 --> 00:00:56.226 predominantly in gynecological pathology.

NOTE Confidence: 0.896323206

00:00:56.226 --> 00:00:59.070 And he is.

NOTE Confidence: 0.896323206

00:00:59.070 --> 00:01:03.370 Serves on the editorial board of several

NOTE Confidence: 0.896323206

00:01:03.370 --> 00:01:05.550 leading prestigious pathology journals,

NOTE Confidence: 0.896323206

00:01:05.550 --> 00:01:08.002 which include Modern Pathology,

NOTE Confidence: 0.896323206

00:01:08.002 --> 00:01:09.228 Human Pathology,

NOTE Confidence: 0.896323206

00:01:09.230 --> 00:01:12.386 Archives of Pathology in Laboratory Medicine,

NOTE Confidence: 0.896323206

00:01:12.390 --> 00:01:13.974 International Journal of

NOTE Confidence: 0.896323206

00:01:13.974 --> 00:01:15.030 Gynecologic Pathology,

NOTE Confidence: 0.896323206

00:01:15.030 --> 00:01:18.306 and American Journal of Clinical Pathology.

NOTE Confidence: 0.896323206

00:01:18.310 --> 00:01:19.510 He was the 20.

NOTE Confidence: 0.896323206

00:01:19.510 --> 00:01:22.008 He was a recipient of the 2018.

NOTE Confidence: 0.896323206

00:01:22.008 --> 00:01:26.894 Arthur Purdist Out Price Without further ado,

NOTE Confidence: 0.896323206

00:01:26.900 --> 00:01:28.808 I'll hand over the floor to

NOTE Confidence: 0.896323206

00:01:28.808 --> 00:01:30.780 Doctor Fedore who will talk about

NOTE Confidence: 0.896323206

00:01:30.780 --> 00:01:32.740 Volvo's famous cell carcinoma

NOTE Confidence: 0.896323206

00:01:32.740 --> 00:01:34.700 and putative precursor lesions,

NOTE Confidence: 0.896323206

00:01:34.700 --> 00:01:35.520 historical evolution,

NOTE Confidence: 0.896323206

00:01:35.520 --> 00:01:37.570 and recent developments in the

NOTE Confidence: 0.896323206

00:01:37.570 --> 00:01:39.660 tale of stasis and progress.

NOTE Confidence: 0.896323206

00:01:39.660 --> 00:01:41.658 At the end of the lecture,

NOTE Confidence: 0.896323206

00:01:41.660 --> 00:01:43.945 please unmute yourself and ask

NOTE Confidence: 0.896323206

00:01:43.945 --> 00:01:47.539 questions or you can post it on the chat.

NOTE Confidence: 0.896323206

00:01:47.540 --> 00:01:47.984 Thank you,

NOTE Confidence: 0.896323206

00:01:47.984 --> 00:01:48.428 Doctor Fedore.

NOTE Confidence: 0.896323206

00:01:48.428 --> 00:01:49.538 I'll hand it to you.

NOTE Confidence: 0.871703007142857

00:01:51.450 --> 00:01:53.802 Thank you Doctor Krishnanodi

NOTE Confidence: 0.871703007142857

00:01:53.802 --> 00:01:55.566 for that introduction.

NOTE Confidence: 0.871703007142857

00:01:55.570 --> 00:01:57.578 It's really a privilege

NOTE Confidence: 0.871703007142857

00:01:57.578 --> 00:02:00.088 to to address y'all today.

NOTE Confidence: 0.871703007142857

00:02:00.090 --> 00:02:03.040 I can hardly believe it's been almost 20

NOTE Confidence: 0.871703007142857

00:02:03.040 --> 00:02:05.650 years since I've completed my training,

NOTE Confidence: 0.871703007142857

00:02:05.650 --> 00:02:10.690 but that's essentially how it goes.

NOTE Confidence: 0.871703007142857

00:02:10.690 --> 00:02:14.518 So this presentation is about

NOTE Confidence: 0.871703007142857

00:02:14.518 --> 00:02:16.159 Volvo squimmerso carcinomer.

NOTE Confidence: 0.871703007142857

00:02:16.160 --> 00:02:18.824 And I will talk about historical

NOTE Confidence: 0.871703007142857

00:02:18.824 --> 00:02:21.069 evolution of the precancerous as

NOTE Confidence: 0.871703007142857

00:02:21.069 --> 00:02:23.039 well as the cancerous lesions,

NOTE Confidence: 0.871703007142857

00:02:23.040 --> 00:02:26.112 as well as pathologic diagnosis and

NOTE Confidence: 0.871703007142857

00:02:26.112 --> 00:02:29.439 various other aspects of those lesions.

NOTE Confidence: 0.871703007142857

00:02:29.440 --> 00:02:32.576 It is often said that ***** cancer

NOTE Confidence: 0.871703007142857

00:02:32.576 --> 00:02:37.280 was initially described in 562AD,

NOTE Confidence: 0.871703007142857

00:02:37.280 --> 00:02:39.536 although if you look at works

NOTE Confidence: 0.871703007142857

00:02:39.536 --> 00:02:41.040 of Asus of Amida,

NOTE Confidence: 0.871703007142857

00:02:41.040 --> 00:02:43.976 who in his classic work to forbid with.

NOTE Confidence: 0.871703007142857

00:02:43.980 --> 00:02:46.253 The last one was focused on ***** cancers,

NOTE Confidence: 0.871703007142857

00:02:46.253 --> 00:02:48.818 and there were several considerations

NOTE Confidence: 0.871703007142857

00:02:48.820 --> 00:02:51.724 of excising ***** cancer and citation

NOTE Confidence: 0.871703007142857

00:02:51.724 --> 00:02:54.379 of previous works prior to that.

NOTE Confidence: 0.871703007142857

00:02:54.380 --> 00:02:56.738 In any event, for whatever reason,

NOTE Confidence: 0.871703007142857

00:02:56.740 --> 00:02:59.550 there was not a lot written for many,

NOTE Confidence: 0.871703007142857

00:02:59.550 --> 00:03:01.375 many years after that documented,

NOTE Confidence: 0.871703007142857

00:03:01.380 --> 00:03:02.940 I should say, for many,

NOTE Confidence: 0.871703007142857

00:03:02.940 --> 00:03:04.508 many years after that.

NOTE Confidence: 0.871703007142857

00:03:04.508 --> 00:03:06.136 Indeed, when you look at some of

NOTE Confidence: 0.871703007142857

00:03:06.136 --> 00:03:07.860 the earliest works in anatomic pathology,

NOTE Confidence: 0.871703007142857

00:03:07.860 --> 00:03:10.260 including this work by Samuel Gross,

NOTE Confidence: 0.871703007142857

00:03:10.260 --> 00:03:12.470 there's no mention whatsoever of.

NOTE Confidence: 0.871703007142857

00:03:12.470 --> 00:03:13.802 ***** all causing numbers.

NOTE Confidence: 0.871703007142857

00:03:13.802 --> 00:03:16.018 These are all the ***** diseases

NOTE Confidence: 0.871703007142857

00:03:16.018 --> 00:03:19.306 that were listed in that text.

NOTE Confidence: 0.871703007142857

00:03:19.310 --> 00:03:19.830 However,

NOTE Confidence: 0.871703007142857

00:03:19.830 --> 00:03:23.250 by the end of the 19th century,

NOTE Confidence: 0.871703007142857

00:03:23.250 --> 00:03:25.710 certainly ***** cancer was well established.

NOTE Confidence: 0.871703007142857

00:03:25.710 --> 00:03:27.750 So much so that if you look at

NOTE Confidence: 0.871703007142857

00:03:27.750 --> 00:03:29.627 this classic text by James Zenwing,

NOTE Confidence: 0.871703007142857

00:03:29.630 --> 00:03:30.695 the last paragraph,

NOTE Confidence: 0.871703007142857

00:03:30.695 --> 00:03:33.214 let's talk about how ***** cancer

NOTE Confidence: 0.871703007142857

00:03:33.214 --> 00:03:36.190 usually terminates without operation,

NOTE Confidence: 0.871703007142857

00:03:36.190 --> 00:03:37.990 you know, within two years after

NOTE Confidence: 0.871703007142857

00:03:37.990 --> 00:03:39.190 discovery of the lesion,

NOTE Confidence: 0.871703007142857

00:03:39.190 --> 00:03:40.330 and indeed.

NOTE Confidence: 0.871703007142857

00:03:40.330 --> 00:03:44.780 When you look at some of the early

NOTE Confidence: 0.871703007142857

00:03:44.780 --> 00:03:47.540 series or the series that were

NOTE Confidence: 0.871703007142857

00:03:47.540 --> 00:03:49.827 published early in the last part of the

NOTE Confidence: 0.871703007142857

00:03:49.827 --> 00:03:51.840 last early part of the last century,

NOTE Confidence: 0.871703007142857

00:03:51.840 --> 00:03:53.877 you can see that the cure rates

NOTE Confidence: 0.871703007142857

00:03:53.877 --> 00:03:55.888 range from anywhere from 8 to 25%.

NOTE Confidence: 0.871703007142857

00:03:55.888 --> 00:03:58.160 It was quite dismal.

NOTE Confidence: 0.871703007142857

00:03:58.160 --> 00:04:00.240 Of course, things have changed.

NOTE Confidence: 0.871703007142857

00:04:00.240 --> 00:04:02.598 This is global gun data and it

NOTE Confidence: 0.871703007142857

00:04:02.598 --> 00:04:04.293 highlights the fact that number

NOTE Confidence: 0.871703007142857

00:04:04.293 --> 00:04:06.149 one vulval cancers are uncommon.

NOTE Confidence: 0.871703007142857

00:04:06.150 --> 00:04:08.172 But out of 45,000 cases you

NOTE Confidence: 0.871703007142857

00:04:08.172 --> 00:04:10.046 can see that 17,000 deaths.

NOTE Confidence: 0.871703007142857

00:04:10.046 --> 00:04:12.186 So things have certainly improved

NOTE Confidence: 0.871703007142857

00:04:12.186 --> 00:04:14.549 with respect to survival rates as

NOTE Confidence: 0.871703007142857

00:04:14.549 --> 00:04:16.894 compared to the turn of the last

NOTE Confidence: 0.871703007142857

00:04:16.961 --> 00:04:18.310 century in the United States.

NOTE Confidence: 0.871703007142857

00:04:18.310 --> 00:04:19.986 You can see that the five year

NOTE Confidence: 0.871703007142857

00:04:19.986 --> 00:04:21.542 relative survival for ***** cancer

NOTE Confidence: 0.871703007142857

00:04:21.542 --> 00:04:24.566 is around 7 to 1.1% and that has

NOTE Confidence: 0.871703007142857

00:04:24.566 --> 00:04:26.990 remained stable for the most part.

NOTE Confidence: 0.871703007142857

00:04:26.990 --> 00:04:29.007 Now the vast majority of ***** cancers

NOTE Confidence: 0.871703007142857

00:04:29.007 --> 00:04:31.492 are are squamous cell carcinomas

NOTE Confidence: 0.871703007142857

00:04:31.492 --> 00:04:34.862 more than 90% and so I would.

NOTE Confidence: 0.871703007142857

00:04:34.862 --> 00:04:36.734 Discussed 6 discrete things.

NOTE Confidence: 0.871703007142857

00:04:36.740 --> 00:04:39.008 A lot of these are controversial

NOTE Confidence: 0.871703007142857

00:04:39.008 --> 00:04:41.948 in some way or there's some

NOTE Confidence: 0.871703007142857

00:04:41.948 --> 00:04:44.060 disagreement in some way about them.

NOTE Confidence: 0.871703007142857

00:04:44.060 --> 00:04:46.580 And so I'll just kind of

NOTE Confidence: 0.871703007142857

00:04:46.580 --> 00:04:49.140 explore some of this items,

NOTE Confidence: 0.871703007142857

00:04:49.140 --> 00:04:51.780 including their pathology,

NOTE Confidence: 0.871703007142857

00:04:51.780 --> 00:04:54.060 the basic pathology,

NOTE Confidence: 0.871703007142857

00:04:54.060 --> 00:04:57.378 the first relates to HVV status,

NOTE Confidence: 0.871703007142857

00:04:57.380 --> 00:05:02.450 this meta analysis of over 8000 patients.

NOTE Confidence: 0.871703007142857

00:05:02.450 --> 00:05:05.270 And numerous dozens of studies show

NOTE Confidence: 0.871703007142857

00:05:05.270 --> 00:05:08.271 that the group prevalence of HPV

NOTE Confidence: 0.871703007142857

00:05:08.271 --> 00:05:10.781 positivity and all the squamous

NOTE Confidence: 0.871703007142857

00:05:10.781 --> 00:05:13.233 cell carcinoma is around 39.1%,

NOTE Confidence: 0.871703007142857

00:05:13.233 --> 00:05:17.211 those that are assessed by P16

NOTE Confidence: 0.871703007142857

00:05:17.211 --> 00:05:20.302 immunostochemistry that is around 34.1%.

NOTE Confidence: 0.871703007142857

00:05:20.302 --> 00:05:22.534 And the best data on the

NOTE Confidence: 0.871703007142857

00:05:22.534 --> 00:05:24.246 significance of HPV positivity

NOTE Confidence: 0.871703007142857

00:05:24.246 --> 00:05:26.836 also comes from a metaanalysis

NOTE Confidence: 0.871703007142857

00:05:26.836 --> 00:05:28.908 wherein the authors concluded

NOTE Confidence: 0.924872583333333

00:05:28.986 --> 00:05:32.199 that woman with HPV positive vulval cancers.

NOTE Confidence: 0.924872583333333

00:05:32.200 --> 00:05:35.798 Have superior survival when compared to those

NOTE Confidence: 0.924872583333333

00:05:35.798 --> 00:05:40.346 that are HPV negative with H R's 0.61 and

NOTE Confidence: 0.924872583333333

00:05:40.346 --> 00:05:43.832 0.75 for five years OS&DFS respectively.

NOTE Confidence: 0.924872583333333

00:05:43.832 --> 00:05:46.928 However, when you look at more

NOTE Confidence: 0.924872583333333

00:05:46.928 --> 00:05:48.893 recent studies, this is studies

NOTE Confidence: 0.924872583333333

00:05:48.893 --> 00:05:50.759 published in the last 10 years,

NOTE Confidence: 0.924872583333333

00:05:50.760 --> 00:05:53.480 the picture becomes a little bit more murky.

NOTE Confidence: 0.924872583333333

00:05:53.480 --> 00:05:55.958 You can see here that most studies,

NOTE Confidence: 0.924872583333333

00:05:55.960 --> 00:05:57.724 about 61% of studies,

NOTE Confidence: 0.924872583333333

00:05:57.724 --> 00:05:59.929 have not found HPV positivity.

NOTE Confidence: 0.924872583333333

00:05:59.930 --> 00:06:04.820 To be associated with better to be to be

NOTE Confidence: 0.924872583333333

00:06:04.820 --> 00:06:06.645 associated with better overall survival.

NOTE Confidence: 0.924872583333333

00:06:06.650 --> 00:06:08.564 And most studies have found it

NOTE Confidence: 0.924872583333333

00:06:08.564 --> 00:06:10.410 to be associated with better

NOTE Confidence: 0.924872583333333

00:06:10.410 --> 00:06:11.928 progression free survival.

NOTE Confidence: 0.924872583333333

00:06:11.930 --> 00:06:13.526 But even by those two measures,

NOTE Confidence: 0.924872583333333

00:06:13.530 --> 00:06:16.302 you can see that there's sizable minorities

NOTE Confidence: 0.924872583333333

00:06:16.302 --> 00:06:19.167 of studies that have found the opposite,

NOTE Confidence: 0.924872583333333

00:06:19.170 --> 00:06:20.448 something like 40%.

NOTE Confidence: 0.924872583333333

00:06:20.448 --> 00:06:22.578 At the University of California,

NOTE Confidence: 0.924872583333333

00:06:22.580 --> 00:06:24.420 San Diego,

NOTE Confidence: 0.924872583333333

00:06:24.420 --> 00:06:27.132 our data falls into that minority

NOTE Confidence: 0.924872583333333

00:06:27.132 --> 00:06:29.473 where HPV positive patients do

NOTE Confidence: 0.924872583333333

00:06:29.473 --> 00:06:32.185 much better than HPV negative case

NOTE Confidence: 0.924872583333333

00:06:32.185 --> 00:06:34.659 patients independent of other factors.

NOTE Confidence: 0.924872583333333

00:06:34.660 --> 00:06:36.675 If you synthesize everything that's

NOTE Confidence: 0.924872583333333

00:06:36.675 --> 00:06:38.690 been published in the literature

NOTE Confidence: 0.924872583333333

00:06:38.752 --> 00:06:39.820 on HPV positivity,

NOTE Confidence: 0.924872583333333

00:06:39.820 --> 00:06:42.865 you find out this patients are generally

NOTE Confidence: 0.924872583333333

00:06:42.865 --> 00:06:45.028 younger, the tumors are smaller,

NOTE Confidence: 0.924872583333333

00:06:45.028 --> 00:06:46.324 they associated with.

NOTE Confidence: 0.924872583333333

00:06:46.330 --> 00:06:48.218 Lower depths of struggle,

NOTE Confidence: 0.924872583333333

00:06:48.218 --> 00:06:48.690 invasion,

NOTE Confidence: 0.924872583333333

00:06:48.690 --> 00:06:50.650 less frequent lymph node metastasis,

NOTE Confidence: 0.924872583333333

00:06:50.650 --> 00:06:52.106 less frequent margin positivity.

NOTE Confidence: 0.924872583333333

00:06:52.106 --> 00:06:54.290 And at least three studies have

NOTE Confidence: 0.924872583333333

00:06:54.348 --> 00:06:55.958 found that for those patients

NOTE Confidence: 0.924872583333333

00:06:55.958 --> 00:06:57.725 that are treated with primary

NOTE Confidence: 0.924872583333333

00:06:57.725 --> 00:07:00.100 radiation or chemo radiation that

NOTE Confidence: 0.924872583333333

00:07:00.100 --> 00:07:01.525 there's greater responsiveness.

NOTE Confidence: 0.924872583333333

00:07:01.530 --> 00:07:03.954 So there seems to be greater

NOTE Confidence: 0.924872583333333

00:07:03.954 --> 00:07:06.063 responsiveness amongst the HPV

NOTE Confidence: 0.924872583333333

00:07:06.063 --> 00:07:09.534 positive group if you compare HPV

NOTE Confidence: 0.924872583333333

00:07:09.534 --> 00:07:12.060 positive and HPV negative cases with

NOTE Confidence: 0.924872583333333

00:07:12.137 --> 00:07:14.967 respect to their mutational profiles.

NOTE Confidence: 0.924872583333333

00:07:14.970 --> 00:07:16.394 It's just,

NOTE Confidence: 0.924872583333333

00:07:16.394 --> 00:07:17.818 you know.

NOTE Confidence: 0.924872583333333

00:07:17.820 --> 00:07:20.400 19HP V positive cases exposed to

NOTE Confidence: 0.924872583333333

00:07:20.400 --> 00:07:23.224 the clinical NGS panel which oped

NOTE Confidence: 0.924872583333333

00:07:23.224 --> 00:07:26.170 another nine institution has 397 genes

NOTE Confidence: 0.924872583333333

00:07:26.170 --> 00:07:29.355 and and these are just the genes

NOTE Confidence: 0.924872583333333

00:07:29.355 --> 00:07:32.819 that show statistically significant

NOTE Confidence: 0.924872583333333

00:07:32.820 --> 00:07:34.800 differences between the HPV positive

NOTE Confidence: 0.924872583333333

00:07:34.800 --> 00:07:37.196 and HPV negative group and are

NOTE Confidence: 0.924872583333333

00:07:37.196 --> 00:07:39.296 more prevalent in the HPV positive.

NOTE Confidence: 0.924872583333333

00:07:39.300 --> 00:07:41.610 You can see that number one

NOTE Confidence: 0.924872583333333

00:07:41.610 --> 00:07:43.150 even the highest mutation.

NOTE Confidence: 0.924872583333333

00:07:43.150 --> 00:07:45.196 Which is like 3C A it's only 28%

NOTE Confidence: 0.924872583333333

00:07:45.196 --> 00:07:47.226 and everything else is lower,

NOTE Confidence: 0.924872583333333

00:07:47.230 --> 00:07:49.449 but these are only the ones that

NOTE Confidence: 0.924872583333333

00:07:49.449 --> 00:07:50.400 show significant differences

NOTE Confidence: 0.924872583333333

00:07:50.456 --> 00:07:52.142 between them and are more common

NOTE Confidence: 0.924872583333333

00:07:52.142 --> 00:07:53.630 than the HPV positive group.

NOTE Confidence: 0.924872583333333

00:07:53.630 --> 00:07:56.040 Amongst the HPV negative group

NOTE Confidence: 0.924872583333333

00:07:56.040 --> 00:07:58.450 however then several genes that

NOTE Confidence: 0.924872583333333

00:07:58.531 --> 00:08:01.086 with high mutation of frequencies

NOTE Confidence: 0.924872583333333

00:08:01.086 --> 00:08:04.633 most notably CP53 and CDK and 2A

NOTE Confidence: 0.924872583333333

00:08:04.633 --> 00:08:07.074 as well as term P and these are

NOTE Confidence: 0.924872583333333

00:08:07.074 --> 00:08:09.468 seen at very high frequencies more

NOTE Confidence: 0.924872583333333

00:08:09.468 --> 00:08:12.148 commonly in the HPV negative group.

NOTE Confidence: 0.941801815384615

00:08:14.170 --> 00:08:16.466 When we look at all prior studies

NOTE Confidence: 0.941801815384615

00:08:16.466 --> 00:08:18.569 that have looked at the question,

NOTE Confidence: 0.941801815384615

00:08:18.570 --> 00:08:20.410 we did this in 2021,

NOTE Confidence: 0.941801815384615

00:08:20.410 --> 00:08:21.866 2020 something like that.

NOTE Confidence: 0.941801815384615

00:08:21.866 --> 00:08:24.050 You can see it's pretty consistent.

NOTE Confidence: 0.941801815384615

00:08:24.050 --> 00:08:26.794 Each bar represents a study that have

NOTE Confidence: 0.941801815384615

00:08:26.794 --> 00:08:31.065 looked at the issue and it's you know TP53

NOTE Confidence: 0.941801815384615

00:08:31.065 --> 00:08:33.690 tends to be the most common mutation.

NOTE Confidence: 0.941801815384615

00:08:33.690 --> 00:08:36.042 That have been identified in the HPV

NOTE Confidence: 0.941801815384615

00:08:36.042 --> 00:08:38.407 negative group which is in the upper graph.

NOTE Confidence: 0.941801815384615

00:08:38.410 --> 00:08:40.458 That's compared to the ones in the lower

NOTE Confidence: 0.941801815384615

00:08:40.458 --> 00:08:42.647 where it tends to be more heterogeneous,

NOTE Confidence: 0.941801815384615

00:08:42.650 --> 00:08:44.434 the HPV positive tumors.

NOTE Confidence: 0.941801815384615

00:08:44.434 --> 00:08:47.110 The mutational profile tends to be

NOTE Confidence: 0.941801815384615

00:08:47.188 --> 00:08:49.973 monitor genius without anyone really

NOTE Confidence: 0.941801815384615

00:08:49.973 --> 00:08:53.342 being overtly dominant the way P53

NOTE Confidence: 0.941801815384615

00:08:53.342 --> 00:08:56.726 does in the HPV negative group.

NOTE Confidence: 0.941801815384615

00:08:56.730 --> 00:09:00.072 The P53 being dominant in the HPV negative

NOTE Confidence: 0.941801815384615

00:09:00.072 --> 00:09:02.427 group also has significance clinically.

NOTE Confidence: 0.941801815384615

00:09:02.430 --> 00:09:04.002 You can see the green line

NOTE Confidence: 0.941801815384615

00:09:04.002 --> 00:09:05.390 represents the HPV positive group,

NOTE Confidence: 0.941801815384615

00:09:05.390 --> 00:09:06.872 patients do better.

NOTE Confidence: 0.941801815384615

00:09:06.872 --> 00:09:10.330 The red line represents the HPV negative

NOTE Confidence: 0.941801815384615

00:09:10.418 --> 00:09:12.950 group that are also P53 mutant.

NOTE Confidence: 0.941801815384615

00:09:12.950 --> 00:09:15.008 And you can see that there's an

NOTE Confidence: 0.941801815384615

00:09:15.008 --> 00:09:16.775 intermediate group where there's HPV

NOTE Confidence: 0.941801815384615

00:09:16.775 --> 00:09:20.030 negative or P53 wild type and those

NOTE Confidence: 0.941801815384615

00:09:20.030 --> 00:09:23.069 patients have intermediate prognosis.

NOTE Confidence: 0.941801815384615

00:09:23.070 --> 00:09:24.801 The notion that.

NOTE Confidence: 0.941801815384615

00:09:24.801 --> 00:09:27.686 P53 alterations is associated with

NOTE Confidence: 0.941801815384615

00:09:27.686 --> 00:09:30.190 ***** cancer was initially reported

NOTE Confidence: 0.941801815384615

00:09:30.190 --> 00:09:33.184 by Pellodian colleagues in 1993

NOTE Confidence: 0.941801815384615

00:09:33.184 --> 00:09:37.310 and it was a small study.

NOTE Confidence: 0.941801815384615

00:09:37.310 --> 00:09:38.990 It was a letter to the editor,

NOTE Confidence: 0.941801815384615

00:09:38.990 --> 00:09:41.174 but they established that the mutations

NOTE Confidence: 0.941801815384615

00:09:41.174 --> 00:09:43.681 were also demonstrable and correlated with

NOTE Confidence: 0.941801815384615

00:09:43.681 --> 00:09:45.665 immunistic chemical staining patterns.

NOTE Confidence: 0.941801815384615

00:09:45.670 --> 00:09:46.310 Of course,

NOTE Confidence: 0.941801815384615

00:09:46.310 --> 00:09:47.270 there've been dozens,

NOTE Confidence: 0.941801815384615

00:09:47.270 --> 00:09:49.670 probably hundreds of studies after that.

NOTE Confidence: 0.941801815384615

00:09:49.670 --> 00:09:52.334 So much so now that we now have.

NOTE Confidence: 0.941801815384615

00:09:52.340 --> 00:09:54.330 Sort of well established staining

NOTE Confidence: 0.941801815384615

00:09:54.330 --> 00:09:56.320 patterns that correlate with the

NOTE Confidence: 0.941801815384615

00:09:56.386 --> 00:09:58.496 presence of an underlying mutation.

NOTE Confidence: 0.941801815384615

00:09:58.500 --> 00:09:59.960 The mutational patterns are

NOTE Confidence: 0.941801815384615

00:09:59.960 --> 00:10:02.251 shown on the left, on the right,

NOTE Confidence: 0.941801815384615

00:10:02.251 --> 00:10:04.190 and this is based on work by

NOTE Confidence: 0.941801815384615

00:10:04.256 --> 00:10:06.356 Tecia Klute and colleagues from

NOTE Confidence: 0.941801815384615

00:10:06.356 --> 00:10:08.484 the Vancouver group And you can

NOTE Confidence: 0.941801815384615

00:10:08.484 --> 00:10:10.500 see that you know the most common

NOTE Confidence: 0.941801815384615

00:10:10.567 --> 00:10:12.952 staining pattern is this parabasal

NOTE Confidence: 0.941801815384615

00:10:12.952 --> 00:10:14.860 diffuse over expression pattern.

NOTE Confidence: 0.941801815384615

00:10:14.860 --> 00:10:17.716 You could also have just staining of the

NOTE Confidence: 0.941801815384615

00:10:17.716 --> 00:10:20.118 basal layers or nulls or cytoplasmic.

NOTE Confidence: 0.941801815384615

00:10:20.120 --> 00:10:22.286 In the wild type staining patterns

NOTE Confidence: 0.941801815384615

00:10:22.286 --> 00:10:24.413 you have no staining of the

NOTE Confidence: 0.941801815384615

00:10:24.413 --> 00:10:26.237 base and some lesions we have,

NOTE Confidence: 0.941801815384615

00:10:26.240 --> 00:10:27.920 even though they may be staining in

NOTE Confidence: 0.941801815384615

00:10:27.920 --> 00:10:30.628 the middle or just scattered sporadic

NOTE Confidence: 0.941801815384615

00:10:30.628 --> 00:10:34.480 staining of individual cells within the nest.

NOTE Confidence: 0.941801815384615

00:10:34.480 --> 00:10:37.763 When that model was applied to an

NOTE Confidence: 0.941801815384615

00:10:37.763 --> 00:10:40.071 independent cohort of over 400

NOTE Confidence: 0.941801815384615

00:10:40.071 --> 00:10:41.484 HPV negative cases,

NOTE Confidence: 0.941801815384615

00:10:41.484 --> 00:10:44.310 the parabasal diffuse expression pattern was

NOTE Confidence: 0.941801815384615

00:10:44.387 --> 00:10:47.435 the most commonly observed staining pattern.

NOTE Confidence: 0.941801815384615

00:10:47.440 --> 00:10:50.028 When I saw the wild type, it's the

NOTE Confidence: 0.941801815384615

00:10:50.028 --> 00:10:52.198 scattered isolated cells being positive.

NOTE Confidence: 0.941801815384615

00:10:52.200 --> 00:10:53.620 So here's some images that

NOTE Confidence: 0.941801815384615

00:10:53.620 --> 00:10:55.040 I just took for this.

NOTE Confidence: 0.941801815384615

00:10:55.040 --> 00:10:57.456 You can see in the top image.

NOTE Confidence: 0.941801815384615

00:10:57.456 --> 00:11:00.170 On initial inspection, it may look like it's.

NOTE Confidence: 0.941801815384615

00:11:00.170 --> 00:11:02.490 HPV mutational type staining pattern,

NOTE Confidence: 0.941801815384615

00:11:02.490 --> 00:11:04.938 but in fact the basal layer is not

NOTE Confidence: 0.941801815384615

00:11:04.938 --> 00:11:06.887 staining so it's P53 wild type.

NOTE Confidence: 0.941801815384615

00:11:06.890 --> 00:11:08.661 Whereas on the bottom it looks like

NOTE Confidence: 0.941801815384615

00:11:08.661 --> 00:11:10.131 the central portion is not staining

NOTE Confidence: 0.941801815384615

00:11:10.131 --> 00:11:11.678 but the base is staining and all

NOTE Confidence: 0.941801815384615

00:11:11.725 --> 00:11:13.285 the cells in between are staining.

NOTE Confidence: 0.941801815384615

00:11:13.290 --> 00:11:16.650 So this is a mutational staining pattern.

NOTE Confidence: 0.941801815384615

00:11:16.650 --> 00:11:19.375 Overall HPV status is recognized

NOTE Confidence: 0.941801815384615

00:11:19.375 --> 00:11:21.010 to be significant,

NOTE Confidence: 0.941801815384615

00:11:21.010 --> 00:11:22.978 but it's not a clinical decision

NOTE Confidence: 0.941801815384615

00:11:22.978 --> 00:11:24.290 point at present time.

NOTE Confidence: 0.941801815384615

00:11:24.290 --> 00:11:26.708 The Who 5th edition does recommend.

NOTE Confidence: 0.941801815384615

00:11:26.710 --> 00:11:29.110 That tumors be classified based

NOTE Confidence: 0.941801815384615

00:11:29.110 --> 00:11:32.050 on the HPV status and the cops.

NOTE Confidence: 0.941801815384615

00:11:32.050 --> 00:11:33.070 Synoptic Report template,

NOTE Confidence: 0.947441742857143

00:11:33.070 --> 00:11:35.650 which Doctor Chris Minoli

NOTE Confidence: 0.947441742857143

00:11:35.650 --> 00:11:40.526 Spences and I CCR guidelines all

NOTE Confidence: 0.947441742857143

00:11:40.526 --> 00:11:42.350 follow The Who classification,

NOTE Confidence: 0.947441742857143

00:11:42.350 --> 00:11:45.630 and Figo 2021 does the same as well.

NOTE Confidence: 0.907416818333333

00:11:48.270 --> 00:11:51.567 The next is the question of tomorrow's

NOTE Confidence: 0.907416818333333

00:11:51.567 --> 00:11:54.240 subtyping in squamous cell carcinoma.

NOTE Confidence: 0.907416818333333

00:11:54.240 --> 00:11:56.110 Here are the various classifications

NOTE Confidence: 0.907416818333333

00:11:56.110 --> 00:11:58.913 over the years of the various subtypes

NOTE Confidence: 0.907416818333333

00:11:58.913 --> 00:12:01.298 of squamous cell carcinoma and you

NOTE Confidence: 0.907416818333333

00:12:01.298 --> 00:12:03.042 can see it all depends on what a

NOTE Confidence: 0.907416818333333

00:12:03.042 --> 00:12:04.519 particular author wants to emphasize.

NOTE Confidence: 0.907416818333333

00:12:04.520 --> 00:12:07.400 What The sense you do get is that,

NOTE Confidence: 0.907416818333333

00:12:07.400 --> 00:12:09.280 and also from my experiences,

NOTE Confidence: 0.907416818333333

00:12:09.280 --> 00:12:12.450 is that the same spectrum of subtypes

NOTE Confidence: 0.907416818333333

00:12:12.450 --> 00:12:14.770 that you see in the skin and elsewhere

NOTE Confidence: 0.907416818333333

00:12:14.770 --> 00:12:16.596 can also be seen in the *****.

NOTE Confidence: 0.907416818333333

00:12:16.600 --> 00:12:19.876 Right now, HPV positivity versus negativity

NOTE Confidence: 0.907416818333333

00:12:19.876 --> 00:12:22.690 is the main classification factor.

NOTE Confidence: 0.907416818333333

00:12:22.690 --> 00:12:25.210 And what we know is that the spindle cell

NOTE Confidence: 0.907416818333333

00:12:25.210 --> 00:12:30.369 and the verrucas are typically HPV negative.

NOTE Confidence: 0.907416818333333

00:12:30.370 --> 00:12:33.079 Everything else can be seen in either

NOTE Confidence: 0.907416818333333

00:12:33.079 --> 00:12:35.967 the HPV positive or HPV negative groups.

NOTE Confidence: 0.907416818333333

00:12:35.970 --> 00:12:38.592 The idea that subtyping relates to

NOTE Confidence: 0.907416818333333

00:12:38.592 --> 00:12:41.237 HPV status was initially proffered by

NOTE Confidence: 0.907416818333333

00:12:41.237 --> 00:12:44.114 Turkey and Kerman in the early 1990s.

NOTE Confidence: 0.907416818333333

00:12:44.120 --> 00:12:46.334 Where they reported that the basiloid

NOTE Confidence: 0.907416818333333

00:12:46.334 --> 00:12:48.508 and warty morphology were more frequently

NOTE Confidence: 0.907416818333333

00:12:48.508 --> 00:12:51.036 seen in the HPV positive group and the

NOTE Confidence: 0.907416818333333

00:12:51.104 --> 00:12:53.445 HPV the caratinizing morphology was more

NOTE Confidence: 0.907416818333333

00:12:53.445 --> 00:12:56.719 frequently seen in the HPV negative group.

NOTE Confidence: 0.907416818333333

00:12:56.720 --> 00:12:59.016 So here for example is the caratinizing

NOTE Confidence: 0.907416818333333

00:12:59.016 --> 00:13:01.219 squamous cell carcinoma and you can see

NOTE Confidence: 0.907416818333333

00:13:01.219 --> 00:13:02.965 that it's basically the three mutational

NOTE Confidence: 0.907416818333333

00:13:03.026 --> 00:13:05.254 type staining pattern or supposed to

NOTE Confidence: 0.907416818333333

00:13:05.254 --> 00:13:08.356 this one which is basiloid and it's P

NOTE Confidence: 0.907416818333333

00:13:08.356 --> 00:13:10.953 16 positive HPV associated or this one

NOTE Confidence: 0.907416818333333

00:13:10.953 --> 00:13:13.819 which is wordy and is similarly HPV.

NOTE Confidence: 0.907416818333333

00:13:13.820 --> 00:13:15.600 Associated however, this one,

NOTE Confidence: 0.907416818333333

00:13:15.600 --> 00:13:18.270 which is also which also has

NOTE Confidence: 0.907416818333333

00:13:18.354 --> 00:13:21.988 warty morphology, is HPV negative,

NOTE Confidence: 0.907416818333333

00:13:21.988 --> 00:13:23.540 P16 negative.

NOTE Confidence: 0.907416818333333

00:13:23.540 --> 00:13:25.655 Now I specifically illustrated this

NOTE Confidence: 0.907416818333333

00:13:25.655 --> 00:13:28.313 case to highlight the the notion

NOTE Confidence: 0.907416818333333

00:13:28.313 --> 00:13:31.139 that HPV status cannot be reliably

NOTE Confidence: 0.907416818333333

00:13:31.139 --> 00:13:33.059 predicted from morphologic evaluation

NOTE Confidence: 0.907416818333333

00:13:33.059 --> 00:13:34.779 only if for example,

NOTE Confidence: 0.907416818333333

00:13:34.780 --> 00:13:36.435 is the keratinize and squintin

NOTE Confidence: 0.907416818333333

00:13:36.435 --> 00:13:38.401 cell carcinoma and you can clearly

NOTE Confidence: 0.907416818333333

00:13:38.401 --> 00:13:40.390 see that it's P 16 positive.

NOTE Confidence: 0.907416818333333

00:13:40.390 --> 00:13:41.120 Indeed,

NOTE Confidence: 0.907416818333333

00:13:41.120 --> 00:13:45.500 the largest studies on the subject

NOTE Confidence: 0.907416818333333

00:13:45.500 --> 00:13:46.828 have found the same.

NOTE Confidence: 0.907416818333333

00:13:46.828 --> 00:13:48.820 This is from the Mobile vaginal

NOTE Confidence: 0.907416818333333

00:13:48.820 --> 00:13:51.352 study group which is only already

NOTE Confidence: 0.907416818333333

00:13:51.352 --> 00:13:52.618 in Natalia Brakislova,

NOTE Confidence: 0.907416818333333

00:13:52.620 --> 00:13:55.770 and you can see here that the

NOTE Confidence: 0.907416818333333

00:13:55.770 --> 00:13:57.580 HPV positive column here

NOTE Confidence: 0.911397074545454

00:13:59.620 --> 00:14:01.625 36.5% of cases are characterizing

NOTE Confidence: 0.911397074545454

00:14:01.625 --> 00:14:04.060 out of the HPV positive cases

NOTE Confidence: 0.911397074545454

00:14:04.060 --> 00:14:06.136 and out of the HPV negative.

NOTE Confidence: 0.911397074545454

00:14:06.140 --> 00:14:08.312 Smaller subset, but still.

NOTE Confidence: 0.911397074545454

00:14:08.312 --> 00:14:12.080 Around 5% are either basiloid or worthy,

NOTE Confidence: 0.911397074545454

00:14:12.080 --> 00:14:13.896 so clearly additional testing

NOTE Confidence: 0.911397074545454

00:14:13.896 --> 00:14:17.040 must be done to establish the HPV

NOTE Confidence: 0.911397074545454

00:14:17.040 --> 00:14:19.399 status if one wants to do that.

NOTE Confidence: 0.911397074545454

00:14:19.400 --> 00:14:21.840 Now there are various modalities

NOTE Confidence: 0.911397074545454

00:14:21.840 --> 00:14:23.718 for those that have been analyzed

NOTE Confidence: 0.911397074545454

00:14:23.718 --> 00:14:25.906 using DNA PCR for high risk HPV

NOTE Confidence: 0.911397074545454

00:14:25.906 --> 00:14:28.200 types and P6 animators to chemistry,

NOTE Confidence: 0.911397074545454

00:14:28.200 --> 00:14:29.800 there will be a discrepancy

NOTE Confidence: 0.911397074545454

00:14:29.800 --> 00:14:31.304 in around 10% of cases.

NOTE Confidence: 0.911397074545454

00:14:31.304 --> 00:14:32.120 In other words,

NOTE Confidence: 0.911397074545454

00:14:32.120 --> 00:14:34.724 you'll find one result using one modality

NOTE Confidence: 0.911397074545454

00:14:34.724 --> 00:14:37.328 and another result using another modality.

NOTE Confidence: 0.911397074545454

00:14:37.330 --> 00:14:39.769 As shown here,

NOTE Confidence: 0.911397074545454

00:14:39.770 --> 00:14:42.090 amongst those cases that are

NOTE Confidence: 0.911397074545454

00:14:42.090 --> 00:14:44.410 P16 positive and PCR negative,

NOTE Confidence: 0.911397074545454

00:14:44.410 --> 00:14:46.420 they tend to be more clinical

NOTE Confidence: 0.911397074545454

00:14:46.420 --> 00:14:48.155 pathologically similar to those that

NOTE Confidence: 0.911397074545454

00:14:48.155 --> 00:14:49.845 are positive by both modalities.

NOTE Confidence: 0.911397074545454

00:14:49.850 --> 00:14:51.314 In other words,

NOTE Confidence: 0.911397074545454

00:14:51.314 --> 00:14:54.242 they're they have background VIN 3,

NOTE Confidence: 0.911397074545454

00:14:54.250 --> 00:14:55.678 they are younger patients,

NOTE Confidence: 0.911397074545454

00:14:55.678 --> 00:14:58.250 maybe they have some warty or visible

NOTE Confidence: 0.911397074545454

00:14:58.250 --> 00:15:00.065 or morphology suggesting that the

NOTE Confidence: 0.911397074545454

00:15:00.065 --> 00:15:02.896 P16 is they are really HPV positive

NOTE Confidence: 0.911397074545454

00:15:02.896 --> 00:15:06.137 irrespective of what this result is showing.

NOTE Confidence: 0.911397074545454

00:15:06.140 --> 00:15:08.863 For those that have the reverse that

NOTE Confidence: 0.911397074545454

00:15:08.863 --> 00:15:11.618 have P16 negative and HPV DNA positive,

NOTE Confidence: 0.911397074545454

00:15:11.620 --> 00:15:13.420 it has to be more heterogeneous,

NOTE Confidence: 0.911397074545454

00:15:13.420 --> 00:15:16.006 but most of them actually look

NOTE Confidence: 0.911397074545454

00:15:16.006 --> 00:15:17.299 like P16 negative,

NOTE Confidence: 0.911397074545454

00:15:17.300 --> 00:15:20.180 HPV DNA negative as well.

NOTE Confidence: 0.911397074545454

00:15:20.180 --> 00:15:23.052 So P 16 overall is an excellent or

NOTE Confidence: 0.911397074545454

00:15:23.052 --> 00:15:25.379 do imperfect surrogate indicator,

NOTE Confidence: 0.911397074545454

00:15:25.380 --> 00:15:29.220 the discrepant rates between P16 IHC

NOTE Confidence: 0.911397074545454

00:15:29.220 --> 00:15:33.618 and things like RNA sexual aboritization.

NOTE Confidence: 0.911397074545454

00:15:33.620 --> 00:15:34.556 Are is less,

NOTE Confidence: 0.911397074545454

00:15:34.556 --> 00:15:37.160 it's tend to be less than 5% but

NOTE Confidence: 0.911397074545454

00:15:37.160 --> 00:15:39.680 there's not enough data in the

NOTE Confidence: 0.911397074545454

00:15:39.680 --> 00:15:43.060 ***** in those particular cases.

NOTE Confidence: 0.911397074545454

00:15:43.060 --> 00:15:45.565 There's been some recent emphasis

NOTE Confidence: 0.911397074545454

00:15:45.565 --> 00:15:48.070 on these so-called double positives

NOTE Confidence: 0.911397074545454

00:15:48.151 --> 00:15:50.489 cases that okay if P6 N is

NOTE Confidence: 0.911397074545454

00:15:50.489 --> 00:15:52.659 significant and P53 is significant,

NOTE Confidence: 0.911397074545454

00:15:52.660 --> 00:15:54.604 well a subset of cases will

NOTE Confidence: 0.911397074545454

00:15:54.604 --> 00:15:55.900 be positive for both.

NOTE Confidence: 0.911397074545454

00:15:55.900 --> 00:15:57.682 These are peer studies that were

NOTE Confidence: 0.911397074545454

00:15:57.682 --> 00:15:59.698 published just within the last two months

NOTE Confidence: 0.911397074545454

00:15:59.700 --> 00:16:02.967 and you can see the Raka Snova found that.

NOTE Confidence: 0.911397074545454

00:16:02.970 --> 00:16:05.490 Two out of seven to six cases were positive

NOTE Confidence: 0.911397074545454

00:16:05.490 --> 00:16:07.686 and both of them were HPV positive.

NOTE Confidence: 0.911397074545454

00:16:07.690 --> 00:16:09.655 But Young and colleagues found

NOTE Confidence: 0.911397074545454

00:16:09.655 --> 00:16:11.634 that four out of 225 were positive

NOTE Confidence: 0.911397074545454

00:16:11.634 --> 00:16:13.809 and all of them were HPV negative.

NOTE Confidence: 0.911397074545454

00:16:13.810 --> 00:16:15.847 They made a big point about saying

NOTE Confidence: 0.911397074545454

00:16:15.850 --> 00:16:18.302 all of the cases that are double

NOTE Confidence: 0.911397074545454

00:16:18.302 --> 00:16:20.294 positive should be classified as HPV

NOTE Confidence: 0.911397074545454

00:16:20.294 --> 00:16:22.370 negative and their data supports that.

NOTE Confidence: 0.911397074545454

00:16:22.370 --> 00:16:24.946 But I'm not sure I quite agree

NOTE Confidence: 0.911397074545454

00:16:24.946 --> 00:16:28.294 with that in echo or you can see

NOTE Confidence: 0.911397074545454

00:16:28.294 --> 00:16:31.620 that 7% of patients that are.

NOTE Confidence: 0.911397074545454

00:16:31.620 --> 00:16:34.362 That have HPV positive tumors also

NOTE Confidence: 0.911397074545454

00:16:34.362 --> 00:16:36.636 have ATV53 mutation and another

NOTE Confidence: 0.911397074545454

00:16:36.636 --> 00:16:38.906 study from Memorial Stone Catering

NOTE Confidence: 0.911397074545454

00:16:38.906 --> 00:16:42.874 found that 27% of cases that are HPV

NOTE Confidence: 0.911397074545454

00:16:42.874 --> 00:16:46.090 positive were also at a P53 mutation.

NOTE Confidence: 0.911397074545454

00:16:46.090 --> 00:16:46.525 Again,

NOTE Confidence: 0.911397074545454

00:16:46.525 --> 00:16:48.700 these are relatively small cores,

NOTE Confidence: 0.911397074545454

00:16:48.700 --> 00:16:49.676 but but you know,

NOTE Confidence: 0.911397074545454

00:16:49.676 --> 00:16:50.896 it's not surprising that there'll

NOTE Confidence: 0.911397074545454

00:16:50.896 --> 00:16:52.535 be a little bit of overlap there.

NOTE Confidence: 0.949059005

00:16:54.660 --> 00:16:58.400 The third item is related

NOTE Confidence: 0.949059005

00:16:58.400 --> 00:17:00.644 to histologic grading.

NOTE Confidence: 0.949059005

00:17:00.650 --> 00:17:02.760 Most gradient of squamous cell

NOTE Confidence: 0.949059005

00:17:02.760 --> 00:17:04.723 carcinoma are based on the

NOTE Confidence: 0.949059005

00:17:04.723 --> 00:17:06.578 border system which was developed

NOTE Confidence: 0.949059005

00:17:06.578 --> 00:17:08.930 in the 1920s for oral cancer,

NOTE Confidence: 0.949059005

00:17:08.930 --> 00:17:11.390 and it talks about count determining

NOTE Confidence: 0.949059005

00:17:11.390 --> 00:17:13.882 the percentage of the tumor that

NOTE Confidence: 0.949059005

00:17:13.882 --> 00:17:15.438 have this undifferentiated cells

NOTE Confidence: 0.949059005

00:17:15.438 --> 00:17:18.410 as a way of stratifying tumors.

NOTE Confidence: 0.949059005

00:17:18.410 --> 00:17:20.150 But the contemporary application

NOTE Confidence: 0.949059005

00:17:20.150 --> 00:17:22.325 of that system is problematic

NOTE Confidence: 0.949059005

00:17:22.325 --> 00:17:24.595 because there are too many variables

NOTE Confidence: 0.949059005

00:17:24.595 --> 00:17:26.365 and everyone is applying it.

NOTE Confidence: 0.949059005

00:17:26.370 --> 00:17:27.414 In different ways.

NOTE Confidence: 0.949059005

00:17:27.414 --> 00:17:31.047 So there tends to be a lot of inter

NOTE Confidence: 0.949059005

00:17:31.047 --> 00:17:32.950 observer variability for the mountain

NOTE Confidence: 0.949059005

00:17:32.950 --> 00:17:35.319 of tumors that are in the mid of the

NOTE Confidence: 0.949059005

00:17:35.319 --> 00:17:37.020 bell curve that that is that are

NOTE Confidence: 0.949059005

00:17:37.020 --> 00:17:38.905 not extremely well differentiated

NOTE Confidence: 0.949059005

00:17:38.905 --> 00:17:41.009 or extremely poorly differentiated.

NOTE Confidence: 0.949059005

00:17:41.010 --> 00:17:42.850 And to make matters worse

NOTE Confidence: 0.949059005

00:17:42.850 --> 00:17:44.322 grading is not significant.

NOTE Confidence: 0.949059005

00:17:44.330 --> 00:17:47.322 So you know here's studies

NOTE Confidence: 0.949059005

00:17:47.322 --> 00:17:49.050 published in the last 10 years,

NOTE Confidence: 0.949059005

00:17:49.050 --> 00:17:52.930 you got 42 studies and none of those

NOTE Confidence: 0.949059005

00:17:52.930 --> 00:17:56.225 studies and when do we ever say 0.

NOTE Confidence: 0.949059005

00:17:56.230 --> 00:17:59.212 But none of those studies have

NOTE Confidence: 0.949059005

00:17:59.212 --> 00:18:02.035 found grading to be associated with

NOTE Confidence: 0.949059005

00:18:02.035 --> 00:18:04.420 overall survival and 83% of them

NOTE Confidence: 0.949059005

00:18:04.420 --> 00:18:06.730 have not found it to be associated

NOTE Confidence: 0.949059005

00:18:06.804 --> 00:18:09.028 with progression free survival.

NOTE Confidence: 0.949059005

00:18:09.030 --> 00:18:10.582 But still, you know,

NOTE Confidence: 0.949059005

00:18:10.582 --> 00:18:12.522 there are alternative forms of

NOTE Confidence: 0.949059005

00:18:12.522 --> 00:18:14.627 grading that have been attempted.

NOTE Confidence: 0.949059005

00:18:14.630 --> 00:18:15.232 You know,

NOTE Confidence: 0.949059005

00:18:15.232 --> 00:18:17.038 GOG had a very influential study

NOTE Confidence: 0.949059005

00:18:17.038 --> 00:18:19.376 from the early 1990s where they had

NOTE Confidence: 0.949059005

00:18:19.376 --> 00:18:21.428 over 600 cases and they modified

NOTE Confidence: 0.949059005

00:18:21.428 --> 00:18:23.415 broader system to basically change

NOTE Confidence: 0.949059005

00:18:23.415 --> 00:18:25.385 the percentages of the grades.

NOTE Confidence: 0.949059005

00:18:25.390 --> 00:18:27.380 And they thought that correlated

NOTE Confidence: 0.949059005

00:18:27.380 --> 00:18:29.370 better with lymph node metastasis

NOTE Confidence: 0.949059005

00:18:29.433 --> 00:18:31.628 as compared with the standardized

NOTE Confidence: 0.949059005

00:18:31.628 --> 00:18:32.506 brother criteria.

NOTE Confidence: 0.949059005

00:18:32.510 --> 00:18:36.626 But this never achieved widespread usage,

NOTE Confidence: 0.949059005

00:18:36.630 --> 00:18:38.382 mostly because I think they never

NOTE Confidence: 0.949059005

00:18:38.382 --> 00:18:40.549 published what is this specific criteria,

NOTE Confidence: 0.949059005

00:18:40.550 --> 00:18:44.228 What do you consider undifferentiated cells

NOTE Confidence: 0.949059005

00:18:44.230 --> 00:18:47.344 kind of. And so it just never took off.

NOTE Confidence: 0.949059005

00:18:47.350 --> 00:18:50.878 Then there's the so-called spray like

NOTE Confidence: 0.949059005

00:18:50.878 --> 00:18:52.894 pattern or the infiltrative pattern.

NOTE Confidence: 0.949059005

00:18:52.894 --> 00:18:55.030 And two studies found it's not

NOTE Confidence: 0.949059005

00:18:55.098 --> 00:18:56.730 associated with recurrence.

NOTE Confidence: 0.949059005

00:18:56.730 --> 00:18:59.621 But Suzanne Jeffers had a nice study

NOTE Confidence: 0.949059005

00:18:59.621 --> 00:19:02.322 from 2015 from the University of

NOTE Confidence: 0.949059005

00:19:02.322 --> 00:19:04.662 Arkansas showing that it's associated

NOTE Confidence: 0.949059005

00:19:04.662 --> 00:19:07.270 with recurrence 2 times more likely

NOTE Confidence: 0.949059005

00:19:07.270 --> 00:19:09.410 to be associated with recurrence.

NOTE Confidence: 0.949059005

00:19:09.410 --> 00:19:11.465 Then there's the Fibro mixoid

NOTE Confidence: 0.949059005

00:19:11.465 --> 00:19:12.287 stromal response,

NOTE Confidence: 0.949059005

00:19:12.290 --> 00:19:14.663 which has been shown since the early

NOTE Confidence: 0.949059005

00:19:14.663 --> 00:19:16.461 1990s and subsequently confirmed by

NOTE Confidence: 0.949059005

00:19:16.461 --> 00:19:18.615 at least two different other studies.

NOTE Confidence: 0.949059005

00:19:18.620 --> 00:19:22.376 That it's associated with poor survival

NOTE Confidence: 0.949059005

00:19:22.380 --> 00:19:24.424 and more extensively metastasis

NOTE Confidence: 0.949059005

00:19:24.424 --> 00:19:27.904 and all the patient group And then

NOTE Confidence: 0.949059005

00:19:27.904 --> 00:19:30.676 finally our group reported a tumor

NOTE Confidence: 0.949059005

00:19:30.676 --> 00:19:32.532 budding that basically said Okay

NOTE Confidence: 0.949059005

00:19:32.532 --> 00:19:35.113 if you classify the level of tumor

NOTE Confidence: 0.949059005

00:19:35.113 --> 00:19:36.996 budding into three groups which

NOTE Confidence: 0.949059005

00:19:36.996 --> 00:19:39.642 has been the same system used at

NOTE Confidence: 0.949059005

00:19:39.642 --> 00:19:41.988 other other organ sites that you

NOTE Confidence: 0.949059005

00:19:41.988 --> 00:19:44.009 have clear separation between in

NOTE Confidence: 0.949059005

00:19:44.009 --> 00:19:46.325 terms of overall survival and DFS.

NOTE Confidence: 0.949059005

00:19:46.330 --> 00:19:49.040 Between the the groups independent

NOTE Confidence: 0.949059005

00:19:49.040 --> 00:19:52.570 of the factors including P53 status

NOTE Confidence: 0.949059005

00:19:52.570 --> 00:19:54.610 and HPV status.

NOTE Confidence: 0.949059005

00:19:54.610 --> 00:19:55.124 However,

NOTE Confidence: 0.949059005

00:19:55.124 --> 00:19:59.236 I think you know and this is mostly

NOTE Confidence: 0.949059005

00:19:59.236 --> 00:20:02.463 hypothesis that all of this are

NOTE Confidence: 0.949059005

00:20:02.463 --> 00:20:05.078 defining a single aggressive subset

NOTE Confidence: 0.949059005

00:20:05.179 --> 00:20:08.023 probably 1 where EMT is operational

NOTE Confidence: 0.949059005

00:20:08.023 --> 00:20:11.488 or activated or most significant.

NOTE Confidence: 0.949059005

00:20:11.490 --> 00:20:13.800 I think that's what this is.

NOTE Confidence: 0.949059005

00:20:13.800 --> 00:20:16.608 We were trying to or we tried to sort

NOTE Confidence: 0.949059005

00:20:16.608 --> 00:20:19.688 of prove that there was a too much

NOTE Confidence: 0.949059005

00:20:19.688 --> 00:20:22.639 overlap to really tell a coherent story.

NOTE Confidence: 0.949059005

00:20:22.640 --> 00:20:25.096 It's the same cases that tended to show

NOTE Confidence: 0.949059005

00:20:25.096 --> 00:20:27.080 the infiltrative pattern and fiber mixer,

NOTE Confidence: 0.949059005

00:20:27.080 --> 00:20:28.870 stroma or tumor body and

NOTE Confidence: 0.949059005

00:20:28.870 --> 00:20:30.660 infiltrative pattern or so on

NOTE Confidence: 0.880026373076923

00:20:30.736 --> 00:20:31.600 and so forth.

NOTE Confidence: 0.880026373076923

00:20:31.600 --> 00:20:32.596 There was a lot of overlap.

NOTE Confidence: 0.880026373076923

00:20:32.600 --> 00:20:34.287 We were able to show that each

NOTE Confidence: 0.880026373076923

00:20:34.287 --> 00:20:35.400 one was significant though,

NOTE Confidence: 0.880026373076923

00:20:35.400 --> 00:20:38.400 but there was such significant overlap.

NOTE Confidence: 0.880026373076923

00:20:38.400 --> 00:20:40.520 So where do we stand at present time?

NOTE Confidence: 0.880026373076923

00:20:40.520 --> 00:20:44.224 Well, gradient is listed as a data element.

NOTE Confidence: 0.880026373076923

00:20:44.230 --> 00:20:46.148 And as a result, there's a required

NOTE Confidence: 0.880026373076923

00:20:46.148 --> 00:20:47.910 element in the caps and optics,

NOTE Confidence: 0.880026373076923

00:20:47.910 --> 00:20:50.750 but I CCR are in the most recent data sets.

NOTE Confidence: 0.880026373076923

00:20:50.750 --> 00:20:52.496 That greeting is not a Co

NOTE Confidence: 0.880026373076923

00:20:52.496 --> 00:20:54.550 item and it's not recommended,

NOTE Confidence: 0.880026373076923

00:20:54.550 --> 00:20:57.898 whereas you know it's still not a

NOTE Confidence: 0.880026373076923

00:20:57.898 --> 00:21:00.706 clinical decision point at present time.

NOTE Confidence: 0.906708138125

00:21:03.910 --> 00:21:06.353 The 4th and the biggest section of

NOTE Confidence: 0.906708138125

00:21:06.353 --> 00:21:08.411 this presentation leads to precursor

NOTE Confidence: 0.906708138125

00:21:08.411 --> 00:21:10.299 lesions and background dermatosis.

NOTE Confidence: 0.906708138125

00:21:10.300 --> 00:21:13.180 Which is really a

NOTE Confidence: 0.906708138125

00:21:13.180 --> 00:21:15.464 controversial area by itself.

NOTE Confidence: 0.906708138125

00:21:15.464 --> 00:21:18.418 We'll start out with the more conventional.

NOTE Confidence: 0.906708138125

00:21:18.420 --> 00:21:23.802 So the original carcinoma insight of skin

NOTE Confidence: 0.906708138125

00:21:23.802 --> 00:21:27.978 was described by Doctor John Bowen in 1912.

NOTE Confidence: 0.906708138125

00:21:27.980 --> 00:21:31.900 It took maybe 10 years for somebody

NOTE Confidence: 0.906708138125

00:21:31.900 --> 00:21:34.180 to find to describe something similar

NOTE Confidence: 0.906708138125

00:21:34.180 --> 00:21:37.336 in the ***** took another 20 years

NOTE Confidence: 0.906708138125

00:21:37.336 --> 00:21:40.330 for somebody to describe the series.

NOTE Confidence: 0.906708138125

00:21:40.330 --> 00:21:42.970 Of lesions and then ten years after that,

NOTE Confidence: 0.906708138125

00:21:42.970 --> 00:21:45.210 15 years after that for the term

NOTE Confidence: 0.906708138125

00:21:45.210 --> 00:21:47.466 custom inside you to be proposed.

NOTE Confidence: 0.906708138125

00:21:47.466 --> 00:21:50.490 And it's kind of highlighted the glacial

NOTE Confidence: 0.906708138125

00:21:50.574 --> 00:21:53.682 pace of progress in the ***** diseases

NOTE Confidence: 0.906708138125

00:21:53.682 --> 00:21:57.809 during the early part of the last century.

NOTE Confidence: 0.906708138125

00:21:57.810 --> 00:21:59.042 But the nomenclature disorder,

NOTE Confidence: 0.906708138125

00:21:59.042 --> 00:22:01.406 as I like to call it, persistent.

NOTE Confidence: 0.906708138125

00:22:01.406 --> 00:22:03.986 With different terms being used.

NOTE Confidence: 0.906708138125

00:22:03.990 --> 00:22:06.120 Remember at that point it had

NOTE Confidence: 0.906708138125

00:22:06.120 --> 00:22:07.870 not been associated with HPV.

NOTE Confidence: 0.906708138125

00:22:07.870 --> 00:22:11.576 In the 60s and 50s it hadn't

NOTE Confidence: 0.906708138125

00:22:11.576 --> 00:22:12.828 been associated with HPV.

NOTE Confidence: 0.906708138125

00:22:12.830 --> 00:22:15.590 So the lesions with different clinical

NOTE Confidence: 0.906708138125

00:22:15.590 --> 00:22:17.883 pathologic basis were getting called

NOTE Confidence: 0.906708138125

00:22:17.883 --> 00:22:20.543 precursor lesions if they had a typia.

NOTE Confidence: 0.906708138125

00:22:20.550 --> 00:22:23.040 So ultimately ISSVD International Society

NOTE Confidence: 0.906708138125

00:22:23.040 --> 00:22:26.564 for the Study of Over Vaginal Diseases

NOTE Confidence: 0.906708138125

00:22:26.564 --> 00:22:29.925 stepped in in 1976 and proposed the term

NOTE Confidence: 0.906708138125

00:22:29.925 --> 00:22:32.110 squamous cell carcinoma inside 2:00 to.

NOTE Confidence: 0.906708138125

00:22:32.110 --> 00:22:34.366 Bring everything in line with similar

NOTE Confidence: 0.906708138125

00:22:34.366 --> 00:22:36.629 terminology in the skin and if you

NOTE Confidence: 0.906708138125

00:22:36.629 --> 00:22:38.735 look at the various the top part of

NOTE Confidence: 0.906708138125

00:22:38.735 --> 00:22:40.667 this table you can see the evolution

NOTE Confidence: 0.906708138125

00:22:40.667 --> 00:22:42.483 and the terminology all the way

NOTE Confidence: 0.906708138125

00:22:42.483 --> 00:22:43.983 to where we are today,

NOTE Confidence: 0.906708138125

00:22:43.990 --> 00:22:46.734 which is based on last guidelines.

NOTE Confidence: 0.906708138125

00:22:46.734 --> 00:22:47.982 L cell,

NOTE Confidence: 0.906708138125

00:22:47.982 --> 00:22:50.562 H cell as shown here.

NOTE Confidence: 0.906708138125

00:22:50.562 --> 00:22:53.670 Now of course nothing has changed about

NOTE Confidence: 0.906708138125

00:22:53.759 --> 00:22:57.590 the pathology of Costnoma inside two or

NOTE Confidence: 0.906708138125

00:22:57.590 --> 00:22:59.885 VIN 3 or however you want to call it.

NOTE Confidence: 0.906708138125

00:22:59.890 --> 00:23:01.490 Except the morphologic spectrum

NOTE Confidence: 0.906708138125

00:23:01.490 --> 00:23:02.690 has gotten expanded,

NOTE Confidence: 0.906708138125

00:23:02.690 --> 00:23:05.660 so basiloid variations and are more

NOTE Confidence: 0.906708138125

00:23:05.660 --> 00:23:08.570 railway recognized or worthy variations.

NOTE Confidence: 0.906708138125

00:23:08.570 --> 00:23:10.814 There's a so-called Divin like pattern

NOTE Confidence: 0.906708138125

00:23:10.814 --> 00:23:13.905 of H cell where in the atypia is

NOTE Confidence: 0.906708138125

00:23:13.905 --> 00:23:16.191 restricted mostly to the basal regions

NOTE Confidence: 0.906708138125

00:23:16.261 --> 00:23:18.222 of the epidermis until one goes down

NOTE Confidence: 0.906708138125

00:23:18.222 --> 00:23:20.009 to look at it and high power it.

NOTE Confidence: 0.906708138125

00:23:20.010 --> 00:23:21.990 And you'd appreciate a lot of

NOTE Confidence: 0.906708138125

00:23:21.990 --> 00:23:24.024 mitotic figures in upper layers of

NOTE Confidence: 0.906708138125

00:23:24.024 --> 00:23:25.644 the epidermis where this doesn't

NOTE Confidence: 0.906708138125

00:23:25.644 --> 00:23:27.659 seem to be basiloid change.

NOTE Confidence: 0.906708138125

00:23:27.660 --> 00:23:30.156 And that hot that that is a clue

NOTE Confidence: 0.906708138125

00:23:30.156 --> 00:23:32.720 that this could be even like H sill.

NOTE Confidence: 0.906708138125

00:23:32.720 --> 00:23:35.669 When you do P6 stain it lights up and

NOTE Confidence: 0.906708138125

00:23:35.669 --> 00:23:38.288 P53 shows that this is a wild type

NOTE Confidence: 0.906708138125

00:23:38.288 --> 00:23:39.958 staining pattern because there's no

NOTE Confidence: 0.906708138125

00:23:39.958 --> 00:23:42.752 staining of the base and this is basal

NOTE Confidence: 0.906708138125

00:23:42.752 --> 00:23:44.140 sparing media epithelial staining.

NOTE Confidence: 0.906708138125

00:23:44.140 --> 00:23:49.340 This is a wild type staining pattern when

NOTE Confidence: 0.906708138125

00:23:49.340 --> 00:23:53.155 H sill is comorbid with lichens sclerosus.

NOTE Confidence: 0.906708138125

00:23:53.160 --> 00:23:55.435 If it can take on this appearance,

NOTE Confidence: 0.906708138125

00:23:55.440 --> 00:23:57.720 this deviant like HCL like appearance.

NOTE Confidence: 0.906708138125

00:23:57.720 --> 00:23:59.344 Here for example at the lower left

NOTE Confidence: 0.906708138125

00:23:59.344 --> 00:24:00.955 you can see the conventional HCL

NOTE Confidence: 0.906708138125

00:24:00.955 --> 00:24:02.964 and then the portions that are above

NOTE Confidence: 0.906708138125

00:24:03.023 --> 00:24:04.685 the like in sclerosis looks almost

NOTE Confidence: 0.906708138125

00:24:04.685 --> 00:24:06.877 normal and low power until you go

NOTE Confidence: 0.906708138125

00:24:06.877 --> 00:24:08.672 in high magnification and appreciate

NOTE Confidence: 0.906708138125

00:24:08.672 --> 00:24:10.280 some of the Ethiopia.

NOTE Confidence: 0.906708138125

00:24:10.280 --> 00:24:12.790 Also more recognized over the

NOTE Confidence: 0.906708138125

00:24:12.790 --> 00:24:15.300 last several decades is palliatory

NOTE Confidence: 0.906708138125

00:24:15.380 --> 00:24:18.096 scatter of of HCL which can result

NOTE Confidence: 0.906708138125

00:24:18.096 --> 00:24:20.216 in P16 sparing the base.

NOTE Confidence: 0.906708138125

00:24:20.220 --> 00:24:21.978 And this you can see here,

NOTE Confidence: 0.906708138125

00:24:21.980 --> 00:24:23.636 probably better shown here.

NOTE Confidence: 0.906708138125

00:24:23.636 --> 00:24:26.120 One can also see this pattern

NOTE Confidence: 0.9459142625

00:24:26.196 --> 00:24:28.316 that the peripheries of regular

NOTE Confidence: 0.9459142625

00:24:28.316 --> 00:24:30.590 HCL where you know this just

NOTE Confidence: 0.9459142625

00:24:30.590 --> 00:24:33.060 scattered and that is a result.

NOTE Confidence: 0.9459142625

00:24:33.060 --> 00:24:35.940 P16 does a single base.

NOTE Confidence: 0.9459142625

00:24:35.940 --> 00:24:38.596 And then finally we reported on a series

NOTE Confidence: 0.9459142625

00:24:38.596 --> 00:24:41.135 of cases that can have such fluorid

NOTE Confidence: 0.9459142625

00:24:41.135 --> 00:24:44.320 edema and inflammation in the dermis.

NOTE Confidence: 0.9459142625

00:24:44.320 --> 00:24:47.280 That it looks like you know it could

NOTE Confidence: 0.9459142625

00:24:47.280 --> 00:24:49.380 be mistaken until one goes on high

NOTE Confidence: 0.9459142625

00:24:49.380 --> 00:24:50.857 magnification to appreciate all the

NOTE Confidence: 0.9459142625

00:24:50.857 --> 00:24:52.960 atypia that's present in in the lesion.

NOTE Confidence: 0.928712271764706

00:24:55.280 --> 00:24:58.311 Now the incidence of HCL has increased

NOTE Confidence: 0.928712271764706

00:24:58.311 --> 00:25:00.131 by several thousand percentage

NOTE Confidence: 0.928712271764706

00:25:00.131 --> 00:25:02.759 points over the last 50 years,

NOTE Confidence: 0.928712271764706

00:25:02.760 --> 00:25:04.890 but the progression rate has

NOTE Confidence: 0.928712271764706

00:25:04.890 --> 00:25:06.594 remained relatively stable with

NOTE Confidence: 0.928712271764706

00:25:06.600 --> 00:25:10.482 about 9% progressing if untreated

NOTE Confidence: 0.928712271764706

00:25:10.482 --> 00:25:13.968 and low percentage less than 5%.

NOTE Confidence: 0.928712271764706

00:25:13.970 --> 00:25:16.682 Of cases we identified are called

NOTE Confidence: 0.928712271764706

00:25:16.682 --> 00:25:19.290 cancer in the resection specimen.

NOTE Confidence: 0.928712271764706

00:25:19.290 --> 00:25:21.174 That said though,

NOTE Confidence: 0.928712271764706

00:25:21.174 --> 00:25:24.314 there still remains this big

NOTE Confidence: 0.928712271764706

00:25:24.314 --> 00:25:26.845 disconnect wherein in most insight

NOTE Confidence: 0.928712271764706

00:25:26.845 --> 00:25:28.970 to lesions are HPV associated,

NOTE Confidence: 0.928712271764706

00:25:28.970 --> 00:25:31.595 but most invasive lesions are

NOTE Confidence: 0.928712271764706

00:25:31.595 --> 00:25:33.822 HPV independent and in the 70s.

NOTE Confidence: 0.928712271764706

00:25:33.822 --> 00:25:36.453 That caused a look back to a study

NOTE Confidence: 0.928712271764706

00:25:36.453 --> 00:25:38.049 that was originally published

NOTE Confidence: 0.928712271764706

00:25:38.049 --> 00:25:41.198 in 1961 by It Built and Goslin.

NOTE Confidence: 0.928712271764706

00:25:41.200 --> 00:25:42.640 And they talked about three

NOTE Confidence: 0.928712271764706

00:25:42.640 --> 00:25:43.792 types of intrepidated costs,

NOTE Confidence: 0.928712271764706

00:25:43.800 --> 00:25:45.528 new line including of the simplex

NOTE Confidence: 0.928712271764706

00:25:45.528 --> 00:25:47.441 type of course of the bonus type

NOTE Confidence: 0.928712271764706

00:25:47.441 --> 00:25:49.367 is what we now refer to as HCL

NOTE Confidence: 0.928712271764706

00:25:49.367 --> 00:25:51.068 and the pygas type we refer to

NOTE Confidence: 0.928712271764706

00:25:51.068 --> 00:25:53.342 as extra mammary pygas disease.

NOTE Confidence: 0.928712271764706

00:25:53.342 --> 00:25:57.080 But the simplex type is what they really,

NOTE Confidence: 0.928712271764706

00:25:57.080 --> 00:25:57.760 you know,

NOTE Confidence: 0.928712271764706

00:25:57.760 --> 00:25:59.158 were initially introducing

NOTE Confidence: 0.928712271764706

00:25:59.158 --> 00:26:01.304 at that point And it was,

NOTE Confidence: 0.928712271764706

00:26:01.304 --> 00:26:03.459 it was I like to highlight this study

NOTE Confidence: 0.928712271764706

00:26:03.459 --> 00:26:05.224 because especially for the trainees

NOTE Confidence: 0.928712271764706

00:26:05.224 --> 00:26:07.118 and the audience it highlights

NOTE Confidence: 0.928712271764706

00:26:07.118 --> 00:26:09.238 the significance of making basic.

NOTE Confidence: 0.928712271764706

00:26:09.240 --> 00:26:10.665 Clinical pathologic observations,

NOTE Confidence: 0.928712271764706

00:26:10.665 --> 00:26:12.090 because everything they've

NOTE Confidence: 0.928712271764706

00:26:12.090 --> 00:26:14.108 ever said really held's true.

NOTE Confidence: 0.928712271764706

00:26:14.108 --> 00:26:16.600 If you look and read that paper,

NOTE Confidence: 0.928712271764706

00:26:16.600 --> 00:26:18.950 they talked about its association

NOTE Confidence: 0.928712271764706

00:26:18.950 --> 00:26:20.360 with leukoplicy vilitis,

NOTE Confidence: 0.928712271764706

00:26:20.360 --> 00:26:21.960 which is like in sclerosis.

NOTE Confidence: 0.928712271764706

00:26:21.960 --> 00:26:23.508 They talked about how it has

NOTE Confidence: 0.928712271764706

00:26:23.508 --> 00:26:24.880 a short insight to face.

NOTE Confidence: 0.928712271764706

00:26:24.880 --> 00:26:26.980 They talked about how it's

NOTE Confidence: 0.928712271764706

00:26:26.980 --> 00:26:29.080 frequently present on the margins.

NOTE Confidence: 0.928712271764706

00:26:29.080 --> 00:26:31.876 All of those have remained true.

NOTE Confidence: 0.928712271764706

00:26:31.880 --> 00:26:33.488 And when you focus on the

NOTE Confidence: 0.928712271764706

00:26:33.488 --> 00:26:34.960 lower portion of this table,

NOTE Confidence: 0.928712271764706

00:26:34.960 --> 00:26:37.408 you can see the evolution in the terminology.

NOTE Confidence: 0.928712271764706

00:26:37.410 --> 00:26:39.684 We started with ISSV D's hypertrophic

NOTE Confidence: 0.928712271764706

00:26:39.684 --> 00:26:42.355 dystrophy and V IM3 of the differentiated

NOTE Confidence: 0.928712271764706

00:26:42.355 --> 00:26:44.527 type to where we are today,

NOTE Confidence: 0.928712271764706

00:26:44.530 --> 00:26:46.648 which is differentiated

NOTE Confidence: 0.928712271764706

00:26:46.648 --> 00:26:48.766 for ventricular pleasure.

NOTE Confidence: 0.928712271764706

00:26:48.770 --> 00:26:50.910 D event is generally seen

NOTE Confidence: 0.928712271764706

00:26:50.910 --> 00:26:53.050 in an older age group.

NOTE Confidence: 0.928712271764706

00:26:53.050 --> 00:26:54.515 There's a school of thought

NOTE Confidence: 0.928712271764706

00:26:54.515 --> 00:26:56.293 that's emerging that D event can

NOTE Confidence: 0.928712271764706

00:26:56.293 --> 00:26:58.085 be seen in the younger and it's

NOTE Confidence: 0.928712271764706

00:26:58.085 --> 00:26:59.809 increasing in the younger age group,

NOTE Confidence: 0.928712271764706

00:26:59.810 --> 00:27:02.096 which is probably related to that

NOTE Confidence: 0.928712271764706

00:27:02.096 --> 00:27:04.594 second peak like in sclerosis which

NOTE Confidence: 0.928712271764706

00:27:04.594 --> 00:27:07.730 occurs in teenagers and younger than 10.

NOTE Confidence: 0.928712271764706

00:27:07.730 --> 00:27:10.089 So those patients probably when they're 30th,

NOTE Confidence: 0.928712271764706

00:27:10.090 --> 00:27:11.610 so may develop the event.

NOTE Confidence: 0.928712271764706

00:27:11.610 --> 00:27:13.362 In any event,

NOTE Confidence: 0.928712271764706

00:27:13.362 --> 00:27:16.058 most patients are postmenopausal age group.

NOTE Confidence: 0.928712271764706

00:27:16.058 --> 00:27:18.350 The event is generally a centrally

NOTE Confidence: 0.928712271764706

00:27:18.412 --> 00:27:20.884 located disease or current inhaler skin

NOTE Confidence: 0.928712271764706

00:27:20.884 --> 00:27:23.250 areas without keratinized and epithelium.

NOTE Confidence: 0.928712271764706

00:27:23.250 --> 00:27:25.546 But of course it can get big and

NOTE Confidence: 0.928712271764706

00:27:25.546 --> 00:27:27.130 extend upward outwards to the

NOTE Confidence: 0.928712271764706

00:27:27.130 --> 00:27:31.210 Libya majora and elsewhere as well.

NOTE Confidence: 0.928712271764706

00:27:31.210 --> 00:27:33.490 Most events are diagnosed

NOTE Confidence: 0.928712271764706

00:27:33.490 --> 00:27:36.340 concurrent with the invasive cancer.

NOTE Confidence: 0.928712271764706

00:27:36.340 --> 00:27:38.314 But cases that are diagnosed in

NOTE Confidence: 0.928712271764706

00:27:38.314 --> 00:27:40.339 isolation are often difficult to diagnose.

NOTE Confidence: 0.928712271764706

00:27:40.340 --> 00:27:40.668 Indeed,

NOTE Confidence: 0.928712271764706

00:27:40.668 --> 00:27:42.636 when you have patients with cancer

NOTE Confidence: 0.928712271764706

00:27:42.636 --> 00:27:45.410 and you go back and look at their

NOTE Confidence: 0.928712271764706

00:27:45.410 --> 00:27:47.300 ostensibly prior lichen sclerosis biopsies,

NOTE Confidence: 0.928712271764706

00:27:47.300 --> 00:27:49.700 a lot of those lichen sclerosis

NOTE Confidence: 0.928712271764706

00:27:49.700 --> 00:27:51.340 biopsies had different in them.

NOTE Confidence: 0.9402536

00:27:53.750 --> 00:27:56.878 In terms of the percentage of the events

NOTE Confidence: 0.9402536

00:27:56.878 --> 00:27:59.106 that found to have cancer follow up,

NOTE Confidence: 0.9402536

00:27:59.110 --> 00:28:02.158 it ranges from 32.8% to what I consider

NOTE Confidence: 0.9402536

00:28:02.158 --> 00:28:04.908 a little bit of an outlier study.

NOTE Confidence: 0.9402536

00:28:04.910 --> 00:28:07.982 They found 85.7% at follow up.

NOTE Confidence: 0.9402536

00:28:07.982 --> 00:28:10.310 This is from the Vancouver group

NOTE Confidence: 0.9402536

00:28:10.310 --> 00:28:12.053 and but I think what everyone would

NOTE Confidence: 0.9402536

00:28:12.053 --> 00:28:13.882 agree on is the time to progression

NOTE Confidence: 0.9402536

00:28:13.882 --> 00:28:16.083 to look at the far right column is

NOTE Confidence: 0.9402536

00:28:16.083 --> 00:28:17.623 that everyone agrees that there's

NOTE Confidence: 0.9402536

00:28:17.623 --> 00:28:20.278 a short median time to progression

NOTE Confidence: 0.9402536

00:28:20.278 --> 00:28:23.734 between the diagnosis of the Devon.

NOTE Confidence: 0.9402536

00:28:23.740 --> 00:28:26.784 By itself, in a biopsy and the subsequent

NOTE Confidence: 0.9402536

00:28:26.784 --> 00:28:29.500 diagnosis of a carcinoma can range widely,

NOTE Confidence: 0.9402536

00:28:29.500 --> 00:28:33.574 but the median time is relatively short.

NOTE Confidence: 0.9402536

00:28:33.580 --> 00:28:36.005 There's a cumulative risk of

NOTE Confidence: 0.9402536

00:28:36.005 --> 00:28:37.460 cancer for defend.

NOTE Confidence: 0.9402536

00:28:37.460 --> 00:28:39.140 If you look at 10 years,

NOTE Confidence: 0.9402536

00:28:39.140 --> 00:28:40.540 regular HCL at 10 years,

NOTE Confidence: 0.9402536

00:28:40.540 --> 00:28:42.220 like I said before, it's only about

NOTE Confidence: 0.9402536

00:28:42.220 --> 00:28:44.516 10% and look at how flat the curve is.

NOTE Confidence: 0.9402536

00:28:44.520 --> 00:28:45.404 On the other hand,

NOTE Confidence: 0.9402536

00:28:45.404 --> 00:28:47.239 when you look at Devin at 10 years,

NOTE Confidence: 0.9402536

00:28:47.240 --> 00:28:49.720 the cumulative risk is close to 50% and

NOTE Confidence: 0.9402536

00:28:49.720 --> 00:28:54.000 the curve is really bumping upwards.

NOTE Confidence: 0.9402536

00:28:54.000 --> 00:28:57.640 However, the diagnosis remains problematic.

NOTE Confidence: 0.9402536

00:28:57.640 --> 00:28:59.700 Here's just a recent

NOTE Confidence: 0.9402536

00:28:59.700 --> 00:29:01.760 study got 4 pathologists,

NOTE Confidence: 0.9402536

00:29:01.760 --> 00:29:03.376 including a gynecological pathologist.

NOTE Confidence: 0.9402536

00:29:03.376 --> 00:29:05.800 The Scala was that gynecological pathologist.

NOTE Confidence: 0.9402536

00:29:05.800 --> 00:29:08.364 He's got 2 dermatopathologist

NOTE Confidence: 0.9402536

00:29:08.364 --> 00:29:10.928 and one general pathologist.

NOTE Confidence: 0.9402536

00:29:10.930 --> 00:29:12.682 And this is not even about

NOTE Confidence: 0.9402536

00:29:12.682 --> 00:29:14.090 diagnosis of divine per se,

NOTE Confidence: 0.9402536

00:29:14.090 --> 00:29:17.093 or what relative value each observer assigns

NOTE Confidence: 0.9402536

00:29:17.093 --> 00:29:20.489 to each of these individual features.

NOTE Confidence: 0.9402536

00:29:20.490 --> 00:29:22.698 It was just are these features

NOTE Confidence: 0.9402536

00:29:22.698 --> 00:29:23.802 present or not?

NOTE Confidence: 0.9402536

00:29:23.810 --> 00:29:28.250 And even that resulted in not entirely

NOTE Confidence: 0.9402536

00:29:28.250 --> 00:29:30.850 reassuring Kappa values in terms

NOTE Confidence: 0.9402536

00:29:30.850 --> 00:29:32.855 of its observer reproducibility.

NOTE Confidence: 0.9402536

00:29:32.855 --> 00:29:35.970 But I think what most would agree

NOTE Confidence: 0.9402536

00:29:35.970 --> 00:29:38.619 on is that basically tepia.

NOTE Confidence: 0.9402536

00:29:38.620 --> 00:29:40.930 Is a requirement for the diagnosis

NOTE Confidence: 0.9402536

00:29:40.930 --> 00:29:46.300 of Divin and recently ISSVD had a a

NOTE Confidence: 0.9402536

00:29:46.300 --> 00:29:48.280 consensus document in which they made

NOTE Confidence: 0.9402536

00:29:48.345 --> 00:29:50.553 that point that the diagnostic features

NOTE Confidence: 0.9402536

00:29:50.553 --> 00:29:53.262 of Divin would be Basilatipia and they

NOTE Confidence: 0.9402536

00:29:53.262 --> 00:29:55.978 defined that which I should talk about,

NOTE Confidence: 0.9402536

00:29:55.980 --> 00:29:56.286 Yeah,

NOTE Confidence: 0.9402536

00:29:56.286 --> 00:29:58.734 the case also needs to be P16 negative,

NOTE Confidence: 0.9402536

00:29:58.740 --> 00:30:01.056 P53 kind of wild type or

NOTE Confidence: 0.9402536

00:30:01.056 --> 00:30:02.214 mutational type staining,

NOTE Confidence: 0.9402536

00:30:02.220 --> 00:30:05.320 they mentioned that their supportive

NOTE Confidence: 0.9402536

00:30:05.320 --> 00:30:05.940 features.

NOTE Confidence: 0.9402536

00:30:05.940 --> 00:30:06.588 You know,

NOTE Confidence: 0.9402536

00:30:06.588 --> 00:30:09.180 all of which are sort of well recognized,

NOTE Confidence: 0.9402536

00:30:09.180 --> 00:30:12.072 but they have to do with most of

NOTE Confidence: 0.9402536

00:30:12.072 --> 00:30:14.602 the keratinized and subtypes into

NOTE Confidence: 0.9402536

00:30:14.602 --> 00:30:16.660 cellular breakdown into cellular

NOTE Confidence: 0.9402536

00:30:16.660 --> 00:30:18.740 vacuoles and prematural maturation.

NOTE Confidence: 0.9402536

00:30:18.740 --> 00:30:20.750 So if we consider the supportive

NOTE Confidence: 0.9402536

00:30:20.750 --> 00:30:23.010 features first here you can

NOTE Confidence: 0.9402536

00:30:23.010 --> 00:30:25.660 see that there's basal etipia.

NOTE Confidence: 0.9402536

00:30:25.660 --> 00:30:28.198 Focal And then there's what they

NOTE Confidence: 0.9402536

00:30:28.198 --> 00:30:30.857 refer to in the ***** context

NOTE Confidence: 0.9402536

00:30:30.857 --> 00:30:33.042 that this keratosis or premature

NOTE Confidence: 0.9402536

00:30:33.042 --> 00:30:35.221 meteoration which terms that may

NOTE Confidence: 0.9402536

00:30:35.221 --> 00:30:37.016 be used differently in Dermpa,

NOTE Confidence: 0.9402536

00:30:37.020 --> 00:30:39.440 but that's how they've been

NOTE Confidence: 0.9402536

00:30:39.440 --> 00:30:41.376 used traditionally in *****.

NOTE Confidence: 0.9402536

00:30:41.380 --> 00:30:44.680 And you can see that the the epidermis

NOTE Confidence: 0.9402536

00:30:44.680 --> 00:30:46.730 turns pink immediately after the

NOTE Confidence: 0.9402536

00:30:46.730 --> 00:30:49.862 basal layer and then there was this

NOTE Confidence: 0.9402536

00:30:49.862 --> 00:30:51.690 splengiosis like degenerative changes

NOTE Confidence: 0.9402536

00:30:51.690 --> 00:30:54.456 and vacuous that are present within it.

NOTE Confidence: 0.9402536

00:30:54.460 --> 00:30:56.700 Regarding the main thing though,

NOTE Confidence: 0.9402536

00:30:56.700 --> 00:30:58.684 which is a typia,

NOTE Confidence: 0.9402536

00:30:58.684 --> 00:31:00.668 they listed criteria including

NOTE Confidence: 0.9402536

00:31:00.668 --> 00:31:02.044 chromatin problems, hypochromasia,

NOTE Confidence: 0.9402536

00:31:02.044 --> 00:31:02.812 nuclear enlargement,

NOTE Confidence: 0.9402536

00:31:02.812 --> 00:31:05.500 something three times the size of a

NOTE Confidence: 0.9402536

00:31:05.558 --> 00:31:07.668 lymphocyte or that's obviously different

NOTE Confidence: 0.9402536

00:31:07.668 --> 00:31:09.778 than background or some pleomorphism.

NOTE Confidence: 0.9402536

00:31:09.780 --> 00:31:12.000 We talk about common features

NOTE Confidence: 0.9402536

00:31:12.000 --> 00:31:13.776 and less common appearances,

NOTE Confidence: 0.9402536

00:31:13.780 --> 00:31:15.658 so of course something like this.

NOTE Confidence: 0.9402536

00:31:15.660 --> 00:31:18.180 We can all probably agree that this is given.

NOTE Confidence: 0.9402536

00:31:18.180 --> 00:31:19.980 This is click up based on the Typia,

NOTE Confidence: 0.86603416375

00:31:19.980 --> 00:31:22.204 it has two features,

NOTE Confidence: 0.86603416375

00:31:22.204 --> 00:31:24.428 hyperchromasia and nuclear enlargement.

NOTE Confidence: 0.86603416375

00:31:24.430 --> 00:31:25.980 And so everyone would agree

NOTE Confidence: 0.86603416375

00:31:25.980 --> 00:31:26.910 that that's basilatipia.

NOTE Confidence: 0.86603416375

00:31:26.910 --> 00:31:28.215 It's pretty true.

NOTE Confidence: 0.86603416375

00:31:28.215 --> 00:31:31.275 Maturation loss of a granular layer and

NOTE Confidence: 0.86603416375

00:31:31.275 --> 00:31:33.945 this is the so-called hypertrophic variant.

NOTE Confidence: 0.86603416375

00:31:33.950 --> 00:31:35.948 And this is another hypertrophic variant.

NOTE Confidence: 0.86603416375

00:31:35.950 --> 00:31:37.950 The basilatipia is more subtle,

NOTE Confidence: 0.86603416375

00:31:37.950 --> 00:31:39.134 but clearly still present.

NOTE Confidence: 0.86603416375

00:31:39.134 --> 00:31:42.541 At the tip of this arrows you can see some

NOTE Confidence: 0.86603416375

00:31:42.541 --> 00:31:44.109 nuclear enlargement and hypochronesia.

NOTE Confidence: 0.86603416375

00:31:44.110 --> 00:31:46.035 Here's one where the granular

NOTE Confidence: 0.86603416375

00:31:46.035 --> 00:31:47.688 layer is preserved, but still.

NOTE Confidence: 0.86603416375

00:31:47.688 --> 00:31:49.431 We can appreciate at the tip of

NOTE Confidence: 0.86603416375

00:31:49.431 --> 00:31:51.703 this iris that there's a nuclear

NOTE Confidence: 0.86603416375

00:31:51.703 --> 00:31:52.879 enlargement and hypochromesure,

NOTE Confidence: 0.86603416375

00:31:52.880 --> 00:31:55.040 and also notice the background

NOTE Confidence: 0.86603416375

00:31:55.040 --> 00:31:56.768 of Michael sclerosis that's

NOTE Confidence: 0.86603416375

00:31:56.768 --> 00:31:58.917 seen in this particular area.

NOTE Confidence: 0.86603416375

00:31:58.920 --> 00:32:01.476 Here's more of the conventional book

NOTE Confidence: 0.86603416375

00:32:01.476 --> 00:32:03.180 where there's irregularly irregular

NOTE Confidence: 0.86603416375

00:32:03.243 --> 00:32:05.368 what they call basal disarray and

NOTE Confidence: 0.86603416375

00:32:05.368 --> 00:32:07.708 announced the most Inritti and basal.

NOTE Confidence: 0.86603416375

00:32:07.708 --> 00:32:09.478 The tip here of course,

NOTE Confidence: 0.86603416375

00:32:09.480 --> 00:32:12.120 and degenerative changes as shown here.

NOTE Confidence: 0.86603416375

00:32:12.120 --> 00:32:13.597 This is species the three I HC.

NOTE Confidence: 0.948487290909091

00:32:16.220 --> 00:32:17.885 There's one where the basaltipia

NOTE Confidence: 0.948487290909091

00:32:17.885 --> 00:32:20.020 is getting more and more subtle,

NOTE Confidence: 0.948487290909091

00:32:20.020 --> 00:32:21.791 but a high magnification then one can

NOTE Confidence: 0.948487290909091

00:32:21.791 --> 00:32:23.620 still get to differentiated then,

NOTE Confidence: 0.948487290909091

00:32:23.620 --> 00:32:24.620 especially if you focus on.

NOTE Confidence: 0.948487290909091

00:32:24.620 --> 00:32:26.097 For example, look at the tip of

NOTE Confidence: 0.948487290909091

00:32:26.097 --> 00:32:27.500 the arrow in the lower left,

NOTE Confidence: 0.948487290909091

00:32:27.500 --> 00:32:29.768 you can appreciate some basaltipia that's

NOTE Confidence: 0.948487290909091

00:32:29.768 --> 00:32:31.780 currently present in these lesions.

NOTE Confidence: 0.948487290909091

00:32:31.780 --> 00:32:32.784 On the other hand,

NOTE Confidence: 0.948487290909091

00:32:32.784 --> 00:32:33.537 something like this,

NOTE Confidence: 0.948487290909091

00:32:33.540 --> 00:32:36.088 which to my eye does not have

NOTE Confidence: 0.948487290909091

00:32:36.088 --> 00:32:37.862 basaltipia but low and behold

NOTE Confidence: 0.948487290909091

00:32:37.862 --> 00:32:40.860 turns out to be a P53 abnormal,

NOTE Confidence: 0.948487290909091

00:32:40.860 --> 00:32:45.500 the so-called subtle variant of DV.

NOTE Confidence: 0.948487290909091

00:32:45.500 --> 00:32:46.544 Which you know,

NOTE Confidence: 0.948487290909091

00:32:46.544 --> 00:32:48.632 sometimes you can sort of your

NOTE Confidence: 0.948487290909091

00:32:48.632 --> 00:32:50.635 yourself way out of being able

NOTE Confidence: 0.948487290909091

00:32:50.635 --> 00:32:52.220 to diagnose the whole thing.

NOTE Confidence: 0.948487290909091

00:32:52.220 --> 00:32:54.340 But in anyway my to my eye this is not

NOTE Confidence: 0.948487290909091

00:32:54.396 --> 00:32:56.736 quite diagnostic at the morphologic level,

NOTE Confidence: 0.948487290909091

00:32:56.740 --> 00:32:59.629 but it is the event and so the so-called

NOTE Confidence: 0.948487290909091

00:32:59.629 --> 00:33:02.220 sort of variant and there are other variants.

NOTE Confidence: 0.948487290909091

00:33:02.220 --> 00:33:03.798 This is atrophic variant to shown

NOTE Confidence: 0.948487290909091

00:33:03.798 --> 00:33:05.486 on the left is more acantalytic

NOTE Confidence: 0.948487290909091

00:33:05.486 --> 00:33:07.806 that's shown on the far right is the

NOTE Confidence: 0.948487290909091

00:33:07.867 --> 00:33:10.057 apotrophic examples of which have shown.

NOTE Confidence: 0.948487290909091

00:33:10.060 --> 00:33:11.940 And here's the intermediate.

NOTE Confidence: 0.948487290909091

00:33:11.940 --> 00:33:12.410 Invariant,

NOTE Confidence: 0.948487290909091

00:33:12.410 --> 00:33:15.322 the one that looks sort of halfway in

NOTE Confidence: 0.948487290909091

00:33:15.322 --> 00:33:17.769 between something that's completely mature,

NOTE Confidence: 0.948487290909091

00:33:17.770 --> 00:33:20.178 premature maturation and all that and

NOTE Confidence: 0.948487290909091

00:33:20.178 --> 00:33:21.810 something that's visible looking.

NOTE Confidence: 0.948487290909091

00:33:21.810 --> 00:33:24.530 And this is a so-called intermediate variant.

NOTE Confidence: 0.948487290909091

00:33:24.530 --> 00:33:26.930 Most of them are non keratinizing,

NOTE Confidence: 0.948487290909091

00:33:26.930 --> 00:33:29.370 but they're also keratinizing variants.

NOTE Confidence: 0.948487290909091

00:33:29.370 --> 00:33:31.890 So here's an intermediate keratinizing.

NOTE Confidence: 0.948487290909091

00:33:31.890 --> 00:33:34.080 You can see it's clinically a

NOTE Confidence: 0.948487290909091

00:33:34.080 --> 00:33:35.860 discrete lesion between the blue

NOTE Confidence: 0.948487290909091

00:33:35.860 --> 00:33:37.610 Marks and a high magnification.

NOTE Confidence: 0.948487290909091

00:33:37.610 --> 00:33:39.310 It looks like it's not

NOTE Confidence: 0.948487290909091

00:33:39.310 --> 00:33:41.090 quite mature in in well.

NOTE Confidence: 0.948487290909091

00:33:41.090 --> 00:33:42.530 It's very minimal base

NOTE Confidence: 0.948487290909091

00:33:42.530 --> 00:33:44.597 of the tippy eye to see.

NOTE Confidence: 0.948487290909091

00:33:44.600 --> 00:33:47.993 To my eye, MP53 lights up that whole area.

NOTE Confidence: 0.911129407142857

00:33:50.760 --> 00:33:53.931 Just like there is a divin like

NOTE Confidence: 0.911129407142857

00:33:53.931 --> 00:33:57.357 pattern of H cell as shown here,

NOTE Confidence: 0.911129407142857

00:33:57.360 --> 00:34:00.160 there is there is also H

NOTE Confidence: 0.911129407142857

00:34:00.160 --> 00:34:01.560 cell like pattern of divin,

NOTE Confidence: 0.911129407142857

00:34:01.560 --> 00:34:03.968 the so-called basaloid divin

NOTE Confidence: 0.911129407142857

00:34:03.968 --> 00:34:06.978 wherein the epidermis is entirely

NOTE Confidence: 0.911129407142857

00:34:06.978 --> 00:34:10.440 basiloid and immature looking.

NOTE Confidence: 0.911129407142857

00:34:10.440 --> 00:34:12.519 But then you do P53 lights up,

NOTE Confidence: 0.911129407142857

00:34:12.520 --> 00:34:13.885 P16 is negative.

NOTE Confidence: 0.911129407142857

00:34:13.885 --> 00:34:16.960 I have not had the misfortune of

NOTE Confidence: 0.911129407142857

00:34:16.960 --> 00:34:20.160 identifying a basil or divine in a biopsy.

NOTE Confidence: 0.911129407142857

00:34:20.160 --> 00:34:21.918 Every case of saying has been

NOTE Confidence: 0.911129407142857

00:34:21.920 --> 00:34:23.560 adjacent to her invasive cancer,

NOTE Confidence: 0.911129407142857

00:34:23.560 --> 00:34:27.277 which of course helps with the diagnosis.

NOTE Confidence: 0.911129407142857

00:34:27.280 --> 00:34:28.744 With respect to immunos,

NOTE Confidence: 0.911129407142857

00:34:28.744 --> 00:34:29.476 to chemistry,

NOTE Confidence: 0.935557274

00:34:31.520 --> 00:34:33.730 the main point of controversy

NOTE Confidence: 0.935557274

00:34:33.730 --> 00:34:36.528 is whether or not there is a

NOTE Confidence: 0.935557274

00:34:36.528 --> 00:34:39.636 thing as a P53 wild type divine.

NOTE Confidence: 0.935557274

00:34:39.636 --> 00:34:41.992 The literature suggests that

NOTE Confidence: 0.935557274

00:34:41.992 --> 00:34:45.692 there is because any up to 35% of

NOTE Confidence: 0.935557274

00:34:45.692 --> 00:34:47.858 cases of reported cases of Divin

NOTE Confidence: 0.935557274

00:34:47.858 --> 00:34:50.274 in the literature, P53 wild type.

NOTE Confidence: 0.935557274

00:34:50.274 --> 00:34:51.762 But of course there's a little

NOTE Confidence: 0.935557274

00:34:51.762 --> 00:34:53.130 bit of circularity there,

NOTE Confidence: 0.935557274

00:34:53.130 --> 00:34:55.260 you know it's called Divin

NOTE Confidence: 0.935557274

00:34:55.260 --> 00:34:57.890 even though it's P53 wild type.

NOTE Confidence: 0.935557274

00:34:57.890 --> 00:34:59.840 Divin is difficult to diagnose

NOTE Confidence: 0.935557274

00:34:59.840 --> 00:35:01.428 by morphology alone, you know.

NOTE Confidence: 0.935557274

00:35:01.428 --> 00:35:02.891 So there's a there's a little bit

NOTE Confidence: 0.935557274

00:35:02.891 --> 00:35:04.338 of circularity in that event.

NOTE Confidence: 0.935557274

00:35:04.340 --> 00:35:06.420 That's what the literature indicates,

NOTE Confidence: 0.935557274

00:35:06.420 --> 00:35:09.156 that you can't have P 53 Watt type

NOTE Confidence: 0.935557274

00:35:09.156 --> 00:35:11.004 and ISSVD certainly supports that.

NOTE Confidence: 0.935557274

00:35:11.004 --> 00:35:14.569 And I and I also know from my personal

NOTE Confidence: 0.935557274

00:35:14.569 --> 00:35:17.041 experience that I've seen cases that

NOTE Confidence: 0.935557274

00:35:17.041 --> 00:35:19.912 are classical Divin with clear cut

NOTE Confidence: 0.935557274

00:35:19.912 --> 00:35:22.297 bisalitipia that are P53 wildfires.

NOTE Confidence: 0.935557274

00:35:22.300 --> 00:35:23.500 So I know it occurs

NOTE Confidence: 0.946657697272727

00:35:25.860 --> 00:35:27.428 with respect to interpretation.

NOTE Confidence: 0.946657697272727

00:35:27.428 --> 00:35:30.380 The same study that I cited earlier,

NOTE Confidence: 0.946657697272727

00:35:30.380 --> 00:35:32.530 Trisi and Clute also talked

NOTE Confidence: 0.946657697272727

00:35:32.530 --> 00:35:34.680 about the side two patterns.

NOTE Confidence: 0.946657697272727

00:35:34.680 --> 00:35:36.852 Including staining of the base that

NOTE Confidence: 0.946657697272727

00:35:36.852 --> 00:35:38.687 extends upward the so-called part

NOTE Confidence: 0.946657697272727

00:35:38.687 --> 00:35:40.940 of basil diffuse pattern or basil

NOTE Confidence: 0.946657697272727

00:35:40.940 --> 00:35:43.760 only staining just the base only,

NOTE Confidence: 0.946657697272727

00:35:43.760 --> 00:35:45.065 not extending upwards.

NOTE Confidence: 0.946657697272727

00:35:45.065 --> 00:35:47.240 A subset of these are

NOTE Confidence: 0.946657697272727

00:35:47.240 --> 00:35:49.280 associated with a P53 mutation,

NOTE Confidence: 0.946657697272727

00:35:49.280 --> 00:35:51.524 but it's a nonspecific staining pattern

NOTE Confidence: 0.946657697272727

00:35:51.524 --> 00:35:54.720 and you get the null in the cytoplasmic.

NOTE Confidence: 0.946657697272727

00:35:54.720 --> 00:35:56.238 The mid epithelia of basal sparing.

NOTE Confidence: 0.946657697272727

00:35:56.240 --> 00:35:58.235 I showed images before when there's no

NOTE Confidence: 0.946657697272727

00:35:58.235 --> 00:36:00.556 staining at the base even though the

NOTE Confidence: 0.946657697272727

00:36:00.556 --> 00:36:02.316 epithelium itself is strongly staining.

NOTE Confidence: 0.946657697272727

00:36:02.320 --> 00:36:03.958 These are wild type staining pattern,

NOTE Confidence: 0.946657697272727

00:36:03.960 --> 00:36:05.752 but the more common wild type staining

NOTE Confidence: 0.946657697272727

00:36:05.752 --> 00:36:07.491 pattern is when you have sporadic

NOTE Confidence: 0.946657697272727

00:36:07.491 --> 00:36:10.596 staining as shown in the left image.

NOTE Confidence: 0.946657697272727

00:36:10.600 --> 00:36:13.870 Now of course in real life

NOTE Confidence: 0.946657697272727

00:36:13.870 --> 00:36:17.000 it's never perfect.

NOTE Confidence: 0.946657697272727

00:36:17.000 --> 00:36:18.785 Everyone can recognize the clay

NOTE Confidence: 0.946657697272727

00:36:18.785 --> 00:36:20.570 cut wild type staining patterns.

NOTE Confidence: 0.946657697272727

00:36:20.570 --> 00:36:22.012 And then there's some cases that it

NOTE Confidence: 0.946657697272727

00:36:22.012 --> 00:36:23.410 looks like it's extending upwards,

NOTE Confidence: 0.946657697272727

00:36:23.410 --> 00:36:26.194 but it's in a discrete area

NOTE Confidence: 0.946657697272727

00:36:26.194 --> 00:36:28.050 without a morphological correlate.

NOTE Confidence: 0.946657697272727

00:36:28.050 --> 00:36:28.842 In other words,

NOTE Confidence: 0.946657697272727

00:36:28.842 --> 00:36:30.690 that area is not atypical at all.

NOTE Confidence: 0.946657697272727

00:36:30.690 --> 00:36:34.274 Or when you have strong staining that

NOTE Confidence: 0.946657697272727

00:36:34.274 --> 00:36:37.282 doesn't extend upwards and it's like okay.

NOTE Confidence: 0.946657697272727

00:36:37.282 --> 00:36:40.240 What do we do with that?

NOTE Confidence: 0.946657697272727

00:36:40.240 --> 00:36:43.200 Seems stronger than expected.

NOTE Confidence: 0.946657697272727

00:36:43.200 --> 00:36:43.568 And again,

NOTE Confidence: 0.946657697272727

00:36:43.568 --> 00:36:44.120 like I said,

NOTE Confidence: 0.946657697272727

00:36:44.120 --> 00:36:45.640 that has been associated with

NOTE Confidence: 0.946657697272727

00:36:45.640 --> 00:36:47.760 the presence of a P53 mutation.

NOTE Confidence: 0.946657697272727

00:36:47.760 --> 00:36:49.713 But you can also see them when

NOTE Confidence: 0.946657697272727

00:36:49.713 --> 00:36:51.040 P53 mutation is absent,

NOTE Confidence: 0.946657697272727

00:36:51.040 --> 00:36:53.679 as in like in sclerosis or liking

NOTE Confidence: 0.946657697272727

00:36:53.680 --> 00:36:55.850 simplex chronicles or other even

NOTE Confidence: 0.946657697272727

00:36:55.850 --> 00:36:58.020 spongeotic dermatitis cases you can

NOTE Confidence: 0.946657697272727

00:36:58.091 --> 00:37:00.198 you can see that pattern as well.

NOTE Confidence: 0.946657697272727

00:37:00.200 --> 00:37:02.072 Or when the standing of the

NOTE Confidence: 0.946657697272727

00:37:02.072 --> 00:37:03.920 base and it extends upwards,

NOTE Confidence: 0.946657697272727

00:37:03.920 --> 00:37:06.248 but in a kind of a wimpy way.

NOTE Confidence: 0.946657697272727

00:37:06.250 --> 00:37:08.689 Slightly and then like what to do with that.

NOTE Confidence: 0.946657697272727

00:37:08.690 --> 00:37:10.657 So in these scenarios it would be

NOTE Confidence: 0.946657697272727

00:37:10.657 --> 00:37:12.725 nice to have additional markers to

NOTE Confidence: 0.946657697272727

00:37:12.725 --> 00:37:15.047 assist with the diagnosis of Divin.

NOTE Confidence: 0.946657697272727

00:37:15.050 --> 00:37:18.566 Unfortunately these markers are not great.

NOTE Confidence: 0.946657697272727

00:37:18.570 --> 00:37:20.670 All the markers that have been

NOTE Confidence: 0.946657697272727

00:37:20.670 --> 00:37:22.355 proffered and listed here that

NOTE Confidence: 0.946657697272727

00:37:22.355 --> 00:37:26.090 are aware of 1 P CK13CK17 sorts 2.

NOTE Confidence: 0.946657697272727

00:37:26.090 --> 00:37:27.786 They're just not ideal.

NOTE Confidence: 0.946657697272727

00:37:27.786 --> 00:37:30.330 They each have their own problems.

NOTE Confidence: 0.946657697272727

00:37:30.330 --> 00:37:31.630 For the main differential,

NOTE Confidence: 0.946657697272727

00:37:31.630 --> 00:37:34.370 we don't really care about Divin versus H,

NOTE Confidence: 0.946657697272727

00:37:34.370 --> 00:37:35.966 so per se.

NOTE Confidence: 0.946657697272727

00:37:35.966 --> 00:37:40.540 We care mostly about D Vin versus Lycos,

NOTE Confidence: 0.946657697272727

00:37:40.540 --> 00:37:44.220 non putative non neoplastic lesions,

NOTE Confidence: 0.946657697272727

00:37:44.220 --> 00:37:45.180 inflammatory disorders,

NOTE Confidence: 0.946657697272727

00:37:45.180 --> 00:37:48.060 that's really what the issue is.

NOTE Confidence: 0.946657697272727

00:37:48.060 --> 00:37:49.866 The one that does show the

NOTE Confidence: 0.946657697272727

00:37:49.866 --> 00:37:51.660 most promise is got a three.

NOTE Confidence: 0.946657697272727

00:37:51.660 --> 00:37:53.557 Got a three was initially reported by

NOTE Confidence: 0.946657697272727

00:37:53.557 --> 00:37:55.523 Dean Yang from the Cleveland Clinic a

NOTE Confidence: 0.946657697272727

00:37:55.523 --> 00:37:58.192 couple of years ago as being lost in

NOTE Confidence: 0.946657697272727

00:37:58.192 --> 00:38:01.379 the basal and para basal layers of D Vin.

NOTE Confidence: 0.946657697272727

00:38:01.380 --> 00:38:03.578 Got a three is normally expressed in

NOTE Confidence: 0.946657697272727

00:38:03.578 --> 00:38:05.098 the epidermis expressed in H cell.

NOTE Confidence: 0.946657697272727

00:38:05.100 --> 00:38:07.168 Difusely, but in Divin,

NOTE Confidence: 0.946657697272727

00:38:07.168 --> 00:38:10.867 apparently it's lost in the basal layer

NOTE Confidence: 0.946657697272727

00:38:10.867 --> 00:38:13.897 and the parabasal layers as well.

NOTE Confidence: 0.946657697272727

00:38:13.900 --> 00:38:16.686 So we examined this and we found

NOTE Confidence: 0.946657697272727

00:38:16.686 --> 00:38:18.660 it to be useful.

NOTE Confidence: 0.946657697272727

00:38:18.660 --> 00:38:19.378 You know,

NOTE Confidence: 0.946657697272727

00:38:19.378 --> 00:38:22.250 this is 19 out of 25 cases showed

NOTE Confidence: 0.946657697272727

00:38:22.337 --> 00:38:25.360 greater than 75% of cells lost in

NOTE Confidence: 0.946657697272727

00:38:25.360 --> 00:38:27.380 the basal and parabasal regions,

NOTE Confidence: 0.946657697272727

00:38:27.380 --> 00:38:30.539 but that still is 2 out of the 25

NOTE Confidence: 0.946657697272727

00:38:30.539 --> 00:38:32.870 cases that had no loss whatsoever.

NOTE Confidence: 0.946657697272727

00:38:32.870 --> 00:38:36.590 We also found a lot of the VIN threes

NOTE Confidence: 0.946657697272727

00:38:36.590 --> 00:38:40.190 showed some loss in a partial or complete.

NOTE Confidence: 0.941027707692307

00:38:40.190 --> 00:38:42.366 But what is useful is that a lot

NOTE Confidence: 0.941027707692307

00:38:42.366 --> 00:38:43.986 of dermatosis like in sclerosis

NOTE Confidence: 0.941027707692307

00:38:43.986 --> 00:38:46.008 like in Simplex Chronicus and a

NOTE Confidence: 0.941027707692307

00:38:46.008 --> 00:38:48.067 variety of others did not show loss.

NOTE Confidence: 0.941027707692307

00:38:48.070 --> 00:38:50.414 We had a rare case that we were

NOTE Confidence: 0.941027707692307

00:38:50.414 --> 00:38:52.029 convinced does not have Divin.

NOTE Confidence: 0.941027707692307

00:38:52.030 --> 00:38:55.108 These are all P53 wall type by the way

NOTE Confidence: 0.941027707692307

00:38:55.108 --> 00:38:57.548 and P16 negative we were convinced,

NOTE Confidence: 0.941027707692307

00:38:57.548 --> 00:39:00.060 not sure divin but still short

NOTE Confidence: 0.941027707692307

00:39:00.060 --> 00:39:03.000 loss of of of this markers.

NOTE Confidence: 0.941027707692307

00:39:03.000 --> 00:39:05.064 So the overall problems can be

NOTE Confidence: 0.941027707692307

00:39:05.064 --> 00:39:06.863 summarized as in sometimes you

NOTE Confidence: 0.941027707692307

00:39:06.863 --> 00:39:08.673 have weak expression throughout the

NOTE Confidence: 0.941027707692307

00:39:08.673 --> 00:39:10.848 epidemics and so you can't tell

NOTE Confidence: 0.941027707692307

00:39:10.848 --> 00:39:12.840 whether there's loss in the base.

NOTE Confidence: 0.941027707692307

00:39:12.840 --> 00:39:13.692 And like I said,

NOTE Confidence: 0.941027707692307

00:39:13.692 --> 00:39:15.985 about 10% of cases show normal expression

NOTE Confidence: 0.941027707692307

00:39:15.985 --> 00:39:18.600 or defiant cases show normal expression.

NOTE Confidence: 0.941027707692307

00:39:18.600 --> 00:39:19.460 And then there's this

NOTE Confidence: 0.941027707692307

00:39:19.460 --> 00:39:20.320 question of partial loss.

NOTE Confidence: 0.941027707692307

00:39:20.320 --> 00:39:22.240 What is partial indeed the,

NOTE Confidence: 0.941027707692307

00:39:22.240 --> 00:39:24.040 you know, we use this numbers

NOTE Confidence: 0.941027707692307

00:39:24.040 --> 00:39:26.200 25 to 75% what is you know,

NOTE Confidence: 0.941027707692307

00:39:26.200 --> 00:39:28.430 I hate any sort of.

NOTE Confidence: 0.941027707692307

00:39:28.430 --> 00:39:30.824 Markers that need to be interpreted

NOTE Confidence: 0.941027707692307

00:39:30.824 --> 00:39:33.334 with numbers in that way and so it

NOTE Confidence: 0.941027707692307

00:39:33.334 --> 00:39:35.115 just you know it it's it's a problem

NOTE Confidence: 0.941027707692307

00:39:35.115 --> 00:39:36.956 but at least it's the one that

NOTE Confidence: 0.941027707692307

00:39:36.956 --> 00:39:38.728 shows the most promise Any marker

NOTE Confidence: 0.941027707692307

00:39:38.728 --> 00:39:41.256 really has to be combined with P50

NOTE Confidence: 0.941027707692307

00:39:41.256 --> 00:39:45.748 degree or and P16 really also in

NOTE Confidence: 0.941027707692307

00:39:45.748 --> 00:39:48.022 this space are these lesions they

NOTE Confidence: 0.941027707692307

00:39:48.022 --> 00:39:50.301 are controversial by the by the

NOTE Confidence: 0.941027707692307

00:39:50.301 --> 00:39:52.150 very nature especially recently or

NOTE Confidence: 0.941027707692307

00:39:52.150 --> 00:39:54.642 that are HP3 independent and P53

NOTE Confidence: 0.941027707692307

00:39:54.642 --> 00:39:58.086 wild type as I alluded to before.

NOTE Confidence: 0.941027707692307

00:39:58.090 --> 00:40:00.970 Most cases of devane are diagnosed

NOTE Confidence: 0.941027707692307

00:40:00.970 --> 00:40:02.890 concurrent with invasive carcinoma,

NOTE Confidence: 0.941027707692307

00:40:02.890 --> 00:40:04.714 and when that happens,

NOTE Confidence: 0.941027707692307

00:40:04.714 --> 00:40:07.330 the P53 mutational status of the

NOTE Confidence: 0.941027707692307

00:40:07.330 --> 00:40:09.980 invasive and inside 2 lesions match

NOTE Confidence: 0.941027707692307

00:40:09.980 --> 00:40:12.830 each other about 78% of the time,

NOTE Confidence: 0.941027707692307

00:40:12.830 --> 00:40:15.250 and then the remaining 21% of

NOTE Confidence: 0.941027707692307

00:40:15.250 --> 00:40:17.250 the time there's a mismatch.

NOTE Confidence: 0.941027707692307

00:40:17.250 --> 00:40:18.900 And that invariably,

NOTE Confidence: 0.941027707692307

00:40:18.900 --> 00:40:21.650 according to one large study,

NOTE Confidence: 0.941027707692307

00:40:21.650 --> 00:40:23.960 is because the invasive cancer

NOTE Confidence: 0.941027707692307

00:40:23.960 --> 00:40:25.346 is P53 abnormal.

NOTE Confidence: 0.941027707692307

00:40:25.350 --> 00:40:30.550 Whereas the lesion adjacent is P53 wild type.

NOTE Confidence: 0.941027707692307

00:40:30.550 --> 00:40:32.272 Now that tells me two things in

NOTE Confidence: 0.941027707692307

00:40:32.272 --> 00:40:34.087 an excision if I see an insight

NOTE Confidence: 0.941027707692307

00:40:34.087 --> 00:40:35.623 to lesion that's at the margin.

NOTE Confidence: 0.941027707692307

00:40:35.630 --> 00:40:37.590 The fact that the P53 is different

NOTE Confidence: 0.941027707692307

00:40:37.590 --> 00:40:41.126 between the excision and the and the

NOTE Confidence: 0.941027707692307

00:40:41.126 --> 00:40:42.866 putative precursor lesion doesn't mean

NOTE Confidence: 0.941027707692307

00:40:42.866 --> 00:40:45.149 I should ignore the precursor lesion.

NOTE Confidence: 0.941027707692307

00:40:45.150 --> 00:40:47.210 I would argue that you know that

NOTE Confidence: 0.941027707692307

00:40:47.210 --> 00:40:48.910 could still be very significant,

NOTE Confidence: 0.941027707692307

00:40:48.910 --> 00:40:51.004 but more importantly at this P53

NOTE Confidence: 0.941027707692307

00:40:51.004 --> 00:40:53.393 wild type insight to lesions that

NOTE Confidence: 0.941027707692307

00:40:53.393 --> 00:40:55.237 are adjacent invasive cancer.

NOTE Confidence: 0.941027707692307

00:40:55.240 --> 00:40:57.040 And what are they? Can they be recognized?

NOTE Confidence: 0.941027707692307

00:40:57.040 --> 00:40:59.890 What is the mutation that's happening

NOTE Confidence: 0.941027707692307

00:40:59.890 --> 00:41:02.560 with them of these lesions?

NOTE Confidence: 0.941027707692307

00:41:02.560 --> 00:41:04.680 Mutation of cancer fraction analysis,

NOTE Confidence: 0.941027707692307

00:41:04.680 --> 00:41:07.460 which as we all know has problems,

NOTE Confidence: 0.941027707692307

00:41:07.460 --> 00:41:10.392 but still have shown that perhaps

NOTE Confidence: 0.941027707692307

00:41:10.392 --> 00:41:13.308 the 53 is not the initiating event

NOTE Confidence: 0.941027707692307

00:41:13.308 --> 00:41:15.996 in this cremence across knowns that

NOTE Confidence: 0.941027707692307

00:41:16.000 --> 00:41:18.160 mutations in a NOx signaling pathway,

NOTE Confidence: 0.941027707692307

00:41:18.160 --> 00:41:21.688 3rd and some others may come first.

NOTE Confidence: 0.941027707692307

00:41:21.690 --> 00:41:24.288 And then they acquire P53 later.

NOTE Confidence: 0.941027707692307

00:41:24.290 --> 00:41:25.982 The question is what is the

NOTE Confidence: 0.941027707692307

00:41:25.982 --> 00:41:27.702 morphology of those cases that don't

NOTE Confidence: 0.941027707692307

00:41:27.702 --> 00:41:30.370 have P53 but have other mutations?

NOTE Confidence: 0.941027707692307

00:41:30.370 --> 00:41:33.367 Does it just look like P53 rod type even?

NOTE Confidence: 0.941027707692307

00:41:33.370 --> 00:41:35.206 Does it look like something else?

NOTE Confidence: 0.941027707692307

00:41:35.210 --> 00:41:36.590 Does it look normal?

NOTE Confidence: 0.941027707692307

00:41:36.590 --> 00:41:39.380 And so that is the question and it's

NOTE Confidence: 0.941027707692307

00:41:39.380 --> 00:41:41.964 not a trivial 1 because like I said,

NOTE Confidence: 0.941027707692307

00:41:41.970 --> 00:41:44.208 a subset of ***** cancers are

NOTE Confidence: 0.941027707692307

00:41:44.208 --> 00:41:46.450 HPV negative and P53 rod type.

NOTE Confidence: 0.941027707692307

00:41:46.450 --> 00:41:48.814 What is the precursor for those

NOTE Confidence: 0.941027707692307

00:41:48.814 --> 00:41:50.390 lesions and those lesions

NOTE Confidence: 0.952146640909091

00:41:50.459 --> 00:41:52.170 represent? Intermediate They

NOTE Confidence: 0.952146640909091

00:41:52.170 --> 00:41:54.210 have intermediate prognosis and

NOTE Confidence: 0.952146640909091

00:41:54.210 --> 00:41:58.558 represent 15% of all Volvo cancers.

NOTE Confidence: 0.952146640909091

00:41:58.558 --> 00:42:02.242 This HPV negative P53 wild time cases.

NOTE Confidence: 0.952146640909091

00:42:02.242 --> 00:42:05.571 So the question is what is the precursor

NOTE Confidence: 0.952146640909091

00:42:05.571 --> 00:42:09.115 lesion for this subset of cases and can

NOTE Confidence: 0.952146640909091

00:42:09.201 --> 00:42:12.627 that lesion be diagnosed by pathologists?

NOTE Confidence: 0.952146640909091

00:42:12.630 --> 00:42:14.667 There have been attempts to do so.

NOTE Confidence: 0.952146640909091

00:42:14.670 --> 00:42:17.400 The first lesion that fits this bill.

NOTE Confidence: 0.952146640909091

00:42:17.400 --> 00:42:21.315 Was was reported on almost 20 years ago as

NOTE Confidence: 0.952146640909091

00:42:21.320 --> 00:42:24.400 low vikentosis with altered differentiation,

NOTE Confidence: 0.952146640909091

00:42:24.400 --> 00:42:26.787 which would be negative P53 well typed

NOTE Confidence: 0.952146640909091

00:42:26.787 --> 00:42:29.137 by definition a subset associated with

NOTE Confidence: 0.952146640909091

00:42:29.137 --> 00:42:31.855 like in sclerosis and by morphology.

NOTE Confidence: 0.952146640909091

00:42:31.855 --> 00:42:34.280 They have the Russiform architecture,

NOTE Confidence: 0.952146640909091

00:42:34.280 --> 00:42:37.000 they have stacked pyrokeratosis

NOTE Confidence: 0.952146640909091

00:42:37.000 --> 00:42:40.200 and the whole spinosum seems

NOTE Confidence: 0.95232968

00:42:43.080 --> 00:42:46.176 pale this pink appearance.

NOTE Confidence: 0.95232968

00:42:46.176 --> 00:42:47.640 Again, they don't have

NOTE Confidence: 0.95232968

00:42:47.640 --> 00:42:48.790 the features of the event,

NOTE Confidence: 0.95232968

00:42:48.790 --> 00:42:52.306 No basal etsypia to speak of.

NOTE Confidence: 0.95232968

00:42:52.310 --> 00:42:54.188 Not all cases are vertical recifonts.

NOTE Confidence: 0.95232968

00:42:54.190 --> 00:42:55.582 Some cases are more on the

NOTE Confidence: 0.95232968

00:42:55.582 --> 00:42:56.510 flattened end of stance,

NOTE Confidence: 0.95232968

00:42:56.510 --> 00:42:59.330 but clearly these cases are oftentimes admix.

NOTE Confidence: 0.95232968

00:42:59.330 --> 00:43:01.990 You can notice the stacked para characters

NOTE Confidence: 0.95232968

00:43:01.990 --> 00:43:05.586 in these cases and no basal etsypia, so the.

NOTE Confidence: 0.95232968

00:43:05.586 --> 00:43:08.574 The first inclination is to dismiss

NOTE Confidence: 0.95232968

00:43:08.574 --> 00:43:11.548 these lesions you know but you know

NOTE Confidence: 0.95232968

00:43:11.548 --> 00:43:13.694 they studies that have looked at it

NOTE Confidence: 0.95232968

00:43:13.694 --> 00:43:15.951 have shown that they do have some

NOTE Confidence: 0.95232968

00:43:15.951 --> 00:43:17.646 driver type mutations within them.

NOTE Confidence: 0.95232968

00:43:17.650 --> 00:43:21.115 You can see you know subset of cases have

NOTE Confidence: 0.95232968

00:43:21.115 --> 00:43:25.470 large one Itras mutations and as well.

NOTE Confidence: 0.95232968

00:43:25.470 --> 00:43:26.990 And there's a related lesion,

NOTE Confidence: 0.95232968

00:43:26.990 --> 00:43:29.070 the so-called differentiated exophytic

NOTE Confidence: 0.95232968

00:43:29.070 --> 00:43:32.290 ***** and trepidal lesion which is defined

NOTE Confidence: 0.95232968

00:43:32.290 --> 00:43:34.909 simply very similarly to to to VAD,

NOTE Confidence: 0.95232968

00:43:34.910 --> 00:43:38.201 except you know this is more prominently

NOTE Confidence: 0.95232968

00:43:38.201 --> 00:43:43.910 a canthotic in the rusi form uniformly

NOTE Confidence: 0.95232968

00:43:43.910 --> 00:43:47.530 that it doesn't have the paleness that

NOTE Confidence: 0.95232968

00:43:47.530 --> 00:43:50.470 we spoke of previously and a smaller

NOTE Confidence: 0.95232968

00:43:50.470 --> 00:43:52.949 subset associated with lichen sclerosis.

NOTE Confidence: 0.95232968

00:43:52.950 --> 00:43:55.490 So that's the so-called devil.

NOTE Confidence: 0.95232968

00:43:55.490 --> 00:43:57.730 And then finally there's the the Russiform,

NOTE Confidence: 0.95232968

00:43:57.730 --> 00:44:00.650 like in Simplex Chronicus.

NOTE Confidence: 0.95232968

00:44:00.650 --> 00:44:02.240 So you know,

NOTE Confidence: 0.95232968

00:44:02.240 --> 00:44:04.890 this is a controversial lesion

NOTE Confidence: 0.95232968

00:44:04.890 --> 00:44:05.950 in which you know,

NOTE Confidence: 0.95232968

00:44:05.950 --> 00:44:08.368 you could argue it one way or the other.

NOTE Confidence: 0.95232968

00:44:08.370 --> 00:44:11.274 I took this image directly from

NOTE Confidence: 0.95232968

00:44:11.274 --> 00:44:13.798 a paper by Roy and colleagues.

NOTE Confidence: 0.95232968

00:44:13.798 --> 00:44:16.290 I see a Simon Roy that's part

NOTE Confidence: 0.95232968

00:44:16.366 --> 00:44:17.530 of our audience.

NOTE Confidence: 0.95232968

00:44:17.530 --> 00:44:21.040 So maybe it's the same Roy in any event.

NOTE Confidence: 0.95232968

00:44:21.040 --> 00:44:22.944 This is a this is this paper is

NOTE Confidence: 0.95232968

00:44:22.944 --> 00:44:25.040 there is from Lycos and Chronicles.

NOTE Confidence: 0.95232968

00:44:25.040 --> 00:44:28.015 We've all seen some iteration of this

NOTE Confidence: 0.95232968

00:44:28.015 --> 00:44:30.860 lesion is defined by papulometosis,

NOTE Confidence: 0.95232968

00:44:30.860 --> 00:44:32.675 prominent hyperglynylosis and

NOTE Confidence: 0.95232968

00:44:32.675 --> 00:44:34.735 hyperkinetosis where the subset

NOTE Confidence: 0.95232968

00:44:34.735 --> 00:44:37.160 associated with like and sclerosis.

NOTE Confidence: 0.95232968

00:44:37.160 --> 00:44:39.734 Over time devil and that started

NOTE Confidence: 0.95232968

00:44:39.734 --> 00:44:42.017 getting lumped together because their

NOTE Confidence: 0.95232968

00:44:42.017 --> 00:44:44.477 morphological features were so similar

NOTE Confidence: 0.95232968

00:44:44.480 --> 00:44:47.516 and they started being considered as

NOTE Confidence: 0.95232968

00:44:47.516 --> 00:44:49.990 precancerous lesions because the same.

NOTE Confidence: 0.95232968

00:44:49.990 --> 00:44:52.114 A spectrum of mutations were found

NOTE Confidence: 0.95232968

00:44:52.114 --> 00:44:55.207 to be present in both the devil and

NOTE Confidence: 0.95232968

00:44:55.207 --> 00:44:56.815 costnoma irrespective of whether

NOTE Confidence: 0.95232968

00:44:56.815 --> 00:45:00.035 or not the costnoma was diagnosed

NOTE Confidence: 0.95232968

00:45:00.035 --> 00:45:01.790 synchronously or metachronously.

NOTE Confidence: 0.95232968

00:45:01.790 --> 00:45:05.070 And also we had a subset of cases

NOTE Confidence: 0.95232968

00:45:05.070 --> 00:45:07.541 where diagnosis of of of devil of

NOTE Confidence: 0.95232968

00:45:07.541 --> 00:45:10.375 that was made and then it recurred

NOTE Confidence: 0.95232968

00:45:10.375 --> 00:45:12.067 as an invasive costnoma.

NOTE Confidence: 0.95232968

00:45:12.070 --> 00:45:14.092 And I certainly have a personal

NOTE Confidence: 0.95232968

00:45:14.092 --> 00:45:17.410 experience with those as well.

NOTE Confidence: 0.95232968

00:45:17.410 --> 00:45:20.280 And and then there's this study from

NOTE Confidence: 0.95232968

00:45:20.280 --> 00:45:25.690 again Roy et all that had 27 cases.

NOTE Confidence: 0.95232968

00:45:25.690 --> 00:45:27.310 And so then essentially the

NOTE Confidence: 0.95232968

00:45:27.310 --> 00:45:29.642 largest study to date and look at

NOTE Confidence: 0.95232968

00:45:29.642 --> 00:45:31.362 the progression rates to squamous

NOTE Confidence: 0.95232968

00:45:31.362 --> 00:45:32.970 cell carcinoma in this courts,

NOTE Confidence: 0.95232968

00:45:32.970 --> 00:45:35.570 it was 46% for that.

NOTE Confidence: 0.95232968

00:45:35.570 --> 00:45:38.090 40% for Devil and about 20 percent,

NOTE Confidence: 0.95232968

00:45:38.090 --> 00:45:41.310 27% for the Russeform and let's see

NOTE Confidence: 0.95232968

00:45:41.310 --> 00:45:43.846 with 37% overall for the whole court.

NOTE Confidence: 0.95232968

00:45:43.850 --> 00:45:45.206 So you know they,

NOTE Confidence: 0.95232968

00:45:45.206 --> 00:45:47.658 they take the position that all of

NOTE Confidence: 0.95232968

00:45:47.658 --> 00:45:50.080 these were part of the same spectrum

NOTE Confidence: 0.95232968

00:45:50.080 --> 00:45:52.530 of lesions and ISSVD has taken the

NOTE Confidence: 0.95232968

00:45:52.530 --> 00:45:54.750 same position prior they took that

NOTE Confidence: 0.95232968

00:45:54.821 --> 00:45:57.930 position one year before that paper,

NOTE Confidence: 0.95232968

00:45:57.930 --> 00:46:00.450 what they call that these lesions,

NOTE Confidence: 0.95232968

00:46:00.450 --> 00:46:03.168 whether it's bad Devil or whatnot.

NOTE Confidence: 0.95232968

00:46:03.170 --> 00:46:05.529 Should all be under the same umbrella

NOTE Confidence: 0.95232968

00:46:05.529 --> 00:46:07.306 called ***** aberrant maturation.

NOTE Confidence: 0.95232968

00:46:07.306 --> 00:46:10.718 And today you find ***** aberrant

NOTE Confidence: 0.95232968

00:46:10.718 --> 00:46:14.058 maturation as essentially HPV independent

NOTE Confidence: 0.95232968

00:46:14.058 --> 00:46:17.730 lesions that combined aberrant maturation,

NOTE Confidence: 0.95232968

00:46:17.730 --> 00:46:21.815 that big hyperkeratosis or parakeratosis

NOTE Confidence: 0.95232968

00:46:21.815 --> 00:46:25.083 and echanthosis and irregular

NOTE Confidence: 0.9150649375

00:46:25.090 --> 00:46:27.538 Richie with minimal nucleotipia.

NOTE Confidence: 0.9150649375

00:46:27.538 --> 00:46:32.147 Also the the lesion needs to be P16

NOTE Confidence: 0.9150649375

00:46:32.147 --> 00:46:36.058 negative and in in P53 wild type.

NOTE Confidence: 0.9150649375

00:46:36.060 --> 00:46:39.616 So here's a lesion which doesn't

NOTE Confidence: 0.9150649375

00:46:39.616 --> 00:46:42.196 seem to be remarkable except

NOTE Confidence: 0.9150649375

00:46:42.196 --> 00:46:44.260 everything looks uncommonly pink.

NOTE Confidence: 0.9150649375

00:46:44.260 --> 00:46:45.940 Thick other keratosis,

NOTE Confidence: 0.9150649375

00:46:45.940 --> 00:46:47.620 Galilei is preserved.

NOTE Confidence: 0.9150649375

00:46:47.620 --> 00:46:49.260 This was signed out descriptively

NOTE Confidence: 0.9150649375

00:46:49.260 --> 00:46:50.900 a couple of years ago.

NOTE Confidence: 0.9150649375

00:46:50.900 --> 00:46:55.020 He came back twice before he was immediately

NOTE Confidence: 0.9150649375

00:46:55.020 --> 00:46:57.200 before he was ultimately excised.

NOTE Confidence: 0.9150649375

00:46:57.200 --> 00:47:00.080 In this excites with negative margins,

NOTE Confidence: 0.9150649375

00:47:00.080 --> 00:47:01.520 but the point is you know

NOTE Confidence: 0.9150649375

00:47:01.520 --> 00:47:03.040 when it was being biopsied,

NOTE Confidence: 0.9150649375

00:47:03.040 --> 00:47:05.240 the idea was they were taking out most of it.

NOTE Confidence: 0.9150649375

00:47:05.240 --> 00:47:07.902 There were tiny lesions to get out but

NOTE Confidence: 0.9150649375

00:47:07.902 --> 00:47:10.434 this is what was there microscopically.

NOTE Confidence: 0.9150649375

00:47:10.440 --> 00:47:12.232 And so this is an example of the

NOTE Confidence: 0.9150649375

00:47:12.232 --> 00:47:13.916 so-called ***** after in maturation.

NOTE Confidence: 0.9150649375

00:47:13.916 --> 00:47:16.800 It is more of a russiform morphology

NOTE Confidence: 0.9150649375

00:47:16.800 --> 00:47:20.616 but you know it was a 24 millimeter

NOTE Confidence: 0.9150649375

00:47:20.616 --> 00:47:24.148 sessile carpet lesion in the right *****.

NOTE Confidence: 0.9150649375

00:47:24.150 --> 00:47:25.310 And so all of it was taken out.

NOTE Confidence: 0.9150649375

00:47:25.310 --> 00:47:27.294 So we don't know what would have happened

NOTE Confidence: 0.9150649375

00:47:27.294 --> 00:47:29.669 to this lesion if it had not been taken out.

NOTE Confidence: 0.9150649375

00:47:29.670 --> 00:47:31.763 And here's a lesion that I'm showing

NOTE Confidence: 0.9150649375

00:47:31.763 --> 00:47:33.942 because I know that this lesion

NOTE Confidence: 0.9150649375

00:47:33.942 --> 00:47:35.967 which was signed out descriptively

NOTE Confidence: 0.9150649375

00:47:35.967 --> 00:47:37.430 initially several years ago,

NOTE Confidence: 0.9150649375

00:47:37.430 --> 00:47:39.162 decades ago,

NOTE Confidence: 0.9150649375

00:47:39.162 --> 00:47:42.748 actually came back as an invasive cancer,

NOTE Confidence: 0.9150649375

00:47:42.750 --> 00:47:44.070 whether that's related or not,

NOTE Confidence: 0.9150649375

00:47:44.070 --> 00:47:46.294 it came back as an invasive cancer at

NOTE Confidence: 0.9150649375

00:47:46.294 --> 00:47:48.507 the exact site that this was removed.

NOTE Confidence: 0.9150649375

00:47:48.510 --> 00:47:51.030 So you know,

NOTE Confidence: 0.9150649375

00:47:51.030 --> 00:47:54.580 11 can sort of make up that one one wishes.

NOTE Confidence: 0.9150649375

00:47:54.580 --> 00:47:57.964 Now there's been a move that says that you

NOTE Confidence: 0.9150649375

00:47:57.964 --> 00:48:01.138 know that van terminology is not ideal,

NOTE Confidence: 0.9150649375

00:48:01.140 --> 00:48:07.178 that perhaps a neo name should be used,

NOTE Confidence: 0.9150649375

00:48:07.180 --> 00:48:09.620 the so-called the russoformic anthrotic

NOTE Confidence: 0.9150649375

00:48:09.620 --> 00:48:11.156 ***** Interpitelian neoplasia,

NOTE Confidence: 0.9150649375

00:48:11.156 --> 00:48:14.730 but then that this more closely reflects the

NOTE Confidence: 0.9150649375

00:48:14.730 --> 00:48:17.060 pathogenesis and the morphologic features.

NOTE Confidence: 0.9150649375

00:48:17.060 --> 00:48:20.740 This was published last year

NOTE Confidence: 0.9150649375

00:48:20.740 --> 00:48:22.580 and the features are basically.

NOTE Confidence: 0.9150649375

00:48:22.580 --> 00:48:24.644 Devil Van Mythology.

NOTE Confidence: 0.9150649375

00:48:24.644 --> 00:48:26.020 No. Basility.

NOTE Confidence: 0.9150649375

00:48:26.020 --> 00:48:26.346 BIA.

NOTE Confidence: 0.9150649375

00:48:26.346 --> 00:48:26.998 You know,

NOTE Confidence: 0.9150649375

00:48:26.998 --> 00:48:28.954 anything that you know can probably

NOTE Confidence: 0.9150649375

00:48:28.954 --> 00:48:31.116 meet criteria for the rules from

NOTE Confidence: 0.9150649375

00:48:31.116 --> 00:48:32.891 like in Saint Brooks Chronicles.

NOTE Confidence: 0.9150649375

00:48:32.900 --> 00:48:34.202 In other words,

NOTE Confidence: 0.9150649375

00:48:34.202 --> 00:48:35.938 no specific popular monstroses

NOTE Confidence: 0.9150649375

00:48:35.940 --> 00:48:37.900 and acantosis and the like.

NOTE Confidence: 0.9150649375

00:48:37.900 --> 00:48:39.121 So you know,

NOTE Confidence: 0.9150649375

00:48:39.121 --> 00:48:41.970 whether or not this name takes and

NOTE Confidence: 0.9150649375

00:48:42.064 --> 00:48:45.096 we end up using Van versus Van Van,

NOTE Confidence: 0.9150649375

00:48:45.100 --> 00:48:47.137 it's not clear that it's still fresh.

NOTE Confidence: 0.9150649375

00:48:47.140 --> 00:48:47.476 Again,

NOTE Confidence: 0.9150649375

00:48:47.476 --> 00:48:49.492 that's why the point of controversy

NOTE Confidence: 0.9150649375

00:48:49.492 --> 00:48:50.500 that's worth discussing.

NOTE Confidence: 0.9150649375

00:48:50.500 --> 00:48:52.188 But I think what matters at the end

NOTE Confidence: 0.9150649375

00:48:52.188 --> 00:48:53.963 of the day is that to highlight that

NOTE Confidence: 0.9150649375

00:48:53.963 --> 00:48:56.009 this is not a typical lesion whose

NOTE Confidence: 0.9150649375

00:48:56.009 --> 00:48:57.134 clinical pathologic significance

NOTE Confidence: 0.9150649375

00:48:57.134 --> 00:49:00.018 is not known, not entirely known,

NOTE Confidence: 0.9150649375

00:49:00.018 --> 00:49:01.776 but you know,

NOTE Confidence: 0.9150649375

00:49:01.780 --> 00:49:04.880 certainly should be removed or

NOTE Confidence: 0.9150649375

00:49:04.880 --> 00:49:08.296 ablated inside one way or the other.

NOTE Confidence: 0.9150649375

00:49:08.300 --> 00:49:11.798 But what it's worth, you know,

NOTE Confidence: 0.9150649375

00:49:11.798 --> 00:49:13.892 in our serious cases that were

NOTE Confidence: 0.9150649375

00:49:13.892 --> 00:49:15.278 called VAM of a bin.

NOTE Confidence: 0.9150649375

00:49:15.280 --> 00:49:17.686 They also in a significant subset

NOTE Confidence: 0.9150649375

00:49:17.686 --> 00:49:19.840 showed aberrant stain for Gala 3.

NOTE Confidence: 0.9150649375

00:49:19.840 --> 00:49:22.330 They said this reduced or loss

NOTE Confidence: 0.9150649375

00:49:22.330 --> 00:49:24.475 of expression in various subsets

NOTE Confidence: 0.9150649375

00:49:24.475 --> 00:49:27.275 suggesting that this is not a way

NOTE Confidence: 0.9150649375

00:49:27.275 --> 00:49:29.518 to separate those lesions out.

NOTE Confidence: 0.9150649375

00:49:29.520 --> 00:49:31.722 Now clearly high risk HPV is

NOTE Confidence: 0.9150649375

00:49:31.722 --> 00:49:33.400 what pursues the diagnosis of

NOTE Confidence: 0.847918297333333

00:49:36.000 --> 00:49:38.065 HCL&D van. There's usually talk

NOTE Confidence: 0.847918297333333

00:49:38.065 --> 00:49:40.130 about inflammatory dermatosis is the

NOTE Confidence: 0.847918297333333

00:49:40.194 --> 00:49:42.199 background in which this happens.

NOTE Confidence: 0.944425801666666

00:49:44.230 --> 00:49:46.638 And and and but really the main

NOTE Confidence: 0.944425801666666

00:49:46.638 --> 00:49:48.067 inflammatory dermatosis that we're

NOTE Confidence: 0.944425801666666

00:49:48.067 --> 00:49:49.757 talking about is lichen sclerosis

NOTE Confidence: 0.944425801666666

00:49:49.757 --> 00:49:52.218 because no one that showed a consistent

NOTE Confidence: 0.944425801666666

00:49:52.218 --> 00:49:54.312 association between any of the others

NOTE Confidence: 0.944425801666666

00:49:54.312 --> 00:49:57.190 and and and deviant or cancer in general.

NOTE Confidence: 0.944425801666666

00:49:57.190 --> 00:49:59.590 So lichen sclerosis is the big player here.

NOTE Confidence: 0.944425801666666

00:49:59.590 --> 00:50:02.870 A smaller subset of the cases of VAM of a

NOTE Confidence: 0.944425801666666

00:50:02.950 --> 00:50:06.010 van also have background lichen sclerosis

NOTE Confidence: 0.944425801666666

00:50:06.010 --> 00:50:09.640 about 30% lichen sclerosis is of course.

NOTE Confidence: 0.944425801666666

00:50:09.640 --> 00:50:12.560 Stats as an intermediate dermatitis,

NOTE Confidence: 0.944425801666666

00:50:12.560 --> 00:50:16.868 kind of a thing that progresses to more

NOTE Confidence: 0.944425801666666

00:50:16.868 --> 00:50:21.808 distinctive sclerosis and oxidative stress

NOTE Confidence: 0.944425801666666

00:50:21.808 --> 00:50:25.840 and alterations in gene expression profiles,

NOTE Confidence: 0.944425801666666

00:50:25.840 --> 00:50:29.100 and ultimately neoplasia in

NOTE Confidence: 0.944425801666666

00:50:29.100 --> 00:50:31.400 a small subset of patients.

NOTE Confidence: 0.944425801666666

00:50:31.400 --> 00:50:36.292 Now the association between lichen sclerosis,

NOTE Confidence: 0.944425801666666

00:50:36.292 --> 00:50:37.916 which was previously called

NOTE Confidence: 0.944425801666666

00:50:37.916 --> 00:50:39.134 the complicative bulbitis.

NOTE Confidence: 0.944425801666666

00:50:39.140 --> 00:50:41.690 And cancer has been recognized since

NOTE Confidence: 0.944425801666666

00:50:41.690 --> 00:50:46.740 at least the mid to late 1800s,

NOTE Confidence: 0.944425801666666

00:50:46.740 --> 00:50:48.882 including this favorite court of mind

NOTE Confidence: 0.944425801666666

00:50:48.882 --> 00:50:51.216 that that association was thought to be

NOTE Confidence: 0.944425801666666

00:50:51.216 --> 00:50:53.336 closer than that of any pathologic lesion,

NOTE Confidence: 0.944425801666666

00:50:53.340 --> 00:50:56.400 with the exception of the modern

NOTE Confidence: 0.944425801666666

00:50:56.400 --> 00:50:57.420 X-ray dermatitis.

NOTE Confidence: 0.944425801666666

00:50:57.420 --> 00:51:00.108 Now it's not uncommon in resection

NOTE Confidence: 0.944425801666666

00:51:00.108 --> 00:51:02.280 specimens for ***** squamous cell

NOTE Confidence: 0.944425801666666

00:51:02.280 --> 00:51:05.150 carcinoma to observe D van like and

NOTE Confidence: 0.944425801666666

00:51:05.150 --> 00:51:07.060 sclerosis and invasive carcinoma

NOTE Confidence: 0.944425801666666

00:51:07.060 --> 00:51:08.964 within the same specimen.

NOTE Confidence: 0.944425801666666

00:51:08.970 --> 00:51:12.466 And in biopsies of DV only you have

NOTE Confidence: 0.944425801666666

00:51:12.466 --> 00:51:14.885 concurrent lycan sclerosis in almost

NOTE Confidence: 0.944425801666666

00:51:14.885 --> 00:51:17.380 90% of cases and for squamous cell

NOTE Confidence: 0.944425801666666

00:51:17.380 --> 00:51:19.609 cost numerous that are HPV negative.

NOTE Confidence: 0.944425801666666

00:51:19.610 --> 00:51:21.430 If you look hard enough you'll find

NOTE Confidence: 0.944425801666666

00:51:21.430 --> 00:51:22.889 like in sclerosis in the background

NOTE Confidence: 0.944425801666666

00:51:22.889 --> 00:51:25.800 in up to 88% of cases.

NOTE Confidence: 0.944425801666666

00:51:25.800 --> 00:51:28.432 Basis of Lycos sclerosis in biopsies have

NOTE Confidence: 0.944425801666666

00:51:28.432 --> 00:51:30.567 been associated with an increased risk

NOTE Confidence: 0.944425801666666

00:51:30.567 --> 00:51:35.197 of ***** cancer with an Sir of over 33.

NOTE Confidence: 0.944425801666666

00:51:35.200 --> 00:51:39.277 So you have a 33 fold higher than expected

NOTE Confidence: 0.944425801666666

00:51:39.280 --> 00:51:41.788 frequency of cancers in women with

NOTE Confidence: 0.944425801666666

00:51:41.788 --> 00:51:44.479 Lycos sclerosis as compared with controls.

NOTE Confidence: 0.944425801666666

00:51:44.480 --> 00:51:46.475 Another way of looking at it is

NOTE Confidence: 0.944425801666666

00:51:46.475 --> 00:51:48.958 to look at what happens when you

NOTE Confidence: 0.944425801666666

00:51:48.958 --> 00:51:50.901 mix Lycos sclerosis with HCL.

NOTE Confidence: 0.944425801666666

00:51:50.901 --> 00:51:53.187 So here's the 10 year accumulated

NOTE Confidence: 0.944425801666666

00:51:53.187 --> 00:51:55.190 incidence of cancer from H cell,

NOTE Confidence: 0.944425801666666

00:51:55.190 --> 00:51:57.326 which as we alluded to before

NOTE Confidence: 0.944425801666666

00:51:57.326 --> 00:51:58.750 is only about 10%.

NOTE Confidence: 0.944425801666666

00:51:58.750 --> 00:52:01.720 You had lichen sclerosis to regulate

NOTE Confidence: 0.944425801666666

00:52:01.720 --> 00:52:04.462 HPV associated H cell and all of a

NOTE Confidence: 0.944425801666666

00:52:04.462 --> 00:52:06.460 sudden the risk moves on to close

NOTE Confidence: 0.944425801666666

00:52:06.460 --> 00:52:07.922 to 40% or 10 years.

NOTE Confidence: 0.944425801666666

00:52:07.922 --> 00:52:10.098 And also the rate of movement of

NOTE Confidence: 0.944425801666666

00:52:10.098 --> 00:52:13.190 this curve is is, is is much higher.

NOTE Confidence: 0.9402536

00:52:15.290 --> 00:52:16.998 And and another way to look at

NOTE Confidence: 0.9402536

00:52:16.998 --> 00:52:18.640 it again were on the significance

NOTE Confidence: 0.9402536

00:52:18.640 --> 00:52:20.621 of the background is to look at

NOTE Confidence: 0.9402536

00:52:20.681 --> 00:52:22.566 what happens with the recurrences.

NOTE Confidence: 0.9402536

00:52:22.570 --> 00:52:25.062 That's a work by Cigarette Regal I

NOTE Confidence: 0.9402536

00:52:25.062 --> 00:52:27.568 thought it's such a nice elegant study

NOTE Confidence: 0.9402536

00:52:27.570 --> 00:52:30.048 that looked at HPV negative *****

NOTE Confidence: 0.9402536

00:52:30.050 --> 00:52:33.667 squad and cell carcinomas and 71%

NOTE Confidence: 0.9402536

00:52:33.667 --> 00:52:37.805 of them were P53 wild type were P 53

NOTE Confidence: 0.9402536

00:52:37.805 --> 00:52:40.115 Newton sorry in the invasive cancer

NOTE Confidence: 0.9402536

00:52:40.115 --> 00:52:43.522 the primary site when they recurred though.

NOTE Confidence: 0.9402536

00:52:43.522 --> 00:52:46.280 Only 88% of them were P53 mutant,

NOTE Confidence: 0.9402536

00:52:46.280 --> 00:52:48.620 so you could argue that 12% of cases

NOTE Confidence: 0.9402536

00:52:48.620 --> 00:52:50.840 were neo cancers that are rising.

NOTE Confidence: 0.9402536

00:52:50.840 --> 00:52:52.634 In this background you can flip

NOTE Confidence: 0.9402536

00:52:52.634 --> 00:52:54.400 it the other way as well.

NOTE Confidence: 0.9402536

00:52:54.400 --> 00:52:57.016 Those cases were initially P50 very

NOTE Confidence: 0.9402536

00:52:57.016 --> 00:52:59.359 well type significant majority of them,

NOTE Confidence: 0.9402536

00:52:59.360 --> 00:53:01.640 57% of them when they recurred

NOTE Confidence: 0.9402536

00:53:01.640 --> 00:53:03.160 had a P53 mutation.

NOTE Confidence: 0.9402536

00:53:03.160 --> 00:53:04.780 Again, we could argue some

NOTE Confidence: 0.9402536

00:53:04.780 --> 00:53:06.076 progression in the subset,

NOTE Confidence: 0.9402536

00:53:06.080 --> 00:53:08.348 but it also argues that a significant

NOTE Confidence: 0.9402536

00:53:08.348 --> 00:53:10.854 subset of these cases are neo cancers

NOTE Confidence: 0.9402536

00:53:10.854 --> 00:53:13.056 that are happening in this background.

NOTE Confidence: 0.9402536

00:53:13.060 --> 00:53:15.500 Of inflammatory dermatosis that may

NOTE Confidence: 0.9402536

00:53:15.500 --> 00:53:17.940 be permissive for the development

NOTE Confidence: 0.9402536

00:53:17.940 --> 00:53:20.670 also bolstering the argument that

NOTE Confidence: 0.9402536

00:53:20.670 --> 00:53:23.588 these are independent cancers is that

NOTE Confidence: 0.9402536

00:53:23.588 --> 00:53:26.136 when you have the same patient with

NOTE Confidence: 0.9402536

00:53:26.136 --> 00:53:28.500 multiple D vents and you look at the

NOTE Confidence: 0.9402536

00:53:28.500 --> 00:53:31.620 the mutational profiles for P53,

NOTE Confidence: 0.9402536

00:53:31.620 --> 00:53:34.962 they have different P53 mutation within

NOTE Confidence: 0.9402536

00:53:34.962 --> 00:53:38.339 different events in the same patient

NOTE Confidence: 0.9402536

00:53:38.340 --> 00:53:42.400 in a subset of patients and also when this.

NOTE Confidence: 0.9402536

00:53:42.400 --> 00:53:45.790 Invasive squamous cell cause normals recur.

NOTE Confidence: 0.9402536

00:53:45.790 --> 00:53:48.645 A significant subset of those

NOTE Confidence: 0.9402536

00:53:48.645 --> 00:53:51.206 recurrences have a set of mutations

NOTE Confidence: 0.9402536

00:53:51.206 --> 00:53:54.110 that are not present in the original,

NOTE Confidence: 0.9402536

00:53:54.110 --> 00:53:56.835 not just more complicated mutations

NOTE Confidence: 0.9402536

00:53:56.835 --> 00:53:58.470 that suggest progression.

NOTE Confidence: 0.9402536

00:53:58.470 --> 00:54:01.284 They have mutations that are new and

NOTE Confidence: 0.9402536

00:54:01.284 --> 00:54:04.043 they don't then that are completely

NOTE Confidence: 0.9402536

00:54:04.043 --> 00:54:07.370 absent from the invasive cancer as well.

NOTE Confidence: 0.9402536

00:54:07.370 --> 00:54:10.866 So for example you know the primary site.

NOTE Confidence: 0.9402536

00:54:10.866 --> 00:54:13.732 May have a P53 mutation and and

NOTE Confidence: 0.9402536

00:54:13.732 --> 00:54:15.597 maybe one or two others.

NOTE Confidence: 0.9402536

00:54:15.600 --> 00:54:18.015 The the recurrence would not have a

NOTE Confidence: 0.9402536

00:54:18.015 --> 00:54:20.385 P53 mutation and would have a different

NOTE Confidence: 0.9402536

00:54:20.385 --> 00:54:23.640 set of other genes that are mutated.

NOTE Confidence: 0.9402536

00:54:23.640 --> 00:54:26.088 So Justin again that these are

NOTE Confidence: 0.9402536

00:54:26.088 --> 00:54:28.777 independent cancers in a subset of

NOTE Confidence: 0.9402536

00:54:28.777 --> 00:54:31.999 recurrences that occur in this setting.

NOTE Confidence: 0.9402536

00:54:32.000 --> 00:54:35.200 And so when we have this H between

NOTE Confidence: 0.9402536

00:54:35.200 --> 00:54:38.817 negative cancers 1 hopes and you have two

NOTE Confidence: 0.9402536

00:54:38.817 --> 00:54:40.960 different defense associated with it.

NOTE Confidence: 0.9402536

00:54:40.960 --> 00:54:42.920 When an invasive cancer arises from it,

NOTE Confidence: 0.9402536

00:54:42.920 --> 00:54:47.516 1 hopes that you know this lesion,

NOTE Confidence: 0.9402536

00:54:47.516 --> 00:54:50.210 this separate D van is clinically

NOTE Confidence: 0.9402536

00:54:50.295 --> 00:54:53.396 evident enough for the surgeon to see.

NOTE Confidence: 0.9402536

00:54:53.400 --> 00:54:55.160 It's pathologically evident enough

NOTE Confidence: 0.9402536

00:54:55.160 --> 00:54:57.360 for the pathologist to see.

NOTE Confidence: 0.9402536

00:54:57.360 --> 00:54:58.356 And if we do see it,

NOTE Confidence: 0.9402536

00:54:58.360 --> 00:55:00.898 that is P53 mutation type to

NOTE Confidence: 0.9402536

00:55:00.898 --> 00:55:03.064 facilitate the diagnosis because it

NOTE Confidence: 0.9402536

00:55:03.064 --> 00:55:05.044 really determines exactly what kind

NOTE Confidence: 0.9402536

00:55:05.044 --> 00:55:07.878 of an excision the patient will get.

NOTE Confidence: 0.9402536

00:55:07.880 --> 00:55:10.876 And that goes to the issue of.

NOTE Confidence: 0.9402536

00:55:10.880 --> 00:55:11.548 The margins,

NOTE Confidence: 0.9402536

00:55:11.548 --> 00:55:13.886 How much of margins should should be

NOTE Confidence: 0.9402536

00:55:13.886 --> 00:55:16.068 obtained given all this activity that

NOTE Confidence: 0.9402536

00:55:16.068 --> 00:55:18.320 are happening around the invasive cancer,

NOTE Confidence: 0.9402536

00:55:18.320 --> 00:55:19.850 the D van,

NOTE Confidence: 0.9402536

00:55:19.850 --> 00:55:23.195 the almost the events that are happening now.

NOTE Confidence: 0.9402536

00:55:23.195 --> 00:55:24.380 The professional organizations

NOTE Confidence: 0.9402536

00:55:24.380 --> 00:55:26.750 recommend that in clearance of around

NOTE Confidence: 0.9402536

00:55:26.806 --> 00:55:28.798 a minimum of 1010 millimeters be be be

NOTE Confidence: 0.9402536

00:55:28.798 --> 00:55:30.714 be done with a histologic clearance

NOTE Confidence: 0.9402536

00:55:30.714 --> 00:55:32.760 for around 8 millimeters to account

NOTE Confidence: 0.9402536

00:55:32.760 --> 00:55:36.966 for shrinkage that #8 millimeters.

NOTE Confidence: 0.9402536

00:55:36.966 --> 00:55:40.578 Comes from studies that have shown

NOTE Confidence: 0.9402536

00:55:40.578 --> 00:55:42.084 in the 1990s,

NOTE Confidence: 0.9402536

00:55:42.090 --> 00:55:43.690 just the three-year old studies,

NOTE Confidence: 0.936899133333334

00:55:43.690 --> 00:55:46.165 that that number is the is the sweet spot.

NOTE Confidence: 0.936899133333334

00:55:46.170 --> 00:55:48.000 Anything that 8 millimeters or

NOTE Confidence: 0.936899133333334

00:55:48.000 --> 00:55:51.208 more has to have less frequency of

NOTE Confidence: 0.936899133333334

00:55:51.208 --> 00:55:53.810 recurrences in this particular setting.

NOTE Confidence: 0.936899133333334

00:55:53.810 --> 00:55:55.635 However, studies published in the

NOTE Confidence: 0.936899133333334

00:55:55.635 --> 00:55:58.241 last 10 years have shown that the

NOTE Confidence: 0.936899133333334

00:55:58.241 --> 00:56:00.036 issue is much more complicated.

NOTE Confidence: 0.936899133333334

00:56:00.040 --> 00:56:03.556 And indeed, most studies have not

NOTE Confidence: 0.936899133333334

00:56:03.556 --> 00:56:06.620 found that 8 millimeter cut off to be

NOTE Confidence: 0.936899133333334

00:56:06.620 --> 00:56:08.875 associated with progression free survival.

NOTE Confidence: 0.936899133333334

00:56:08.880 --> 00:56:11.184 In fact, some of the others of the

NOTE Confidence: 0.936899133333334

00:56:11.184 --> 00:56:13.728 original study have now essentially

NOTE Confidence: 0.936899133333334

00:56:13.728 --> 00:56:15.920 recanted because additional data

NOTE Confidence: 0.936899133333334

00:56:15.920 --> 00:56:18.560 have shown that you know it.

NOTE Confidence: 0.936899133333334

00:56:18.560 --> 00:56:19.800 It did not influence risk,

NOTE Confidence: 0.936899133333334

00:56:19.800 --> 00:56:21.335 that that's more free margin

NOTE Confidence: 0.936899133333334

00:56:21.335 --> 00:56:23.040 distance whether you use an 8,

NOTE Confidence: 0.936899133333334

00:56:23.040 --> 00:56:25.460 five or three millimeters.

NOTE Confidence: 0.936899133333334

00:56:25.460 --> 00:56:27.880 What does influence recurrences?

NOTE Confidence: 0.936899133333334

00:56:27.880 --> 00:56:30.120 Is finding deviant and lichen

NOTE Confidence: 0.936899133333334

00:56:30.120 --> 00:56:31.912 sclerosis at the margin.

NOTE Confidence: 0.936899133333334

00:56:31.920 --> 00:56:34.958 Finding deviant by itself at the margin

NOTE Confidence: 0.936899133333334

00:56:34.960 --> 00:56:37.144 are the one are the things that affect

NOTE Confidence: 0.936899133333334

00:56:37.144 --> 00:56:39.039 recurrences in patient revolving cancer.

NOTE Confidence: 0.936899133333334

00:56:39.040 --> 00:56:41.580 Lichen sclerosis by itself

NOTE Confidence: 0.936899133333334

00:56:41.580 --> 00:56:44.120 did not affect recurrences,

NOTE Confidence: 0.936899133333334

00:56:44.120 --> 00:56:47.222 but recognizing the abnormality around this

NOTE Confidence: 0.936899133333334

00:56:47.222 --> 00:56:50.439 invasive cancer continues to be problematic.

NOTE Confidence: 0.936899133333334

00:56:50.440 --> 00:56:52.057 So we look at this little ditzel

NOTE Confidence: 0.936899133333334

00:56:52.057 --> 00:56:53.640 of an excision that we received,

NOTE Confidence: 0.936899133333334

00:56:53.640 --> 00:56:54.663 which is typical.

NOTE Confidence: 0.936899133333334

00:56:54.663 --> 00:56:56.368 And there's abnormal area adjacent

NOTE Confidence: 0.936899133333334

00:56:56.368 --> 00:56:58.648 to it that we can all recognize.

NOTE Confidence: 0.936899133333334

00:56:58.650 --> 00:57:00.150 And then there's what looks like

NOTE Confidence: 0.936899133333334

00:57:00.150 --> 00:57:01.330 normal skin adjacent to it.

NOTE Confidence: 0.936899133333334

00:57:01.330 --> 00:57:02.728 It looked normal to the surgeon.

NOTE Confidence: 0.936899133333334

00:57:02.730 --> 00:57:04.487 They thought they were getting the margin.

NOTE Confidence: 0.936899133333334

00:57:04.490 --> 00:57:06.968 It looked normal to the gross prosector,

NOTE Confidence: 0.936899133333334

00:57:06.970 --> 00:57:08.690 but microscopically it was not.

NOTE Confidence: 0.936899133333334

00:57:08.690 --> 00:57:11.860 It was full of differentiated Vin and

NOTE Confidence: 0.936899133333334

00:57:11.860 --> 00:57:14.820 indeed when having a saying the P53 on

NOTE Confidence: 0.936899133333334

00:57:14.820 --> 00:57:19.530 all blocks of all margins around their

NOTE Confidence: 0.936899133333334

00:57:19.530 --> 00:57:21.948 P53 null LOVA squamous cell cancer.

NOTE Confidence: 0.936899133333334

00:57:21.950 --> 00:57:24.267 Four out of 13 cases became positive

NOTE Confidence: 0.936899133333334

00:57:24.267 --> 00:57:26.628 margins and those that were more

NOTE Confidence: 0.936899133333334

00:57:26.628 --> 00:57:28.368 focally positive before became

NOTE Confidence: 0.936899133333334

00:57:28.368 --> 00:57:30.229 more extensively possible for DVN.

NOTE Confidence: 0.936899133333334

00:57:30.230 --> 00:57:32.518 And the DVN that were in this newly

NOTE Confidence: 0.936899133333334

00:57:32.518 --> 00:57:34.470 identified margins tended to be very subtle.

NOTE Confidence: 0.936899133333334

00:57:34.470 --> 00:57:35.995 And this was recently confirmed

NOTE Confidence: 0.936899133333334

00:57:35.995 --> 00:57:37.906 earlier this year by the Vancouver

NOTE Confidence: 0.936899133333334

00:57:37.906 --> 00:57:39.868 group showing that when they did

NOTE Confidence: 0.936899133333334

00:57:39.870 --> 00:57:42.467 P53I EC just on the closest margin

NOTE Confidence: 0.936899133333334

00:57:42.470 --> 00:57:46.027 that 29% additional cases of DVN

NOTE Confidence: 0.936899133333334

00:57:46.027 --> 00:57:47.929 or at least P53 abnormal insight

NOTE Confidence: 0.936899133333334

00:57:47.929 --> 00:57:51.270 to lesions were identified and.

NOTE Confidence: 0.936899133333334

00:57:51.270 --> 00:57:53.004 These lesions were so subtle the

NOTE Confidence: 0.936899133333334

00:57:53.004 --> 00:57:55.381 more you move away from the invasive

NOTE Confidence: 0.936899133333334

00:57:55.381 --> 00:57:57.697 cancer that they thought they were

NOTE Confidence: 0.936899133333334

00:57:57.697 --> 00:57:59.645 morphologically occult could not be

NOTE Confidence: 0.936899133333334

00:57:59.645 --> 00:58:01.149 identified by morphology unknown.

NOTE Confidence: 0.936899133333334

00:58:01.150 --> 00:58:03.574 And it's not like P53 signature

NOTE Confidence: 0.936899133333334

00:58:03.574 --> 00:58:07.014 where it's like whatever this one is

NOTE Confidence: 0.936899133333334

00:58:07.014 --> 00:58:10.054 actually associated with a threefold

NOTE Confidence: 0.936899133333334

00:58:10.054 --> 00:58:13.079 increased risk of recurrence finding

NOTE Confidence: 0.936899133333334

00:58:13.079 --> 00:58:15.324 AP53 abnormality at the margin

NOTE Confidence: 0.936899133333334

00:58:15.324 --> 00:58:17.780 even though there's no morphologic

NOTE Confidence: 0.936899133333334

00:58:17.780 --> 00:58:20.665 correlate for that P53 abnormality.

NOTE Confidence: 0.936899133333334

00:58:20.670 --> 00:58:24.189 And that goes to the what has happened when,

NOTE Confidence: 0.936899133333334

00:58:24.190 --> 00:58:24.826 what has,

NOTE Confidence: 0.936899133333334

00:58:24.826 --> 00:58:26.416 what has happened with respect

NOTE Confidence: 0.936899133333334

00:58:26.416 --> 00:58:28.110 to how patients are treated.

NOTE Confidence: 0.936899133333334

00:58:28.110 --> 00:58:29.990 So prior to 1995,

NOTE Confidence: 0.936899133333334

00:58:29.990 --> 00:58:31.870 surgeries were more draconian,

NOTE Confidence: 0.936899133333334

00:58:31.870 --> 00:58:34.366 you know lot of radical valvectomies

NOTE Confidence: 0.936899133333334

00:58:34.366 --> 00:58:36.750 for small lesions and the like.

NOTE Confidence: 0.936899133333334

00:58:36.750 --> 00:58:39.200 And so there was no difference between

NOTE Confidence: 0.936899133333334

00:58:39.200 --> 00:58:41.149 HPV positive and HPV negative.

NOTE Confidence: 0.936899133333334

00:58:41.150 --> 00:58:43.496 But those differences emerged after we

NOTE Confidence: 0.936899133333334

00:58:43.496 --> 00:58:45.730 moved to more conservative surgeries.

NOTE Confidence: 0.936899133333334

00:58:45.730 --> 00:58:47.648 So what tended to happen prior to

NOTE Confidence: 0.936899133333334

00:58:47.650 --> 00:58:49.174 1995 was that they were taking

NOTE Confidence: 0.936899133333334

00:58:49.174 --> 00:58:50.782 out the invasive cancer as well

NOTE Confidence: 0.936899133333334

00:58:50.782 --> 00:58:52.127 as everything in the background.

NOTE Confidence: 0.936899133333334

00:58:52.130 --> 00:58:53.450 And that's again that's speculative,

NOTE Confidence: 0.936899133333334

00:58:53.450 --> 00:58:55.376 but that's probably what was happening

NOTE Confidence: 0.936899133333334

00:58:55.376 --> 00:58:57.680 that they were taking out the invasive

NOTE Confidence: 0.936899133333334

00:58:57.680 --> 00:58:59.606 cancer and everything else around it.

NOTE Confidence: 0.918779692631579

00:58:59.610 --> 00:59:01.866 So it it behaved more like an in

NOTE Confidence: 0.918779692631579

00:59:01.866 --> 00:59:03.558 positive case where you're taking

NOTE Confidence: 0.918779692631579

00:59:03.558 --> 00:59:05.682 the discrete lesion in the duct,

NOTE Confidence: 0.918779692631579

00:59:05.690 --> 00:59:07.010 but that has changed.

NOTE Confidence: 0.918779692631579

00:59:07.010 --> 00:59:09.476 So what really matters now is identifying

NOTE Confidence: 0.918779692631579

00:59:09.476 --> 00:59:12.416 whether or not those cases but even

NOTE Confidence: 0.918779692631579

00:59:12.416 --> 00:59:14.299 surgical excision is appropriate.

NOTE Confidence: 0.918779692631579

00:59:14.300 --> 00:59:17.020 For all those lesions adjacent,

NOTE Confidence: 0.918779692631579

00:59:17.020 --> 00:59:20.076 whether or not once you think about more

NOTE Confidence: 0.918779692631579

00:59:20.076 --> 00:59:21.954 aggressive ablation insight to insight

NOTE Confidence: 0.918779692631579

00:59:21.954 --> 00:59:24.852 to for for those lesions after the

NOTE Confidence: 0.918779692631579

00:59:24.852 --> 00:59:27.538 main invasive cancer has been removed.

NOTE Confidence: 0.918779692631579

00:59:27.540 --> 00:59:31.804 I'll end by by showing this to explain

NOTE Confidence: 0.918779692631579

00:59:31.804 --> 00:59:34.268 the title of my of this presentation

NOTE Confidence: 0.918779692631579

00:59:34.268 --> 00:59:37.252 we just talked about a stay a tale of

NOTE Confidence: 0.918779692631579

00:59:37.252 --> 00:59:39.590 stasis and this is the survival rate.

NOTE Confidence: 0.918779692631579

00:59:39.590 --> 00:59:42.110 Is the upper curve talks about,

NOTE Confidence: 0.918779692631579

00:59:42.110 --> 00:59:44.510 you know, new Volvo cancer cases

NOTE Confidence: 0.918779692631579

00:59:44.510 --> 00:59:46.760 that have been diagnosed based on

NOTE Confidence: 0.918779692631579

00:59:46.760 --> 00:59:49.950 Co data going back to 1975 and look

NOTE Confidence: 0.918779692631579

00:59:49.950 --> 00:59:52.386 at the flat death rate associated

NOTE Confidence: 0.918779692631579

00:59:52.386 --> 00:59:54.430 with it over the last 50 years.

NOTE Confidence: 0.918779692631579

00:59:54.430 --> 00:59:56.590 Despite all of those progress,

NOTE Confidence: 0.918779692631579

00:59:56.590 --> 00:59:59.122 all the advances prognosis

NOTE Confidence: 0.918779692631579

00:59:59.122 --> 01:00:01.246 remains roughly just bad.

NOTE Confidence: 0.918779692631579

01:00:01.246 --> 01:00:02.958 There's been no significant

NOTE Confidence: 0.918779692631579

01:00:02.958 --> 01:00:04.551 improvement overall in, in,

NOTE Confidence: 0.918779692631579

01:00:04.551 --> 01:00:07.260 in in the survival rates for Volvo

NOTE Confidence: 0.918779692631579

01:00:07.338 --> 01:00:09.966 cancer over the last half century.

NOTE Confidence: 0.918779692631579

01:00:09.970 --> 01:00:11.930 But there is also a tale of progress.

NOTE Confidence: 0.918779692631579

01:00:11.930 --> 01:00:14.660 RFS has improved to some

NOTE Confidence: 0.918779692631579

01:00:14.660 --> 01:00:16.155 extent and so recurrences,

NOTE Confidence: 0.918779692631579

01:00:16.155 --> 01:00:18.550 which is really the main thing

NOTE Confidence: 0.918779692631579

01:00:18.550 --> 01:00:21.684 to some extent has improved.

NOTE Confidence: 0.918779692631579

01:00:21.684 --> 01:00:23.369 But there are clearly a

NOTE Confidence: 0.918779692631579

01:00:23.369 --> 01:00:25.209 lot of work to be done.

NOTE Confidence: 0.918779692631579

01:00:25.210 --> 01:00:27.022 And the question is for pathology

NOTE Confidence: 0.918779692631579

01:00:27.022 --> 01:00:29.281 really it's about what is the true

NOTE Confidence: 0.918779692631579

01:00:29.281 --> 01:00:30.605 morphologic spectrum for Devin,

NOTE Confidence: 0.918779692631579

01:00:30.610 --> 01:00:32.974 as well as this HBV negative

NOTE Confidence: 0.918779692631579

01:00:32.974 --> 01:00:35.250 P53 raw type precursor regions,

NOTE Confidence: 0.918779692631579

01:00:35.250 --> 01:00:37.914 the biomarkers for Devin.

NOTE Confidence: 0.918779692631579

01:00:37.914 --> 01:00:39.246 Urgently needed.

NOTE Confidence: 0.918779692631579

01:00:39.250 --> 01:00:41.610 And then what to do with the three

NOTE Confidence: 0.918779692631579

01:00:41.610 --> 01:00:43.204 mutations and the margins and

NOTE Confidence: 0.918779692631579

01:00:43.204 --> 01:00:45.088 exactly how do we handle that?

NOTE Confidence: 0.918779692631579

01:00:45.090 --> 01:00:48.290 And of course identifying the

NOTE Confidence: 0.918779692631579

01:00:48.290 --> 01:00:51.040 aggressive subset using the mythology

NOTE Confidence: 0.918779692631579

01:00:51.040 --> 01:00:53.490 essentially is so much great.

NOTE Confidence: 0.918779692631579

01:00:53.490 --> 01:00:56.164 So thanks again for the privilege and

NOTE Confidence: 0.918779692631579

01:00:56.170 --> 01:00:57.730 I will be happy to make any questions.

NOTE Confidence: 0.905982325

01:00:59.810 --> 01:01:01.110 Thank you Doctor Fedori

NOTE Confidence: 0.905982325

01:01:01.110 --> 01:01:02.410 for a wonderful lecture,

NOTE Confidence: 0.905982325

01:01:02.410 --> 01:01:04.866 particularly focusing on the

NOTE Confidence: 0.905982325

01:01:04.866 --> 01:01:06.708 challenging HPV independent.

NOTE Confidence: 0.905982325

01:01:06.710 --> 01:01:08.290 Volvo in Preptelian lesions,

NOTE Confidence: 0.905982325

01:01:08.290 --> 01:01:10.265 in the interest of time,

NOTE Confidence: 0.905982325

01:01:10.270 --> 01:01:14.156 I'll hand it open it up for please

NOTE Confidence: 0.905982325

01:01:14.156 --> 01:01:16.986 unmute yourself and ask questions.

NOTE Confidence: 0.928932275

01:01:18.910 --> 01:01:20.910 Hi. Hi, this is, this is Pale Lou.

NOTE Confidence: 0.928932275

01:01:20.910 --> 01:01:24.430 You can hear me. Yes, I can, I think.

NOTE Confidence: 0.928932275

01:01:24.430 --> 01:01:26.885 Thank you for bringing this

NOTE Confidence: 0.928932275

01:01:26.885 --> 01:01:29.004 timely update in this ground.

NOTE Confidence: 0.928932275

01:01:29.004 --> 01:01:32.310 But the vova cancer in the precursor lesions.

NOTE Confidence: 0.928932275

01:01:32.310 --> 01:01:34.742 There's lots of details,

NOTE Confidence: 0.928932275

01:01:34.742 --> 01:01:37.014 interesting discoveries in recent decades,

NOTE Confidence: 0.928932275

01:01:37.014 --> 01:01:39.510 so I do have a question.

NOTE Confidence: 0.928932275

01:01:39.510 --> 01:01:41.070 We'll see. What do you think?

NOTE Confidence: 0.928932275

01:01:41.070 --> 01:01:44.458 Do you think the diving as a

NOTE Confidence: 0.928932275

01:01:44.458 --> 01:01:47.263 whole is a single kernel event

NOTE Confidence: 0.928932275

01:01:47.263 --> 01:01:49.067 of any dealing associated?

NOTE Confidence: 0.928932275

01:01:49.070 --> 01:01:50.042 Squints are customized.

NOTE Confidence: 0.928932275

01:01:50.042 --> 01:01:51.986 This could be a field effect,

NOTE Confidence: 0.94025354

01:01:55.430 --> 01:01:58.027 I think. Because of Divin of course,

NOTE Confidence: 0.94025354

01:01:58.030 --> 01:02:00.286 like I said, it's the subset of them

NOTE Confidence: 0.94025354

01:02:00.286 --> 01:02:02.380 are diagnosed by themselves and are

NOTE Confidence: 0.94025354

01:02:02.380 --> 01:02:04.215 never actually diagnosed with squamous

NOTE Confidence: 0.94025354

01:02:04.215 --> 01:02:06.790 cell carcinoma that clearly and in

NOTE Confidence: 0.94025354

01:02:06.790 --> 01:02:10.035 those cases do have you know the

NOTE Confidence: 0.94025354

01:02:10.035 --> 01:02:13.327 expected mutation of profile of PCC3,

NOTE Confidence: 0.94025354

01:02:13.327 --> 01:02:18.263 PIC, 3C, A HRAS and the like that

NOTE Confidence: 0.94025354

01:02:18.270 --> 01:02:20.545 number one it can occur by itself.

NOTE Confidence: 0.94025354

01:02:20.550 --> 01:02:22.308 We have enough data for that

NOTE Confidence: 0.94025354

01:02:22.310 --> 01:02:25.290 when we see Divin.

NOTE Confidence: 0.94025354

01:02:25.290 --> 01:02:27.309 Associated with invasive

NOTE Confidence: 0.94025354

01:02:27.309 --> 01:02:29.328 squamous cell carcinoma,

NOTE Confidence: 0.94025354

01:02:29.330 --> 01:02:33.370 most of those deviant lesions have

NOTE Confidence: 0.94025354

01:02:33.370 --> 01:02:36.170 a similar mutation or profile,

NOTE Confidence: 0.94025354

01:02:36.170 --> 01:02:38.330 at least based on the limited NGS panels

NOTE Confidence: 0.94025354

01:02:38.330 --> 01:02:40.817 that have been used as the squamous

NOTE Confidence: 0.94025354

01:02:40.817 --> 01:02:44.100 cell carcinoma that are adjacent to them.

NOTE Confidence: 0.94025354

01:02:44.100 --> 01:02:46.820 So I think what's probably

NOTE Confidence: 0.94025354

01:02:46.820 --> 01:02:49.540 happening is that multiple factors,

NOTE Confidence: 0.94025354

01:02:49.540 --> 01:02:51.630 some of them are independent

NOTE Confidence: 0.94025354

01:02:51.630 --> 01:02:53.720 new lesions that are entirely

NOTE Confidence: 0.94025354

01:02:53.798 --> 01:02:56.178 unrelated to the invasive cancer,

NOTE Confidence: 0.94025354

01:02:56.180 --> 01:02:58.852 but I think a subset are indeed field

NOTE Confidence: 0.94025354

01:02:58.852 --> 01:03:01.811 effect that are happening that are sort of

NOTE Confidence: 0.94025354

01:03:01.811 --> 01:03:04.378 related to the invasive cancer as well.

NOTE Confidence: 0.94025354

01:03:04.380 --> 01:03:05.211 So with that,

NOTE Confidence: 0.94025354

01:03:05.211 --> 01:03:07.820 so have you seen or read the articles,

NOTE Confidence: 0.94025354

01:03:07.820 --> 01:03:09.720 investigations where you show?

NOTE Confidence: 0.94025354

01:03:09.720 --> 01:03:11.620 Different patches of divings,

NOTE Confidence: 0.94025354

01:03:11.620 --> 01:03:13.700 they have different P53 mutations.

NOTE Confidence: 0.94025354

01:03:13.700 --> 01:03:17.956 Or have you seen a diving or

NOTE Confidence: 0.94025354

01:03:17.956 --> 01:03:21.253 revovactum of diving where you see

NOTE Confidence: 0.94025354

01:03:21.253 --> 01:03:23.217 different P53 staining patterns?

NOTE Confidence: 0.94025354

01:03:23.220 --> 01:03:25.770 Like you you have focally diffuse

NOTE Confidence: 0.94025354

01:03:25.770 --> 01:03:28.426 positive and the other focus will

NOTE Confidence: 0.94025354

01:03:28.426 --> 01:03:31.054 be now or the others possibly

NOTE Confidence: 0.94025354

01:03:31.054 --> 01:03:32.140 cytoplasmic P53 alteration?

NOTE Confidence: 0.94025354

01:03:32.140 --> 01:03:33.100 I don't know.

NOTE Confidence: 0.94025354

01:03:33.100 --> 01:03:34.535 Have you read it or have you

NOTE Confidence: 0.94025354

01:03:34.535 --> 01:03:35.460 seen such a case?

NOTE Confidence: 0.94025354

01:03:35.460 --> 01:03:36.620 I don't think there is.

NOTE Confidence: 0.94025354

01:03:36.620 --> 01:03:38.040 I don't think that has

NOTE Confidence: 0.94025354

01:03:38.040 --> 01:03:40.314 been reported I I I I must.

NOTE Confidence: 0.94025354

01:03:40.314 --> 01:03:42.582 I'm familiar with just by everything

NOTE Confidence: 0.94025354

01:03:42.582 --> 01:03:44.539 that's written in the space.

NOTE Confidence: 0.94025354

01:03:44.540 --> 01:03:47.015 The the first question that

NOTE Confidence: 0.94025354

01:03:47.015 --> 01:03:50.319 you know the same devins with

NOTE Confidence: 0.94025354

01:03:50.319 --> 01:03:52.884 different patterns has been shown.

NOTE Confidence: 0.94025354

01:03:52.884 --> 01:03:55.952 You know if you read the the small

NOTE Confidence: 0.94025354

01:03:55.952 --> 01:03:59.340 case series by Pinto had one was

NOTE Confidence: 0.94025354

01:03:59.340 --> 01:04:02.700 nonsense the other one was missense,

NOTE Confidence: 0.94025354

01:04:02.700 --> 01:04:04.500 different devins in the same patient.

NOTE Confidence: 0.9578644975

01:04:06.900 --> 01:04:08.100 Mutations and so they had

NOTE Confidence: 0.9578644975

01:04:08.100 --> 01:04:08.820 different staining patterns.

NOTE Confidence: 0.9578644975

01:04:08.820 --> 01:04:10.577 One was null and the other one

NOTE Confidence: 0.9578644975

01:04:10.577 --> 01:04:12.650 was null for expression and so,

NOTE Confidence: 0.9578644975

01:04:12.650 --> 01:04:14.660 so we know that that happens.

NOTE Confidence: 0.9578644975

01:04:14.660 --> 01:04:18.931 I for one have not seen a case where

NOTE Confidence: 0.9578644975

01:04:18.931 --> 01:04:21.517 you know in a resection specimen

NOTE Confidence: 0.9578644975

01:04:21.517 --> 01:04:23.663 there are multiple devins associated

NOTE Confidence: 0.9578644975

01:04:23.663 --> 01:04:25.601 with an invasive cancer and they

NOTE Confidence: 0.9578644975

01:04:25.601 --> 01:04:27.060 have different staining patterns.

NOTE Confidence: 0.9578644975

01:04:27.060 --> 01:04:28.698 The devins have different staining patterns

NOTE Confidence: 0.946657506363636

01:04:31.060 --> 01:04:32.705 and I don't think, I don't think

NOTE Confidence: 0.946657506363636

01:04:32.705 --> 01:04:33.900 it's been documented elsewhere.

NOTE Confidence: 0.94830432

01:04:46.240 --> 01:04:48.320 On a slightly different note,

NOTE Confidence: 0.94830432

01:04:48.320 --> 01:04:49.960 what are your thoughts and this

NOTE Confidence: 0.94830432

01:04:49.960 --> 01:04:51.820 new method of depth of invasion

NOTE Confidence: 0.94830432

01:04:51.886 --> 01:04:53.438 on HPV independent cancers?

NOTE Confidence: 0.882016433333333

01:04:56.400 --> 01:04:59.040 Well, I guess time would tell.

NOTE Confidence: 0.882016433333333

01:04:59.040 --> 01:05:01.240 I think time would tell whether or not

NOTE Confidence: 0.9402536

01:05:03.840 --> 01:05:06.038 I always like new things like that,

NOTE Confidence: 0.9402536

01:05:06.040 --> 01:05:08.624 especially if it improves.

NOTE Confidence: 0.9402536

01:05:08.624 --> 01:05:10.562 Prognostication or stratification

NOTE Confidence: 0.9402536

01:05:10.562 --> 01:05:14.436 of patients. I think once it's

NOTE Confidence: 0.9402536

01:05:14.436 --> 01:05:15.976 introduced then we'll analyze it,

NOTE Confidence: 0.9402536

01:05:15.980 --> 01:05:19.572 we'll do a lot of you know review

NOTE Confidence: 0.9402536

01:05:19.572 --> 01:05:22.388 of it and see whether or not it

NOTE Confidence: 0.9402536

01:05:22.388 --> 01:05:23.580 actually performs as indicated.

NOTE Confidence: 0.9402536

01:05:23.580 --> 01:05:25.260 I think it's easy to do.

NOTE Confidence: 0.9402536

01:05:25.260 --> 01:05:28.081 We currently doing the study right now

NOTE Confidence: 0.9402536

01:05:28.081 --> 01:05:31.201 on that same subject we'll we'll we'll

NOTE Confidence: 0.9402536

01:05:31.201 --> 01:05:33.820 see what what it shows ultimately.

NOTE Confidence: 0.9402536

01:05:33.820 --> 01:05:35.140 So I I without judgment until

NOTE Confidence: 0.9402536

01:05:35.140 --> 01:05:36.020 we see that either.

NOTE Confidence: 0.9402536

01:05:39.080 --> 01:05:42.640 So thank you again for a wonderful talk.

NOTE Confidence: 0.9402536

01:05:42.640 --> 01:05:44.320 It's a shame you couldn't be in person,

NOTE Confidence: 0.9402536

01:05:44.320 --> 01:05:46.840 but we understand. So hopefully.

NOTE Confidence: 0.94830432

01:05:48.560 --> 01:05:50.240 Well, thanks again. It's again,

NOTE Confidence: 0.94830432

01:05:50.240 --> 01:05:52.262 it's an absolute pleasure and it's

NOTE Confidence: 0.94830432

01:05:52.262 --> 01:05:56.000 good to to see faces of friends,

NOTE Confidence: 0.94830432

01:05:56.000 --> 01:05:57.915 colleagues and mentors.

NOTE Confidence: 0.94830432

01:05:57.915 --> 01:06:01.245 And so thanks again for the

NOTE Confidence: 0.94830432

01:06:01.245 --> 01:06:03.170 invitation and you'll have a

NOTE Confidence: 0.94830432

01:06:03.170 --> 01:06:04.960 great rest of your day. Thank you.