WEBVTT

NOTE duration:"01:11:05"

NOTE recognizability:0.867

NOTE language:en-us

NOTE Confidence: 0.96568607

00:00:00.000 --> 00:00:02.920 Good afternoon.

NOTE Confidence: 0.96568607

00:00:02.920 --> 00:00:07.000 This year's McAllister Award recipient

NOTE Confidence: 0.96568607

00:00:07.000 --> 00:00:11.240 is Doctor Christina Antonescu. Dr.

NOTE Confidence: 0.96568607

00:00:11.240 --> 00:00:15.097 Antonescu is a renowned bone and soft

NOTE Confidence: 0.96568607

00:00:15.097 --> 00:00:17.520 tissue pathologist from Memorial

NOTE Confidence: 0.96568607

00:00:17.520 --> 00:00:20.678 Sloan Kettering Cancer Center where

NOTE Confidence: 0.96568607

00:00:20.678 --> 00:00:24.304 she's the director of the Bone and

NOTE Confidence: 0.96568607

00:00:24.304 --> 00:00:27.334 soft tissue subspeciality and also

NOTE Confidence: 0.96568607

00:00:27.334 --> 00:00:31.120 Co Director of the Sarcoma Center.

NOTE Confidence: 0.96568607

00:00:31.120 --> 00:00:33.404 Doctor Antonescu completed her

NOTE Confidence: 0.96568607

00:00:33.404 --> 00:00:36.560 MD from Bucharest, Romania where

NOTE Confidence: 0.96568607

00:00:36.560 --> 00:00:40.160 she began a pathology residency,

NOTE Confidence: 0.96568607

00:00:40.160 --> 00:00:44.440 but she completed it in 1996 at

NOTE Confidence: 0.96568607

00:00:44.440 --> 00:00:47.920 Lenox Hill Hospital in New York.

NOTE Confidence: 0.96568607

00:00:47.920 --> 00:00:51.720 After that, she went on to do a

NOTE Confidence: 0.96568607

00:00:51.720 --> 00:00:53.987 three-year fellowship at Memorial

NOTE Confidence: 0.96568607

00:00:53.987 --> 00:00:56.435 Zone Kettering Cancer Center,

NOTE Confidence: 0.96568607

00:00:56.440 --> 00:01:00.703 doing the first two years in general

NOTE Confidence: 0.96568607

00:01:00.703 --> 00:01:03.566 oncologic surgical pathology and the

NOTE Confidence: 0.96568607

00:01:03.566 --> 00:01:06.842 third year as a special Research fellow

NOTE Confidence: 0.96568607

00:01:06.842 --> 00:01:10.318 in born and Soft Tissue Pathology.

NOTE Confidence: 0.96568607

00:01:10.320 --> 00:01:14.776 And then she stayed on to become an

NOTE Confidence: 0.96568607

00:01:14.776 --> 00:01:20.792 attending at the same center at the bottom.

NOTE Confidence: 0.96568607

00:01:20.792 --> 00:01:21.416 Dr.

NOTE Confidence: 0.96568607

00:01:21.416 --> 00:01:24.536 Antonescu is a consummate surgical

NOTE Confidence: 0.96568607

00:01:24.536 --> 00:01:28.244 pathologist and she went on to build

NOTE Confidence: 0.96568607

00:01:28.244 --> 00:01:31.637 her scientific research on an excellent

NOTE Confidence: 0.96568607

00:01:31.637 --> 00:01:34.712 foundation of morphology to become

NOTE Confidence: 0.96568607

00:01:34.712 --> 00:01:38.680 a well funded clinician scientist.

NOTE Confidence: 0.96568607

00:01:38.680 --> 00:01:43.640 She's published more than 450 original

NOTE Confidence: 0.96568607

00:01:43.640 --> 00:01:47.400 articles, 24 review articles,

NOTE Confidence: 0.96568607

00:01:47.400 --> 00:01:50.520 written nearly forty book chapters,

NOTE Confidence: 0.96568607

00:01:50.520 --> 00:01:53.088 and co-authored 4 books.

NOTE Confidence: 0.96568607

00:01:53.088 --> 00:01:56.298 She's a She's made significant

NOTE Confidence: 0.96568607

00:01:56.298 --> 00:01:59.676 contribution to The Who Blue Book series,

NOTE Confidence: 0.96568607

00:01:59.680 --> 00:02:02.116 The Bone and Soft Tissue Tumors

NOTE Confidence: 0.96568607

00:02:02.120 --> 00:02:04.160 for more than 20 years,

NOTE Confidence: 0.96568607

00:02:04.160 --> 00:02:07.290 starting starting when when she

NOTE Confidence: 0.96568607

00:02:07.290 --> 00:02:09.741 was a junior attending.

NOTE Confidence: 0.96568607

00:02:09.741 --> 00:02:14.880 She's many awards and honors to her credit,

NOTE Confidence: 0.96568607

00:02:14.880 --> 00:02:17.680 starting from her training days,

NOTE Confidence: 0.96568607

00:02:17.680 --> 00:02:20.676 but I'll mention only two of those,

NOTE Confidence: 0.96568607

00:02:20.680 --> 00:02:23.920 the Ramsay Cortrans Young Investigator

NOTE Confidence: 0.96568607

00:02:23.920 --> 00:02:28.920 Award at given at US CAP in 2012 and

NOTE Confidence: 0.96568607

00:02:28.920 --> 00:02:35.200 the Maude Abbott Lecture in 2022.

NOTE Confidence: 0.96568607

00:02:35.200 --> 00:02:37.870 Doctor Antonesca has dedicated her work

NOTE Confidence: 0.96568607

00:02:37.870 --> 00:02:40.769 to the discovery of unique molecular

NOTE Confidence: 0.96568607

00:02:40.769 --> 00:02:43.359 signatures to help in defining,

NOTE Confidence: 0.96568607

00:02:43.360 --> 00:02:46.432 redefining and reclassifying sarcomas,

NOTE Confidence: 0.96568607

00:02:46.432 --> 00:02:50.833 and a brief list includes reporting

NOTE Confidence: 0.96568607

00:02:50.833 --> 00:02:54.151 the CHOP gene fusions and liposarcomas

NOTE Confidence: 0.96568607

00:02:54.151 --> 00:02:56.920 early on in her career.

NOTE Confidence: 0.96568607

00:02:56.920 --> 00:03:01.054 Expanding on EWSR 1 fusion partners

NOTE Confidence: 0.96568607

00:03:01.054 --> 00:03:04.760 in various soft tissue tumors,

NOTE Confidence: 0.96568607

00:03:04.760 --> 00:03:08.407 defining B core family of round cell

NOTE Confidence: 0.96568607

00:03:08.407 --> 00:03:12.475 tumors and sick fusion sarcomas and

NOTE Confidence: 0.96568607

00:03:12.475 --> 00:03:16.480 more recently in epithelioid hemangio

NOTE Confidence: 0.96568607

00:03:16.480 --> 00:03:19.391 endotheliomas defining the CAMPTOR 1

NOTE Confidence: 0.96568607

00:03:19.391 --> 00:03:23.512 fusion and the YAP 1 TFE 3 gene fusions.

NOTE Confidence: 0.96568607

00:03:23.512 --> 00:03:25.480 Even more recently,

NOTE Confidence: 0.96568607

00:03:25.480 --> 00:03:28.680 she's defined the genomic landscape

NOTE Confidence: 0.96568607

00:03:28.680 --> 00:03:32.280 of post radiation angiosarcomas

NOTE Confidence: 0.96568607

00:03:32.280 --> 00:03:36.466 and has laid down the criteria for

NOTE Confidence: 0.96568607

00:03:36.466 --> 00:03:39.840 grading primary breast angiosarcomas.

NOTE Confidence: 0.96568607

00:03:39.840 --> 00:03:41.008 In short,

NOTE Confidence: 0.96568607

00:03:41.008 --> 00:03:43.344 Doctor Antonesco's work touches

NOTE Confidence: 0.96568607

00:03:43.344 --> 00:03:46.840 on almost every sub speciality,

NOTE Confidence: 0.96568607

00:03:46.840 --> 00:03:50.606 and she is indeed a futuristic model

NOTE Confidence: 0.96568607

00:03:50.606 --> 00:03:54.639 of a general surgical pathologist.

NOTE Confidence: 0.604302842

00:04:03.230 --> 00:04:04.990 Thank you, Manju. Oops. Sorry.

NOTE Confidence: 0.878072394

00:04:08.790 --> 00:04:09.462 Thank you, Manju.

NOTE Confidence: 0.878072394

00:04:09.462 --> 00:04:10.400 Thank you. The committee.

NOTE Confidence: 0.878072394

00:04:10.400 --> 00:04:11.870 Are you hearing me well or?

NOTE Confidence: 0.878072394

00:04:11.870 --> 00:04:16.790 It's a bit? Yeah. OK.

NOTE Confidence: 0.878072394

00:04:16.790 --> 00:04:20.638 It's a great honor to be here,

NOTE Confidence: 0.878072394

00:04:20.638 --> 00:04:22.894 to be back in this amphitheater

NOTE Confidence: 0.878072394

00:04:22.894 --> 00:04:25.398 and to give the McAllister

NOTE Confidence: 0.878072394

00:04:25.398 --> 00:04:27.276 lecture and awards.

NOTE Confidence: 0.545185536

00:04:29.520 --> 00:04:32.160 Mind you, you, you know, overdid it.

NOTE Confidence: 0.545185536

00:04:32.160 --> 00:04:35.360 You, you guys treated me as royalty today.

NOTE Confidence: 0.545185536

00:04:35.360 --> 00:04:37.652 So I'm I'm very grateful and

NOTE Confidence: 0.545185536

00:04:37.652 --> 00:04:39.918 thankful so we can we can start

NOTE Confidence: 0.955803497142857

00:04:42.240 --> 00:04:45.600 since we have a diverse audience here.

NOTE Confidence: 0.955803497142857

00:04:45.600 --> 00:04:47.280 I will start with a very,

NOTE Confidence: 0.955803497142857

00:04:47.280 --> 00:04:50.100 very brief introduction of the

NOTE Confidence: 0.955803497142857

00:04:50.100 --> 00:04:52.920 sarcoma field where as you've

NOTE Confidence: 0.955803497142857

00:04:53.021 --> 00:04:56.096 heard I spend most of my efforts

NOTE Confidence: 0.955803497142857

00:04:56.096 --> 00:04:59.360 clinical and research energy.

NOTE Confidence: 0.955803497142857

00:04:59.360 --> 00:05:01.652 Sarcomas pose certain challenges

NOTE Confidence: 0.955803497142857

00:05:01.652 --> 00:05:06.120 as you as you know they are rare.

NOTE Confidence: 0.955803497142857

00:05:06.120 --> 00:05:08.970 They have a wide morphologic spectrums

NOTE Confidence: 0.955803497142857

00:05:08.970 --> 00:05:11.959 with more than 100 tumor types.

NOTE Confidence: 0.955803497142857

00:05:11.960 --> 00:05:15.350 The research level there is also

NOTE Confidence: 0.955803497142857

00:05:15.350 --> 00:05:18.154 limited number of cell models,

NOTE Confidence: 0.955803497142857

00:05:18.154 --> 00:05:22.960 both in vitro models and and mouse models.

NOTE Confidence: 0.955803497142857

00:05:22.960 --> 00:05:25.198 And what's very important is that

NOTE Confidence: 0.955803497142857

00:05:25.198 --> 00:05:27.848 you know at the clinical level that

NOTE Confidence: 0.955803497142857

00:05:27.848 --> 00:05:30.823 there is a still a huge gap between

NOTE Confidence: 0.955803497142857

00:05:30.823 --> 00:05:34.064 the advances that we've made in the

NOTE Confidence: 0.955803497142857

00:05:34.064 --> 00:05:36.614 pathogenesis of sarcomas and the

NOTE Confidence: 0.955803497142857

00:05:36.614 --> 00:05:39.788 available drugs and therapies out there

NOTE Confidence: 0.955803497142857

00:05:39.788 --> 00:05:42.558 that our colleagues medical oncologist

NOTE Confidence: 0.955803497142857

00:05:42.560 --> 00:05:46.520 can provide to the sarcoma patients.

NOTE Confidence: 0.955803497142857

00:05:46.520 --> 00:05:49.768 So in order to simplify our understanding and

NOTE Confidence: 0.955803497142857

00:05:49.768 --> 00:05:53.319 give a perspective to their pathogenesis,

NOTE Confidence: 0.955803497142857

00:05:53.320 --> 00:05:56.170 sarcomas can be defined divided

NOTE Confidence: 0.955803497142857

00:05:56.170 --> 00:05:59.772 in two main categories based on

NOTE Confidence: 0.955803497142857

00:05:59.772 --> 00:06:02.360 simple versus complex genomics.

NOTE Confidence: 0.955803497142857

00:06:02.360 --> 00:06:04.551 The first category are sarcomas that are

NOTE Confidence: 0.955803497142857

00:06:04.551 --> 00:06:07.239 driven by a single specific alterations,

NOTE Confidence: 0.955803497142857

00:06:07.240 --> 00:06:10.540 either a fusion or a activating

NOTE Confidence: 0.955803497142857

00:06:10.540 --> 00:06:13.785 mutation such as kitting GIST and

NOTE Confidence: 0.955803497142857

00:06:13.785 --> 00:06:16.510 these tumors have historically being

NOTE Confidence: 0.955803497142857

00:06:16.510 --> 00:06:19.122 diagnosed at the molecular level

NOTE Confidence: 0.955803497142857

00:06:19.122 --> 00:06:22.680 by a single assay molecular test.

NOTE Confidence: 0.955803497142857

00:06:22.680 --> 00:06:28.084 The second category is is represented

NOTE Confidence: 0.955803497142857

00:06:28.084 --> 00:06:30.994 by sarcomas with complex genomics,

NOTE Confidence: 0.955803497142857

00:06:31.000 --> 00:06:33.960 typically mutations in tumor suppressor

NOTE Confidence: 0.955803497142857

00:06:33.960 --> 00:06:36.920 genes or copy number alterations.

NOTE Confidence: 0.955803497142857

00:06:36.920 --> 00:06:38.424 And in this category,

NOTE Confidence: 0.955803497142857

00:06:38.424 --> 00:06:41.478 we have most of the adults 5 sarcomas

NOTE Confidence: 0.955803497142857

00:06:41.478 --> 00:06:44.339 such as UPS, mix of fibrosarcoma,

NOTE Confidence: 0.955803497142857

00:06:44.339 --> 00:06:47.584 liomal sarcoma support and these tumors

NOTE Confidence: 0.955803497142857

00:06:47.584 --> 00:06:51.440 can be best approached by an NGS tool.

NOTE Confidence: 0.916494616666667

00:06:55.040 --> 00:06:57.422 The impact of molecular discoveries to

NOTE Confidence: 0.916494616666667

00:06:57.422 --> 00:07:00.120 the sarcoma field have been remarkable,

NOTE Confidence: 0.916494616666667

00:07:00.120 --> 00:07:03.024 especially at the diagnosis

NOTE Confidence: 0.916494616666667

00:07:03.024 --> 00:07:04.942 and classification area,

NOTE Confidence: 0.916494616666667

00:07:04.942 --> 00:07:08.638 and mainly because it allowed us to have

NOTE Confidence: 0.916494616666667

00:07:08.638 --> 00:07:13.110 a more objective interpretation as well

NOTE Confidence: 0.916494616666667

00:07:13.110 --> 00:07:15.885 as empowering surgical pathologists that

NOTE Confidence: 0.916494616666667

00:07:15.885 --> 00:07:20.240 do not have a special sarcoma expertise.

NOTE Confidence: 0.916494616666667

00:07:20.240 --> 00:07:23.278 It also allowed us some of our

NOTE Confidence: 0.916494616666667

00:07:23.278 --> 00:07:25.518 objective diagnosis when the material

NOTE Confidence: 0.916494616666667

00:07:25.518 --> 00:07:29.800 was very scant or suboptimal.

NOTE Confidence: 0.916494616666667

00:07:29.800 --> 00:07:33.906 As we became more and more aware of

NOTE Confidence: 0.916494616666667

00:07:33.906 --> 00:07:37.036 the genomic complexity of sarcomas,

NOTE Confidence: 0.916494616666667

00:07:37.040 --> 00:07:40.373 as well as due to the continuous

NOTE Confidence: 0.916494616666667

00:07:40.373 --> 00:07:44.838 decrease in sequence sequencing costs,

NOTE Confidence: 0.916494616666667

00:07:44.840 --> 00:07:48.963 we have witnessed for the past decade

NOTE Confidence: 0.916494616666667

00:07:48.963 --> 00:07:52.275 a significant platform shift from a

NOTE Confidence: 0.916494616666667

00:07:52.275 --> 00:07:56.850 single gene assay to a targeted NGS panel.

NOTE Confidence: 0.916494616666667

00:07:56.850 --> 00:08:01.773 Almost obsolete these days are RTPCR

NOTE Confidence: 0.916494616666667

00:08:01.773 --> 00:08:05.845 tests for fusion detection or DNAPCR

NOTE Confidence: 0.916494616666667

00:08:05.845 --> 00:08:09.475 tests for a single activating mutation.

NOTE Confidence: 0.916494616666667

00:08:09.480 --> 00:08:11.800 Even FISH assay that interrogates

NOTE Confidence: 0.916494616666667

00:08:11.800 --> 00:08:14.513 only one gene rearrangement at the

NOTE Confidence: 0.916494616666667

00:08:14.513 --> 00:08:17.065 time is not as popular as before and

NOTE Confidence: 0.916494616666667

00:08:17.065 --> 00:08:19.894 the main reasons being that it has

NOTE Confidence: 0.916494616666667

00:08:19.894 --> 00:08:22.388 low resolution and cannot be cannot

NOTE Confidence: 0.916494616666667

00:08:22.388 --> 00:08:24.558 pick up certain translocation such

NOTE Confidence: 0.916494616666667

00:08:24.558 --> 00:08:27.231 as cryptic or intrachromosomal that

NOTE Confidence: 0.916494616666667

00:08:27.231 --> 00:08:29.800 will go over in more detail later.

NOTE Confidence: 0.916494616666667

00:08:29.800 --> 00:08:32.584 There also also limited number of

NOTE Confidence: 0.916494616666667

00:08:32.584 --> 00:08:34.440 FISH probes available commercially

NOTE Confidence: 0.916494616666667

00:08:34.518 --> 00:08:35.678 that can be used.

NOTE Confidence: 0.916494616666667

00:08:35.680 --> 00:08:39.816 And even if we have a positive

NOTE Confidence: 0.916494616666667

00:08:39.816 --> 00:08:43.344 FISH result due to the significant

NOTE Confidence: 0.916494616666667

00:08:43.344 --> 00:08:46.144 gene promiscuity that we we know,

NOTE Confidence: 0.916494616666667

00:08:46.144 --> 00:08:49.479 especially in the EWS gene family of tumors,

NOTE Confidence: 0.916494616666667

00:08:49.480 --> 00:08:51.640 we may not necessarily know what

NOTE Confidence: 0.916494616666667

00:08:51.640 --> 00:08:54.088 the accurate diagnosis is.

NOTE Confidence: 0.916494616666667

00:08:54.088 --> 00:08:55.480 And lastly,

NOTE Confidence: 0.916494616666667

00:08:55.480 --> 00:08:58.240 even in the assets like array,

NOTE Confidence: 0.916494616666667

00:08:58.240 --> 00:09:00.104 CGH or SNIP array,

NOTE Confidence: 0.916494616666667

00:09:00.104 --> 00:09:02.900 they are not not necessary anymore

NOTE Confidence: 0.916494616666667

00:09:02.992 --> 00:09:05.944 since most of the copy number

NOTE Confidence: 0.916494616666667

00:09:05.944 --> 00:09:08.697 alterations results can be obtained

NOTE Confidence: 0.916494616666667

00:09:08.697 --> 00:09:13.359 from an Ng targeted NGS panel.

NOTE Confidence: 0.916494616666667

00:09:13.360 --> 00:09:17.070 This diagram just gives you a glimpse

NOTE Confidence: 0.916494616666667

00:09:17.070 --> 00:09:20.361 of the current complexity of sarcomas

NOTE Confidence: 0.916494616666667

00:09:20.361 --> 00:09:24.670 that are driven by EWS or FUS gene

NOTE Confidence: 0.916494616666667

00:09:24.670 --> 00:09:28.210 fusions and you can imagine EWS

NOTE Confidence: 0.916494616666667

00:09:28.210 --> 00:09:32.063 positive FISH may definitely not tell

NOTE Confidence: 0.916494616666667

00:09:32.063 --> 00:09:35.999 the whole story and the diagnosis.

NOTE Confidence: 0.916494616666667

00:09:36.000 --> 00:09:37.800 In particular for small blue

NOTE Confidence: 0.916494616666667

00:09:37.800 --> 00:09:38.880 round cell tumors,

NOTE Confidence: 0.916494616666667

00:09:38.880 --> 00:09:40.692 which is the panel in the

NOTE Confidence: 0.916494616666667

00:09:40.692 --> 00:09:42.360 center with the black boxes,

NOTE Confidence: 0.916494616666667

00:09:42.360 --> 00:09:47.768 it is not unusual for for a case to

NOTE Confidence: 0.916494616666667

00:09:47.768 --> 00:09:51.262 be tested by 4 to 5 FISH probes before

NOTE Confidence: 0.916494616666667

00:09:51.262 --> 00:09:53.554 we arrive to the correct diagnosis.

NOTE Confidence: 0.916494616666667

00:09:53.560 --> 00:09:56.656 And that's not saving us any

NOTE Confidence: 0.916494616666667

00:09:56.656 --> 00:09:58.720 time or any costs.

NOTE Confidence: 0.916494616666667

00:09:58.720 --> 00:10:03.692 So the most widely applied targeted RNA

NOTE Confidence: 0.916494616666667

00:10:03.692 --> 00:10:06.848 sequencing is Archer and I understand

NOTE Confidence: 0.916494616666667

00:10:06.848 --> 00:10:10.196 that's what you're using here as well.

NOTE Confidence: 0.916494616666667

00:10:10.200 --> 00:10:11.912 And in our department,

NOTE Confidence: 0.916494616666667

00:10:11.912 --> 00:10:16.624 we use a panel of 123 genes that are

NOTE Confidence: 0.916494616666667

00:10:16.624 --> 00:10:19.440 commonly involved in in sarcomas as well.

NOTE Confidence: 0.916494616666667

00:10:19.440 --> 00:10:23.437 Archer is a anchor Multiplex PCR that

NOTE Confidence: 0.916494616666667

00:10:23.437 --> 00:10:28.163 uses a one side nested primers and is

NOTE Confidence: 0.916494616666667

00:10:28.163 --> 00:10:31.276 able to detect agnostically a gene

NOTE Confidence: 0.916494616666667

00:10:31.276 --> 00:10:33.721 rearrangement by targeting a gene

NOTE Confidence: 0.916494616666667

00:10:33.721 --> 00:10:36.920 that is commonly involved in the fusion.

NOTE Confidence: 0.916494616666667

00:10:36.920 --> 00:10:40.016 It requires 7 to 10 on stain slides and

NOTE Confidence: 0.916494616666667

00:10:40.016 --> 00:10:42.995 the results are out in about a week.

NOTE Confidence: 0.81979853

00:10:46.000 --> 00:10:51.076 For the targeted DNA based NGS,

NOTE Confidence: 0.81979853

00:10:51.080 --> 00:10:53.336 most platforms out there

NOTE Confidence: 0.81979853

00:10:53.336 --> 00:10:56.156 include about 500 cancer genes.

NOTE Confidence: 0.81979853

00:10:56.160 --> 00:10:58.680 They have high coverage in our

NOTE Confidence: 0.81979853

00:10:58.680 --> 00:11:01.578 hospital more than 700 range and

NOTE Confidence: 0.81979853

00:11:01.578 --> 00:11:04.694 the the report of the targeted

NOTE Confidence: 0.81979853

00:11:04.694 --> 00:11:07.940 NGS will provide information on a

NOTE Confidence: 0.81979853

00:11:07.940 --> 00:11:11.269 number of things including single

NOTE Confidence: 0.81979853

00:11:11.269 --> 00:11:14.129 nucleotide variants and intra

NOTE Confidence: 0.81979853

00:11:14.129 --> 00:11:17.750 genic alterations as well as arm

NOTE Confidence: 0.81979853

00:11:17.750 --> 00:11:20.690 level copy number changes which are

NOTE Confidence: 0.81979853

00:11:20.690 --> 00:11:23.299 deletions or amplifications and a

NOTE Confidence: 0.81979853

00:11:23.299 --> 00:11:26.341 very limited number of gene fusions

NOTE Confidence: 0.81979853

00:11:26.434 --> 00:11:29.360 such as EWS and and track fusions.

NOTE Confidence: 0.81979853

00:11:29.360 --> 00:11:31.538 It's required more materials such as

NOTE Confidence: 0.81979853

00:11:31.538 --> 00:11:33.757 10 to 20 unstained slides depending

NOTE Confidence: 0.81979853

00:11:33.757 --> 00:11:37.024 on the size of the tissue and the

NOTE Confidence: 0.81979853

00:11:37.024 --> 00:11:41.760 estimated turn around time is about a month.

NOTE Confidence: 0.81979853

00:11:41.760 --> 00:11:44.800 So this is what we use at MSK.

NOTE Confidence: 0.81979853

00:11:44.800 --> 00:11:48.314 Is this in house targeted NGS panel?

NOTE Confidence: 0.81979853

00:11:48.320 --> 00:11:50.920 We call it MSK impact.

NOTE Confidence: 0.81979853

00:11:50.920 --> 00:11:54.675 And this particular platform requires

NOTE Confidence: 0.81979853

00:11:54.675 --> 00:11:58.880 both tumor and germline normal DNA

NOTE Confidence: 0.81979853

00:11:58.880 --> 00:12:01.742 and therefore a patient consent is

NOTE Confidence: 0.81979853

00:12:01.742 --> 00:12:05.285 required as part of a protocol and

NOTE Confidence: 0.81979853

00:12:05.285 --> 00:12:08.363 can be activated only by medical

NOTE Confidence: 0.81979853

00:12:08.363 --> 00:12:10.997 oncologist and not by pathologist.

NOTE Confidence: 0.81979853

00:12:11.000 --> 00:12:11.486 Briefly,

NOTE Confidence: 0.81979853

00:12:11.486 --> 00:12:14.888 the tumor and the normal DNA is

NOTE Confidence: 0.81979853

00:12:14.888 --> 00:12:17.820 being pulled together with the

NOTE Confidence: 0.81979853

00:12:17.820 --> 00:12:21.305 Multiplex cup captures of the bio

NOTE Confidence: 0.81979853

00:12:21.305 --> 00:12:25.105 biotelated probes and then it's being

NOTE Confidence: 0.81979853

00:12:25.105 --> 00:12:28.279 sequenced and provided 100 base pair

NOTE Confidence: 0.691823646666667

00:12:30.480 --> 00:12:33.600 paired and fragments and then these

NOTE Confidence: 0.691823646666667

00:12:33.600 --> 00:12:37.182 are runs through an OPPO KB pipeline

NOTE Confidence: 0.691823646666667

00:12:37.182 --> 00:12:41.634 and a report is being generated.

NOTE Confidence: 0.691823646666667

00:12:41.640 --> 00:12:45.376 In contrast, most of the targeted NGS

NOTE Confidence: 0.691823646666667

00:12:45.376 --> 00:12:48.784 panels that are commercially available or

NOTE Confidence: 0.691823646666667

00:12:48.784 --> 00:12:53.160 that are running other academic places,

NOTE Confidence: 0.691823646666667

00:12:53.160 --> 00:12:56.524 they require only tumor DNA and because

NOTE Confidence: 0.691823646666667

00:12:56.524 --> 00:12:59.420 of that those reports may not be able

NOTE Confidence: 0.691823646666667

00:12:59.497 --> 00:13:01.759 to tell you the difference between

NOTE Confidence: 0.691823646666667

00:13:01.759 --> 00:13:04.599 a germline and a somatic mutation.

NOTE Confidence: 0.691823646666667

00:13:04.600 --> 00:13:06.885 So that's the major difference

NOTE Confidence: 0.691823646666667

00:13:06.885 --> 00:13:08.713 between the two platforms.

NOTE Confidence: 0.87740231

00:13:11.200 --> 00:13:15.092 So why am I giving this talk

NOTE Confidence: 0.87740231

00:13:15.092 --> 00:13:17.906 to you now and the reason,

NOTE Confidence: 0.87740231

00:13:17.906 --> 00:13:21.037 the main reason being that more than 10

NOTE Confidence: 0.87740231

00:13:21.037 --> 00:13:23.662 years have passed since we at Memorial

NOTE Confidence: 0.87740231

00:13:23.662 --> 00:13:25.925 have been using a systematically

NOTE Confidence: 0.87740231

00:13:25.925 --> 00:13:28.315 NGS in our clinical practice.

NOTE Confidence: 0.87740231

00:13:28.320 --> 00:13:31.050 So a lot of time has a lot of data

NOTE Confidence: 0.87740231

00:13:31.134 --> 00:13:33.944 has accumulated and analyzed in

NOTE Confidence: 0.87740231

00:13:33.944 --> 00:13:36.192 different projects and studies.

NOTE Confidence: 0.87740231

00:13:36.200 --> 00:13:38.400 As you will see.

NOTE Confidence: 0.87740231

00:13:38.400 --> 00:13:42.285 It also gives me an opportunity to

NOTE Confidence: 0.87740231

00:13:42.285 --> 00:13:45.156 discuss the contributions for NGS

NOTE Confidence: 0.87740231

00:13:45.156 --> 00:13:47.376 in diagnosis and classification

NOTE Confidence: 0.87740231

00:13:47.376 --> 00:13:51.100 and to highlight the the pros of

NOTE Confidence: 0.87740231

00:13:51.100 --> 00:13:53.986 of this method in contrast with

NOTE Confidence: 0.87740231

00:13:53.986 --> 00:13:56.758 FISH or PCR or so forth.

NOTE Confidence: 0.87740231

00:13:56.760 --> 00:13:59.182 And I would also like to give

NOTE Confidence: 0.87740231

00:13:59.182 --> 00:14:01.586 you some examples to make the

NOTE Confidence: 0.87740231

00:14:01.586 --> 00:14:03.726 case that there are additional

NOTE Confidence: 0.87740231

00:14:03.726 --> 00:14:06.279 applications to NGS besides diagnosis.

NOTE Confidence: 0.87740231

00:14:06.280 --> 00:14:09.240 So for this talk,

NOTE Confidence: 0.87740231

00:14:09.240 --> 00:14:13.216 I will try to cover five different topics

NOTE Confidence: 0.87740231

00:14:13.216 --> 00:14:16.439 including with the impact on diagnosis,

NOTE Confidence: 0.87740231

00:14:16.440 --> 00:14:18.528 impact on survival,

NOTE Confidence: 0.87740231

00:14:18.528 --> 00:14:19.920 targeted therapy,

NOTE Confidence: 0.87740231

00:14:19.920 --> 00:14:22.038 risk stratification and at the end,

NOTE Confidence: 0.87740231

00:14:22.040 --> 00:14:25.587 if we have time also to give you

NOTE Confidence: 0.87740231

00:14:25.587 --> 00:14:28.552 an example how NGS can be used in

NOTE Confidence: 0.87740231

00:14:28.552 --> 00:14:30.852 the genomic sub classification

NOTE Confidence: 0.87740231

00:14:30.852 --> 00:14:33.152 of molecularly complex sarcomas.

NOTE Confidence: 0.87740231

00:14:33.160 --> 00:14:36.037 So we can start with the obvious,

NOTE Confidence: 0.87740231

00:14:36.040 --> 00:14:39.036 the use of NGS in routine diagnosis.

NOTE Confidence: 0.87740231

00:14:39.040 --> 00:14:42.988 And here I will first discuss the

NOTE Confidence: 0.87740231

00:14:42.988 --> 00:14:45.560 NGS increased diagnostic accuracy

NOTE Confidence: 0.87740231

00:14:45.560 --> 00:14:47.420 in undifferentiated tumors,

NOTE Confidence: 0.87740231

00:14:47.420 --> 00:14:50.873 mainly where the the morphology and

NOTE Confidence: 0.87740231

00:14:50.873 --> 00:14:53.546 immunostoc chemistry has failed to

NOTE Confidence: 0.87740231

00:14:53.546 --> 00:14:56.276 provide a more specific characterization.

NOTE Confidence: 0.87740231

00:14:56.280 --> 00:15:00.376 And then a few examples of the NGS

NOTE Confidence: 0.87740231

00:15:00.376 --> 00:15:02.375 increased sensitivity of detection

NOTE Confidence: 0.87740231

00:15:02.375 --> 00:15:05.448 if you we compare it to other

NOTE Confidence: 0.87740231

00:15:05.448 --> 00:15:07.719 lower resolution methods.

NOTE Confidence: 0.87740231

00:15:07.720 --> 00:15:11.900 So in order to give some examples of

NOTE Confidence: 0.87740231

00:15:11.900 --> 00:15:14.319 the NGS increased diagnostic accuracy,

NOTE Confidence: 0.87740231

00:15:14.320 --> 00:15:17.224 I selected few examples that I

NOTE Confidence: 0.87740231

00:15:17.224 --> 00:15:20.368 believe there are a little bit

NOTE Confidence: 0.87740231

00:15:20.368 --> 00:15:23.680 more often pitfalls in our soft

NOTE Confidence: 0.87740231

00:15:23.680 --> 00:15:25.760 tissue sarcoma practice.

NOTE Confidence: 0.87740231

00:15:25.760 --> 00:15:28.960 And I will start with an example

NOTE Confidence: 0.87740231

00:15:28.960 --> 00:15:30.640 of undifferentiated leomorphic

NOTE Confidence: 0.87740231

00:15:30.640 --> 00:15:32.880 sarcoma of the extremity.

NOTE Confidence: 0.87740231

00:15:32.880 --> 00:15:35.771 And this is how the morphology of

NOTE Confidence: 0.87740231

00:15:35.771 --> 00:15:38.042 the resection specimen look like

NOTE Confidence: 0.87740231

00:15:38.042 --> 00:15:39.958 had had different components.

NOTE Confidence: 0.87740231

00:15:39.960 --> 00:15:43.056 This was a 34 year old man with the

NOTE Confidence: 0.87740231

00:15:43.056 --> 00:15:46.018 11 CM tumor of the thigh and you

NOTE Confidence: 0.87740231

00:15:46.018 --> 00:15:49.384 can see on the lower panel very

NOTE Confidence: 0.87740231

00:15:49.384 --> 00:15:52.360 leomorphic spindle bizarre cells.

NOTE Confidence: 0.87740231

00:15:52.360 --> 00:15:54.676 The tumor also has some ossification

NOTE Confidence: 0.87740231

00:15:54.676 --> 00:15:57.369 and the upper panel if you can

NOTE Confidence: 0.87740231

00:15:57.369 --> 00:15:59.796 appreciate they were had a completely

NOTE Confidence: 0.87740231

00:15:59.796 --> 00:16:01.604 different morphology with mononuclear

NOTE Confidence: 0.87740231

00:16:01.604 --> 00:16:03.720 cells and osteoclastive giant cells.

NOTE Confidence: 0.87740231

00:16:03.720 --> 00:16:06.138 So our interpretation on this case

NOTE Confidence: 0.87740231

00:16:06.138 --> 00:16:09.488 is that was most likely a Sarcomatus

NOTE Confidence: 0.87740231

00:16:09.488 --> 00:16:11.700 transformation in a tenosynovial

NOTE Confidence: 0.87740231

00:16:11.700 --> 00:16:13.359 giant cell tumor.

NOTE Confidence: 0.87740231

00:16:13.360 --> 00:16:13.736 However,

NOTE Confidence: 0.87740231

00:16:13.736 --> 00:16:15.616 the patient developed lung meds

NOTE Confidence: 0.87740231

00:16:15.616 --> 00:16:17.120 and the local recurrence.

NOTE Confidence: 0.87740231

00:16:17.120 --> 00:16:19.605 So he behaved in a very aggressive

NOTE Confidence: 0.87740231

00:16:19.605 --> 00:16:22.520 fashion and as it happens to all

NOTE Confidence: 0.87740231

00:16:22.520 --> 00:16:24.720 these recurrent metastatic cases that

NOTE Confidence: 0.87740231

00:16:24.804 --> 00:16:27.916 the tumor are being tested by MSK impact.

NOTE Confidence: 0.87740231

00:16:27.920 --> 00:16:29.728 And to our surprise,

NOTE Confidence: 0.87740231

00:16:29.728 --> 00:16:32.968 the results showed a very high level

NOTE Confidence: 0.87740231

00:16:32.968 --> 00:16:36.432 of amplification of MDM two and CDK 4,

NOTE Confidence: 0.87740231

00:16:36.440 --> 00:16:38.768 so that raising the possibility of

NOTE Confidence: 0.87740231

00:16:38.768 --> 00:16:40.320 a day differentiated liposarcoma.

NOTE Confidence: 0.87740231

00:16:40.320 --> 00:16:43.180 Of course we did the immunos based

NOTE Confidence: 0.87740231

00:16:43.180 --> 00:16:46.180 on this result which showed strong

NOTE Confidence: 0.87740231

00:16:46.180 --> 00:16:48.450 nuclear positivity for both markers.

NOTE Confidence: 0.87740231

00:16:48.450 --> 00:16:51.410 And of course we went back to the

NOTE Confidence: 0.87740231

00:16:51.410 --> 00:16:53.775 specimen and we tried to find

NOTE Confidence: 0.87740231

00:16:53.775 --> 00:16:55.695 any areas of well differentiated

NOTE Confidence: 0.87740231

00:16:55.775 --> 00:16:58.840 liposarcoma and indeed we did in

NOTE Confidence: 0.87740231

00:16:58.840 --> 00:17:02.636 probably in in retrospect these were

NOTE Confidence: 0.87740231

00:17:02.636 --> 00:17:05.450 interpreted as as normal fat which

NOTE Confidence: 0.87740231

00:17:05.534 --> 00:17:08.240 is being infiltrated by the tumor.

NOTE Confidence: 0.831744103076923

00:17:08.240 --> 00:17:11.565 The second example is one that refers

NOTE Confidence: 0.831744103076923

00:17:11.565 --> 00:17:14.920 and relates to round cell sarcomas.

NOTE Confidence: 0.831744103076923

00:17:14.920 --> 00:17:18.196 A few years back we we did this small

NOTE Confidence: 0.831744103076923

00:17:18.196 --> 00:17:21.358 study with Doctor Argani from Hopkins.

NOTE Confidence: 0.831744103076923

00:17:21.360 --> 00:17:24.240 He had a couple of cases of round

NOTE Confidence: 0.831744103076923

00:17:24.240 --> 00:17:26.880 cell sarcomas of the kidney in young

NOTE Confidence: 0.831744103076923

00:17:26.880 --> 00:17:29.400 adults that were CD 34 negative,

NOTE Confidence: 0.831744103076923

00:17:29.400 --> 00:17:31.904 B core strongly positive.

NOTE Confidence: 0.831744103076923

00:17:31.904 --> 00:17:34.453 And the leading diagnosis for

NOTE Confidence: 0.831744103076923

00:17:34.453 --> 00:17:37.039 for these tumors was a clear

NOTE Confidence: 0.831744103076923

00:17:37.039 --> 00:17:39.278 cell sarcoma of the kidney.

NOTE Confidence: 0.831744103076923

00:17:39.280 --> 00:17:40.876 And to our surprise,

NOTE Confidence: 0.831744103076923

00:17:40.876 --> 00:17:43.688 when we did the RNA sequencing on

NOTE Confidence: 0.831744103076923

00:17:43.688 --> 00:17:46.376 these cases and NAP to STAT 6 fusion

NOTE Confidence: 0.831744103076923

00:17:46.376 --> 00:17:49.497 was discovered in keeping with the

NOTE Confidence: 0.831744103076923

00:17:49.497 --> 00:17:52.197 malignant solitary fibrous tumor which

NOTE Confidence: 0.831744103076923

00:17:52.200 --> 00:17:55.104 triggered of course an immuno stain

NOTE Confidence: 0.831744103076923

00:17:55.104 --> 00:17:58.718 which showed 4 plus STAT 6 positivity.

NOTE Confidence: 0.831744103076923

00:17:58.720 --> 00:18:01.198 We were truly puzzled of the B

NOTE Confidence: 0.831744103076923

00:18:01.198 --> 00:18:03.895 core of our expression of these

NOTE Confidence: 0.831744103076923

00:18:03.895 --> 00:18:06.475 malignant SFTS in the kidney.

NOTE Confidence: 0.831744103076923

00:18:06.480 --> 00:18:09.324 And we look back at the RNA sig data

NOTE Confidence: 0.831744103076923

00:18:09.324 --> 00:18:11.413 which showed indeed I don't know

NOTE Confidence: 0.831744103076923

00:18:11.413 --> 00:18:14.284 if you see on that panel very high

NOTE Confidence: 0.831744103076923

00:18:14.284 --> 00:18:17.176 expression or B core at MIRMRNA level,

NOTE Confidence: 0.831744103076923

00:18:17.176 --> 00:18:19.816 suggesting that what we see

NOTE Confidence: 0.831744103076923

00:18:19.816 --> 00:18:20.872 on immunostochemistry,

NOTE Confidence: 0.831744103076923

00:18:20.880 --> 00:18:23.760 it's not some kind of background

NOTE Confidence: 0.831744103076923

00:18:23.760 --> 00:18:25.200 false positive result.

NOTE Confidence: 0.831744103076923

00:18:25.200 --> 00:18:27.846 We then expanded the study with

NOTE Confidence: 0.831744103076923

00:18:27.846 --> 00:18:30.700 other non renal SFT and indeed

NOTE Confidence: 0.831744103076923

00:18:30.700 --> 00:18:33.205 the majority of malignant SFT

NOTE Confidence: 0.831744103076923

00:18:33.205 --> 00:18:36.520 also Co expressed B core that may

NOTE Confidence: 0.831744103076923

00:18:36.520 --> 00:18:39.520 represent the pitfall in diagnosis.

NOTE Confidence: 0.831744103076923

00:18:39.520 --> 00:18:42.720 And the last example I want to briefly

NOTE Confidence: 0.831744103076923

00:18:42.720 --> 00:18:45.960 go over is the NGS contribution to

NOTE Confidence: 0.831744103076923

00:18:45.960 --> 00:18:47.440 undifferentiated sarcomatoidiaeoplasm.

NOTE Confidence: 0.831744103076923

00:18:47.440 --> 00:18:51.880 So this was a tough case.

NOTE Confidence: 0.831744103076923

00:18:51.880 --> 00:18:53.896 This was a 70 year old man

NOTE Confidence: 0.831744103076923

00:18:53.896 --> 00:18:55.918 with the arms of tissue mask.

NOTE Confidence: 0.831744103076923

00:18:55.920 --> 00:18:58.405 It looked like this blue

NOTE Confidence: 0.831744103076923

00:18:58.405 --> 00:18:59.399 vesicular monomorphic.

NOTE Confidence: 0.831744103076923

00:18:59.400 --> 00:19:01.104 Our leading diagnosis was

NOTE Confidence: 0.831744103076923

00:19:01.104 --> 00:19:03.234 a high grade and PNSD.

NOTE Confidence: 0.831744103076923

00:19:03.240 --> 00:19:03.811 However,

NOTE Confidence: 0.831744103076923

00:19:03.811 --> 00:19:07.237 the immuno profile was not supportive

NOTE Confidence: 0.831744103076923

00:19:07.240 --> 00:19:10.036 S100 Sox the negative and the

NOTE Confidence: 0.831744103076923

00:19:10.040 --> 00:19:11.940 H3K27 trimethyl was retained.

NOTE Confidence: 0.831744103076923

00:19:11.940 --> 00:19:15.120 He had a very high proliferation rate,

NOTE Confidence: 0.831744103076923

00:19:15.120 --> 00:19:17.920 which is kind of unusual for sarcomas,

NOTE Confidence: 0.831744103076923

00:19:17.920 --> 00:19:21.021 so close to 90% and the Archer

NOTE Confidence: 0.831744103076923

00:19:21.021 --> 00:19:23.200 was negative for fusions.

NOTE Confidence: 0.831744103076923

00:19:23.200 --> 00:19:25.744 So then the patient next year

NOTE Confidence: 0.831744103076923

00:19:25.744 --> 00:19:28.400 developed a small bowel metastasis,

NOTE Confidence: 0.831744103076923

00:19:28.400 --> 00:19:30.344 which once again is quite unusual

NOTE Confidence: 0.831744103076923

00:19:30.344 --> 00:19:32.518 for sarcomas to go in the bowel.

NOTE Confidence: 0.831744103076923

00:19:32.520 --> 00:19:33.640 We've seen it of course,

NOTE Confidence: 0.831744103076923

00:19:33.640 --> 00:19:36.880 but and then we of course ran the

NOTE Confidence: 0.831744103076923

00:19:36.880 --> 00:19:39.998 impact and the impact show the high

NOTE Confidence: 0.831744103076923

00:19:40.000 --> 00:19:44.110 tumor mutation burden of 20 mutations

NOTE Confidence: 0.831744103076923

00:19:44.110 --> 00:19:47.480 And then of course the diagnostic piece,

NOTE Confidence: 0.831744103076923

00:19:47.480 --> 00:19:50.630 the B RAF V 600 E mutation as well as

NOTE Confidence: 0.831744103076923

00:19:50.717 --> 00:19:54.294 the GA and CT transition mutations that

NOTE Confidence: 0.831744103076923

00:19:54.294 --> 00:19:57.358 were consistent with the UV signature.

NOTE Confidence: 0.831744103076923

00:19:57.360 --> 00:20:00.678 So the diagnosis of the differentiated

NOTE Confidence: 0.831744103076923

00:20:00.678 --> 00:20:03.760 spindle cell Melanoma was rendered.

NOTE Confidence: 0.831744103076923

00:20:03.760 --> 00:20:06.360 The patient was treated successfully

NOTE Confidence: 0.831744103076923

00:20:06.360 --> 00:20:08.960 with the immune checkpoint inhibitors.

NOTE Confidence: 0.831744103076923

00:20:08.960 --> 00:20:11.529 And he's still alive 2023 with the

NOTE Confidence: 0.831744103076923

00:20:11.529 --> 00:20:14.952 liver meth and and then we had the

NOTE Confidence: 0.831744103076923

00:20:14.952 --> 00:20:17.197 opportunity to run the immunosochemistry

NOTE Confidence: 0.831744103076923

00:20:17.278 --> 00:20:20.197 for B RAF which was diffusely positive.

NOTE Confidence: 0.831744103076923

00:20:20.200 --> 00:20:25.020 So moving on to the next topic,

NOTE Confidence: 0.831744103076923

00:20:25.020 --> 00:20:29.475 the increased sensitivity of detection of

NOTE Confidence: 0.831744103076923

00:20:29.475 --> 00:20:33.360 NGS compared to other molecular methods.

NOTE Confidence: 0.831744103076923

00:20:33.360 --> 00:20:38.111 And here I think 1 good example are

NOTE Confidence: 0.831744103076923

00:20:38.111 --> 00:20:41.128 tumors that are driven by a wide

NOTE Confidence: 0.831744103076923

00:20:41.128 --> 00:20:44.400 spectrum of alteration in one gene,

NOTE Confidence: 0.831744103076923

00:20:44.400 --> 00:20:46.724 such as the loss of function mutation

NOTE Confidence: 0.831744103076923

00:20:46.724 --> 00:20:50.696 in smart B1, which can be deletions,

NOTE Confidence: 0.831744103076923

00:20:50.696 --> 00:20:52.742 mutations, arm level deletions,

NOTE Confidence: 0.831744103076923

00:20:52.742 --> 00:20:54.478 translocation and so forth.

NOTE Confidence: 0.831744103076923

00:20:54.480 --> 00:20:57.560 And you can imagine such a spectrum

NOTE Confidence: 0.831744103076923

00:20:57.560 --> 00:21:00.224 of alterations can be picked up

NOTE Confidence: 0.831744103076923

00:21:00.224 --> 00:21:03.360 mainly by NGS and not by other

NOTE Confidence: 0.864929959545455

00:21:03.360 --> 00:21:04.728 low resolution studies.

NOTE Confidence: 0.864929959545455

00:21:04.728 --> 00:21:08.568 So few years ago we we looked specifically

NOTE Confidence: 0.864929959545455

00:21:08.568 --> 00:21:11.922 at the spectrum of mutations alterations

NOTE Confidence: 0.864929959545455

00:21:11.922 --> 00:21:15.240 in smart P1 deficient sarcoma.

NOTE Confidence: 0.864929959545455

00:21:15.240 --> 00:21:17.039 As it is, as you probably know,

NOTE Confidence: 0.864929959545455

00:21:17.040 --> 00:21:19.305 it's a growing family of

NOTE Confidence: 0.864929959545455

00:21:19.305 --> 00:21:21.117 bonus of tissue tumors.

NOTE Confidence: 0.864929959545455

00:21:21.120 --> 00:21:23.360 And our main question was,

NOTE Confidence: 0.864929959545455

00:21:23.360 --> 00:21:28.376 can can we tell if the type of genetic

NOTE Confidence: 0.864929959545455

00:21:28.376 --> 00:21:31.399 alteration may correlate with Histology,

NOTE Confidence: 0.864929959545455

00:21:31.400 --> 00:21:37.072 with the histotype So included 78 such

NOTE Confidence: 0.864929959545455

00:21:37.072 --> 00:21:40.288 cases including epithelial sarcoma,

NOTE Confidence: 0.864929959545455

00:21:40.288 --> 00:21:42.892 rhabdoid tumors, epithelial and

NOTE Confidence: 0.864929959545455

00:21:42.892 --> 00:21:44.996 PNSD pro differentiated cordoma,

NOTE Confidence: 0.864929959545455

00:21:45.000 --> 00:21:48.800 all of them being I and I-1 deficient.

NOTE Confidence: 0.864929959545455

00:21:48.800 --> 00:21:51.386 And we studied them all with

NOTE Confidence: 0.864929959545455

00:21:51.386 --> 00:21:53.720 NGS as well as FISH.

NOTE Confidence: 0.864929959545455

00:21:53.720 --> 00:21:55.300 So the short answer to

NOTE Confidence: 0.864929959545455

00:21:55.300 --> 00:21:56.880 our question it was no,

NOTE Confidence: 0.864929959545455

00:21:56.880 --> 00:22:00.192 there was no correlation between alter

NOTE Confidence: 0.864929959545455

00:22:00.192 --> 00:22:02.400 genetic alteration and Histology.

NOTE Confidence: 0.864929959545455

00:22:02.400 --> 00:22:05.110 Most Histology showed large homozygous

NOTE Confidence: 0.864929959545455

00:22:05.110 --> 00:22:08.666 deletion of SMART B1 and about

NOTE Confidence: 0.864929959545455

00:22:08.666 --> 00:22:11.438 1/3 showed introgenic alterations.

NOTE Confidence: 0.864929959545455

00:22:11.440 --> 00:22:12.452 So I'm trying to,

NOTE Confidence: 0.864929959545455

00:22:12.452 --> 00:22:12.958 you know,

NOTE Confidence: 0.864929959545455

00:22:12.960 --> 00:22:16.025 hear that obviously would never

NOTE Confidence: 0.864929959545455

00:22:16.025 --> 00:22:19.400 be picked up by FISH assays.

NOTE Confidence: 0.864929959545455

00:22:19.400 --> 00:22:21.776 We then wanted to look more

NOTE Confidence: 0.864929959545455

00:22:21.776 --> 00:22:24.566 into this and and see if the

NOTE Confidence: 0.864929959545455

00:22:24.566 --> 00:22:27.156 extent of the deletion at 22 Q,

NOTE Confidence: 0.864929959545455

00:22:27.160 --> 00:22:30.654 the locus of I91 may correlate

NOTE Confidence: 0.864929959545455

00:22:30.654 --> 00:22:31.468 with histotype.

NOTE Confidence: 0.864929959545455

00:22:31.468 --> 00:22:33.503 And although there was no

NOTE Confidence: 0.864929959545455

00:22:33.503 --> 00:22:35.118 black and white answer,

NOTE Confidence: 0.864929959545455

00:22:35.120 --> 00:22:37.825 it became clear that some

NOTE Confidence: 0.864929959545455

00:22:37.825 --> 00:22:39.448 histologies like epithelial

NOTE Confidence: 0.864929959545455

00:22:39.448 --> 00:22:41.913 sarcomas have smaller deletions

NOTE Confidence: 0.864929959545455

00:22:41.913 --> 00:22:44.564 mostly centered on SMART B1,

NOTE Confidence: 0.864929959545455

00:22:44.564 --> 00:22:47.069 while tumors like a poor

NOTE Confidence: 0.864929959545455

00:22:47.069 --> 00:22:49.211 differentiated cordoma here in

NOTE Confidence: 0.864929959545455

00:22:49.211 --> 00:22:51.279 yellow have larger deletions

NOTE Confidence: 0.864929959545455

00:22:51.280 --> 00:22:53.030 showing code deletions of other

NOTE Confidence: 0.864929959545455

00:22:53.030 --> 00:22:55.440 gene on both sides of SMART V1.

NOTE Confidence: 0.828263944

00:22:57.880 --> 00:23:01.516 OK, moving on to a different example

NOTE Confidence: 0.828263944

00:23:01.516 --> 00:23:05.824 to show the NGS increase sensitivity

NOTE Confidence: 0.828263944

00:23:05.824 --> 00:23:09.839 detection in a certain translocation

NOTE Confidence: 0.828263944

00:23:09.840 --> 00:23:11.730 and the there are two examples

NOTE Confidence: 0.828263944

00:23:11.730 --> 00:23:14.318 here that I would I would like to

NOTE Confidence: 0.828263944

00:23:14.318 --> 00:23:16.208 share with you the unbalanced or

NOTE Confidence: 0.828263944

00:23:16.277 --> 00:23:19.277 cryptic translocation as well as

NOTE Confidence: 0.828263944

00:23:19.277 --> 00:23:20.477 intrachromosomal translocation.

NOTE Confidence: 0.828263944

00:23:20.480 --> 00:23:23.343 And by far the best example of

NOTE Confidence: 0.828263944

00:23:23.343 --> 00:23:25.387 cryptic translocation is the EWS

NOTE Confidence: 0.828263944

00:23:25.387 --> 00:23:27.984 Org fusion which is the second most

NOTE Confidence: 0.828263944

00:23:27.984 --> 00:23:30.518 common alteration in Ewing sarcoma.

NOTE Confidence: 0.828263944

00:23:30.520 --> 00:23:33.537 And the reason that this results in

NOTE Confidence: 0.828263944

00:23:33.537 --> 00:23:35.921 a cryptic alteration is because EWS

NOTE Confidence: 0.828263944

00:23:35.921 --> 00:23:38.424 and Org show opposite directions

NOTE Confidence: 0.828263944

00:23:38.424 --> 00:23:39.640 of transcription.

NOTE Confidence: 0.828263944

00:23:39.640 --> 00:23:42.506 So in order to form a functional fusion,

NOTE Confidence: 0.828263944

00:23:42.506 --> 00:23:44.638 they needs to invert.

NOTE Confidence: 0.828263944

00:23:44.640 --> 00:23:45.920 And in order to invert,

NOTE Confidence: 0.828263944

00:23:45.920 --> 00:23:50.000 they usually lose genetic material that

NOTE Confidence: 0.828263944

00:23:50.000 --> 00:23:53.680 cannot then be picked up by fish resolution.

NOTE Confidence: 0.828263944

00:23:53.680 --> 00:23:55.728 So the idea here is that if you

NOTE Confidence: 0.828263944

00:23:55.728 --> 00:23:58.196 have a case that looks like Ewings,

NOTE Confidence: 0.828263944

00:23:58.200 --> 00:24:00.760 stained like Ewings and EWS,

NOTE Confidence: 0.828263944

00:24:00.760 --> 00:24:01.825 fish is negative,

NOTE Confidence: 0.828263944

00:24:01.825 --> 00:24:03.600 which actually can be negative

NOTE Confidence: 0.828263944

00:24:03.600 --> 00:24:06.480 in 50% of these cases, right?

NOTE Confidence: 0.828263944

00:24:06.480 --> 00:24:08.624 The next step would be for you to

NOTE Confidence: 0.828263944

00:24:08.624 --> 00:24:14.092 do the Archer and GS panel talking

NOTE Confidence: 0.828263944

00:24:14.092 --> 00:24:16.408 about intracromosomal fusions

NOTE Confidence: 0.828263944

00:24:16.408 --> 00:24:21.040 that also can be not can.

NOTE Confidence: 0.828263944

00:24:21.040 --> 00:24:23.330 Fish cannot be reliable for

NOTE Confidence: 0.828263944

00:24:23.330 --> 00:24:26.115 detection and here one very good

NOTE Confidence: 0.828263944

00:24:26.115 --> 00:24:28.957 example are the N track 1 fusions.

NOTE Confidence: 0.828263944

00:24:28.960 --> 00:24:31.600 Most of these fusions are intracromosomal,

NOTE Confidence: 0.828263944

00:24:31.600 --> 00:24:35.795 either deletion such as INTRAC 1

NOTE Confidence: 0.828263944

00:24:35.795 --> 00:24:38.918 LMNA which is by far the most common,

NOTE Confidence: 0.828263944

00:24:38.920 --> 00:24:41.032 as well as inversions,

NOTE Confidence: 0.828263944

00:24:41.032 --> 00:24:43.672 either TPM three or TPR.

NOTE Confidence: 0.828263944

00:24:43.680 --> 00:24:44.840 Here on the left side,

NOTE Confidence: 0.828263944

00:24:44.840 --> 00:24:47.666 the diagram shows one of these

NOTE Confidence: 0.828263944

00:24:47.666 --> 00:24:50.113 inversions of these two genes

NOTE Confidence: 0.828263944

00:24:50.113 --> 00:24:53.800 that are truly nearby on one Q.

NOTE Confidence: 0.828263944

00:24:53.800 --> 00:24:55.600 So once again,

NOTE Confidence: 0.828263944

00:24:55.600 --> 00:24:58.155 in order to have a functional fusion,

NOTE Confidence: 0.828263944

00:24:58.160 --> 00:25:00.986 you have to have inversion and

NOTE Confidence: 0.828263944

00:25:00.986 --> 00:25:03.959 that cannot be picked up by fish.

NOTE Confidence: 0.828263944

00:25:03.960 --> 00:25:06.770 Just briefly mentioning the anthrax

NOTE Confidence: 0.828263944

00:25:06.770 --> 00:25:09.018 fusion positive spindle cell

NOTE Confidence: 0.828263944

00:25:09.018 --> 00:25:12.292 tumor is a relatively new entity

NOTE Confidence: 0.828263944

00:25:12.292 --> 00:25:14.396 emerging in AWHO classification.

NOTE Confidence: 0.828263944

00:25:14.400 --> 00:25:17.255 It's composed of these monomorphic

NOTE Confidence: 0.828263944

00:25:17.255 --> 00:25:19.539 spindle cells or patternless

NOTE Confidence: 0.828263944

00:25:19.539 --> 00:25:21.608 pattern and very characteristic.

NOTE Confidence: 0.828263944

00:25:21.608 --> 00:25:25.535 There are these stromal collagen bands

NOTE Confidence: 0.828263944

00:25:25.535 --> 00:25:30.056 and very vascular rings which are,

NOTE Confidence: 0.828263944

00:25:30.056 --> 00:25:32.480 you know, highly,

NOTE Confidence: 0.828263944

00:25:32.480 --> 00:25:35.080 highly suspicious of this entity.

NOTE Confidence: 0.828263944

00:25:35.080 --> 00:25:38.237 And another clue to the diagnosis is

NOTE Confidence: 0.828263944

00:25:38.237 --> 00:25:42.320 the Co expression of S100 and CD34.

NOTE Confidence: 0.828263944

00:25:42.320 --> 00:25:44.680 Pan and track is helpful.

NOTE Confidence: 0.828263944

00:25:44.680 --> 00:25:46.260 Of course, it's sensitive,

NOTE Confidence: 0.828263944

00:25:46.260 --> 00:25:48.235 but far from being specific.

NOTE Confidence: 0.828263944

00:25:48.240 --> 00:25:53.352 So this diagnosis has a very

NOTE Confidence: 0.828263944

00:25:53.352 --> 00:25:55.560 important impact on therapy.

NOTE Confidence: 0.828263944

00:25:55.560 --> 00:25:58.211 So in our opinion that when

NOTE Confidence: 0.828263944

00:25:58.211 --> 00:25:59.477 you have a case like this,

NOTE Confidence: 0.828263944

00:25:59.480 --> 00:26:02.636 a molecular confirmation is truly required.

NOTE Confidence: 0.951922711666667

00:26:04.680 --> 00:26:07.560 OK. And the last example here,

NOTE Confidence: 0.951922711666667

00:26:07.560 --> 00:26:10.680 the increased sensitivity in alterations,

NOTE Confidence: 0.951922711666667

00:26:10.680 --> 00:26:12.240 in unusual gene alterations.

NOTE Confidence: 0.951922711666667

00:26:12.240 --> 00:26:15.669 And here I thought a good example maybe

NOTE Confidence: 0.951922711666667

00:26:15.669 --> 00:26:18.199 B core internal tandem duplication.

NOTE Confidence: 0.951922711666667

00:26:18.200 --> 00:26:20.594 So what are what is the B core ITD?

NOTE Confidence: 0.951922711666667

00:26:20.600 --> 00:26:26.640 Are these Reds small strips of

NOTE Confidence: 0.951922711666667

00:26:26.640 --> 00:26:30.880 of DNA illustrated here in red.

NOTE Confidence: 0.951922711666667

00:26:30.880 --> 00:26:34.010 They're duplicated at the last at

NOTE Confidence: 0.951922711666667

00:26:34.010 --> 00:26:37.720 the portion of elastic B core exon,

NOTE Confidence: 0.951922711666667

00:26:37.720 --> 00:26:42.676 which somehow up regulate B core expression.

NOTE Confidence: 0.951922711666667

00:26:42.680 --> 00:26:47.198 B core ITD are the driver of about 40%

NOTE Confidence: 0.951922711666667

00:26:47.200 --> 00:26:49.636 of round cells sarcomas in infants.

NOTE Confidence: 0.951922711666667

00:26:49.640 --> 00:26:53.696 So this is very important to to remember

NOTE Confidence: 0.951922711666667

00:26:53.696 --> 00:26:57.928 as well as most tumors of the primitive

NOTE Confidence: 0.951922711666667

00:26:57.928 --> 00:27:01.480 mixed with mesenchymal tumor of infancy.

NOTE Confidence: 0.951922711666667

00:27:01.480 --> 00:27:04.364 However, the B core ITD have later

NOTE Confidence: 0.951922711666667

00:27:04.364 --> 00:27:07.265 on show to you know to be present

NOTE Confidence: 0.951922711666667

00:27:07.265 --> 00:27:08.597 in other undifferentiated sarcomas.

NOTE Confidence: 0.951922711666667

00:27:08.600 --> 00:27:11.506 It's something that you should be familiar

NOTE Confidence: 0.951922711666667

00:27:11.506 --> 00:27:14.957 and aware of regardless of your specialty.

NOTE Confidence: 0.951922711666667

00:27:14.960 --> 00:27:18.502 So these are pretty much in 90% of

NOTE Confidence: 0.951922711666667

00:27:18.502 --> 00:27:20.554 clear cells sarcoma of the kidney,

NOTE Confidence: 0.951922711666667

00:27:20.560 --> 00:27:24.808 the CNS peanuts with B core ITD as well

NOTE Confidence: 0.951922711666667

00:27:24.808 --> 00:27:26.960 as and these are not pediatric cases,

NOTE Confidence: 0.951922711666667

00:27:26.960 --> 00:27:30.400 some high grade endometrial stromosarcoma

NOTE Confidence: 0.951922711666667

00:27:30.400 --> 00:27:34.795 as we have noted some shared histologic

NOTE Confidence: 0.951922711666667

00:27:34.795 --> 00:27:37.520 features among all these members.

NOTE Confidence: 0.951922711666667

00:27:37.520 --> 00:27:40.656 They are not perfect but clearly some

NOTE Confidence: 0.951922711666667

00:27:40.656 --> 00:27:43.052 shared features as well as diffuse

NOTE Confidence: 0.951922711666667

00:27:43.052 --> 00:27:46.348 up regulation of B core both at RNA

NOTE Confidence: 0.951922711666667

00:27:46.348 --> 00:27:48.958 level as well as protein level,

NOTE Confidence: 0.951922711666667

00:27:48.960 --> 00:27:52.520 which can be used again for diagnosis.

NOTE Confidence: 0.951922711666667

00:27:52.520 --> 00:27:54.440 However, as we saw,

NOTE Confidence: 0.951922711666667

00:27:54.440 --> 00:27:57.080 SFTS can show as high level.

NOTE Confidence: 0.951922711666667

00:27:57.080 --> 00:28:00.696 So for this diagnosis,

NOTE Confidence: 0.951922711666667

00:28:00.696 --> 00:28:04.800 NGS again is the gold standard.

NOTE Confidence: 0.951922711666667

00:28:04.800 --> 00:28:08.032 Moving on to the second big topic to

NOTE Confidence: 0.951922711666667

00:28:08.032 --> 00:28:11.840 discuss the impact of NGS on survival.

NOTE Confidence: 0.951922711666667

00:28:11.840 --> 00:28:15.088 So here we'll talk about the driver

NOTE Confidence: 0.951922711666667

00:28:15.088 --> 00:28:17.358 gene alteration impact as well as

NOTE Confidence: 0.951922711666667

00:28:17.360 --> 00:28:20.930 the global landscape beyond the

NOTE Confidence: 0.951922711666667

00:28:20.930 --> 00:28:22.358 driver alteration.

NOTE Confidence: 0.951922711666667

00:28:22.360 --> 00:28:25.678 So for the driver gene alteration,

NOTE Confidence: 0.951922711666667

00:28:25.680 --> 00:28:27.840 I picked two different

NOTE Confidence: 0.951922711666667

00:28:27.840 --> 00:28:30.000 example in Rhabdomyo sarcoma,

NOTE Confidence: 0.951922711666667

00:28:30.000 --> 00:28:33.479 MYO D1 mutation and Dicer 1 alteration.

NOTE Confidence: 0.951922711666667

00:28:33.480 --> 00:28:36.168 And then we'll give some examples

NOTE Confidence: 0.951922711666667

00:28:36.168 --> 00:28:38.560 of fusions in round cells.

NOTE Confidence: 0.951922711666667

00:28:38.560 --> 00:28:41.596 So let's start with MYO D1.

NOTE Confidence: 0.951922711666667

00:28:41.600 --> 00:28:44.491 You may know that MYO D1 mutation

NOTE Confidence: 0.951922711666667

00:28:44.491 --> 00:28:47.024 defines a very specific and

NOTE Confidence: 0.951922711666667

00:28:47.024 --> 00:28:50.034 aggressive type of Rhabdoma sarcoma,

NOTE Confidence: 0.951922711666667

00:28:50.040 --> 00:28:52.520 spindle and sclerosing Rhabdoma sarcoma,

NOTE Confidence: 0.951922711666667

00:28:52.520 --> 00:28:56.840 which is included now a standalone

NOTE Confidence: 0.951922711666667

00:28:56.840 --> 00:28:59.080 entity from embryoner Rhabdoma

NOTE Confidence: 0.951922711666667

00:28:59.080 --> 00:29:01.880 sarcoma and The Who classification.

NOTE Confidence: 0.951922711666667

00:29:01.880 --> 00:29:03.492 And why is that?

NOTE Confidence: 0.951922711666667

00:29:03.492 --> 00:29:05.507 Because it has distinct morphology

NOTE Confidence: 0.951922711666667

00:29:05.507 --> 00:29:08.324 can either be spindle or more common

NOTE Confidence: 0.951922711666667

00:29:08.324 --> 00:29:10.824 is composed of these uniform round

NOTE Confidence: 0.951922711666667

00:29:10.824 --> 00:29:13.656 to avoid cells that are separated

NOTE Confidence: 0.951922711666667

00:29:13.656 --> 00:29:16.239 by this sclerosing stroma.

NOTE Confidence: 0.951922711666667

00:29:16.240 --> 00:29:19.560 Also importantly, as I mentioned,

NOTE Confidence: 0.951922711666667

00:29:19.560 --> 00:29:22.598 they have a very aggressive outcome even

NOTE Confidence: 0.951922711666667

00:29:22.598 --> 00:29:25.279 worse than alveolar abdominal sarcoma.

NOTE Confidence: 0.951922711666667

00:29:25.280 --> 00:29:27.893 In our study they showed an 18%

NOTE Confidence: 0.951922711666667

00:29:27.893 --> 00:29:29.492 four year survival.

NOTE Confidence: 0.951922711666667

00:29:29.492 --> 00:29:32.157 They typically are occurring older

NOTE Confidence: 0.951922711666667

00:29:32.157 --> 00:29:35.400 children and young adults and more often

NOTE Confidence: 0.951922711666667

00:29:35.400 --> 00:29:41.559 in the head and neck and and and trunk.

NOTE Confidence: 0.951922711666667

00:29:41.560 --> 00:29:44.464 This is to be distinguished from

NOTE Confidence: 0.951922711666667

00:29:44.464 --> 00:29:46.883 another spindle cell Rhabdoma sarcoma

NOTE Confidence: 0.951922711666667

00:29:46.883 --> 00:29:50.075 that occurs at birth or or or infants.

NOTE Confidence: 0.951922711666667

00:29:50.080 --> 00:29:53.505 Yeah that have this vesicular

NOTE Confidence: 0.951922711666667

00:29:53.505 --> 00:29:55.560 herring bone appearance.

NOTE Confidence: 0.951922711666667

00:29:55.560 --> 00:29:58.072 These particular Rhabdoma sarcomas

NOTE Confidence: 0.951922711666667

00:29:58.072 --> 00:30:01.212 are characterized by recurrent fusions

NOTE Confidence: 0.951922711666667

00:30:01.212 --> 00:30:05.560 either involving site two or NCOA 2.

NOTE Confidence: 0.951922711666667

00:30:05.560 --> 00:30:06.109 Importantly,

NOTE Confidence: 0.951922711666667

00:30:06.109 --> 00:30:09.403 these tumors have a very favorable

NOTE Confidence: 0.951922711666667

00:30:09.403 --> 00:30:12.200 outcome with almost no metastatic

NOTE Confidence: 0.951922711666667

00:30:12.200 --> 00:30:15.386 potential and therefore they behave more

NOTE Confidence: 0.951922711666667

00:30:15.386 --> 00:30:19.679 in keeping with an infantile fibrosarcoma.

NOTE Confidence: 0.951922711666667

00:30:19.680 --> 00:30:23.556 Moving on to to touch base

NOTE Confidence: 0.8668509725

00:30:23.560 --> 00:30:26.680 a little bit on the Dicer 1 alterations.

NOTE Confidence: 0.8668509725

00:30:26.680 --> 00:30:32.080 It's a, you know new expanding fields.

NOTE Confidence: 0.8668509725

00:30:32.080 --> 00:30:34.462 We recently did this study that

NOTE Confidence: 0.8668509725

00:30:34.462 --> 00:30:37.185 we presented at USE CAP this year

NOTE Confidence: 0.8668509725

00:30:37.185 --> 00:30:41.696 comparing a a molecularly a group of

NOTE Confidence: 0.8668509725

00:30:41.696 --> 00:30:45.064 botuloids type for Rhabdomyo sarcoma

NOTE Confidence: 0.8668509725

00:30:45.064 --> 00:30:48.194 with a conventional Rhabdomyo sarcoma.

NOTE Confidence: 0.8668509725

00:30:48.200 --> 00:30:52.136 And the short story is that we observed

NOTE Confidence: 0.8668509725

00:30:52.136 --> 00:30:55.282 Dicer 1 alterations either somatic

NOTE Confidence: 0.8668509725

00:30:55.282 --> 00:30:59.398 or germline only in the boteroid

NOTE Confidence: 0.8668509725

00:30:59.400 --> 00:31:03.180 type Rhabdomyo sarcoma and that was

NOTE Confidence: 0.8668509725

00:31:03.180 --> 00:31:05.684 associated with a very favorable outcome

NOTE Confidence: 0.8668509725

00:31:05.684 --> 00:31:08.199 as you can see here the red line.

NOTE Confidence: 0.91703232

00:31:10.280 --> 00:31:14.480 OK, moving on to discuss few

NOTE Confidence: 0.91703232

00:31:14.480 --> 00:31:17.800 fusions that truly have an impact

NOTE Confidence: 0.91703232

00:31:17.800 --> 00:31:20.329 on survival and therefore a,

NOTE Confidence: 0.91703232

00:31:20.329 --> 00:31:23.983 you know, detailed NGS or Archer

NOTE Confidence: 0.91703232

00:31:23.983 --> 00:31:26.560 character characterization is needed.

NOTE Confidence: 0.91703232

00:31:26.560 --> 00:31:30.571 And of course we will start with

NOTE Confidence: 0.91703232

00:31:30.571 --> 00:31:33.896 chick docs probably all being aware

NOTE Confidence: 0.91703232

00:31:33.896 --> 00:31:37.768 of this small borons of sarcoma that

NOTE Confidence: 0.91703232

00:31:37.768 --> 00:31:41.254 is characterized by a fusion that

NOTE Confidence: 0.91703232

00:31:41.254 --> 00:31:43.889 results in switching the function

NOTE Confidence: 0.91703232

00:31:43.889 --> 00:31:47.077 of CHICK from a repressor to an

NOTE Confidence: 0.91703232

00:31:47.080 --> 00:31:50.664 oncogenic activator of transcription

NOTE Confidence: 0.91703232

00:31:50.664 --> 00:31:54.153 especially up regulating ATV1ATV4.

NOTE Confidence: 0.91703232

00:31:54.153 --> 00:31:57.512 And because of this function ETV 4 as

NOTE Confidence: 0.91703232

00:31:57.512 --> 00:31:59.832 shown here is by immunostochemistry

NOTE Confidence: 0.91703232

00:31:59.832 --> 00:32:04.256 is one of the most reliable ancillary

NOTE Confidence: 0.91703232

00:32:04.256 --> 00:32:07.270 immuno marker in the diagnosis

NOTE Confidence: 0.91703232

00:32:07.270 --> 00:32:09.120 of chick ducks for sarcomas.

NOTE Confidence: 0.91703232

00:32:09.120 --> 00:32:13.400 These tumors occurs in the deep soft tissues.

NOTE Confidence: 0.91703232

00:32:13.400 --> 00:32:15.997 They are large heterogeneous as shown here.

NOTE Confidence: 0.91703232

00:32:16.000 --> 00:32:18.960 They occur in young adults.

NOTE Confidence: 0.91703232

00:32:18.960 --> 00:32:24.040 They rarely are seen in children or bone.

NOTE Confidence: 0.91703232

00:32:24.040 --> 00:32:25.740 And morphologically they look

NOTE Confidence: 0.91703232

00:32:25.740 --> 00:32:27.440 like small blue round.

NOTE Confidence: 0.91703232

00:32:27.440 --> 00:32:30.635 So tumor at a very quick low power view.

NOTE Confidence: 0.91703232

00:32:30.640 --> 00:32:33.195 However at the higher power they have

NOTE Confidence: 0.91703232

00:32:33.200 --> 00:32:36.609 you know more cytoplasm and we look

NOTE Confidence: 0.91703232

00:32:36.609 --> 00:32:39.118 epithelioidal focus spindling and so forth.

NOTE Confidence: 0.91703232

00:32:39.120 --> 00:32:39.735 Importantly,

NOTE Confidence: 0.91703232

00:32:39.735 --> 00:32:42.810 the diagnosis is required because

NOTE Confidence: 0.91703232

00:32:42.810 --> 00:32:45.850 of the very poor outcome and you

NOTE Confidence: 0.91703232

00:32:45.850 --> 00:32:48.623 can see here in this couple mark

NOTE Confidence: 0.91703232

00:32:48.623 --> 00:32:51.269 comparison with the E wing sarcoma

NOTE Confidence: 0.91703232

00:32:51.269 --> 00:32:54.118 which are you're matched for stage

NOTE Confidence: 0.91703232

00:32:54.120 --> 00:32:56.952 and you can see that the chick docs

NOTE Confidence: 0.91703232

00:32:56.952 --> 00:33:00.125 four has a five year survival of 43%

NOTE Confidence: 0.91703232

00:33:00.125 --> 00:33:03.800 compared to 77% the E wing sarcoma.

NOTE Confidence: 0.91703232

00:33:03.800 --> 00:33:05.384 And more than that,

NOTE Confidence: 0.91703232

00:33:05.384 --> 00:33:08.254 why the clinicians need to know about

NOTE Confidence: 0.91703232

00:33:08.254 --> 00:33:11.080 this is because they do not respond

NOTE Confidence: 0.91703232

00:33:11.080 --> 00:33:13.080 well to even sarcoma regimens.

NOTE Confidence: 0.91703232

00:33:13.080 --> 00:33:15.596 And so far that was, you know,

NOTE Confidence: 0.91703232

00:33:15.596 --> 00:33:17.744 the only type of therapy that

NOTE Confidence: 0.91703232

00:33:17.744 --> 00:33:19.877 was used as the first line.

NOTE Confidence: 0.91703232

00:33:19.880 --> 00:33:23.396 However, nowadays knowing that these are,

NOTE Confidence: 0.91703232

00:33:23.400 --> 00:33:25.276 you know, quite resistant,

NOTE Confidence: 0.91703232

00:33:25.276 --> 00:33:28.646 they may be approached with more adult

NOTE Confidence: 0.91703232

00:33:28.646 --> 00:33:31.320 type sarcoma chemotherapy such as AIM.

NOTE Confidence: 0.860113052142857

00:33:34.440 --> 00:33:37.380 One caveat here that we've noticed

NOTE Confidence: 0.860113052142857

00:33:37.380 --> 00:33:40.991 is that the chick docks for sarcomas

NOTE Confidence: 0.860113052142857

00:33:40.991 --> 00:33:44.617 have a high risk of negative results

NOTE Confidence: 0.860113052142857

00:33:44.717 --> 00:33:47.637 both by fish as well as by NGS.

NOTE Confidence: 0.860113052142857

00:33:47.640 --> 00:33:50.559 And that is due to the very

NOTE Confidence: 0.860113052142857

00:33:50.559 --> 00:33:52.719 repetitive sequences of docks for.

NOTE Confidence: 0.860113052142857

00:33:52.720 --> 00:33:54.164 So when that happens,

NOTE Confidence: 0.860113052142857

00:33:54.164 --> 00:33:57.198 if our suspicion is a chick docks for

NOTE Confidence: 0.860113052142857

00:33:57.198 --> 00:33:59.580 and every other Archer is negative

NOTE Confidence: 0.860113052142857

00:33:59.580 --> 00:34:02.517 for other fusions is to look manually,

NOTE Confidence: 0.860113052142857

00:34:02.520 --> 00:34:05.481 you know to ask the molecular lab to look

NOTE Confidence: 0.860113052142857

00:34:05.481 --> 00:34:08.120 manually at the levels of ETV 1/4 and five.

NOTE Confidence: 0.860113052142857

00:34:08.120 --> 00:34:10.360 And you can see here there are

NOTE Confidence: 0.860113052142857

00:34:10.360 --> 00:34:12.621 very high levels of over expression

NOTE Confidence: 0.860113052142857

00:34:12.621 --> 00:34:14.372 compared to other sarcomas,

NOTE Confidence: 0.860113052142857

00:34:14.372 --> 00:34:16.236 which confirms the diagnosis

NOTE Confidence: 0.860113052142857

00:34:16.236 --> 00:34:19.040 of a chick docs for fusion.

NOTE Confidence: 0.860113052142857

00:34:19.040 --> 00:34:22.036 This has been shown by many groups

NOTE Confidence: 0.860113052142857

00:34:22.036 --> 00:34:24.748 including our showing that by RNA sequencing,

NOTE Confidence: 0.860113052142857

00:34:24.748 --> 00:34:28.304 the chick docs for sarcomas have their

NOTE Confidence: 0.860113052142857

00:34:28.304 --> 00:34:31.076 own cluster on the group separate

NOTE Confidence: 0.860113052142857

00:34:31.076 --> 00:34:34.240 from all the other round cell tumors.

NOTE Confidence: 0.860113052142857

00:34:34.240 --> 00:34:37.354 So this chip docs 4 makes a very good

NOTE Confidence: 0.860113052142857

00:34:37.360 --> 00:34:41.320 contrast with the B core CCNB 3 sarcomas.

NOTE Confidence: 0.860113052142857

00:34:41.320 --> 00:34:45.160 B core CCNB 3 is a very peculiar

NOTE Confidence: 0.860113052142857

00:34:45.160 --> 00:34:48.440 translocation which is an

NOTE Confidence: 0.860113052142857

00:34:48.440 --> 00:34:51.720 intrachromosomal X paracentric inversion.

NOTE Confidence: 0.860113052142857

00:34:51.720 --> 00:34:54.756 Again cannot be detected by FISH.

NOTE Confidence: 0.860113052142857

00:34:54.760 --> 00:34:59.158 It requires Archer for the diagnosis.

NOTE Confidence: 0.860113052142857

00:34:59.160 --> 00:35:02.648 Clinically the demographics are

NOTE Confidence: 0.860113052142857

00:35:02.648 --> 00:35:05.280 more closer to E wing sarcoma and

NOTE Confidence: 0.860113052142857

00:35:05.351 --> 00:35:07.436 very different than CHIC docs.

NOTE Confidence: 0.860113052142857

00:35:07.440 --> 00:35:10.674 They occur in bone mostly in in

NOTE Confidence: 0.860113052142857

00:35:10.674 --> 00:35:12.570 children and morphologically they

NOTE Confidence: 0.860113052142857

00:35:12.570 --> 00:35:15.538 have a hybrid morphology between an E

NOTE Confidence: 0.860113052142857

00:35:15.538 --> 00:35:18.238 wing sarcoma and a synovial sarcoma.

NOTE Confidence: 0.860113052142857

00:35:18.240 --> 00:35:21.066 They have both round and spindle

NOTE Confidence: 0.860113052142857

00:35:21.066 --> 00:35:23.989 cell components and of course the

NOTE Confidence: 0.860113052142857

00:35:23.989 --> 00:35:26.992 important stain here is the B core

NOTE Confidence: 0.860113052142857

00:35:26.992 --> 00:35:29.478 which shows 4 plus positivity.

NOTE Confidence: 0.860113052142857

00:35:29.480 --> 00:35:30.051 Clinically.

NOTE Confidence: 0.860113052142857

00:35:30.051 --> 00:35:30.622 Again,

NOTE Confidence: 0.860113052142857

00:35:30.622 --> 00:35:33.894 very important since B core does

NOTE Confidence: 0.860113052142857

00:35:33.894 --> 00:35:36.378 much better than chick ducks four

NOTE Confidence: 0.860113052142857

00:35:36.378 --> 00:35:38.760 and pretty much similar outcome

NOTE Confidence: 0.860113052142857

00:35:38.760 --> 00:35:40.320 with synovial sarcoma.

NOTE Confidence: 0.947840863333333

00:35:43.360 --> 00:35:47.475 OK, so we looked at the impact of driver

NOTE Confidence: 0.947840863333333

00:35:47.475 --> 00:35:50.600 alterations either mutations or fusions.

NOTE Confidence: 0.947840863333333

00:35:50.600 --> 00:35:53.015 Now let's look at the impact and

NOTE Confidence: 0.947840863333333

00:35:53.015 --> 00:35:55.320 survival on like secondary events,

NOTE Confidence: 0.947840863333333

00:35:55.320 --> 00:35:58.250 right global landscape besides the

NOTE Confidence: 0.947840863333333

00:35:58.250 --> 00:36:01.024 driver and in translocation associates

NOTE Confidence: 0.947840863333333

00:36:01.024 --> 00:36:03.754 sarcoma secondary events are rare,

NOTE Confidence: 0.947840863333333

00:36:03.760 --> 00:36:05.220 but when they occur,

NOTE Confidence: 0.947840863333333

00:36:05.220 --> 00:36:07.410 they usually are associated very bad

NOTE Confidence: 0.947840863333333

00:36:07.482 --> 00:36:09.917 outcome and resistant to chemotherapy.

NOTE Confidence: 0.947840863333333

00:36:09.920 --> 00:36:12.272 So if we take the example

NOTE Confidence: 0.947840863333333

00:36:12.272 --> 00:36:13.840 of Ewing sarcoma here,

NOTE Confidence: 0.947840863333333

00:36:13.840 --> 00:36:16.440 the secondary events are usually

NOTE Confidence: 0.947840863333333

00:36:16.440 --> 00:36:19.040 alteration in tumor suppressor genes.

NOTE Confidence: 0.947840863333333

00:36:19.040 --> 00:36:23.675 As you can see P53 citican 2A stacks 2,

NOTE Confidence: 0.947840863333333

00:36:23.680 --> 00:36:26.040 about 8 to 10% each,

NOTE Confidence: 0.947840863333333

00:36:26.040 --> 00:36:27.753 usually mutually exclusive.

NOTE Confidence: 0.947840863333333

00:36:27.753 --> 00:36:31.285 But when these occur, as I said,

NOTE Confidence: 0.947840863333333

00:36:31.285 --> 00:36:33.360 the the evening sarcoma patients

NOTE Confidence: 0.947840863333333

00:36:33.360 --> 00:36:36.688 do very badly as a whole of

NOTE Confidence: 0.947840863333333

00:36:36.688 --> 00:36:38.194 translocation associates sarcoma.

NOTE Confidence: 0.947840863333333

00:36:38.200 --> 00:36:40.570 The secondary events most common

NOTE Confidence: 0.947840863333333

00:36:40.570 --> 00:36:43.988 are the P16P-15 deletion as well

NOTE Confidence: 0.947840863333333

00:36:43.988 --> 00:36:47.073 as a turret promoter alteration.

NOTE Confidence: 0.947840863333333

00:36:47.080 --> 00:36:48.948 So very recently we,

NOTE Confidence: 0.947840863333333

00:36:48.948 --> 00:36:51.283 we performed this study which

NOTE Confidence: 0.947840863333333

00:36:51.283 --> 00:36:53.774 where we included sarcomas that

NOTE Confidence: 0.947840863333333

00:36:53.774 --> 00:36:56.678 are defined by EWS Kreb fusions,

NOTE Confidence: 0.947840863333333

00:36:56.680 --> 00:36:59.840 right, ITF Kreb Kreb one.

NOTE Confidence: 0.947840863333333

00:36:59.840 --> 00:37:02.440 And we wanted to, to,

NOTE Confidence: 0.947840863333333

00:37:02.440 --> 00:37:06.514 to question to address if the secondary

NOTE Confidence: 0.947840863333333

00:37:06.514 --> 00:37:08.799 genetic events may be different

NOTE Confidence: 0.947840863333333

00:37:08.799 --> 00:37:10.234 in different histotypes, right?

NOTE Confidence: 0.947840863333333

00:37:10.234 --> 00:37:12.118 So here we have angiomatoid fibro,

NOTE Confidence: 0.947840863333333

00:37:12.120 --> 00:37:14.640 he's just cytoma clears as sarcoma,

NOTE Confidence: 0.947840863333333

00:37:14.640 --> 00:37:15.680 gastrointestinal creases,

NOTE Confidence: 0.947840863333333

00:37:15.680 --> 00:37:17.760 sarcoma and so forth.

NOTE Confidence: 0.947840863333333

00:37:17.760 --> 00:37:19.820 So although was not again

NOTE Confidence: 0.947840863333333

00:37:19.820 --> 00:37:21.880 a black and white picture,

NOTE Confidence: 0.947840863333333

00:37:21.880 --> 00:37:23.200 we noted that there are,

NOTE Confidence: 0.947840863333333

00:37:23.200 --> 00:37:24.072 you know,

NOTE Confidence: 0.947840863333333

00:37:24.072 --> 00:37:26.252 some alterations were called more

NOTE Confidence: 0.947840863333333

00:37:26.252 --> 00:37:28.863 common in certain histologies like AFH

NOTE Confidence: 0.947840863333333

00:37:28.863 --> 00:37:31.719 had more common CDKN to AB deletion,

NOTE Confidence: 0.947840863333333

00:37:31.720 --> 00:37:35.224 while all the tarts promoter mutations

NOTE Confidence: 0.947840863333333

00:37:35.224 --> 00:37:38.439 or card in clearances or coma.

NOTE Confidence: 0.947840863333333

00:37:38.440 --> 00:37:40.040 So then we wanted to,

NOTE Confidence: 0.947840863333333

00:37:40.040 --> 00:37:43.718 to see if these alterations also

NOTE Confidence: 0.947840863333333

00:37:43.720 --> 00:37:45.901 have an impact on survival, right?

NOTE Confidence: 0.947840863333333

00:37:45.901 --> 00:37:47.947 Because that's that's why we do

NOTE Confidence: 0.947840863333333

00:37:47.947 --> 00:37:50.193 NGS on these patients that we

NOTE Confidence: 0.947840863333333

00:37:50.193 --> 00:37:52.113 already know the fusion type.

NOTE Confidence: 0.947840863333333

00:37:52.120 --> 00:37:56.278 And the answer was truly clear cut.

NOTE Confidence: 0.947840863333333

00:37:56.280 --> 00:37:58.990 Here you have the AFHS

NOTE Confidence: 0.947840863333333

00:37:58.990 --> 00:38:00.074 angiomotor fibrohistocytoma.

NOTE Confidence: 0.947840863333333

00:38:00.080 --> 00:38:02.776 The only two patients that had CDKN 2

NOTE Confidence: 0.947840863333333

00:38:02.776 --> 00:38:05.557 AB were the ones that metastasized.

NOTE Confidence: 0.947840863333333

00:38:05.560 --> 00:38:08.073 And here you have the clears of

NOTE Confidence: 0.947840863333333

00:38:08.073 --> 00:38:10.784 sarcoma and you have the the patients

NOTE Confidence: 0.947840863333333

00:38:10.784 --> 00:38:13.118 in green that died of disease

NOTE Confidence: 0.947840863333333

00:38:13.202 --> 00:38:15.466 were highly enriched by cases

NOTE Confidence: 0.947840863333333

00:38:15.466 --> 00:38:17.996 that had secondary genetic events

NOTE Confidence: 0.9235372575

00:38:20.240 --> 00:38:23.100 moving away from translocation.

NOTE Confidence: 0.9235372575

00:38:23.100 --> 00:38:26.378 This is another textbook example

NOTE Confidence: 0.9235372575

00:38:26.378 --> 00:38:28.886 that I'm sure the pediatric folks

NOTE Confidence: 0.9235372575

00:38:28.886 --> 00:38:31.280 here are very familiar with.

NOTE Confidence: 0.9235372575

00:38:31.280 --> 00:38:35.900 And this is about the impact of P53

NOTE Confidence: 0.9235372575

00:38:35.900 --> 00:38:40.400 mutation in Embraer abdominal sarcoma,

NOTE Confidence: 0.9235372575

00:38:40.400 --> 00:38:43.076 which of course has clinical implication,

NOTE Confidence: 0.9235372575

00:38:43.080 --> 00:38:47.154 risk escalation, more chemo and so forth.

NOTE Confidence: 0.9235372575

00:38:47.160 --> 00:38:48.520 And of course different

NOTE Confidence: 0.9235372575

00:38:48.520 --> 00:38:50.560 survival as you can see here.

NOTE Confidence: 0.9235372575

00:38:50.560 --> 00:38:53.360 And you may, you may say, well,

NOTE Confidence: 0.9235372575

00:38:53.360 --> 00:38:55.620 the presence of anaplasia

NOTE Confidence: 0.9235372575

00:38:55.620 --> 00:38:57.315 on Histology correlates,

NOTE Confidence: 0.9235372575

00:38:57.320 --> 00:39:00.715 correlates with the mutation with a genotype.

NOTE Confidence: 0.9235372575

00:39:00.720 --> 00:39:02.598 And that's true for most parts.

NOTE Confidence: 0.9235372575

00:39:02.600 --> 00:39:04.464 However, we've seen discrepancy

NOTE Confidence: 0.9235372575

00:39:04.464 --> 00:39:07.260 cases that do not have anaplasia

NOTE Confidence: 0.9235372575

00:39:07.341 --> 00:39:09.760 and AP53 mutation and vice versa.

NOTE Confidence: 0.9235372575

00:39:09.760 --> 00:39:12.840 So I mean, at least at our institution,

NOTE Confidence: 0.9235372575

00:39:12.840 --> 00:39:17.440 we do NGS on all Enbrana abdominal sarcomas,

NOTE Confidence: 0.9235372575

00:39:17.440 --> 00:39:18.535 especially since sometimes

NOTE Confidence: 0.9235372575

00:39:18.535 --> 00:39:20.360 our sample is so small,

NOTE Confidence: 0.9235372575

00:39:20.360 --> 00:39:24.080 they may not catch the anaplasia.

NOTE Confidence: 0.9235372575

00:39:24.080 --> 00:39:26.156 OK, moving on to third topic,

NOTE Confidence: 0.9235372575

00:39:26.160 --> 00:39:28.918 the impact of NGS to targeted therapy.

NOTE Confidence: 0.9235372575

00:39:28.920 --> 00:39:30.920 This will be by brief.

NOTE Confidence: 0.9235372575

00:39:30.920 --> 00:39:34.475 I assembled here a list for you of highly

NOTE Confidence: 0.9235372575

00:39:34.475 --> 00:39:37.400 relevant examples for soft tissue field.

NOTE Confidence: 0.9235372575

00:39:37.400 --> 00:39:38.784 And of course, top,

NOTE Confidence: 0.9235372575

00:39:38.784 --> 00:39:42.320 top of the list are the mutations in KIT,

NOTE Confidence: 0.9235372575

00:39:42.320 --> 00:39:45.120 PDGFR alpha and B Raff in GIST.

NOTE Confidence: 0.9235372575

00:39:45.120 --> 00:39:46.372 I don't have to,

NOTE Confidence: 0.9235372575

00:39:46.372 --> 00:39:46.998 you know,

NOTE Confidence: 0.9235372575

00:39:47.000 --> 00:39:47.960 tell you much,

NOTE Confidence: 0.9235372575

00:39:47.960 --> 00:39:49.560 but based on these mutations,

NOTE Confidence: 0.9235372575

00:39:49.560 --> 00:39:52.880 we choose what type of thyroid

NOTE Confidence: 0.9235372575

00:39:52.880 --> 00:39:54.080 tyrosine kinase inhibitor

NOTE Confidence: 0.9235372575

00:39:54.080 --> 00:39:56.080 and based on this alteration,

NOTE Confidence: 0.9235372575

00:39:56.080 --> 00:40:00.192 we may decide if the patient is a

NOTE Confidence: 0.9235372575

00:40:00.192 --> 00:40:03.957 candidate for adjuvant therapy or not.

NOTE Confidence: 0.9235372575

00:40:03.960 --> 00:40:06.459 The second example are sarcomas that are

NOTE Confidence: 0.9235372575

00:40:06.459 --> 00:40:09.118 driven by MDM to CDK 4 amplification.

NOTE Confidence: 0.9235372575

00:40:09.120 --> 00:40:12.984 And here we care about this

NOTE Confidence: 0.9235372575

00:40:12.984 --> 00:40:16.150 because they are for a while

NOTE Confidence: 0.9235372575

00:40:16.150 --> 00:40:18.200 now CDK 4 inhibitors available

NOTE Confidence: 0.9235372575

00:40:18.200 --> 00:40:20.160 with relatively good responses,

NOTE Confidence: 0.9235372575

00:40:20.160 --> 00:40:22.758 at least in the D flypool.

NOTE Confidence: 0.9235372575

00:40:22.760 --> 00:40:24.972 The third example here,

NOTE Confidence: 0.9235372575

00:40:24.972 --> 00:40:28.290 I cannot stress enough how important

NOTE Confidence: 0.9235372575

00:40:28.383 --> 00:40:31.673 it is for us pathologists to recognize

NOTE Confidence: 0.9235372575

00:40:31.673 --> 00:40:35.480 in real life the kinase fusion tumors.

NOTE Confidence: 0.9235372575

00:40:35.480 --> 00:40:38.728 And that is of course because of

NOTE Confidence: 0.9235372575

00:40:38.728 --> 00:40:41.248 the dramatic responses that we have

NOTE Confidence: 0.9235372575

00:40:41.248 --> 00:40:43.479 seen with kinase inhibitors and

NOTE Confidence: 0.9235372575

00:40:43.479 --> 00:40:46.930 depending on what type of kinase or

NOTE Confidence: 0.9235372575

00:40:47.021 --> 00:40:48.802 different tyrosine kinase inhibitors.

NOTE Confidence: 0.9235372575

00:40:48.802 --> 00:40:50.806 So for INTRAC of course is

NOTE Confidence: 0.9235372575

00:40:50.806 --> 00:40:51.840 lateral tracting it,

NOTE Confidence: 0.9235372575

00:40:51.840 --> 00:40:55.248 but now they have a second and third

NOTE Confidence: 0.9235372575

00:40:55.248 --> 00:40:57.720 generation of INTRAC inhibitors.

NOTE Confidence: 0.9235372575

00:40:57.720 --> 00:41:00.352 The next point here are the the

NOTE Confidence: 0.9235372575

00:41:00.352 --> 00:41:03.320 Smart B1 loss of function sarcomas,

NOTE Confidence: 0.9235372575

00:41:03.320 --> 00:41:05.475 again very important to diagnose

NOTE Confidence: 0.9235372575

00:41:05.475 --> 00:41:07.630 them correctly since now we

NOTE Confidence: 0.9235372575

00:41:07.707 --> 00:41:09.717 have a targeted therapy for,

NOTE Confidence: 0.9235372575

00:41:09.720 --> 00:41:11.280 for this disease,

NOTE Confidence: 0.9235372575

00:41:11.280 --> 00:41:14.592 the easy H2 inhibitor called tazemetostat,

NOTE Confidence: 0.9235372575

00:41:14.592 --> 00:41:18.052 which have shown decent responses,

NOTE Confidence: 0.9235372575

00:41:18.052 --> 00:41:21.276 especially in epithelial sarcoma.

NOTE Confidence: 0.9235372575

00:41:21.280 --> 00:41:23.810 The differentiating Melanoma I guess

NOTE Confidence: 0.9235372575

00:41:23.810 --> 00:41:26.265 with the UV signature completely

NOTE Confidence: 0.9235372575

00:41:26.265 --> 00:41:28.815 different therapy than sarcomas with the

NOTE Confidence: 0.9235372575

00:41:28.815 --> 00:41:30.680 immune checkpoint inhibitors with very,

NOTE Confidence: 0.9235372575

00:41:30.680 --> 00:41:34.199 very good responses.

NOTE Confidence: 0.9235372575

00:41:34.200 --> 00:41:35.298 And lastly,

NOTE Confidence: 0.9235372575

00:41:35.298 --> 00:41:39.690 I want to share with you 2 examples

NOTE Confidence: 0.9235372575

00:41:39.806 --> 00:41:42.920 of something completely unexpected to

NOTE Confidence: 0.9235372575

00:41:42.920 --> 00:41:47.080 us in which the secondary alterations

NOTE Confidence: 0.9235372575

00:41:47.080 --> 00:41:49.900 became were were targetable while

NOTE Confidence: 0.9235372575

00:41:49.900 --> 00:41:52.720 the driver mutation was not.

NOTE Confidence: 0.9235372575

00:41:52.720 --> 00:41:56.479 Sounds a bit confusing, but let's see.

NOTE Confidence: 0.9235372575

00:41:56.480 --> 00:41:59.553 So the first example is this patient

NOTE Confidence: 0.9235372575

00:41:59.553 --> 00:42:01.640 with an angiomatoid fibrocystiocytoma

NOTE Confidence: 0.9235372575

00:42:01.640 --> 00:42:04.400 having a fulminant course,

NOTE Confidence: 0.9235372575

00:42:04.400 --> 00:42:06.455 rapid local recurrences,

NOTE Confidence: 0.9235372575

00:42:06.455 --> 00:42:09.880 metastasis to the adrenal gland.

NOTE Confidence: 0.9235372575

00:42:09.880 --> 00:42:12.340 Archer confirmed the classic

NOTE Confidence: 0.9235372575

00:42:12.340 --> 00:42:15.816 AWS Kreb 1 fusion impact showed.

NOTE Confidence: 0.9235372575

00:42:15.816 --> 00:42:16.832 In addition,

NOTE Confidence: 0.9235372575

00:42:16.832 --> 00:42:20.804 CDK into AB which we know it can

NOTE Confidence: 0.9235372575

00:42:20.804 --> 00:42:23.276 happen in this disease as well

NOTE Confidence: 0.9235372575

00:42:23.276 --> 00:42:26.116 as AB RAF V 600 E mutation

NOTE Confidence: 0.896336106

00:42:26.120 --> 00:42:30.526 which is almost unheard of to see

NOTE Confidence: 0.896336106

00:42:30.526 --> 00:42:32.941 this mutation in in translocation

NOTE Confidence: 0.896336106

00:42:32.941 --> 00:42:35.880 associated sarcoma as a secondary event.

NOTE Confidence: 0.896336106

00:42:35.880 --> 00:42:38.571 And you can see here the tumor was also

NOTE Confidence: 0.896336106

00:42:38.571 --> 00:42:41.000 positive by this marker immunostochemistry

NOTE Confidence: 0.864060900769231

00:42:43.680 --> 00:42:46.935 patient of course was had first line

NOTE Confidence: 0.864060900769231

00:42:46.935 --> 00:42:49.558 the sarcoma chemotherapy aim and failed.

NOTE Confidence: 0.864060900769231

00:42:49.560 --> 00:42:52.465 And then because of the B RAF

NOTE Confidence: 0.864060900769231

00:42:52.465 --> 00:42:54.798 second side mutation was put on a

NOTE Confidence: 0.72622445

00:42:57.120 --> 00:43:00.438 combo therapy of RAF and make inhibitor.

NOTE Confidence: 0.72622445

00:43:00.440 --> 00:43:02.198 And this is the the imaging,

NOTE Confidence: 0.72622445

00:43:02.200 --> 00:43:05.528 the MRI and CAT scan showing on the

NOTE Confidence: 0.72622445

00:43:05.528 --> 00:43:08.004 upper panel the primary time mask.

NOTE Confidence: 0.72622445

00:43:08.004 --> 00:43:11.958 The 1st 2 show the dramatic increase in size.

NOTE Confidence: 0.72622445

00:43:11.960 --> 00:43:16.048 This is before the targeted therapy and

NOTE Confidence: 0.72622445

00:43:16.048 --> 00:43:19.720 the last one is after a few months of

NOTE Confidence: 0.72622445

00:43:19.720 --> 00:43:21.556 the ancorafenibinimetinib combination.

NOTE Confidence: 0.72622445

00:43:21.556 --> 00:43:25.228 And here lower is the adrenal

NOTE Confidence: 0.72622445

00:43:25.228 --> 00:43:27.998 gland metastasis that you know,

NOTE Confidence: 0.72622445

00:43:28.000 --> 00:43:30.016 grew extremely fast in one month

NOTE Confidence: 0.72622445

00:43:30.016 --> 00:43:32.044 and then decreased in size after

NOTE Confidence: 0.72622445

00:43:32.044 --> 00:43:33.599 a few months on therapy.

NOTE Confidence: 0.72622445

00:43:33.600 --> 00:43:37.040 So this was a remarkable result,

NOTE Confidence: 0.72622445

00:43:37.040 --> 00:43:40.725 unexpected and you know, I,

NOTE Confidence: 0.72622445

00:43:40.725 --> 00:43:43.000 I think even if the the clinician

NOTE Confidence: 0.72622445

00:43:43.000 --> 00:43:45.776 had the results in hand still is

NOTE Confidence: 0.72622445

00:43:45.776 --> 00:43:48.752 they will start with first line

NOTE Confidence: 0.72622445

00:43:48.752 --> 00:43:52.119 chemotherapy as as a sarcoma protocol.

NOTE Confidence: 0.72622445

00:43:52.120 --> 00:43:54.385 OK, Second example as dramatic

NOTE Confidence: 0.72622445

00:43:54.385 --> 00:43:56.197 as the first one.

NOTE Confidence: 0.72622445

00:43:56.200 --> 00:44:00.238 This was a Dicer one associated

NOTE Confidence: 0.72622445

00:44:00.240 --> 00:44:03.800 anaplastic sarcoma of the kidney

NOTE Confidence: 0.72622445

00:44:03.800 --> 00:44:07.344 young patient again fulminant

NOTE Confidence: 0.72622445

00:44:07.344 --> 00:44:10.320 course failed sarcoma chemotherapy

NOTE Confidence: 0.72622445

00:44:10.320 --> 00:44:14.520 and then IMPACT was done and show

NOTE Confidence: 0.72622445

00:44:14.520 --> 00:44:18.240 2 somatic dicer 1 alterations.

NOTE Confidence: 0.72622445

00:44:18.240 --> 00:44:21.690 So there was no germline in addition

NOTE Confidence: 0.72622445

00:44:21.690 --> 00:44:25.800 to a PDGFR alpha hotspot mutation.

NOTE Confidence: 0.72622445

00:44:25.800 --> 00:44:29.526 You can see here the the panel E shows

NOTE Confidence: 0.72622445

00:44:29.526 --> 00:44:33.598 the strong PDGFR alpha expression.

NOTE Confidence: 0.72622445

00:44:33.600 --> 00:44:37.760 So then this patient got was treated

NOTE Confidence: 0.72622445

00:44:37.760 --> 00:44:40.015 with a PDGFR alpha inhibitor,

NOTE Confidence: 0.72622445

00:44:40.015 --> 00:44:42.040 which is called Ava pritinib.

NOTE Confidence: 0.72622445

00:44:42.040 --> 00:44:43.942 And you can see appreciate here

NOTE Confidence: 0.72622445

00:44:43.942 --> 00:44:46.118 based on CAT scan and PET scan,

NOTE Confidence: 0.72622445

00:44:46.120 --> 00:44:48.472 the decrease in size and metabolic

NOTE Confidence: 0.72622445

00:44:48.472 --> 00:44:50.040 activity after this treatment.

NOTE Confidence: 0.72622445

00:44:50.040 --> 00:44:51.580 So again,

NOTE Confidence: 0.72622445

00:44:51.580 --> 00:44:55.052 quite remarkable change of clinical

NOTE Confidence: 0.72622445

00:44:55.052 --> 00:44:58.272 course due to these unexpected

NOTE Confidence: 0.72622445

00:44:58.272 --> 00:45:01.039 targetable secondary genetic events.

NOTE Confidence: 0.923887716363636

00:45:03.280 --> 00:45:05.912 OK topic #4 I hope we are

NOTE Confidence: 0.923887716363636

00:45:05.912 --> 00:45:07.600 doing good with time.

NOTE Confidence: 0.923887716363636

00:45:07.600 --> 00:45:12.560 I don't know is the impact of

NOTE Confidence: 0.923887716363636

00:45:12.560 --> 00:45:15.080 NGS in risk stratification.

NOTE Confidence: 0.923887716363636

00:45:15.080 --> 00:45:18.752 And here I, I want to share our very

NOTE Confidence: 0.923887716363636

00:45:18.752 --> 00:45:22.470 recent work on GIST where we developed

NOTE Confidence: 0.923887716363636

00:45:22.470 --> 00:45:25.920 the next generation genomic nomogram

NOTE Confidence: 0.923887716363636

00:45:25.920 --> 00:45:29.025 that truly incorporates both the

NOTE Confidence: 0.923887716363636

00:45:29.025 --> 00:45:31.509 traditional clinical pathologic factors

NOTE Confidence: 0.923887716363636

00:45:31.509 --> 00:45:35.275 as well the genomic alteration from NGS.

NOTE Confidence: 0.923887716363636

00:45:35.280 --> 00:45:37.764 So I don't know how many GI pathologists or

NOTE Confidence: 0.923887716363636

00:45:37.764 --> 00:45:40.397 soft tissue pathologists are in the audience,

NOTE Confidence: 0.923887716363636

00:45:40.400 --> 00:45:42.608 but you know, risk,

NOTE Confidence: 0.923887716363636

00:45:42.608 --> 00:45:45.920 risk prognostication in GIST is not,

NOTE Confidence: 0.923887716363636

00:45:45.920 --> 00:45:47.744 not a pickle, right?

NOTE Confidence: 0.923887716363636

00:45:47.744 --> 00:45:49.064 It's kind of complex.

NOTE Confidence: 0.923887716363636

00:45:49.064 --> 00:45:50.792 You have to have this cheat,

NOTE Confidence: 0.923887716363636

00:45:50.800 --> 00:45:52.557 you know, with you all the time.

NOTE Confidence: 0.923887716363636

00:45:52.560 --> 00:45:55.200 And here are some of them,

NOTE Confidence: 0.923887716363636

00:45:55.200 --> 00:45:59.442 all of these different tier systems schemes,

NOTE Confidence: 0.923887716363636

00:45:59.442 --> 00:46:02.900 the two most common you probably know

NOTE Confidence: 0.923887716363636

00:46:02.985 --> 00:46:05.995 are the Fletcher and IH and Yetinen.

NOTE Confidence: 0.923887716363636

00:46:06.000 --> 00:46:08.025 Even between these two there

NOTE Confidence: 0.923887716363636

00:46:08.025 --> 00:46:09.240 are significant differences.

NOTE Confidence: 0.923887716363636

00:46:09.240 --> 00:46:12.102 Yetinen has five tier system because

NOTE Confidence: 0.923887716363636

00:46:12.102 --> 00:46:14.840 they include a benign category,

NOTE Confidence: 0.923887716363636

00:46:14.840 --> 00:46:16.636 while Fletcher has four.

NOTE Confidence: 0.923887716363636

00:46:16.636 --> 00:46:19.971 Fletcher and IH does not take into

NOTE Confidence: 0.923887716363636

00:46:19.971 --> 00:46:22.716 consideration the anatomic site and

NOTE Confidence: 0.923887716363636

00:46:22.716 --> 00:46:25.550 therefore because of that this is

NOTE Confidence: 0.923887716363636

00:46:25.550 --> 00:46:27.755 a chit chat for the gastric tumors,

NOTE Confidence: 0.923887716363636

00:46:27.760 --> 00:46:31.100 it typically overestimates the gastric

NOTE Confidence: 0.923887716363636

00:46:31.100 --> 00:46:33.790 GIST with low mitotic activity.

NOTE Confidence: 0.923887716363636

00:46:33.790 --> 00:46:36.040 So as you can see,

NOTE Confidence: 0.923887716363636

00:46:36.040 --> 00:46:37.520 there are problems with this,

NOTE Confidence: 0.923887716363636

00:46:37.520 --> 00:46:38.121 right,

NOTE Confidence: 0.923887716363636

00:46:38.121 --> 00:46:41.126 problems with these especially for

NOTE Confidence: 0.923887716363636

00:46:41.126 --> 00:46:44.934 clinicians that use this as a gold

NOTE Confidence: 0.923887716363636

00:46:44.934 --> 00:46:47.993 standard to select patients who are at

NOTE Confidence: 0.923887716363636

00:46:48.087 --> 00:46:52.559 moderate to high risk for adjuvant therapy.

NOTE Confidence: 0.923887716363636

00:46:52.560 --> 00:46:54.760 So we are at Memorial,

NOTE Confidence: 0.923887716363636

00:46:54.760 --> 00:46:57.384 we do a lot of sequencing and most

NOTE Confidence: 0.923887716363636

00:46:57.384 --> 00:46:59.480 just patients are being sequenced.

NOTE Confidence: 0.923887716363636

00:46:59.480 --> 00:47:02.262 We get these fancy reports, right?

NOTE Confidence: 0.923887716363636

00:47:02.262 --> 00:47:03.648 They're very comprehensive.

NOTE Confidence: 0.923887716363636

00:47:03.648 --> 00:47:05.034 And then what,

NOTE Confidence: 0.923887716363636

00:47:05.040 --> 00:47:08.266 what exactly is being used from the report,

NOTE Confidence: 0.923887716363636

00:47:08.266 --> 00:47:08.528 right?

NOTE Confidence: 0.923887716363636

00:47:08.528 --> 00:47:10.100 We spent a lot of money

NOTE Confidence: 0.923887716363636

00:47:10.163 --> 00:47:11.555 and we want to know what,

NOTE Confidence: 0.923887716363636

00:47:11.560 --> 00:47:13.674 what can we get out of it.

NOTE Confidence: 0.923887716363636

00:47:13.680 --> 00:47:16.264 So the first information we get out of

NOTE Confidence: 0.923887716363636

00:47:16.264 --> 00:47:18.696 it is the primary alteration, right?

NOTE Confidence: 0.923887716363636

00:47:18.696 --> 00:47:20.040 The primary driver,

NOTE Confidence: 0.923887716363636

00:47:20.040 --> 00:47:23.535 the kit PDGFR alpha and we can

NOTE Confidence: 0.923887716363636

00:47:23.535 --> 00:47:25.422 tell if it's responsive or not

NOTE Confidence: 0.923887716363636

00:47:25.422 --> 00:47:27.396 to E nothing even based on that,

NOTE Confidence: 0.923887716363636

00:47:27.400 --> 00:47:29.992 you know the the clinicians make

NOTE Confidence: 0.923887716363636

00:47:29.992 --> 00:47:32.767 certain decisions on type of TKI or

NOTE Confidence: 0.923887716363636

00:47:32.767 --> 00:47:35.760 decision to to put the patient on adjuvant.

NOTE Confidence: 0.923887716363636

00:47:35.760 --> 00:47:39.370 The second information they use

NOTE Confidence: 0.923887716363636

00:47:39.370 --> 00:47:41.713 from this report is the secondary

NOTE Confidence: 0.923887716363636

00:47:41.713 --> 00:47:44.278 site mutation usually in kit.

NOTE Confidence: 0.923887716363636

00:47:44.280 --> 00:47:47.152 And this is just to inform them on

NOTE Confidence: 0.923887716363636

00:47:47.152 --> 00:47:49.350 the mechanism of resistance to the

NOTE Confidence: 0.923887716363636

00:47:49.350 --> 00:47:51.887 TKI when they are going to switch

NOTE Confidence: 0.923887716363636

00:47:51.887 --> 00:47:54.679 the TKI to the second type of drug.

NOTE Confidence: 0.923887716363636

00:47:54.680 --> 00:47:57.557 And based on the second site mutation,

NOTE Confidence: 0.923887716363636

00:47:57.560 --> 00:47:59.280 they may do those decisions.

NOTE Confidence: 0.923887716363636

00:47:59.280 --> 00:48:03.640 So this is pretty much what's being used.

NOTE Confidence: 0.923887716363636

00:48:03.640 --> 00:48:06.040 So what is not used?

NOTE Confidence: 0.923887716363636

00:48:06.040 --> 00:48:08.440 When we started study, we were,

NOTE Confidence: 0.923887716363636

00:48:08.440 --> 00:48:09.172 you know,

NOTE Confidence: 0.923887716363636

00:48:09.172 --> 00:48:11.734 kind of perplex that a lot of

NOTE Confidence: 0.923887716363636

00:48:11.734 --> 00:48:13.318 stuff it's not used.

NOTE Confidence: 0.923887716363636

00:48:13.320 --> 00:48:16.392 We don't use any of this data for

NOTE Confidence: 0.923887716363636

00:48:16.392 --> 00:48:18.980 risk certification and we do not use

NOTE Confidence: 0.923887716363636

00:48:18.980 --> 00:48:22.284 any information from the non kits,

NOTE Confidence: 0.923887716363636

00:48:22.284 --> 00:48:24.237 non driver alterations.

NOTE Confidence: 0.923887716363636

00:48:24.240 --> 00:48:26.400 So then we, you know,

NOTE Confidence: 0.923887716363636

00:48:26.400 --> 00:48:28.080 set up,

NOTE Confidence: 0.923887716363636

00:48:28.080 --> 00:48:31.116 trying working very closely with a

NOTE Confidence: 0.923887716363636

00:48:31.116 --> 00:48:33.872 bioinformatic person and use machine

NOTE Confidence: 0.923887716363636

00:48:33.872 --> 00:48:36.040 learning methods called Oncocast.

NOTE Confidence: 0.923887716363636

00:48:36.040 --> 00:48:38.680 This has been used at Memorial

NOTE Confidence: 0.923887716363636

00:48:38.680 --> 00:48:40.799 trying to do genome risk,

NOTE Confidence: 0.923887716363636

00:48:40.800 --> 00:48:43.312 risk stratification in lung

NOTE Confidence: 0.923887716363636

00:48:43.312 --> 00:48:45.196 cancer in mesothelioma.

NOTE Confidence: 0.923887716363636

00:48:45.200 --> 00:48:46.032 So we,

NOTE Confidence: 0.923887716363636

00:48:46.032 --> 00:48:49.360 we applied that in GIST and this is

NOTE Confidence: 0.863492740909091

00:48:49.464 --> 00:48:52.235 this, these are the results in gastric GIST.

NOTE Confidence: 0.863492740909091

00:48:52.240 --> 00:48:55.481 So using this method that as I

NOTE Confidence: 0.863492740909091

00:48:55.481 --> 00:48:57.396 said incorporates traditional size

NOTE Confidence: 0.863492740909091

00:48:57.396 --> 00:49:00.525 mitosis as well as the most recurrent

NOTE Confidence: 0.863492740909091

00:49:00.525 --> 00:49:03.280 alteration that we're seeing on impact.

NOTE Confidence: 0.863492740909091

00:49:03.280 --> 00:49:04.280 And you can see here,

NOTE Confidence: 0.863492740909091

00:49:04.280 --> 00:49:06.646 we were able to divide the gastric

NOTE Confidence: 0.863492740909091

00:49:06.646 --> 00:49:08.719 gist in three genomic tears.

NOTE Confidence: 0.863492740909091

00:49:08.720 --> 00:49:11.600 The first one here in red is high risk,

NOTE Confidence: 0.863492740909091

00:49:11.600 --> 00:49:14.988 which is which is defined by 1P

NOTE Confidence: 0.863492740909091

00:49:14.988 --> 00:49:17.760 deletion or SDHB alterations.

NOTE Confidence: 0.863492740909091

00:49:17.760 --> 00:49:20.420 The one in green is intermediate risk

NOTE Confidence: 0.863492740909091

00:49:20.420 --> 00:49:23.916 with 14 Q deletion here and what else?

NOTE Confidence: 0.863492740909091

00:49:23.920 --> 00:49:26.752 An absence of KIT X111 mutation

NOTE Confidence: 0.863492740909091

00:49:26.752 --> 00:49:28.640 which is very important.

NOTE Confidence: 0.863492740909091

00:49:28.640 --> 00:49:30.440 Same thing in the small bowel.

NOTE Confidence: 0.863492740909091

00:49:30.440 --> 00:49:32.520 You may not be able to see it very well.

NOTE Confidence: 0.863492740909091

00:49:32.520 --> 00:49:33.573 3 tier system.

NOTE Confidence: 0.863492740909091

00:49:33.573 --> 00:49:37.141 The red one is high risk if if the gist

NOTE Confidence: 0.863492740909091

00:49:37.141 --> 00:49:40.245 has a mutation in the mic Max axis RB

NOTE Confidence: 0.863492740909091

00:49:40.245 --> 00:49:43.422 or CD can to A then it's high risk.

NOTE Confidence: 0.863492740909091

00:49:43.422 --> 00:49:48.580 If not, if it does what presence of

NOTE Confidence: 0.863492740909091

00:49:48.580 --> 00:49:51.400 1P deletions or five Q amplification?

NOTE Confidence: 0.863492740909091

00:49:51.400 --> 00:49:54.586 That's it's intermediate risk and the

NOTE Confidence: 0.863492740909091

00:49:54.586 --> 00:49:56.976 same alterations could be confirmed

NOTE Confidence: 0.863492740909091

00:49:56.976 --> 00:50:00.296 only if we looked at Exoni Lucky

NOTE Confidence: 0.863492740909091

00:50:00.296 --> 00:50:02.116 Taxon 11 small bulges.

NOTE Confidence: 0.863492740909091

00:50:02.120 --> 00:50:05.072 So we wanted to validate this since it was,

NOTE Confidence: 0.863492740909091

00:50:05.080 --> 00:50:06.210 you know,

NOTE Confidence: 0.863492740909091

00:50:06.210 --> 00:50:09.600 relatively new method used in GIST.

NOTE Confidence: 0.863492740909091

00:50:09.600 --> 00:50:12.680 So we we used a different statistical method,

NOTE Confidence: 0.863492740909091

00:50:12.680 --> 00:50:14.740 the multivariate cost proportional

NOTE Confidence: 0.863492740909091

00:50:14.740 --> 00:50:18.519 hazard and we confirm pretty much the

NOTE Confidence: 0.863492740909091

00:50:18.519 --> 00:50:21.549 same alterations that were statistically

NOTE Confidence: 0.863492740909091

00:50:21.549 --> 00:50:24.592 significant with the machine learning

NOTE Confidence: 0.863492740909091

00:50:24.592 --> 00:50:27.876 method even in the SDH deficient GIST.

NOTE Confidence: 0.863492740909091

00:50:27.880 --> 00:50:30.484 And you may probably know these

NOTE Confidence: 0.863492740909091

00:50:30.484 --> 00:50:33.936 are have a different biology,

NOTE Confidence: 0.863492740909091

00:50:33.936 --> 00:50:36.699 different clinical behavior and

NOTE Confidence: 0.863492740909091

00:50:36.699 --> 00:50:38.695 the current risk certification

NOTE Confidence: 0.863492740909091

00:50:38.695 --> 00:50:41.880 does not apply to these at all.

NOTE Confidence: 0.863492740909091

00:50:41.880 --> 00:50:44.970 Using the same methods we were

NOTE Confidence: 0.863492740909091

00:50:44.970 --> 00:50:47.600 able to distinguish a more high

NOTE Confidence: 0.863492740909091

00:50:47.600 --> 00:50:51.136 risk of SDH mutagists that have

NOTE Confidence: 0.863492740909091

00:50:51.136 --> 00:50:54.556 P53 mutations or 1Q amplification.

NOTE Confidence: 0.863492740909091

00:50:54.560 --> 00:50:58.578 So we we are very optimistic and

NOTE Confidence: 0.863492740909091

00:50:58.578 --> 00:51:01.280 positive about these results.

NOTE Confidence: 0.863492740909091

00:51:01.280 --> 00:51:04.424 We are hoping to maybe apply

NOTE Confidence: 0.863492740909091

00:51:04.424 --> 00:51:05.996 in other sarcomas.

NOTE Confidence: 0.863492740909091

00:51:06.000 --> 00:51:07.248 Of course comma sarcomas

NOTE Confidence: 0.863492740909091

00:51:07.248 --> 00:51:09.120 you need a lot of numbers.

NOTE Confidence: 0.863492740909091

00:51:09.120 --> 00:51:12.600 You cannot do this in chick ducks 4.

NOTE Confidence: 0.863492740909091

00:51:12.600 --> 00:51:18.550 So we think that this will be very

NOTE Confidence: 0.863492740909091

00:51:18.550 --> 00:51:21.315 useful for the clinicians that may help

NOTE Confidence: 0.863492740909091

00:51:21.315 --> 00:51:24.164 them at a different level to choose

NOTE Confidence: 0.863492740909091

00:51:24.164 --> 00:51:26.180 the patients for adjuvant therapy.

NOTE Confidence: 0.863492740909091

00:51:26.180 --> 00:51:28.640 We also think that it might

NOTE Confidence: 0.863492740909091

00:51:28.640 --> 00:51:31.266 bypass of the heterogeneity I just

NOTE Confidence: 0.863492740909091

00:51:31.266 --> 00:51:33.858 mentioned in the beginning on the

NOTE Confidence: 0.863492740909091

00:51:33.939 --> 00:51:35.890 traditional risks stratification,

NOTE Confidence: 0.863492740909091

00:51:35.890 --> 00:51:39.280 especially knowing that all of these

NOTE Confidence: 0.863492740909091

00:51:39.280 --> 00:51:41.315 were designed before the imatinib

NOTE Confidence: 0.863492740909091

00:51:41.315 --> 00:51:44.298 era and they do not take into

NOTE Confidence: 0.863492740909091

00:51:44.298 --> 00:51:48.200 account the kid mutation pattern.

NOTE Confidence: 0.863492740909091

00:51:48.200 --> 00:51:52.050 So our work also for the first

NOTE Confidence: 0.863492740909091

00:51:52.050 --> 00:51:55.546 time raises the the point of that

NOTE Confidence: 0.863492740909091

00:51:55.546 --> 00:51:57.510 kid independent gene alterations

NOTE Confidence: 0.863492740909091

00:51:57.595 --> 00:51:59.768 may play a role in survival.

NOTE Confidence: 0.863492740909091

00:51:59.768 --> 00:52:03.046 And of course this can be we think

NOTE Confidence: 0.863492740909091

00:52:03.046 --> 00:52:05.746 that this can be widely applied

NOTE Confidence: 0.863492740909091

00:52:05.746 --> 00:52:08.416 because most of the targeted NGS

NOTE Confidence: 0.863492740909091

00:52:08.416 --> 00:52:11.356 panels out there give information

NOTE Confidence: 0.863492740909091

00:52:11.356 --> 00:52:14.209 about the single nucleotide variants

NOTE Confidence: 0.863492740909091

00:52:14.209 --> 00:52:18.169 make Max RB and so forth that can

NOTE Confidence: 0.863492740909091

00:52:18.263 --> 00:52:21.719 easily applied in non impact targets.

NOTE Confidence: 0.863492740909091

00:52:21.720 --> 00:52:22.313 OK.

NOTE Confidence: 0.863492740909091

00:52:22.313 --> 00:52:22.906 Lastly,

NOTE Confidence: 0.863492740909091

00:52:22.906 --> 00:52:25.278 if we have time,

NOTE Confidence: 0.863492740909091

00:52:25.280 --> 00:52:29.648 we can go over the additional

NOTE Confidence: 0.863492740909091

00:52:29.648 --> 00:52:34.466 applications of NGS and here I

NOTE Confidence: 0.863492740909091

00:52:34.466 --> 00:52:37.528 thought to share with you the

NOTE Confidence: 0.863492740909091

00:52:37.528 --> 00:52:41.112 importance of NGS in working with

NOTE Confidence: 0.863492740909091

00:52:41.112 --> 00:52:43.320 genomically complex sarcomas.

NOTE Confidence: 0.863492740909091

00:52:43.320 --> 00:52:46.224 And the first example here is

NOTE Confidence: 0.863492740909091

00:52:46.224 --> 00:52:49.111 this relatively new entity mixoid

NOTE Confidence: 0.863492740909091

00:52:49.111 --> 00:52:50.839 neomorphic liposarcoma.

NOTE Confidence: 0.972975991111111

00:52:50.840 --> 00:52:54.152 You may or may have not heard of this

NOTE Confidence: 0.972975991111111

00:52:54.160 --> 00:52:58.400 last WHA classification has been

NOTE Confidence: 0.972975991111111

00:52:58.400 --> 00:53:01.536 made a stand stand alone subtype of

NOTE Confidence: 0.972975991111111

00:53:01.536 --> 00:53:04.520 liposarcoma as a hybrid morphology.

NOTE Confidence: 0.972975991111111

00:53:04.520 --> 00:53:06.758 In areas looks like mixoid liposarcoma,

NOTE Confidence: 0.972975991111111

00:53:06.760 --> 00:53:10.318 in areas looks like theomorphic liposarcoma.

NOTE Confidence: 0.972975991111111

00:53:10.320 --> 00:53:12.180 It occurs in young patients

NOTE Confidence: 0.972975991111111

00:53:12.180 --> 00:53:14.040 in the media Steiner mainly.

NOTE Confidence: 0.972975991111111

00:53:14.040 --> 00:53:16.680 But then we've seen a wide

NOTE Confidence: 0.972975991111111

00:53:16.680 --> 00:53:18.440 age range and locations.

NOTE Confidence: 0.972975991111111

00:53:18.440 --> 00:53:20.648 And if we just look at the NGS

NOTE Confidence: 0.972975991111111

00:53:20.648 --> 00:53:22.839 of these three different types,

NOTE Confidence: 0.972975991111111

00:53:22.840 --> 00:53:24.760 the green is mixed with pleomorphic,

NOTE Confidence: 0.972975991111111

00:53:24.760 --> 00:53:26.986 the red is pleomorphic lipo and

NOTE Confidence: 0.972975991111111

00:53:26.986 --> 00:53:30.396 the blue is the mixoid round cell.

NOTE Confidence: 0.972975991111111

00:53:30.400 --> 00:53:32.940 The mixoid pleomorphic liposarcoma

NOTE Confidence: 0.972975991111111

00:53:32.940 --> 00:53:35.920 is a closer genomic signature

NOTE Confidence: 0.972975991111111

00:53:35.920 --> 00:53:38.120 with the pleomorphic lipo and

NOTE Confidence: 0.972975991111111

00:53:38.120 --> 00:53:39.880 very different than Mixoide.

NOTE Confidence: 0.972975991111111

00:53:39.880 --> 00:53:43.156 And this maybe not so unexpected right?

NOTE Confidence: 0.972975991111111

00:53:43.160 --> 00:53:46.118 Mixo liposarcoma have starts mutations and

NOTE Confidence: 0.972975991111111

00:53:46.118 --> 00:53:49.878 have the peak peak three CA alterations.

NOTE Confidence: 0.972975991111111

00:53:49.880 --> 00:53:52.768 But then when we looked at the allele

NOTE Confidence: 0.972975991111111

00:53:52.768 --> 00:53:55.189 specific copy number here on top right,

NOTE Confidence: 0.972975991111111

00:53:55.189 --> 00:53:57.283 a completely different picture could be

NOTE Confidence: 0.972975991111111

00:53:57.283 --> 00:54:00.359 seen in in Mixoide theomorphic liposarcoma,

NOTE Confidence: 0.972975991111111

00:54:00.360 --> 00:54:02.720 very different than theomorphic liposarcoma,

NOTE Confidence: 0.972975991111111

00:54:02.720 --> 00:54:03.946 for example,

NOTE Confidence: 0.972975991111111

00:54:03.946 --> 00:54:06.398 showing this widespread loss

NOTE Confidence: 0.972975991111111

00:54:06.398 --> 00:54:08.237 of hell heterozygosity,

NOTE Confidence: 0.972975991111111

00:54:08.240 --> 00:54:10.670 which was pretty much globally more

NOTE Confidence: 0.972975991111111

00:54:10.670 --> 00:54:14.258 than 85% of the genome shows this LOH

NOTE Confidence: 0.972975991111111

00:54:14.258 --> 00:54:16.918 type signature compared to for example,

NOTE Confidence: 0.972975991111111

00:54:16.920 --> 00:54:19.800 a mixer lipo here that is very flat.

NOTE Confidence: 0.972975991111111

00:54:19.800 --> 00:54:23.424 In addition, they have very interesting

NOTE Confidence: 0.972975991111111

00:54:23.424 --> 00:54:26.559 copy number alterations here on top.

NOTE Confidence: 0.972975991111111

00:54:26.560 --> 00:54:29.470 It's a primary tumor or mixopleomorphic

NOTE Confidence: 0.972975991111111

00:54:29.470 --> 00:54:29.955 liposarcoma.

NOTE Confidence: 0.972975991111111

00:54:29.960 --> 00:54:31.520 You probably don't see it,

NOTE Confidence: 0.972975991111111

00:54:31.520 --> 00:54:34.391 but this is a near haploid that here you

NOTE Confidence: 0.972975991111111

00:54:34.391 --> 00:54:37.119 have #1 which is total of copy number.

NOTE Confidence: 0.972975991111111

00:54:37.120 --> 00:54:40.200 And then in the metastasis, it became 2,

NOTE Confidence: 0.972975991111111

00:54:40.200 --> 00:54:44.960 meaning that you have a hyper deployed,

NOTE Confidence: 0.972975991111111

00:54:44.960 --> 00:54:48.560 deployed after doubling of the

NOTE Confidence: 0.972975991111111

00:54:48.560 --> 00:54:49.520 haploid phenotype.

NOTE Confidence: 0.972975991111111

00:54:49.520 --> 00:54:52.640 So very intriguing, very specific,

NOTE Confidence: 0.972975991111111

00:54:52.640 --> 00:54:54.839 very different alterations.

NOTE Confidence: 0.972975991111111

00:54:54.839 --> 00:54:59.237 And all this information would be

NOTE Confidence: 0.972975991111111

00:54:59.237 --> 00:55:02.760 extracted from our Impact NGS panel.

NOTE Confidence: 0.972975991111111

00:55:02.760 --> 00:55:03.594 So no,

NOTE Confidence: 0.972975991111111

00:55:03.594 --> 00:55:06.513 no whole genome or no whole transcriptome,

NOTE Confidence: 0.972975991111111

00:55:06.520 --> 00:55:09.736 everything that you see was extracted

NOTE Confidence: 0.972975991111111

00:55:09.736 --> 00:55:12.520 from the targeted DNA panel.

NOTE Confidence: 0.972975991111111

00:55:12.520 --> 00:55:13.768 Why is this important?

NOTE Confidence: 0.972975991111111

00:55:13.768 --> 00:55:16.440 Well, it's important because once again,

NOTE Confidence: 0.972975991111111

00:55:16.440 --> 00:55:19.518 you know the impact on survival.

NOTE Confidence: 0.972975991111111

00:55:19.520 --> 00:55:21.992 The mixed with theomorphic do even

NOTE Confidence: 0.972975991111111

00:55:21.992 --> 00:55:24.520 worse than the pleomorphic liposarcoma,

NOTE Confidence: 0.972975991111111

00:55:24.520 --> 00:55:26.272 although these are young patients and

NOTE Confidence: 0.972975991111111

00:55:26.272 --> 00:55:28.232 these are older patients, of course,

NOTE Confidence: 0.972975991111111

00:55:28.232 --> 00:55:31.400 much better than the mixed with drone cell.

NOTE Confidence: 0.972975991111111

00:55:31.400 --> 00:55:32.144 OK.

NOTE Confidence: 0.972975991111111

00:55:32.144 --> 00:55:35.824 And one last example, you know,

NOTE Confidence: 0.972975991111111

00:55:35.824 --> 00:55:36.880 is, is to,

NOTE Confidence: 0.972975991111111

00:55:36.880 --> 00:55:40.152 to illustrate our recent work that we can

NOTE Confidence: 0.972975991111111

00:55:40.152 --> 00:55:43.647 use NGS in the differential diagnosis

NOTE Confidence: 0.972975991111111

00:55:43.647 --> 00:55:46.235 of genomically complex sarcomas.

NOTE Confidence: 0.972975991111111

00:55:46.240 --> 00:55:49.838 We've seen too many mistakes or errors.

NOTE Confidence: 0.972975991111111

00:55:49.840 --> 00:55:51.480 So we, you know,

NOTE Confidence: 0.972975991111111

00:55:51.480 --> 00:55:53.940 in various diseases that we thought

NOTE Confidence: 0.972975991111111

00:55:54.020 --> 00:55:56.416 let's look at this more carefully.

NOTE Confidence: 0.972975991111111

00:55:56.416 --> 00:56:00.525 And here I will give you 2 examples,

NOTE Confidence: 0.972975991111111

00:56:00.525 --> 00:56:02.580 embryonorabdomal sarcoma to

NOTE Confidence: 0.972975991111111

00:56:02.580 --> 00:56:05.320 distinguish from Triton tumor

NOTE Confidence: 0.972975991111111

00:56:05.320 --> 00:56:07.997 and embryonorabdomal sarcoma to

NOTE Confidence: 0.972975991111111

00:56:07.997 --> 00:56:10.437 distinguish from theomorphic Raptor.

NOTE Confidence: 0.972975991111111

00:56:10.440 --> 00:56:14.720 So this first study that we did recently

NOTE Confidence: 0.972975991111111

00:56:14.720 --> 00:56:17.378 was to compare embryonorabdo with Triton

NOTE Confidence: 0.972975991111111

00:56:17.378 --> 00:56:20.479 tumor or MPNST with Raptor component.

NOTE Confidence: 0.972975991111111

00:56:20.480 --> 00:56:23.938 And you may not know that in fact NF1

NOTE Confidence: 0.972975991111111

00:56:23.938 --> 00:56:26.926 alterations is the second most common

NOTE Confidence: 0.972975991111111

00:56:26.926 --> 00:56:29.800 genetic event in embryonoraptil.

NOTE Confidence: 0.972975991111111

00:56:29.800 --> 00:56:32.000 So having an F1 alterations,

NOTE Confidence: 0.972975991111111

00:56:32.000 --> 00:56:34.080 you cannot distinguish between

NOTE Confidence: 0.972975991111111

00:56:34.080 --> 00:56:36.160 umbrella and tritone tumor.

NOTE Confidence: 0.972975991111111

00:56:36.160 --> 00:56:37.568 So that's one thing.

NOTE Confidence: 0.972975991111111

00:56:37.568 --> 00:56:37.920 Second,

NOTE Confidence: 0.972975991111111

00:56:37.920 --> 00:56:40.965 that this particular study was

NOTE Confidence: 0.972975991111111

00:56:40.965 --> 00:56:44.520 triggered by three cases that were

NOTE Confidence: 0.972975991111111

00:56:44.520 --> 00:56:47.004 three cases of tritone tumor that

NOTE Confidence: 0.972975991111111

00:56:47.004 --> 00:56:48.660 were misdiagnosis and Bronner

NOTE Confidence: 0.972975991111111

00:56:48.729 --> 00:56:51.387 reptile and one of them had

NOTE Confidence: 0.972975991111111

00:56:51.387 --> 00:56:52.273 therapeutic repercussions.

NOTE Confidence: 0.921046371

00:56:52.280 --> 00:56:55.472 The other two the diagnosis was changed

NOTE Confidence: 0.921046371

00:56:55.472 --> 00:56:59.240 in real time due to the impact results.

NOTE Confidence: 0.921046371

00:56:59.240 --> 00:57:02.278 So I know it's a complicated figure,

NOTE Confidence: 0.921046371

00:57:02.280 --> 00:57:07.145 but you have to kind of believe me that

NOTE Confidence: 0.921046371

00:57:07.145 --> 00:57:11.404 tritone tumor has the same genomics as MPNST.

NOTE Confidence: 0.921046371

00:57:11.404 --> 00:57:14.512 They have alteration in the PRC two

NOTE Confidence: 0.921046371

00:57:14.512 --> 00:57:17.480 complex as well as the CDKN 2AB.

NOTE Confidence: 0.921046371

00:57:17.480 --> 00:57:20.576 While the embryonic of the master coma has

NOTE Confidence: 0.921046371

00:57:20.576 --> 00:57:23.355 Ras mutations and B core loss of function.

NOTE Confidence: 0.921046371

00:57:23.360 --> 00:57:26.289 So for most cases,

NOTE Confidence: 0.921046371

00:57:26.289 --> 00:57:29.400 if you look at uncle prints of the impact,

NOTE Confidence: 0.921046371

00:57:29.400 --> 00:57:32.080 you can actually favor one over the other.

NOTE Confidence: 0.921046371

00:57:32.080 --> 00:57:33.568 I'm not saying that this can

NOTE Confidence: 0.921046371

00:57:33.568 --> 00:57:35.553 be done in 100% of the cases,

NOTE Confidence: 0.921046371

00:57:35.553 --> 00:57:38.144 but in more than 70% of the cases,

NOTE Confidence: 0.921046371

00:57:38.144 --> 00:57:40.660 we are able to tell the genomic

NOTE Confidence: 0.921046371

00:57:40.660 --> 00:57:43.360 difference between a tritone slash

NOTE Confidence: 0.921046371

00:57:43.360 --> 00:57:46.480 MPNST versus and Bronner Optima circle.

NOTE Confidence: 0.718830528461538

00:57:49.000 --> 00:57:51.020 OK, what's important? Well,

NOTE Confidence: 0.718830528461538

00:57:51.020 --> 00:57:54.979 the the survival again it's like black and

NOTE Confidence: 0.718830528461538

00:57:54.979 --> 00:57:59.440 white and Branarabdo very good prognosis.

NOTE Confidence: 0.718830528461538

00:57:59.440 --> 00:58:02.310 The NF one mutant and Branarabdo responds

NOTE Confidence: 0.718830528461538

00:58:02.310 --> 00:58:06.229 very well to like any other and the NPNST are

NOTE Confidence: 0.718830528461538

00:58:06.229 --> 00:58:09.559 doing the Triton tumor are doing very poorly.

NOTE Confidence: 0.718830528461538

00:58:09.560 --> 00:58:15.292 And lastly, we used NGS to try to distinguish

NOTE Confidence: 0.718830528461538

00:58:15.292 --> 00:58:17.957 and Branarabdo from theomorphic rhabdo.

NOTE Confidence: 0.718830528461538

00:58:17.960 --> 00:58:19.276 And why is that, you may ask?

NOTE Confidence: 0.718830528461538

00:58:19.280 --> 00:58:21.890 Because we seen embryonorabdo with

NOTE Confidence: 0.718830528461538

00:58:21.890 --> 00:58:25.000 anaplasia in young adults or even,

NOTE Confidence: 0.718830528461538

00:58:25.000 --> 00:58:26.560 you know, not so young adults.

NOTE Confidence: 0.718830528461538

00:58:26.560 --> 00:58:29.758 So we struggle sometimes, you know,

NOTE Confidence: 0.718830528461538

00:58:29.760 --> 00:58:32.118 is it truly an embryon anaplasia?

NOTE Confidence: 0.718830528461538

00:58:32.120 --> 00:58:33.092 Is it pleomorphic?

NOTE Confidence: 0.718830528461538

00:58:33.092 --> 00:58:35.788 So we try to look into this more

NOTE Confidence: 0.718830528461538

00:58:35.788 --> 00:58:37.840 carefully to see if, you know,

NOTE Confidence: 0.718830528461538

00:58:37.840 --> 00:58:40.400 since we have all this data available anyway,

NOTE Confidence: 0.718830528461538

00:58:40.400 --> 00:58:40.817 right?

NOTE Confidence: 0.718830528461538

00:58:40.817 --> 00:58:43.319 These are sequenced as I mentioned.

NOTE Confidence: 0.718830528461538

00:58:43.320 --> 00:58:45.920 So why not just to try to see if in,

NOTE Confidence: 0.718830528461538

00:58:45.920 --> 00:58:47.320 you know, a challenging case.

NOTE Confidence: 0.718830528461538

00:58:47.320 --> 00:58:49.196 Could this be helpful?

NOTE Confidence: 0.718830528461538

00:58:49.196 --> 00:58:51.072 And again embryonorabdomal sarcoma

NOTE Confidence: 0.718830528461538

00:58:51.072 --> 00:58:53.959 has NF1 mutation and Ras mutation,

NOTE Confidence: 0.718830528461538

00:58:53.960 --> 00:58:55.880 V core alteration very different.

NOTE Confidence: 0.718830528461538

00:58:55.880 --> 00:58:59.800 While pleomorphic rhabdoma sarcoma

NOTE Confidence: 0.718830528461538

00:58:59.800 --> 00:59:02.265 has the same alterations as

NOTE Confidence: 0.718830528461538

00:59:02.265 --> 00:59:04.237 any other pleomorphic sarcoma.

NOTE Confidence: 0.718830528461538

00:59:04.240 --> 00:59:05.716 So if you look at this,

NOTE Confidence: 0.718830528461538

00:59:05.720 --> 00:59:08.177 so on the left you have pleomorphic

NOTE Confidence: 0.718830528461538

00:59:08.177 --> 00:59:09.840 rhabdom and then you have

NOTE Confidence: 0.718830528461538

00:59:09.840 --> 00:59:11.976 undifferential pleomorphic sarcoma,

NOTE Confidence: 0.718830528461538

00:59:11.976 --> 00:59:13.400 pleomorphic liposarcoma.

NOTE Confidence: 0.718830528461538

00:59:13.400 --> 00:59:16.158 Here it looks pretty much the same.

NOTE Confidence: 0.718830528461538

00:59:16.160 --> 00:59:21.108 So pleomorphic rhabdom has the same genomics,

NOTE Confidence: 0.718830528461538

00:59:21.108 --> 00:59:24.016 the same signature and any other adult

NOTE Confidence: 0.718830528461538

00:59:24.016 --> 00:59:26.555 theomorphic sarcoma and just supported

NOTE Confidence: 0.718830528461538

00:59:26.555 --> 00:59:30.558 the fact that these are included in the

NOTE Confidence: 0.718830528461538

00:59:30.558 --> 00:59:32.930 therapeutic bracket of pleomorphic sarcoma.

NOTE Confidence: 0.718830528461538

00:59:32.930 --> 00:59:35.380 So if you ask a sarcoma medical

NOTE Confidence: 0.718830528461538

00:59:35.446 --> 00:59:37.356 oncologist how you treat pleomorphic

NOTE Confidence: 0.718830528461538

00:59:37.356 --> 00:59:40.221 crap that they will say like any

NOTE Confidence: 0.718830528461538

00:59:40.221 --> 00:59:41.556 other pleomorphic sarcoma,

NOTE Confidence: 0.718830528461538

00:59:41.560 --> 00:59:44.025 not with Embryon Arab the

NOTE Confidence: 0.718830528461538

00:59:44.025 --> 00:59:45.997 protocol which makes sense.

NOTE Confidence: 0.718830528461538

00:59:46.000 --> 00:59:46.402 However,

NOTE Confidence: 0.718830528461538

00:59:46.402 --> 00:59:49.618 it is our role to make sure we

NOTE Confidence: 0.718830528461538

00:59:49.618 --> 00:59:51.359 distinguish the two of them.

NOTE Confidence: 0.718830528461538

00:59:51.360 --> 00:59:56.120 So final thoughts if we need any.

NOTE Confidence: 0.718830528461538

00:59:56.120 --> 01:00:00.564 I hope I convinced you giving you so many

NOTE Confidence: 0.718830528461538

01:00:00.564 --> 01:00:03.030 examples about the wide application of

NOTE Confidence: 0.718830528461538

01:00:03.110 --> 01:00:06.000 NGS beyond diagnosis and classification.

NOTE Confidence: 0.718830528461538

01:00:06.000 --> 01:00:09.510 And the last point here is that our role

NOTE Confidence: 0.718830528461538

01:00:09.510 --> 01:00:13.000 as pathologist seems to be evolving.

NOTE Confidence: 0.718830528461538

01:00:13.000 --> 01:00:16.619 A lot during the NGS era and

NOTE Confidence: 0.718830528461538

01:00:16.619 --> 01:00:20.144 it's advisable if you ask me to

NOTE Confidence: 0.718830528461538

01:00:20.144 --> 01:00:22.439 keep an active role in,

NOTE Confidence: 0.718830528461538

01:00:22.439 --> 01:00:23.317 you know,

NOTE Confidence: 0.718830528461538

01:00:23.317 --> 01:00:25.073 incorporating and interpreting all

NOTE Confidence: 0.718830528461538

01:00:25.073 --> 01:00:27.720 these NGS tests and putting together

NOTE Confidence: 0.718830528461538

01:00:27.720 --> 01:00:30.630 with the remaining of the findings for,

NOTE Confidence: 0.718830528461538

01:00:30.630 --> 01:00:31.410 you know,

NOTE Confidence: 0.718830528461538

01:00:31.410 --> 01:00:33.750 an improved diagnosis and a better

NOTE Confidence: 0.718830528461538

01:00:33.750 --> 01:00:35.438 management for these patients.

NOTE Confidence: 0.718830528461538

01:00:35.440 --> 01:00:36.640 Thank you very much.

NOTE Confidence: 0.68865725

01:00:50.920 --> 01:00:51.400 Any questions?

NOTE Confidence: 0.921259345

01:00:54.720 --> 01:00:56.118 I guess I was very clear,

NOTE Confidence: 0.5861593

01:01:03.920 --> 01:01:05.340 are these affiliations

NOTE Confidence: 0.5861593

01:01:05.340 --> 01:01:06.920 detectable or liquid files?

NOTE Confidence: 0.912833257777778

01:01:09.080 --> 01:01:10.691 Very good question.

NOTE Confidence: 0.912833257777778

01:01:10.691 --> 01:01:14.864 So we have a similar panel with IMPACT.

NOTE Confidence: 0.912833257777778

01:01:14.864 --> 01:01:18.640 IMPACT has 500 genes we call MSK Access,

NOTE Confidence: 0.912833257777778

01:01:18.640 --> 01:01:21.665 which does the sequencing from

NOTE Confidence: 0.912833257777778

01:01:21.665 --> 01:01:24.106 the circulating DNA includes

NOTE Confidence: 0.912833257777778

01:01:24.106 --> 01:01:27.236 I believe 70 something genes.

NOTE Confidence: 0.912833257777778

01:01:27.240 --> 01:01:28.880 It's not very reliable,

NOTE Confidence: 0.912833257777778

01:01:28.880 --> 01:01:30.520 it's not very accurate.

NOTE Confidence: 0.912833257777778

01:01:30.520 --> 01:01:32.668 So I guess if you're looking

NOTE Confidence: 0.912833257777778

01:01:32.668 --> 01:01:34.477 at a specific alteration like

NOTE Confidence: 0.912833257777778

01:01:34.477 --> 01:01:36.506 just you look at kits, you know,

NOTE Confidence: 0.912833257777778

01:01:36.506 --> 01:01:38.530 this may work well in the blood if

NOTE Confidence: 0.912833257777778

01:01:38.587 --> 01:01:40.597 you know exactly what you're after,

NOTE Confidence: 0.912833257777778

01:01:40.600 --> 01:01:42.970 but not not for these genomically

NOTE Confidence: 0.912833257777778

01:01:42.970 --> 01:01:44.155 complex circle ones.

NOTE Confidence: 0.498123358

01:01:47.200 --> 01:01:50.480 See, I do have a question.

NOTE Confidence: 0.59600711

01:01:53.080 --> 01:01:55.666 You mentioned earlier reverse morphology

NOTE Confidence: 0.59600711

01:01:55.666 --> 01:01:58.842 with the genomic data, NGS data,

NOTE Confidence: 0.59600711

01:01:58.842 --> 01:02:02.720 then you go back and look at the tumor.

NOTE Confidence: 0.59600711

01:02:02.720 --> 01:02:07.596 Do you think that the NGS data should be

NOTE Confidence: 0.59600711

01:02:07.600 --> 01:02:10.320 signed out by the surgeon pathologist?

NOTE Confidence: 0.782692677222222

01:02:14.160 --> 01:02:16.015 I, I think it should be signed

NOTE Confidence: 0.782692677222222

01:02:16.015 --> 01:02:17.529 about the molecular pathologist to

NOTE Confidence: 0.782692677222222

01:02:17.529 --> 01:02:19.515 make sure that everything you know,

NOTE Confidence: 0.782692677222222

01:02:19.520 --> 01:02:21.610 the quality control and everything

NOTE Confidence: 0.782692677222222

01:02:21.610 --> 01:02:24.559 and then to be discussed the results

NOTE Confidence: 0.782692677222222

01:02:24.560 --> 01:02:26.438 in like a molecular tumor board.

NOTE Confidence: 0.782692677222222

01:02:26.440 --> 01:02:28.560 And I think that's what we are missing.

NOTE Confidence: 0.782692677222222

01:02:28.560 --> 01:02:30.960 We missed this link. I agree with you.

NOTE Confidence: 0.782692677222222

01:02:30.960 --> 01:02:32.335 That's very important to kind

NOTE Confidence: 0.782692677222222

01:02:32.335 --> 01:02:33.160 of put together.

NOTE Confidence: 0.782692677222222

01:02:33.160 --> 01:02:34.372 I mean, you know,

NOTE Confidence: 0.782692677222222

01:02:34.372 --> 01:02:36.753 doesn't make sense with what we see and

NOTE Confidence: 0.782692677222222

01:02:36.753 --> 01:02:39.115 a lot of time it makes sense and then

NOTE Confidence: 0.782692677222222

01:02:39.115 --> 01:02:41.327 they trigger us to do additional tests

NOTE Confidence: 0.782692677222222

01:02:41.327 --> 01:02:43.478 that we didn't even think about that right.

NOTE Confidence: 0.782692677222222

01:02:43.480 --> 01:02:46.720 So I gave a number of examples here,

NOTE Confidence: 0.782692677222222

01:02:46.720 --> 01:02:49.042 but I truly think they should be signed on

NOTE Confidence: 0.782692677222222

01:02:49.042 --> 01:02:51.596 by molecular pathologists that would know,

NOTE Confidence: 0.782692677222222

01:02:51.600 --> 01:02:54.078 you know, the pitfalls all the.

NOTE Confidence: 0.782692677222222

01:02:54.080 --> 01:02:54.560 So there's

NOTE Confidence: 0.49307067

01:02:56.680 --> 01:02:59.826 a question in chat that's you've been

NOTE Confidence: 0.49307067

01:02:59.826 --> 01:03:03.840 settled in the collation so far.

NOTE Confidence: 0.49307067

01:03:03.840 --> 01:03:06.330 Yeah, it's used, but not, not great,

NOTE Confidence: 0.49307067

01:03:06.330 --> 01:03:08.885 no, at least the cases I've sent

NOTE Confidence: 0.49307067

01:03:08.885 --> 01:03:11.720 to methylation in our department,

NOTE Confidence: 0.49307067

01:03:11.720 --> 01:03:14.400 maybe because I send zebras

NOTE Confidence: 0.49307067

01:03:14.400 --> 01:03:16.880 so usually say no match.

NOTE Confidence: 0.49307067

01:03:16.880 --> 01:03:18.714 So actually I've not been sending much.

NOTE Confidence: 0.49307067

01:03:18.720 --> 01:03:20.672 I mean, I, I have a question.

NOTE Confidence: 0.49307067

01:03:20.672 --> 01:03:23.960 I mean, the, the workup takes a long time,

NOTE Confidence: 0.49307067

01:03:23.960 --> 01:03:25.840 right? So I'm a drastic guy.

NOTE Confidence: 0.49307067

01:03:25.840 --> 01:03:27.640 I get questions from my own

NOTE Confidence: 0.49307067

01:03:27.640 --> 01:03:29.826 colleagues more or less the same day

NOTE Confidence: 0.49307067

01:03:29.826 --> 01:03:31.399 that you've got the whole answer.

NOTE Confidence: 0.601854092857143

01:03:33.440 --> 01:03:34.959 These these workups take a long time.

NOTE Confidence: 0.601854092857143

01:03:34.960 --> 01:03:37.354 And every time there's a typical workflow,

NOTE Confidence: 0.601854092857143

01:03:37.360 --> 01:03:38.540 you get a biopsy, say London's

NOTE Confidence: 0.601854092857143

01:03:38.540 --> 01:03:40.260 going to sell something or other,

NOTE Confidence: 0.601854092857143

01:03:40.260 --> 01:03:41.440 you get a reflection,

NOTE Confidence: 0.601854092857143

01:03:41.440 --> 01:03:43.435 and then you spend your time working it up.

NOTE Confidence: 0.601854092857143

01:03:43.435 --> 01:03:44.995 Yeah, that's sort of the way it works.

NOTE Confidence: 0.601854092857143

01:03:45.000 --> 01:03:47.025 And then you don't have that issue

NOTE Confidence: 0.601854092857143

01:03:47.025 --> 01:03:48.360 about how fast you have to work.

NOTE Confidence: 0.601854092857143

01:03:48.360 --> 01:03:49.388 You've got, you know,

NOTE Confidence: 0.601854092857143

01:03:49.388 --> 01:03:50.679 you can work, take a month,

NOTE Confidence: 0.601854092857143

01:03:50.680 --> 01:03:53.040 and it's not a big deal. Yes,

NOTE Confidence: 0.926203964285714

01:03:55.560 --> 01:03:57.114 I mean it depends. As I said,

NOTE Confidence: 0.926203964285714

01:03:57.120 --> 01:04:00.276 we cannot activate these NGS tests.

NOTE Confidence: 0.926203964285714

01:04:00.280 --> 01:04:01.488 It's all by clinician.

NOTE Confidence: 0.926203964285714

01:04:01.488 --> 01:04:02.998 So we just emailed them.

NOTE Confidence: 0.926203964285714

01:04:03.000 --> 01:04:04.400 I said hey, you know,

NOTE Confidence: 0.926203964285714

01:04:04.400 --> 01:04:05.600 I don't know what this is,

NOTE Confidence: 0.926203964285714

01:04:05.600 --> 01:04:06.560 please get consent,

NOTE Confidence: 0.926203964285714

01:04:06.560 --> 01:04:08.800 get blood from the patient so we,

NOTE Confidence: 0.926203964285714

01:04:08.800 --> 01:04:11.600 we can activate the NGS right away.

NOTE Confidence: 0.926203964285714

01:04:11.600 --> 01:04:13.478 I will sign out the biopsy,

NOTE Confidence: 0.926203964285714

01:04:13.480 --> 01:04:15.040 you know, if I if I think it's,

NOTE Confidence: 0.926203964285714

01:04:15.040 --> 01:04:17.320 you know, high grade or whatever,

NOTE Confidence: 0.926203964285714

01:04:17.320 --> 01:04:19.774 I would say undifferentiated and then

NOTE Confidence: 0.926203964285714

01:04:19.774 --> 01:04:22.458 the classification will be done on the

NOTE Confidence: 0.926203964285714

01:04:22.458 --> 01:04:24.740 resection or I will suggest material if

NOTE Confidence: 0.926203964285714

01:04:24.808 --> 01:04:27.560 it's from outside to do Archer or whatever,

NOTE Confidence: 0.926203964285714

01:04:27.560 --> 01:04:29.680 if it's monomorphic Archer,

NOTE Confidence: 0.926203964285714

01:04:29.680 --> 01:04:31.800 if it's piomorphic NGS.

NOTE Confidence: 0.926203964285714

01:04:31.800 --> 01:04:33.416 But yeah, I mean,

NOTE Confidence: 0.926203964285714

01:04:33.416 --> 01:04:36.640 everybody wants to the result the same day,

NOTE Confidence: 0.926203964285714

01:04:36.640 --> 01:04:38.840 but and even the resection,

NOTE Confidence: 0.926203964285714

01:04:38.840 --> 01:04:41.234 I sign it out and then impact,

NOTE Confidence: 0.926203964285714

01:04:41.240 --> 01:04:43.120 you know, comes back in a month later.

NOTE Confidence: 0.926203964285714

01:04:43.120 --> 01:04:44.944 And I always say that make

NOTE Confidence: 0.926203964285714

01:04:44.944 --> 01:04:46.690 fun of myself said, you know,

NOTE Confidence: 0.926203964285714

01:04:46.690 --> 01:04:48.906 my diagnosis is as good as, you know,

NOTE Confidence: 0.926203964285714

01:04:48.906 --> 01:04:50.784 one month because then then I'll

NOTE Confidence: 0.926203964285714

01:04:50.784 --> 01:04:52.637 have the results of the NGS.

NOTE Confidence: 0.926203964285714

01:04:52.640 --> 01:04:55.152 And then I may have to, yeah,

NOTE Confidence: 0.926203964285714

01:04:55.152 --> 01:04:56.328 reconsider my diagnosis,

NOTE Confidence: 0.926203964285714

01:04:56.328 --> 01:04:57.344 which, you know,

NOTE Confidence: 0.926203964285714

01:04:57.344 --> 01:04:59.840 happens as I showed you couple of times.

NOTE Confidence: 0.926203964285714

01:04:59.840 --> 01:05:01.320 But this, this is great.

NOTE Confidence: 0.926203964285714

01:05:01.320 --> 01:05:01.890 You know,

NOTE Confidence: 0.926203964285714

01:05:01.890 --> 01:05:03.600 these are finally some objective tools.

NOTE Confidence: 0.926203964285714

01:05:03.600 --> 01:05:06.239 Some some sometimes doesn't all make sense,

NOTE Confidence: 0.926203964285714

01:05:06.240 --> 01:05:09.184 but most of the time if they find

NOTE Confidence: 0.926203964285714

01:05:09.184 --> 01:05:11.997 an alterations or a fusion and we

NOTE Confidence: 0.926203964285714

01:05:11.997 --> 01:05:14.400 confirm by immuno chemistry, it's real.

NOTE Confidence: 0.926203964285714

01:05:14.400 --> 01:05:16.000 So we, you know,

NOTE Confidence: 0.926203964285714

01:05:16.000 --> 01:05:17.400 we changed the diagnosis.

NOTE Confidence: 0.740177468333333

01:05:20.080 --> 01:05:22.504 Finally some questions. Yeah,

NOTE Confidence: 0.740177468333333

01:05:22.504 --> 01:05:25.477 I just wanted to come back to the question,

NOTE Confidence: 0.740177468333333

01:05:25.480 --> 01:05:27.790 some of the stuff you mentioned about

NOTE Confidence: 0.740177468333333

01:05:27.790 --> 01:05:29.275 GIST and actually one question kind

NOTE Confidence: 0.740177468333333

01:05:29.275 --> 01:05:32.270 of came up with Rob's point for the

NOTE Confidence: 0.740177468333333

01:05:32.270 --> 01:05:34.040 GIST and she asked do you do that?

NOTE Confidence: 0.740177468333333

01:05:34.040 --> 01:05:36.101 Do you need a clinician order for that or

NOTE Confidence: 0.740177468333333

01:05:36.101 --> 01:05:38.032 do you do that in her complexity manner?

NOTE Confidence: 0.740177468333333

01:05:38.032 --> 01:05:40.596 I cannot, I cannot. It's just a patient

NOTE Confidence: 0.740177468333333

01:05:40.596 --> 01:05:42.920 need to be consent to draw blood.

NOTE Confidence: 0.740177468333333

01:05:42.920 --> 01:05:46.637 So and because you see Mati Nibben,

NOTE Confidence: 0.740177468333333

01:05:46.640 --> 01:05:49.313 you know TKI, they do it on every case.

NOTE Confidence: 0.740177468333333

01:05:49.320 --> 01:05:52.209 I don't have to tell them that the GIST

NOTE Confidence: 0.740177468333333

01:05:52.209 --> 01:05:53.870 sarcoma oncologist are outstanding.

NOTE Confidence: 0.740177468333333

01:05:53.870 --> 01:05:56.040 So I don't have to tell them.

NOTE Confidence: 0.740177468333333

01:05:56.040 --> 01:05:58.980 But yes, it's being done on every

NOTE Confidence: 0.740177468333333

01:05:58.980 --> 01:06:02.396 case and with the normal gram that you

NOTE Confidence: 0.740177468333333

01:06:02.396 --> 01:06:04.504 described that incorporates the genomic

NOTE Confidence: 0.740177468333333

01:06:04.504 --> 01:06:06.840 data is I don't know if I missed it.

NOTE Confidence: 0.740177468333333

01:06:06.840 --> 01:06:07.884 Maybe you shouldn't,

NOTE Confidence: 0.740177468333333

01:06:07.884 --> 01:06:10.048 but is that could be look at

NOTE Confidence: 0.740177468333333

01:06:10.048 --> 01:06:11.584 that anywhere or is that posted

NOTE Confidence: 0.740177468333333

01:06:11.584 --> 01:06:12.998 anywhere on the it's published,

NOTE Confidence: 0.740177468333333

01:06:13.000 --> 01:06:15.370 so published you can cut

NOTE Confidence: 0.740177468333333

01:06:15.370 --> 01:06:17.478 it and I'm just kidding.

NOTE Confidence: 0.740177468333333

01:06:17.478 --> 01:06:19.146 Yeah, it's published, Yeah,

NOTE Confidence: 0.740177468333333

01:06:19.146 --> 01:06:23.194 it's published last year and we also have

NOTE Confidence: 0.740177468333333

01:06:23.194 --> 01:06:26.239 recently done a similar one in Lyle.

NOTE Confidence: 0.740177468333333

01:06:26.240 --> 01:06:26.440 Yeah.

NOTE Confidence: 0.740177468333333

01:06:26.440 --> 01:06:26.640 One

NOTE Confidence: 0.6559178925

01:06:29.680 --> 01:06:32.200 thing that I think some of the patients,

NOTE Confidence: 0.6559178925

01:06:32.200 --> 01:06:33.998 any paths might not be pick up from

NOTE Confidence: 0.282236375

01:06:34.400 --> 01:06:35.160 our like hard scale.

NOTE Confidence: 0.915832943636364

01:06:40.120 --> 01:06:42.502 Yeah, that's the hardest part because

NOTE Confidence: 0.915832943636364

01:06:42.502 --> 01:06:44.800 most of the commercially available,

NOTE Confidence: 0.915832943636364

01:06:44.800 --> 01:06:47.542 they don't provide them and even

NOTE Confidence: 0.915832943636364

01:06:47.542 --> 01:06:50.520 even within our own departments,

NOTE Confidence: 0.915832943636364

01:06:50.520 --> 01:06:52.680 different molecular pathologists

NOTE Confidence: 0.915832943636364

01:06:52.680 --> 01:06:54.840 use different thresholds.

NOTE Confidence: 0.915832943636364

01:06:54.840 --> 01:06:55.964 So it may depend.

NOTE Confidence: 0.915832943636364

01:06:55.964 --> 01:06:57.650 So a lot of the studies

NOTE Confidence: 0.915832943636364

01:06:57.720 --> 01:06:58.941 that we do copy number,

NOTE Confidence: 0.915832943636364

01:06:58.941 --> 01:07:01.773 we had to go back to the raw data to

NOTE Confidence: 0.915832943636364

01:07:01.773 --> 01:07:03.837 make sure that everything is accurate.

NOTE Confidence: 0.915832943636364

01:07:03.840 --> 01:07:06.720 So you're perfectly right.

NOTE Confidence: 0.915832943636364

01:07:06.720 --> 01:07:10.781 This is still very subjective field,

NOTE Confidence: 0.915832943636364

01:07:10.781 --> 01:07:13.547 you know, to report the arm

NOTE Confidence: 0.915832943636364

01:07:13.547 --> 01:07:15.640 level copy number changes

NOTE Confidence: 0.880308271111111

01:07:18.280 --> 01:07:19.900 also because our clinicians don't

NOTE Confidence: 0.880308271111111

01:07:19.900 --> 01:07:21.746 really care that much, you know,

NOTE Confidence: 0.880308271111111

01:07:21.746 --> 01:07:22.838 they're all after mutations,

NOTE Confidence: 0.880308271111111

01:07:22.840 --> 01:07:23.932 fusions, you know,

NOTE Confidence: 0.880308271111111

01:07:23.932 --> 01:07:26.480 so then maybe it's not so much,

NOTE Confidence: 0.880308271111111

01:07:26.480 --> 01:07:28.390 you know, detail or is no, no,

NOTE Confidence: 0.880308271111111

01:07:28.390 --> 01:07:32.240 no certain standards that are being applied.

NOTE Confidence: 0.880308271111111

01:07:32.240 --> 01:07:35.120 I don't know what what's the situation here?

NOTE Confidence: 0.880308271111111

01:07:35.120 --> 01:07:36.880 And signing out molecular, but

NOTE Confidence: 0.709552546666667

01:07:39.080 --> 01:07:41.516 right, yeah, most commercial the same.

NOTE Confidence: 0.709552546666667

01:07:41.520 --> 01:07:43.840 They are not reported.

NOTE Confidence: 0.709552546666667

01:07:43.840 --> 01:07:47.720 So when we we did the the the

NOTE Confidence: 0.709552546666667

01:07:47.720 --> 01:07:50.944 prognostication in LYO, LYO is a disease.

NOTE Confidence: 0.709552546666667

01:07:50.944 --> 01:07:54.773 Lyo is a disease of copy number, right.

NOTE Confidence: 0.709552546666667

01:07:54.773 --> 01:07:56.638 It's not necessarily like just,

NOTE Confidence: 0.709552546666667

01:07:56.640 --> 01:07:59.952 it's truly you have to have very good data.

NOTE Confidence: 0.709552546666667

01:07:59.960 --> 01:08:02.640 So we were not able to find a,

NOTE Confidence: 0.709552546666667

01:08:02.640 --> 01:08:04.284 a validation cohort.

NOTE Confidence: 0.709552546666667

01:08:04.284 --> 01:08:08.300 So in the end, we have to take from

NOTE Confidence: 0.709552546666667

01:08:08.300 --> 01:08:10.520 like the Genie project of ACR,

NOTE Confidence: 0.709552546666667

01:08:10.520 --> 01:08:12.840 get all the raw data,

NOTE Confidence: 0.709552546666667

01:08:12.840 --> 01:08:15.306 redo our own copy number in order for us

NOTE Confidence: 0.709552546666667

01:08:15.306 --> 01:08:17.880 to be able to compare with the impact.

NOTE Confidence: 0.709552546666667

01:08:17.880 --> 01:08:22.120 So it was really very, very hard.

NOTE Confidence: 0.709552546666667

01:08:22.120 --> 01:08:23.191 I don't know,

NOTE Confidence: 0.709552546666667

01:08:23.191 --> 01:08:25.690 maybe in the future they will standardize

NOTE Confidence: 0.709552546666667

01:08:25.764 --> 01:08:27.616 this better and maybe will come

NOTE Confidence: 0.709552546666667

01:08:27.616 --> 01:08:29.320 from if the clinicians require it.

NOTE Confidence: 0.8546047475

01:08:32.960 --> 01:08:34.480 I just want to thank you for coming.

NOTE Confidence: 0.8546047475

01:08:34.480 --> 01:08:36.800 I really enjoyed it.

NOTE Confidence: 0.8546047475

01:08:36.800 --> 01:08:38.564 I remember signing out with you and

NOTE Confidence: 0.8546047475

01:08:38.564 --> 01:08:40.636 one of the first things you said to

NOTE Confidence: 0.8546047475

01:08:40.636 --> 01:08:42.718 me was is there blood in the system?

NOTE Confidence: 0.8546047475

01:08:42.720 --> 01:08:45.560 And now I can see why that was such

NOTE Confidence: 0.8546047475

01:08:45.560 --> 01:08:47.240 an important question for for me to.

NOTE Confidence: 0.8546047475

01:08:47.240 --> 01:08:48.398 Yeah, I can't.

NOTE Confidence: 0.8546047475

01:08:48.398 --> 01:08:51.640 Yeah, I'm sure the fellows think I'm crazy.

NOTE Confidence: 0.8546047475

01:08:51.640 --> 01:08:52.960 You know, every, you know,

NOTE Confidence: 0.8546047475

01:08:52.960 --> 01:08:54.336 like we are looking at the slides and

NOTE Confidence: 0.8546047475

01:08:54.336 --> 01:08:55.718 said is there blood in the system?

NOTE Confidence: 0.8546047475

01:08:55.720 --> 01:08:58.120 Like why? It's like this question,

NOTE Confidence: 0.8546047475

01:08:58.120 --> 01:08:59.560 so very

NOTE Confidence: 0.592319183333333

01:09:02.000 --> 01:09:02.759 important question. I'm

NOTE Confidence: 0.57902911125

01:09:10.680 --> 01:09:11.560 just so thank you.

NOTE Confidence: 0.57902911125

01:09:11.560 --> 01:09:12.664 Thank you so much. Oh, OK.

NOTE Confidence: 0.57902911125

01:09:12.664 --> 01:09:14.800 OK. Let me, let me just.

NOTE Confidence: 0.57902911125

01:09:14.800 --> 01:09:21.040 Yeah, it's my great honor. OK.

NOTE Confidence: 0.57902911125

01:09:21.040 --> 01:09:22.440 I just want to give this award.

NOTE Confidence: 0.57902911125

01:09:22.440 --> 01:09:24.720 OK, guys, could you stay for two seconds?

NOTE Confidence: 0.57902911125

01:09:24.720 --> 01:09:25.956 I'm going to make it short.

NOTE Confidence: 0.57902911125

01:09:25.960 --> 01:09:28.160 All right? OK, Don't worry.

NOTE Confidence: 0.57902911125

01:09:28.160 --> 01:09:28.570 Don't worry.

NOTE Confidence: 0.57902911125

01:09:28.570 --> 01:09:29.800 I have to do it officially.

NOTE Confidence: 0.57902911125

01:09:29.800 --> 01:09:31.640 All right,

NOTE Confidence: 0.57902911125

01:09:31.640 --> 01:09:33.140 So it's my great pleasure

NOTE Confidence: 0.57902911125

01:09:33.140 --> 01:09:36.198 and honor to present the

NOTE Confidence: 0.57902911125

01:09:36.200 --> 01:09:37.840 Doctor McAllister Actorship

NOTE Confidence: 0.57902911125

01:09:37.840 --> 01:09:39.440 Award to our today's speaker,

NOTE Confidence: 0.692316155

01:09:39.440 --> 01:09:40.500 Doctor Antonescu,

NOTE Confidence: 0.692316155

01:09:40.500 --> 01:09:43.120 on behalf of the entire department.

NOTE Confidence: 0.692316155

01:09:43.120 --> 01:09:46.078 So just briefly about Doctor McAllister.

NOTE Confidence: 0.692316155

01:09:46.080 --> 01:09:48.360 He was a graduate of a Yale College.

NOTE Confidence: 0.692316155

01:09:48.360 --> 01:09:50.040 Then he went to John Hopkins

NOTE Confidence: 0.692316155

01:09:50.040 --> 01:09:52.440 where he graduated from Med school

NOTE Confidence: 0.936480641428571

01:09:52.440 --> 01:09:54.757 and finished his residency there as well,

NOTE Confidence: 0.950707032

01:09:55.280 --> 01:09:58.320 and actually came back here as the chief

NOTE Confidence: 0.950707032

01:09:58.320 --> 01:10:00.012 of surgical pathology for the Memorial

NOTE Confidence: 0.950707032

01:10:00.012 --> 01:10:02.120 unit of the Yale New Haven Hospital

NOTE Confidence: 0.967327533333333

01:10:02.120 --> 01:10:08.360 for 25 years from 1953 to 1978.

NOTE Confidence: 0.967327533333333

01:10:08.360 --> 01:10:10.720 He was regarded as one of the

NOTE Confidence: 0.967327533333333

01:10:10.720 --> 01:10:12.386 best diagnosticians, educator,

NOTE Confidence: 0.967327533333333

01:10:12.386 --> 01:10:14.766 great mentor, advisor,

NOTE Confidence: 0.967327533333333

01:10:14.766 --> 01:10:18.720 and friend to many students, residents,

NOTE Confidence: 0.967327533333333

01:10:18.720 --> 01:10:20.834 and all colleagues in in our hospital

NOTE Confidence: 0.73717107375

01:10:20.840 --> 01:10:23.990 system. So I think you really truly

NOTE Confidence: 0.73717107375

01:10:23.990 --> 01:10:26.560 represent what this lectureship award

NOTE Confidence: 0.823336806923077

01:10:26.560 --> 01:10:28.947 is for and we are very grateful

NOTE Confidence: 0.823336806923077

01:10:28.947 --> 01:10:30.959 that you came to us today.

NOTE Confidence: 0.95659464

01:10:29.080 --> 01:10:30.960 So thank you so much. So

NOTE Confidence: 0.88738695

01:10:30.960 --> 01:10:33.920 this is, it's not big, but it's from heart.