WEBVTT
NOTE duration:"01:20:20"
NOTE language:en-us
NOTE Confidence: 0.836859365789474
00:00:00.000 --> 00:00:02.790 GAIL breast cancer CME series.
NOTE Confidence: 0.836859365789474
00:00:02.790 --> 00:00:06.320 Really excited and fortunate to have
NOTE Confidence: 0.836859365789474
00:00:06.320 --> 00:00:10.220 three phenomenal speakers in our medical
NOTE Confidence: 0.836859365789474
00:00:10.220 --> 00:00:12.855 oncology colleagues in this session.
NOTE Confidence: 0.836859365789474
00:00:12.855 --> 00:00:15.525 We’re going to first start off
NOTE Confidence: 0.836859365789474
00:00:15.525 --> 00:00:17.831 with Doctor Maryam Lustberg,
NOTE Confidence: 0.836859365789474
00:00:17.834 --> 00:00:22.388 who is our incoming breast program director,
NOTE Confidence: 0.836859365789474
00:00:22.390 --> 00:00:23.338 packing her bags,
NOTE Confidence: 0.836859365789474
00:00:23.338 --> 00:00:26.184 and on our way from Ohio State to Yale
NOTE Confidence: 0.836859365789474
00:00:26.184 --> 00:00:28.448 in the in the next couple of weeks,
NOTE Confidence: 0.836859365789474
00:00:28.450 --> 00:00:30.786 she’s going to be talking about a really,
NOTE Confidence: 0.836859365789474
00:00:30.790 --> 00:00:32.934 really interesting area area
NOTE Confidence: 0.836859365789474
00:00:32.934 --> 00:00:35.078 just so much excitement,
NOTE Confidence: 0.836859365789474
00:00:35.080 --> 00:00:38.216 change and controversy on when do we
NOTE Confidence: 0.836859365789474
00:00:38.216 --> 00:00:41.182 deescalate and when do we escalate
NOTE Confidence: 0.836859365789474
00:00:41.182 --> 00:00:43.238 for breast oncology therapies?
NOTE Confidence: 0.836859365789474
00:00:43.240 --> 00:00:44.868 Then we'll go to.
NOTE Confidence: 0.836859365789474
00:00:44.868 --> 00:00:46.089 Doctor Michael D.
NOTE Confidence: 0.836859365789474
00:00:46.090 --> 00:00:48.280 Geovanna is going to be discussing
NOTE Confidence: 0.836859365789474
00:00:48.280 --> 00:00:49.740 recent advances in systemic
NOTE Confidence: 0.836859365789474
00:00:49.799 --> 00:00:51.327 therapy for breast cancer,
NOTE Confidence: 0.836859365789474
00:00:51.330 --> 00:00:53.688 and you know each year whether it’s at ASCO,
NOTE Confidence: 0.836859365789474
00:00:53.690 --> 00:00:55.242 ESMO or San Antonio.
NOTE Confidence: 0.836859365789474
00:00:55.242 --> 00:00:57.182 There’s so many really exciting
NOTE Confidence: 0.836859365789474
00:00:57.190 --> 00:00:59.625 developments in drug therapy that
NOTE Confidence: 0.836859365789474
00:00:59.625 --> 00:01:03.247 come out and it’ll be great to to
NOTE Confidence: 0.836859365789474
00:01:03.247 --> 00:01:05.569 hear about those and certainly last
NOTE Confidence: 0.836859365789474
00:01:05.569 --> 00:01:08.848 but not least is Doctor Andrea Silber
NOTE Confidence: 0.836859365789474
00:01:08.848 --> 00:01:11.310 discussing really super important topic
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of breast cancer epidemiology in 2021.

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Risk factors, and specifically in our vulnerable population.

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We’re going to leave some time at the end to answer any questions, but please feel free to put in questions either into the chat box or to the question and answer box. It will try to answer some of those in real time and then at the end.

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And with that, I’d like to turn the podium over to Doctor Doctor, Maryam,
Lustberg, Deescalation, and escalation of breast cancer therapy. Current status.

Thank you doctor Lester.

Thank you Doctor Gosain and thank you to the participants for joining today.

I’ll start with sharing with you patient perspectives on the escalation of medical oncology therapies.

This was a recent publication where patients and advocates were engaged on what they thought about the escalation of their trials and what were some of their perceived barriers and facilitators. And in these discussions,
it's interesting that up too close to half of patients expressed.
Some unwillingness to participate in a deescalation medical oncology trial and some of it was actually centered around terminology they actually did not like the term deescalation and the most preferred terminology was actually the lowest effective chemotherapy goes.
Listed here are some of the facilitators that patients expressed and a lot of this centered around the hope that deescalated therapy would have less physical side effects, less impact on day-to-day life, and less out of pocket expenses.
The biggest barriers were related to fear that the cancer would come back, or that they would have decision, regret, and so this. These data highlight the importance of good patient and provider communication. Other standards continue to change, and breast cancer, and as we have mounting evidence for better deescalated therapies. Thankfully, due to ongoing clinical trials, I will highlight in the next few slides some of the latest advances in the escalation in medical oncology.
There are so many that I won’t be able to highlight all of them but to recap our goals and medical oncology and the escalation.

The calls aren’t you reduced chemotherapy use while still having the most effective regiment.

Making regiments better tolerated, both acute and long term stamping therapies that are not shown to be effective in reducing costs.

So starting with your positive disease. Most of you are familiar with the Taylor R ask RX perspective study using the 21 gene expression assay or Oncotype DX. Which should that?
Most patients with low required scores. There really was no improvement in outcomes by the addition of chemotherapy to standard of care and open therapy, and this has of course changed our standard of care care and has significantly reduced chemotherapy use in ER positive breast cancer.

Going on to just kind of delving into the data a little bit more, the benefits of D escalation in the younger cohort where a little less clear based on the Taylor Taylor RX study Hall, and I think we can see here in those patients who are 50 or younger.
between the required scores of 16 to 25.

What the data was showing is that there was a lower at that rate do too with chemotherapy when it preceded undergoing therapy.

So is this what is leading to this better outcome and this is continues to be widely debated.

Is it ovarian suppression, effect of chemotherapy, or is it actually the cytotoxic effects of chemotherapy, and several models have been proposed and several perspective studies are.

And to answer this question and different medical oncologists have
very strong opinions about this that I’m sure you’ve heard about. So what about the escalation in ER positive node, positive disease and there is on your study was reported out in the last San Antonio. And as you can see in this schema, those patients with up to three positive nodes with the crime scores of 0 to 25 were randomized to standard care which was chemotherapy. Plus under compare P versus Anderson therapy alone. Those with high recurrence
scores actually came up study.

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Receive standard of care chemotherapy.

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Close to 5000 patients were enrolled.

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And as you can see,

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there was no significant difference in

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invasive disease free survival with

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additional chemotherapy for those

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with requests for between zero to 25.

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After immediate follow up of five years,

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so this is obviously practice changing and.

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A wonderful set of data for us

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to reassure our patients with not

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positive disease with favorable

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features on gentleman profiling.

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But again, similar to the Taylor RX study,

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how we approach the younger cohort of
patients is a little less clear in the study that premenopausal cohort appeared to have significant difference in outcomes when chemotherapy was used. And again whether this was due to the chemotherapy affect or to the effect of ovarian suppression from chemotherapy. These data are not going to answer that specific question. Although, interestingly, when we actually look at the type of endocrine therapy that was used in this study,
only 16% and then they can therapy,
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arm actually had a variance.
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Regression therapy administered
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and only 3% in the chemotherapy
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arm had a variance oppression.
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Straight so so where do we go from here?
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How do we synthesize these data
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and how do we?
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How do we approach that younger
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patients with no positive disease?
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And I think the data are
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continuing to evolve,
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and it’s important to also highlight
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some new data that represented
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also in the last time Junior
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breast meeting by Nadia Harbucks,
Group of the ADAPT Study. And here they use dynamic K 67 monitoring where those who actually had favorable K 67 numbers after three to four weeks of endocrine therapy, regardless of their age, even if they had low nodal disease burden. Actually did fine without chemotherapy. So so. So there’s this kind of adds to the body of data of if we have better biological predictors to be able to better pluck out, patients were at higher risk.
versus lower risk,

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00:08:46.960 --> 00:08:50.140 can be better tailor our therapies
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00:08:50.140 --> 00:08:52.284 in this endocrine responsive
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00:08:52.284 --> 00:08:55.500 group that had this lower post
NOTE Confidence: 0.86163117

00:08:55.599 --> 00:08:58.847 Ki 67 levels after a short pre
NOTE Confidence: 0.86163117

00:08:58.847 --> 00:09:01.188 operative in therapy at the data
NOTE Confidence: 0.86163117

00:09:01.188 --> 00:09:03.400 I just showed you in the previous
NOTE Confidence: 0.86163117

00:09:03.472 --> 00:09:05.788 slide tend to do relatively well.
NOTE Confidence: 0.86163117

00:09:05.790 --> 00:09:06.741 Start a push.
NOTE Confidence: 0.86163117

00:09:06.741 --> 00:09:08.960 I I did a nice job summarizing
NOTE Confidence: 0.86163117

00:09:09.036 --> 00:09:11.328 these data as a discussion in
NOTE Confidence: 0.86163117

00:09:11.328 --> 00:09:12.856 the last thing Antonio,
NOTE Confidence: 0.86163117

00:09:12.860 --> 00:09:14.384 and as I mentioned,
NOTE Confidence: 0.86163117

00:09:14.384 --> 00:09:16.670 these data are continuing to evolve.
NOTE Confidence: 0.876628236470588

00:09:16.670 --> 00:09:19.570 What we know for sure is that we do need
NOTE Confidence: 0.876628236470588

00:09:19.651 --> 00:09:22.556 to take into account on anatomical risk,
use some type of baseline
gene expression profiling,
whether it’s Uncle Type DX,
mammaprint and then whether we should
also use some type of endocrine therapy
response guided measurements I think.
It remains to still be determined
whether this is additive or superior.
I don’t think we can say for sure,
but but the data are continuing to evolve
pretty rapidly in the in this space,
and I’m sure I’m giving this
talk in two years.
Will have additional data to share with
you moving on to her two positive disease,
a huge area of the escalation strategy
has been with the use of another site plans since her to direct the therapies carried cardio toxicity risk.
And as you enter cyclins, there has been continued effort looking at whether we can safely eliminate anthracyclines in her two positive therapies.
So this was one of the first studies that showed that where non after after cycling, taxane plus Carbo regiment less stressed him out was compared to two AC TH. And other numerically the numbers favor that the answer cycling regimen there was actually no statistical difference
in outcomes between the two groups, but certainly higher toxicity with increased cardiac toxicity as well as. Secondary malignancies with anthracite news. But this numerical difference still was unsettling for some oncologists, and I think many of us had continued to use anthracite playing for very high risk. Her two positive disease and inflammatory breast cancer and said that the after cycling news has persisted. But just in the last month the results of the perspective train two study were reported out. This was originally presented.
in the last ASKO, where a more modern regiment including for choosing map was used. And as you can see, there is absolutely no difference between the upper side pain and not after cycling group and no difference in overall survival. So I think additional reassuring data that answer cycling is can be deescalated and in the majority of our for two positive cases, what about staging won her two and positive breast cancer? Obviously you know we used to use multi pomp chemotherapy for these tumors as well,
But what if we use less than the APITI study, set the standard that using single agent taxing question has chosen not followed by.

He requested to not lead to very highly effective outcomes, and it was certainly better tolerated than multi agent chemotherapy so so so it was a very reassuring results that continue to to persist as the data mature.

Can we further deescalate this therapy and this was the attempt trial looking at what if we substituted the taxing percept in ARM with TDM one which tends to be better tolerated in some respects.

I can have a little less neuropathy,
not hair loss, and that time study showed that there was some similar efficacy between the two arms. However, to the surprise of some of the people who are looking at the data, it was not necessarily better tolerated and there was actually higher discontinuation rates in the TV on one arm. Which had led to the next, the escalation trial design account too, which is looking at a shorter to UTM one arm, not a whole year. And this is still in development, but certainly highlights for you another. Further attempt at Deescalating stage one her two positive chemotherapy.
Many of you are familiar with the Compass study and I would like to just highlight that it’s.

It’s a nice combination of both the escalation, an escalation of therapy where D escalating carboplatinum and.

After cycling, but at the same time, given that we know that her two positive disease is at higher risk of CNS relapse for patients with residual disease, there is an opportunity to build on the data of the Katherine study and essentially add a small molecule inhibitor to catch them which has
been shown to have great CNS activity that will show in a little bit. And we always need chemotherapy for her two positive disease. This area is rapidly changing and very exciting. I think there is an opportunity to potentially look at imaging biomarkers to identify patients who are more likely to achieve PCR without chemotherapy with just the use of dual. Her two targeted therapy. So this was recently reported by Rosen Connelly and this approach using PET imaging as a Biomarker for picking the patients.
that can have a deescalated approach
is actually going to be prospectively evaluated in any thoughts that they coming up.
Keep an eye out on another presentation from Nadia hard working Group.
Looking also at chemotherapy for you edge events coming up in the upcoming ASCO.
Moving on to triple negative breast cancer. Certainly, given the more aggressive phenotype of triple negative disease, we’ve been much more cautious about the escalating therapies in triple negative breast cancer,
but I would be remiss if I didn’t mention that there’s a body of work with tumor in simple, implicating lymphocytes as a measure of good prognosis, and this is something that can lead to potentially DFD. Escalated immunotherapy based treatments, or even elimination or chemotherapy. I will highlight one such study. Where stage one, triple negative breast cancers with high tells actually did just as well with or without chemotherapy. Certainly a lot of ongoing, exciting,
effective efforts are going on in the till space before we can safely deescalate therapy and triple negative breast cancer. But they are coming. An exciting abstract and presentation will be presented in this year’s ASCO looking at part inhibitor alone as preoperative neoadjuvant chemotherapy and BRCA one and two tumors. This is without any chemotherapy patients with these types of tumors actually had pretty high on PCR rates, so these are exciting data that will be further represented in
this coming as still coming up.

So we talked a lot about Deescalation,

but obviously.

We need to just kind of touch on

some of the escalation approaches.

Certainly we’ve made a lot of progress,

but we still have over 40,000

individuals with breast cancer

so it goes without saying that our current

strip strategies have significant gaps.

One of the great successes of escalation,

has been the introduction of the CD.

That’s, ER, positive that they have led
00:16:33.586 --> 00:16:35.620 to improved progression free survival.

00:16:35.620 --> 00:16:38.230 Anne continued more and more overall

00:16:38.230 --> 00:16:40.772 survival data are maturing and will

00:16:40.772 --> 00:16:42.950 be presented in this year’s ASCO,

00:16:42.950 --> 00:16:46.072 so you can look at it as

00:16:46.072 --> 00:16:47.410 an escalation approach,

00:16:47.410 --> 00:16:50.250 but also deescalation approach because.

00:16:50.250 --> 00:16:53.010 What the data to show also is at work for

00:16:53.083 --> 00:16:55.820 a long time to initiation of chemotherapy

00:16:55.820 --> 00:16:58.749 in patients with metastatic breast cancer.

00:16:58.750 --> 00:17:00.222 What about escalating argument

00:17:00.222 --> 00:17:02.062 underground therapy in early stage?

00:17:02.070 --> 00:17:03.160 Breast cancer.

00:17:03.160 --> 00:17:06.430 Three studies have been reported out,

00:17:06.430 --> 00:17:09.762 but only monarchy with Emoci club has

00:17:09.762 -->

28
been shown to to to improve outcomes.

I think the data are still maturing and I would say we are not ready
too too too too too too.

Add city 46 inhibitors.

Agile and therapy.

At this point in time.

And when you further inspect the data,

that question has been why?

Why has Monarch even the only positive study, Penelope B and Palace were not an?

There's a very nice presentation coming looking at the composition of tumors that actually
tend to be of the luminal before iety,
00:17:49.570 --> 00:17:51.614 so I think kind of the biology
00:17:51.614 --> 00:17:52.490 of these chambers.
00:17:52.490 --> 00:17:53.990 Whether we can kind of phenotype,
00:17:53.990 --> 00:17:56.020 the tumors that are more likely to
00:17:56.020 --> 00:17:57.929 benefit from agile and taxi for 1600.
00:17:57.930 --> 00:18:00.730 Happy, I think it’s the next step.
00:18:00.730 --> 00:18:03.130 Brain metastases are huge gap and
00:18:03.130 --> 00:18:06.130 we need to do better to catnap
00:18:06.130 --> 00:18:08.130 inverted climb with an important
00:18:08.130 --> 00:18:10.883 study and as the basis of adjutant
00:18:10.883 --> 00:18:13.548 to catnip that I mentioned in the
00:18:13.548 --> 00:18:15.726 in the compass study coming up.
00:18:15.730 --> 00:18:21.018 And I will wrap up with escalation of
00:18:21.018 --> 00:18:23.694 our preoperative chemotherapy regiments
00:18:23.694 --> 00:18:27.050 in triple negative breast cancer.
Certainly we have approval for two checkpoint inhibitors in the metastatic setting, but what about in the pre operative setting? Keynote 522 has been in the news quite a bit recently. The patients and in the intervention arm essentially got everything they had, carbo, attacks all they got after cycling symbolism as well as a year of her Pember Lizum app after after surgery. So the kitchen sink was given and improved PCR rates in the intervention arm improved event free survival.
With these data, Merck went to FDA ODAC and ask for approval of pembrolizumab for pre operative.

Want to get chemotherapy and it was denied.

Why was it denied?

Really?

The Act committee wanted to see results of analysis for an even potentially the final analysis.

Analysis For results actually became available in May,

and they were positive whether they’re going to go back in after time .4 or wait until the final analysis remains to be seen.

But generally I think most of us think
that potential approval is getting close.

I wanted to highlight an important abstract that you will hear about in the next ASCO coming up with our rule of Mob that Jeffrey Nova study, which did not throw the kitchen sink applications. There was no carbo. There wasn’t a year of immunotherapy and they still had very remarkable results. So I think data are mounting that for appropriate. We can select the patients most likely to benefit from immunotherapy. This is something that potentially could help. Our patients.
I'm gonna wrap up with a saying that won't have time to discuss in great length. Our escalation strategies and metastatic breast cancer, but a lot of exciting work is going on in this area and it will be a focus of our future discussions. So in conclusion, it's about right side therapy, not D, escalation or escalation. We have a way to go to achieve this for every individual diagnosed with breast Cancer Research, patient engagement, and collaborations.
00:20:46.014 --> 00:20:47.790 are the path forward.
NOTE Confidence: 0.875422415833334

00:20:47.790 --> 00:20:49.218 Thank you so much for your attention.
NOTE Confidence: 0.856699082307692

00:20:50.720 --> 00:20:53.114 Thank you Doctor Lustberg that was
NOTE Confidence: 0.856699082307692

00:20:53.114 --> 00:20:55.683 really fantastic and I know I have
NOTE Confidence: 0.856699082307692

00:20:55.683 --> 00:20:58.268 a bunch of questions for you at the
NOTE Confidence: 0.856699082307692

00:20:58.268 --> 00:21:00.308 end and hopefully our audience,
NOTE Confidence: 0.856699082307692

00:21:00.310 --> 00:21:02.640 whether they’re locally here in
NOTE Confidence: 0.856699082307692

00:21:02.640 --> 00:21:04.038 Connecticut or internationally,
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00:21:04.040 --> 00:21:06.416 will put some questions in the
NOTE Confidence: 0.856699082307692

00:21:06.416 --> 00:21:09.407 question to answer a chat box for you.
NOTE Confidence: 0.856699082307692

00:21:09.410 --> 00:21:11.036 Next, we’re going to move on
NOTE Confidence: 0.856699082307692

00:21:11.036 --> 00:21:12.120 to Doctor Michael D.
NOTE Confidence: 0.856699082307692

00:21:12.120 --> 00:21:14.980 Geovanna and discussing recent advances
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00:21:20.000 --> 00:21:21.788 Thank you doctor Cubana.
NOTE Confidence: 0.892945618

00:21:56.780 --> 00:21:58.980 Sorry for the technical problems,
thank you for having me and for all of the attendees being on the conference. I will hit some highlights and advances in therapy for each of the types of breast cancer and I'll start with her two positive breast cancer we now have. Eight different targeted drugs for treating her two positive breast cancer, so it’s been wonderful progress in this field and of these eight, there’s actually been five new FDA approvals in just the last two years. Those are the ones that I’ve highlighted in red here, and that does not even include FDA approvals.
00:22:32.381 --> 00:22:34.397 approvals for a biosimilars or
NOTE Confidence: 0.892945618
00:22:34.397 --> 00:22:37.043 subq preparations of some of these.
NOTE Confidence: 0.892945618
00:22:37.050 --> 00:22:39.577 So the first drug I'll mention is
NOTE Confidence: 0.892945618
00:22:39.577 --> 00:22:42.639 TDM one or trastuzumab in fanzine.
NOTE Confidence: 0.892945618
00:22:42.640 --> 00:22:44.272 This was first approved a number
NOTE Confidence: 0.892945618
00:22:44.272 --> 00:22:45.088 of years ago,
NOTE Confidence: 0.892945618
00:22:45.090 --> 00:22:47.130 as per the Amelia trial,
NOTE Confidence: 0.892945618
00:22:47.130 --> 00:22:49.278 showing that in second line therapy
NOTE Confidence: 0.892945618
00:22:49.278 --> 00:22:52.248 for her two positive metastatic disease TDM,
NOTE Confidence: 0.892945618
00:22:52.250 --> 00:22:54.754 one was superior to what was then most
NOTE Confidence: 0.892945618
00:22:54.754 --> 00:22:56.850 commonly used second line therapy of
NOTE Confidence: 0.892945618
00:22:56.850 --> 00:22:59.505 lapetina been capeside of been with improved
NOTE Confidence: 0.892945618
00:22:59.505 --> 00:23:01.970 progression free survival response rate,
NOTE Confidence: 0.892945618
00:23:01.970 --> 00:23:03.110 and overall survival,
NOTE Confidence: 0.892945618
00:23:03.110 --> 00:23:05.010 as well as less toxicity,
NOTE Confidence: 0.892945618
00:23:05.010 --> 00:23:07.544 and this became the standard second line.
B for metastatic disease at that time, bumping the patent Open Cape, cited being to third line and then the other really important.

Recent results using this drug were the results of the Catherine trial that looked at this drug in the post neoadjuvant setting in patients who had been treated in the neoadjuvant setting with trust using map based therapy and those who did not achieve a pathological complete response were randomized to standard of care which was to complete a year of the trustees and map.
Or switching to TDM one instead, and there was quite remarkable results in terms of switching with almost a 50% decrease in disease free survival and freedom from distant response and overall survival looking promising as well. Just in the past month, published online is an update of the Catherine trial with subgroup analysis and I'll just mention a couple of the important follow line subgroup analysis from this trial. One is that the improvement with the switch to TDM one came both in patients who were treated with an for cycling as well as those who were
not treated with anthracyclines.

It came even in patients with the very highest risk disease categories.

The improvement was seen regardless of hormone receptor status, positive or negative.

and in this trial, about 70 patients entered initially having clinical stage one disease and still had residual disease.

Those who got switched to TDM seemed to have a benefit,
although it’s small numbers and so we can’t really pull statistics. But there were six disease free survival events in those that continued trastuzumab, and none in the arm that was switched to TDM. One and of these events, three of them were non CNS distant recurrences, two or CNS recurrences, and one was a contralateral breast cancer. So although small numbers it gives us pause to think about even using this strategy in patients who present with clinical stage one disease, and that’s a controversial area whether to use this strategy or not.
But the Catherine trial did set a new paradigm for treating her two positive disease, which is in general we could debate stage one disease, but in general patients with her two positive disease, now we think should get neoadjuvant therapy, because if they get a non path CR we can improve their long term outcome by switching to TDM one and this paradigm. Now we also apply to the triple negative subset because the create X trial showed that in triple negative patients who get neoadjuvant chemo.
Therapy.

Those who do not get a path CR and we now have a worse outcome can have their outcome improved by the use of edge of in Cape cited mean.

So I think for both her two positive and triple negative disease we should always think about neoadjuvant therapy. For these reasons, because in the post neoadjuvant setting we can improve long term outcome by intervening.

The next drug I wanted to talk about is to cotton. If so, this is a her two
tyrosine kinase inhibitor.

We now have three.

Her two tyrosine kinase inhibitors to choose from and low to captain.

If unlike the other two is highly selective just for her two without hitting the other members of the her two receptor family.

Let Patton in has an Nurettin. You can see here that there's no activity against the EGF receptor.

Let Patton in has an Nurettin. They both have equivalent activity against the EGF receptor interaction.

If actually inhibits all of the receptors in this family.
So the HER2 climb trial looked at the introduction of Takata nib in the metastatic setting for patients who had prior first line therapy with trastuzumab and second line therapy with TDM one. The really important part of this trial as Merriam has shown you is that this trial welcomed patients with brain metastases and not only treated brain metastases but even untreated or progressing brain.

Test ices because the earlier phase trials with this drug showed good activity in the CNS, and so patients in this trial were randomized to therapy with trastuzumab in the metastatic setting for patients who had prior first line therapy with trastuzumab and second line therapy with TDM one. The really important part of this trial as Merriam has shown you is that this trial welcomed patients with brain metastases and not only treated brain metastases but even untreated or progressing brain.
00:27:50.297 --> 00:27:54.210 capeside of being with or without to continu.

00:27:54.210 --> 00:27:56.142 And in this trial,

00:27:59.139 --> 00:28:01.110 almost half of the patients entered

00:28:01.110 --> 00:28:03.100 About 60% of them were

00:28:03.100 --> 00:28:04.294 treated brain metastases,

00:28:04.300 --> 00:28:07.120 but the rest were untreated

00:28:07.120 --> 00:28:09.376 or treated but progressing.

00:28:09.380 --> 00:28:12.345 And the overall population showed

00:28:12.345 --> 00:28:14.717 an improvement in progression

00:28:14.717 --> 00:28:16.996 free survival of 2.2 months.

00:28:16.996 --> 00:28:18.586 An improvement in overall survival

00:28:18.586 --> 00:28:20.369 of four and a half months.

00:28:20.370 --> 00:28:22.603 So this was an important trial showing

00:28:22.603 --> 00:28:24.589 an improvement in overall survival.
And the response rate nearly doubled from 23% to 41%. 

In patients with brain metastases who entered the trial, they achieved the same benefit of a 2.2% month improvement in progression free survival. 

Interestingly, the objective response in the brain metastases of patients who had active brain metastases by resist criteria were 47% versus 20% because we know Cape cited being also does cross the blood brain barrier. So remarkably, almost half of patients had objective response by recist criteria in their brain metastases.
that were active brain metastases.

So this drug is quite active.

In the CNS and this slide shows

the CNS progression,

free survival of the patients

with brain metastases,

which improved by nearly six

months from 4.2 months.

Median progression free survival to

almost 10 months and at one year 40% of the patients had not had brain

progression in the experimental arm,

whereas none of the patients in the

standard arm still are without progression.

And this show is in the
patients with brain metastases.

The overall survival, which was improved by six months from 12 months to 18 months, so really important results in the CNS.

And because this is such a active drug and with these good results, it’s now being tested in the second line in the her two climb 02 trial which is looking at second line T DM one versus T DM 1 + 2 cotton.

The next drug I want to talk about is trastuzumab. Dear XD can this is another antibody drug conjugate like TDM.
00:30:20.795 --> 00:30:22.705 compares it to TDM one TDM.
00:30:22.705 --> 00:30:24.630 One has the payload being a tubulin inhibitor.
00:30:24.630 --> 00:30:25.785 This drug has a topoisomerase one inhibitor and this drug also has what’s called a stand by a bystander effect because when the targeted drug when the payload is cleared from the antibody, it actually can diffuse. Through the membrane of the cell.
00:30:35.264 --> 00:30:37.404 targeted drug when the payload is cleared from the antibody, it actually can diffuse. Through the membrane of the cell.
00:30:45.722 --> 00:30:47.890 the her two expression in a tumor, you can get killing of cells that perhaps have lower levels of her two.
By this bystander effect. And in phase one trials, this drug was extremely active in her two positive breast cancer and her two positive gastric cancer as well as even breast cancers that had lower levels of her two. Perhaps because of this bystander effect in cells that had heterogeneous levels of her two expression and in phase one trials overall 86% of subjects had at least some tumor shrinkage. And so the trial that got this drug, FDA approved was the destiny of 1 trial, which was a single arm phase, two trial and patients in the
metastatic setting had to have prior trastuzumab an prior TDM one and 2/3 of them also had prior per Susan Mab. Almost all of them had visceral metastases, and this was a fairly late line trial with the median number of lines of prior therapy being 6. And despite this being a Lateline And despite this being a Lateline trial once again, the activity was really dramatic with almost all patients having at least some shrinkage of their tumor by recist criteria, a 60% confirmed objective response rate, a Disease Control rate of 97%,
an 11 out of 168 patients with complete
responses in their metastatic disease.
So an amazingly active drug,
even in a very late line setting.
These were really durable responses
as well with their median duration
of response of almost 15 months
and overall survival at one year
still being 86% despite being
six line therapy on average.
The one huge caveat with this drug
is to watch out for the side effect
of interstitial lung disease,
or pneumonitis,
which occur in almost 14% of patients and in two point 2% of patients. It was actually a fatal, so the one caveat with this drug is to be highly vision vigilant for any respiratory symptoms that could indicate pneumonitis. And because this drug is so active, it’s being tested in a number of other settings now. We have accelerated approval based on the single ARM trial that I just showed you the destiny O2 trial is the definitive trial. Comparing this drug to treatment of
00:33:20.392 --> 00:33:22.550 physicians choice in a phase three setting.
NOTE Confidence: 0.819517523
00:33:22.550 --> 00:33:24.140 With these options,
NOTE Confidence: 0.819517523
00:33:24.140 --> 00:33:26.790 the Destiny 03 is comparing
NOTE Confidence: 0.819517523
00:33:26.790 --> 00:33:29.404 this after first line therapy
NOTE Confidence: 0.819517523
00:33:29.404 --> 00:33:32.326 head to head against TDM one.
NOTE Confidence: 0.819517523
00:33:32.330 --> 00:33:33.845 So it’s just using web
NOTE Confidence: 0.819517523
00:33:33.845 --> 00:33:35.057 touristy can versus TDM.
NOTE Confidence: 0.8611110825
00:33:35.060 --> 00:33:36.308 One in second line.
NOTE Confidence: 0.8611110825
00:33:36.308 --> 00:33:38.573 The Destiny 04 trial is looking at
NOTE Confidence: 0.8611110825
00:33:38.573 --> 00:33:40.553 her two low breast cancer patients
NOTE Confidence: 0.8611110825
00:33:40.553 --> 00:33:42.649 because I showed you in phase one.
NOTE Confidence: 0.8611110825
00:33:42.650 --> 00:33:44.830 Trials responses in those patients.
NOTE Confidence: 0.8611110825
00:33:44.830 --> 00:33:48.286 So this is just using map touristy can
NOTE Confidence: 0.8611110825
00:33:48.286 --> 00:33:50.799 versus chemotherapy of physicians choice,
NOTE Confidence: 0.8611110825
00:33:50.800 --> 00:33:52.900 and in Destiny 05 it’s actually
NOTE Confidence: 0.8611110825
00:33:52.900 --> 00:33:55.433 being compared to TDM one in the
NOTE Confidence: 0.8611110825
00:33:55.433 --> 00:33:57.208 in the post neoadjuvant setting.
NOTE Confidence: 0.8611110825
00:33:57.210 --> 00:33:58.884 As per the Catherine trial where
NOTE Confidence: 0.8611110825
00:33:58.884 --> 00:34:00.397 patients who get into management
NOTE Confidence: 0.8611110825
00:34:00.397 --> 00:34:02.102 therapy and have residual disease
NOTE Confidence: 0.8611110825
00:34:02.102 --> 00:34:04.026 will be randomized to TDM one
NOTE Confidence: 0.8611110825
00:34:04.026 --> 00:34:05.538 or try D'souza Mabdi rixty cat.
NOTE Confidence: 0.8611110825
00:34:05.540 --> 00:34:08.504 So being tested in all of
NOTE Confidence: 0.8611110825
00:34:08.504 --> 00:34:09.986 these different settings.
NOTE Confidence: 0.8611110825
00:34:09.990 --> 00:34:13.161 Another her two targeting drug that was
NOTE Confidence: 0.8611110825
00:34:13.161 --> 00:34:15.769 just recently approved is margetuximab,
NOTE Confidence: 0.8611110825
00:34:15.770 --> 00:34:19.417 and this is actually a derivative of
NOTE Confidence: 0.8611110825
00:34:19.417 --> 00:34:23.134 her of trastuzumab that has the FC
NOTE Confidence: 0.8611110825
00:34:23.134 --> 00:34:25.584 Gamma portion replaced by another
NOTE Confidence: 0.8611110825
00:34:25.584 --> 00:34:28.296 FC Gamma alteration that has a
NOTE Confidence: 0.8611110825
00:34:28.296 --> 00:34:30.644 higher affinity for activating FC
NOTE Confidence: 0.8611110825
Gamma receptor and a lower affinity for inhibitory FC Gamma receptor. This is based on the fact that we know trastuzumab is not only targeted signal transduction, but it also recruit the immune system. That was thought by making transducer maps more able to actively recruit the immune system. It may give it enhanced activity, so this was tested in the Sophia trial, which was a phase three trial of chemotherapy versus margetuximab plus chemotherapy in later line therapy.
and there was a fairly small positive result.

As you can see here in progression.

Free survival improving by about two months,

so not a huge result,

but enough to get this drug FDA approved.

So it’s now part of our armamentarium

and the final her two targeting

drug recently approved is narrative,

which was tested in the Nala trial and

this was a trial of Neurontin and Capeside,

it being versus LA patented capeside

of being in patients who had at

least two prior therapies for their

metastatic her two positive disease

and the new rotten if compared to

NOTE Confidence: 0.8611110825

NOTE Confidence: 0.8611110825

NOTE Confidence: 0.8611110825

NOTE Confidence: 0.8611110825

NOTE Confidence: 0.8611110825

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NOTE Confidence: 0.8611110825

NOTE Confidence: 0.8611110825
La Pata nib did have an improved progression free survival. Overall response, and perhaps a little bit in overall survival. None of these patients had prior to continue, and so in the era now of using two continents, it will be difficult to know if there really is a place for new routine in metastatic. Her two positive disease. And so, as I showed you, we now have many drugs to choose from. An I oppose this as a reasonable order sequence of therapy that we can use for her two positive
NOTE Confidence: 0.8611110825
00:36:14.231 --> 00:36:15.840 metastatic disease patients.
NOTE Confidence: 0.8611110825
00:36:15.840 --> 00:36:17.140 In the first line,
NOTE Confidence: 0.8611110825
00:36:17.140 --> 00:36:18.440 therapy should have pertuzumab,
NOTE Confidence: 0.8611110825
00:36:18.440 --> 00:36:18.950 trastuzumab,
NOTE Confidence: 0.8611110825
00:36:18.950 --> 00:36:22.010 and taxane because of the remarkable
NOTE Confidence: 0.8611110825
00:36:22.010 --> 00:36:23.980 overall survival benefit seen
NOTE Confidence: 0.8611110825
00:36:23.980 --> 00:36:25.815 in the Cleopatra trial TDM,
NOTE Confidence: 0.8611110825
00:36:25.820 --> 00:36:28.039 one is still considered the second line
NOTE Confidence: 0.8611110825
00:36:28.039 --> 00:36:30.173 therapy as per the Amelia trial and
NOTE Confidence: 0.8611110825
00:36:30.173 --> 00:36:32.689 we now can consider a third line therapy.
NOTE Confidence: 0.8611110825
00:36:32.690 --> 00:36:34.622 Being just do some AB capeside it
NOTE Confidence: 0.8611110825
00:36:34.622 --> 00:36:36.716 being into cotton if since we have
NOTE Confidence: 0.8611110825
00:36:36.716 --> 00:36:38.231 seen an improvement in overall
NOTE Confidence: 0.8611110825
00:36:38.231 --> 00:36:39.913 survival in the her two climb
NOTE Confidence: 0.8611110825
00:36:39.913 --> 00:36:41.238 study and this is especially
NOTE Confidence: 0.837415576470588
of course attractive for patients who may already have brain metastases from their her two positive disease and then perhaps enforced line therapy, we could use a trust. Susan abjure Exede can, although this may ultimately compete with the her two climb regimen for third line therapy and then in late line therapy, perhaps we might want to use margetuximab for the slight edge it might have over therapy using map in the Wave line therapy. Moving on to triple negative breast cancer. We now have five or six targeted drugs that are approved for triple negative breast cancer.
We have two park inhibitors are lab rib and no tell is operated as Merriam showed you, we now have two checkpoint inhibitors, anti PDL, one drugs at Season 11 map and Pember Lism AB.

We have an antibody drug conjugate and I kind of include carboplatin as a targeted therapy for triple negative breast cancer because if you remember from the TNT trial, particularly patients who had germline BRCA. Mutations. They had a remarkable high response rate to single agent carboplatin about a 60% response rate for germline
carriers and that is applies to not only triple negative disease but any germ line BRCA mutation carriers.

So in terms of immunotherapy, we have two positive results in the metastatic setting. I think the results aren’t as enormously impressive as they are in some other types of cancer, like Melanoma or lung cancer, but they are positive results.

atisa lism AB versus placebo was added to nab paclitaxel, an in the PDL 1 positive patients.
There was a two to three month improvement in progression Free Survival, a significant improvement in response rate, and if this holds up, but perhaps an impressive improvement in overall survival, the Keynote 355 was a similar trial using Pember Lizum app, and the chemotherapy might have been nap after taxol or path that axle or gem carbo in first line. Setting again and in those with the CPS score greater than 10%, an improvement in progression free survival of almost four months.
And so we now have either of these drugs atisa lism AB or embolism AB for approval for PD L1 positive patients by the appropriate assay I might add in the first line setting with these chemotherapy agents there was another trial looking at a teasel is a map with paclitaxel, this was a flat out negative trial with no improvement in progression. the impassioned 131 and interesting Lee. This was a flat out negative trial with no improvement in progression. Free survival, minimal improvement in response rate and no improvement in overall survival. And the only difference between this and the 130 child was a nap attack,
00:39:38.420 --> 00:39:39.701 slow versus paclitaxel.
00:39:39.701 --> 00:39:42.263 So we don’t really understand why
00:39:42.263 --> 00:39:44.048 is this one negative?
00:39:44.050 --> 00:39:46.416 Is there a difference in the patient
00:39:46.416 --> 00:39:48.040 population that was enrolled?
00:39:48.040 --> 00:39:49.391 It’s hard to see that on the
00:39:49.391 --> 00:39:50.520 surface it was first line.
00:39:50.520 --> 00:39:51.888 Triple negative patients.
00:39:51.888 --> 00:39:53.712 Is there truly some
00:39:53.712 --> 00:39:55.080 magical difference between
00:39:55.148 --> 00:39:57.050 Napa Taxol and path that axle?
00:39:57.050 --> 00:39:58.286 I suspect nabbed paclitaxel
00:40:00.140 --> 00:40:01.814 but is it really so much of an edge
00:40:01.814 --> 00:40:03.446 that it would make this difference?
Or is it just chance because the results with immunotherapy are not tremendously impressive? And is it possible that some private trials might look positive? Some might look at negative? We don’t know the answer, but for now, if we use atezolizumab, we should use it with nab Papa Taxol and not paclitaxel. What about the use of immunotherapy in early stages of triple negative breast cancer? Miriam mentioned this child, the keynote 522 trial and the first interim analysis was published in the New England Journal,
at which point 600 patients were enrolled and it showed an impressive difference in pathological complete response rate for the addition of Pember Lism AB to the kitchen sink, as Merriam explained with a 14% improvement in pathologic complete response rate. And we do know in this disease that pathologic complete response is a very strong predictor of long term outcome. And we know that the FDA in the past has said that they would consider drug approvals based on improvement in pathologic complete response for this type of disease.
This is not yet approved,

and as Marion mentioned in February,

the pharmaceutical company actually

asked the FDA to consider accelerated

approval based on these early results.

As she mentioned,

there was an ODAC meeting in February

and the Odacon the FDA decided at that

time not yet to grant accelerated approval.

Wanting further follow up and more

endpoints that were still premature.

In terms of event free survival

and overall survival,

and in fact at the time of this

meeting the trial was up to over

1100 patients and the path CR rate
delta was a little bit different than it was with the 1st 600 patients. There was a 7% difference at that time. The P value was still quite good, but because the statistics were allowing multiple analysis, there was very high stringency for what the P value would need to be an it actually didn’t hit it. Yet at this point, and Merriam showed you that there is ongoing analysis and we might hear about this soon.
But meanwhile we have to decide to do what to do with our triple negative patients who present, especially if there are high risk patients and I will tell you that for some young, very high risk multiple node positive patients who I have encountered since the publication of the first data. I have used this regimen even though it is not FDA approved and we still don’t know the long term outcome. I’ve had insurance companies agree to improve this approved. The immunotherapy on the basis of what data we have so far.
It's not clear that we should all be doing this for every patient, but we have to discuss with the patient sitting before us. Whether we do this or not. And I will say that I've done it with a couple of patients so far. We now have an antibody drug conjugate for treating metastatic triple negative breast cancer. That's quite a good active drug. It's sacituzumab gobatti can the antigen is trope too, which is present on many breast cancers and the active moiety is a topa one inhibitor.
It’s actually SN 38, which is the business molecule, the active metabolite of Irene Attican. Ann, this was tested in the ascent trial versus treatment of chemotherapy of physicians choice, and this antibody, drug conjugate, was quite active with an improvement in progression free survival. A six month improvement in overall survival and of substantial improvement in the response rate. So this was approved for triple negative metastatic breast cancer. After two or more prior chemotherapies, and it’s actually now being tested.
in hormone receptor positive as well.

We are participating in that trial and I've had patients with hormone receptor positive disease in the trial. Had good responses as well.

We often think of an antibody drug conjugate as a much more tolerable therapy than a naked chemotherapy, but actually I have to say this particular drug does have toxicities that are on par with chemotherapy, including neutropenia, nausea and vomiting, diarrhea, abdominal symptoms, complete alopecia, low blood counts.
decreased appetite, and rash.

So although it’s a very active drug in a good drug, it doesn’t seem in terms of toxicity.

Would be a free ride compared to chemotherapy.

And then finally, in the last few minutes I’ll just a few words about hormone receptor positive disease.

We now have five biological agents that we can combine with our endocrine therapies.

The three CDK 46 inhibitors everolimus and alkalis sub alkalis, is active only in those tumors that have a PR 3 kinase mutation,
which is about 40% of metastatic hormone receptor positive breast cancer in the solar one trial that was published almost two years ago now, which was a randomized phase three looking at full strength, with or without alkalis. If there was a significant improvement, progression free survival and response rate. So this is now considered standard therapy for patients in combination with focus strength to have a PR 3 kinase mutation. This can have some substantial toxicity as well, including diarrhea.
Hyperglycemia that requires aggressive management, an erracht as well that can be prevented by using an antihistamine. We have the three CDK 46 inhibitors which have remarkable activity in the metastatic setting in first line, and says the second line nearly doubling response rate and nearly doubling progression free survival and in the metastatic setting they really all seem to have nearly identical activity. There’s maybe a slight edge for abemaciclib in that it has a little bit of single agent activity, which the other two seem not to,
and perhaps some potential to cross the CNS. Blood brain barrier and some CNS activity.

But for the most part in the metastatic setting they seem to be extremely active and equally active. So as Miriam mentioned, the big question is will these be able to be moved into the early stage setting and she mentioned that we have one positive trial, the monarchy trial, which looked at very high risk patients with four or more nodes positive or one to three nodes positive and other high risk features and enrolled.
Over 5000 patients and looked at the use of abemaciclib for two years with the edge of an enderman therapy versus not at this at early. At about a year and a half follow up as seems to be a positive trial so far in terms of reduction in distant relapse. Free survival. But as far as Marion mentioned, what we have looking at us in the face is two other early stage trials with palbociclib that seemed to be negative and so is there really a difference between abemaciclib in pablum? Albo psych lab? Is there a difference in the
Is there some other explanation and we have an ongoing trial with Ribociclib which hasn’t reported yet. Now the interesting thing is, these results are reported at different time points and there were different treatment durations. So in the Penelope B trial, which looked at patients who had residual disease after neoadjuvant therapy, this analysis is out at 43 months. And if you looked at the two year mark, there was a 4% difference in favor of the palbociclib.
but that went down at three years,

and at the four year follow-up Timepoint,

essentially no difference between the arms.

When we look at the monarchy

with abemaciclib,

which appears to be a positive trial so far.

The treatment duration is 2 years,

but the follow up so far is

only 19 months and so it may be

that we see some effect of these

while the therapy is going on.

But once the therapy is completed over time,

the difference between the

two arms might go away.

So we need more study,

more follow up and we need to
00:48:31.931 --> 00:48:33.870 see the results of the Natalie trial which is using recycled for three years in high risk disease.

00:48:35.910 --> 00:48:38.018 That’s my last slide.

00:48:40.850 --> 00:48:41.898 One thing I wanted to say once again getting back to dealing with the person to sitting in front of you question arises.

00:48:43.688 --> 00:48:45.351 It’s not FDA approved.

00:48:47.050 --> 00:48:49.794 Should we act on this data with abemaciclib?

00:48:49.800 --> 00:48:51.172 We really don’t know if this is going to hold up in the long term, but I will tell you that I have brought this up sometimes with patients.
12 nodes positive and was starting her regimen therapy and I discussed with her whether to add emoti clip because it’s enormously high risk to have. Well, no, it’s positive and I prescribed with emoti clip for this woman. It would be covered by her insurance company. Again, we don’t know if we should be doing this. We sometimes act early. We may be giving therapy that has toxicity that in the long run doesn’t help, but I consider it in very high risk patients based on this data. So I stuck my neck out in a couple of areas there, but that’s my last slide and I’ll
00:49:36.451 --> 00:49:38.189 be happy to take any questions

00:49:38.189 --> 00:49:40.025 now or at the discussion time.

00:49:42.090 --> 00:49:43.746 Thank you Doctor Digiovanni,

00:49:43.746 --> 00:49:46.653 that was fantastic and there are questions

00:49:46.653 --> 00:49:49.124 that are trickling in and they both

00:49:49.124 --> 00:49:51.799 in the chat in question and answer.

00:49:51.800 --> 00:49:54.690 Certainly not last and least,

00:49:54.690 --> 00:50:00.980 but we have Professor Andreas Silvers.

00:49:55.800 --> 00:49:59.620 Gonna really give us a exciting

00:49:59.620 --> 00:50:06.200 update on breast cancer

00:50:01.044 --> 00:50:02.900 epidemiology for risk factors,

00:50:02.900 --> 00:50:06.200 especially in our vulnerable populations so.

00:50:06.200 --> 00:50:07.169 Thank you, Andrea.

00:50:10.159 --> 00:50:12.400 You’re on mute still.
thank you for that introduction.

It’s my pleasure to present today and I will start out by describing the topography of breast cancer in 2021 and I reviewed current epidemiology and how we got here.

Sure, but it’s not advancing.

And as you can see on this slide, breast cancer in the United States is extremely common. It’s not the most common cause of death that is lung cancer.

You can compare the results of deaths that are anticipated in 2021.
for lung cancer, which is 100 and
It's a very common tumor in elderly women.
7% of all breast cancers will appear in women over the age of 70.
Just want to highlight a little bit that breast cancer is heterogeneous and there are multiple subtypes there. Subtypes within the subtypes such as Lumenal A and luminal B.
The significance of this is going to become clear when we talk about etiology and prevention and also keep in mind that breast cancer subtypes.
00:52:07.966 --> 00:52:10.871 actually can change in up to 25% of patients when they metastasize.
NOTE Confidence: 0.853695164
00:52:10.871 --> 00:52:13.976 Their breast cancer has changed subtype and the most common change that one sees is going from luminal,
NOTE Confidence: 0.853695164
00:52:13.980 --> 00:52:16.195 a two triple negative.
NOTE Confidence: 0.870443961111111
00:52:16.195 --> 00:52:21.713 And here’s the breakdown of breast cancer by subtype,
NOTE Confidence: 0.870443961111111
00:52:21.720 --> 00:52:23.500 hormone receptor positive breast cancer,
NOTE Confidence: 0.870443961111111
00:52:23.500 --> 00:52:25.880 and you can see that luminal a specifically,
NOTE Confidence: 0.870443961111111
00:52:25.880 --> 00:52:28.245 but hormone receptor positive breast cancer,
NOTE Confidence: 0.870443961111111
00:52:28.245 --> 00:52:30.137 is the most common type,
NOTE Confidence: 0.870443961111111
00:52:30.140 --> 00:52:34.388 regardless of age or race,
NOTE Confidence: 0.870443961111111
00:52:34.390 --> 00:52:37.828 and it’s six times more common than the triple negative breast cancer.
NOTE Confidence: 0.870443961111111
00:52:37.830 --> 00:52:42.900 Let’s move ahead and talk about risk factors.
NOTE Confidence: 0.87256719625
00:52:42.900 --> 00:52:50.320 I think from my previous slide,
00:52:56.360 --> 00:52:59.897 you can tell one of the risk factors is

00:52:59.897 --> 00:53:03.349 being female and another is being older,

00:53:03.350 --> 00:53:07.109 but those are non modifiable risk factors.

00:53:07.110 --> 00:53:10.362 Personal history of invasive or non

00:53:10.362 --> 00:53:13.849 invasive breast cancer predisposes to both

00:53:13.849 --> 00:53:16.325 contralateral and ipsilateral primaries.

00:53:16.330 --> 00:53:19.940 Benign breast disease with atypia.

00:53:19.940 --> 00:53:22.364 Family history and this is regardless

00:53:22.364 --> 00:53:24.511 of whether there’s a mutation

00:53:24.511 --> 00:53:26.776 for women with family history.

00:53:26.780 --> 00:53:32.107 Only 5 to 6% have identifiable mutations,

00:53:32.110 --> 00:53:34.840 and when you look at known

00:53:34.840 --> 00:53:37.074 mutations that comprises less than

00:53:37.074 --> 00:53:39.100 10% of all breast cancers.

00:53:39.100 --> 00:53:42.103 Breast density I will get into that

NOTE Confidence: 0.87256719625

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a little more later in the talk, but let’s talk about increased exposure to estrogen throughout the female lifetime, early menses. Menses now starts below the age of 11 in the United States. This was not true. A generation ago, delayed childbearing or no lipperhey late menopause. Menopause is occurring later now, it said. Between 50 and 51, that was not true. A generation ago, exogenous estrogen that has been given to women to help them through the menopause and that estrogen is
more of a risk when it’s combined with progestin and previous studies, it looks like the estrogen that’s given as a single agent to women who have had hysterectomies is not as risky and transgender women. Due to increased exposure of estrogen. Moving along to radiation, that’s radiation therapy, which is given to children or mantle radiation for Hodgkin’s disease. Radiation therapy is the highest risk when it’s given during adolescence, between age 10 to. When the breast is most
actively proliferating,
but there’s also an increased risk from radiation exposure,
either accidental, such as Chernobyl, or intentional such as warfare, and this also was shown to be most active for the adolescent girls and wasn’t as seen to be a risk factor after the age of 45. Drinking alcohol. As little as one alcoholic beverage per day in several studies has shown a slightly increased risk of breast cancer and then obesity. Just wanted to highlight breast density.
You can see here that there are some women who have extremely dense breasts, and for those women at level 4 that increases the odds ratio 6 fold. So that’s a very very important risk factor. Greater parity was associated with a lower risk of hormone receptor positive breast cancer, but it is an increased risk for...
triple negative breast cancer.
Breastfeeding can cut the risk for triple negative breast cancer by 50%.
Well, that's not true for receptor positive breast cancer.
So these two women on the cover of Good Housekeeping show. How are modern women more likely to have risk factors for hormone receptor positive breast cancer by delaying childbearing having fewer children and those things increase the risk. As a matter of fact, breast cancer is more common in areas like the I-95 corridor, an in Marin County,
not due to environment,
but due to cluster of risk factor for the type of women that live in these areas,
and modern women are taller.
Bigger also are more likely to be diverse in this country,
and these are reasons to increase the risk for breast cancer.
Let’s move ahead to looking at the rest of the world.
Global incidence is increasing.
And you can see that breast cancer is different in different types of countries.
In highly developed countries,
most women get breast cancer when they’re
older and less developed countries.

That's the reverse, and it's thought to have to do with the wealthier countries having higher rates of obesity.

But as you can imagine, the case fatality rate is lowest in highly developed countries, and this is even true in our own country.

When you look at the case fatality rate in a state like Connecticut, which has the second highest rate of breast cancer, the case fatality rate is the lowest Ann.

You compare that to some of our Southern states that may have lower incidence.
but higher case fatality rates, and this may have to do with insurance in these various states in our country. When we look at the nationality, the United States doesn’t even make the top 15. Belgium is the number one. But when we look at Survival Worldwide, you can see a very different story. The five year survival in the United States is 95%. Compare that to what you see in South Africa and Mongolia. And survival rate in the United States does vary by subtype. The hormone receptor positive breast cancers.
Looking at the most recent SEER data have an excellent prognosis and even the five year survival for the triple negatives when they are localized have a better prognosis than you see in other countries.

But survival rates don’t really tell the whole story. First of all, women being diagnosed with breast cancer today may have better outcomes. We’ll see in the most recent SEER data, but diagnostics and treatments continue to improve overtime, and there’s good access in highly developed countries and highly developed cities.
but these numbers don’t take everything into account. First of all, survival rates for hormone receptor positive breast cancer. 50% of the patients that are going to relapse will relapse after five years. So the five year survival rate kind of skews things and some of the survival rates, although they may be due to stage, they may really have to do with overall health response, an access to treatment so different subtypes may predict timing of relapse. But there are so many other things I’m
going to be a little controversial here and say geopolitics can determine outcome. Look at a situation in Puerto Rico during Hurricane Maria where it really decimated their health system. That does change screening. It does change treatment and it will change outcome. Let’s take geopolitical changes in our own country. For the pandemic may have changed patterns of screening change patterns. patterns of treatment and I hate to say it women have been known to increase their alcohol intake during the pandemic.
Are we going to see changes in epidemiology due to the pandemic? So who are the most vulnerable that we see now? Black women, particularly younger women. They are more likely to be diagnosed with triple negative breast cancer and more likely to be diagnosed. Diagnosed at a younger age. Blacks are more likely to die of breast cancer at any age. They presented a later stage, but their insurance status is worse twice as likely to be uninsured. Well,
immigrants from less developed nations we talked about what you see with global breast cancer and I'll talk a little bit about sexual minorities as well.

The NCI talks about risks in terms of cancer health disparities, and you can see it. Women who are African American have a higher risk of dying from breast cancer, but let's get into the various groups that are more likely to suffer cancer health disparities, and I think I'm going to describe for you how many of these apply to breast cancer.
We already talked about women of color and breast cancer outcome, and women of different ancestry or recent immigrants made. We also have a higher risk of both getting breast cancer or particularly their outcomes. Individuals of lower socioeconomic status have decreased. Access to screening, decreased access to treatment. An also may have associated health problems that make treatment problematic. Well, individuals with disabilities are less likely to get screened, and that’s been looked at.
At mammographic screening in wheelchair population.

Again, individuals who have poor insurance coverage are less likely to get the best possible care.

We talked about the rural areas in the United States in the South that those patients have worse insurance coverage and are less likely to have access to care.

LGBT women are less likely to be screened and also have some of the estrogen during lifetime risk factors that would increase their risk.
We talked about immigrants, refugees, and the elderly who are more likely to get breast cancer. So breast cancer rates are declining in our country and this is due to diagnostic advances and some of the things that Mariam and Mike talked about. But risk factors have been identified and they really vary depending on the subtype. There are certain regions in the world, but in our own country that are increased risk for adverse outcomes and special populations. In the United States are disproportionately
vulnerable to adverse outcomes.

It will require an enormous collaborative effort not only on the part of the medical community, but on the part of all citizens to transform cancer care for all people, regardless of their race, ethnicity, immigration status, age, gender, sexual orientation or socioeconomic status, one of the biggest risk factors is the communities that people grew up in.

And thank you for your attention, and I always like to mention those I seen with breast cancer or
have been affected by the disease.

Thank you doctor.

So that was fantastic and you know, thank you for all three of our speakers for you know, three really phenomenal presentations that you know show the breadth of the care and services that we provide here at Yale. But more importantly, you know the the options and therapies that are available to women and some of the challenges that we have moving forward in terms of not only screening but...
treatment of our more vulnerable.

Populations there were a couple of questions in the chat box and hopefully others will come in in the question and answer until we get some more.

I wanted to start with a question to for Doctor Lustberg and the others on D escalation of therapy, and I guess how do you approach that question to patients when you’re trying to offer a trial?

That’s going to do less rather than more, especially for that anxious patient who’s you know, main concern is living and survival and.

I’m not necessarily trying to sell
that trial to them on deescalation, but kind of.

How do you make them feel comfortable moving forward down that route?

Yeah, that’s a great question. I think it takes a lot of open communication, listening understanding their fears, goals of care, but also spending time laying out the rationale. I like to say these trials were conceived by the best minds in breast cancer, essentially synthesizing all the best data that we have to date.
And here’s why.

We’re thinking that more is not necessarily more so it does take more time.

But I think I tend to use that as an educational opportunity, and certainly if they don’t feel comfortable, that’s their choice. But I think regardless it opens up the dialogue for potentially an additional trials down the road just to get them comfortable the road just to get them comfortable.

I think it opens up the dialogue for potentially an additional trials down the road just to get them comfortable. And that we would never consciously give a therapy that is known to be so far.
Angel, in a safer, vulnerable population. So many women have to work and have to take care of their families during treatment. And it's not a choice. And if we can deescalate it can be the difference between being unemployed and maybe losing housing and losing ability to take care of the rest of their life so they can be attractive. Slowly. There is a question in the chat box from Carolyn Friedman and maybe Andrew. You want to tackle this first and then.
the other is why are dense breast
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dense breasted women still getting
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yearly mammograms and nothing else?
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And maybe a little bit about
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the difference between kinetic
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and maybe some other states.
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I'm, well, Connecticut was one of the
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first states to pass a wonderful law
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mandating that women are identified
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as having dense breasts and making
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sure that there is insurance
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coverage for additional testing
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either an ultrasound or an MRI.
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An Carolyn, you bring up a great point.
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Many states have signed on to this.
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But not all States and you ask a question.
I think it’s a matter of priorities.

Connecticut has been very good in terms of advocacy, and there was a tremendous advocate who got this through after her own experience of having a mammographic undetectable tumor. That was an advanced cancer.

Thank you Andrea. A question for. Michael, I’m here Chesapeake early on, about two years ago it posed a question in an editorial where to platinum salts it in triple negative breast cancer in the neoadjuvant setting.

You know, have things changed,
or is it still something that were?

You know struggling through case by case and differences maybe between bracca specific T NBC versus sporadic.

It’s a good question and we still do struggle with it an it’s we it. I think it’s fair to say it’s still not standard of care. There are a number of trials that that have shown that when it’s incorporated into the neoadjuvant setting, it improves the pathological complete response rate.

So if you are of the mind that the goal of treating early stage triple negative breast cancer is to maximize the triple,
the maximized, the pathological complete response rate because we know those patients are the best to be cured. Then it’s reasonable to consider incorporating it. One might not think it’s worth incorporating it in a relatively lower anatomical risk, so maybe a stage one patient or, and as you said, we know from the metastatic setting with the TNT trial that the response rate for BRCA germline mutation carriers is quite high,
01:11:41.230 --> 01:11:43.396 so it may be worth incorporating
NOTE Confidence: 0.858326927333333
01:11:43.396 --> 01:11:44.840 it in that standpoint,
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01:11:44.840 --> 01:11:46.950 although there was an early
NOTE Confidence: 0.858326927333333
01:11:46.950 --> 01:11:48.638 stage trial that compared.
NOTE Confidence: 0.858326927333333
01:11:48.640 --> 01:11:48.975 Yes,
NOTE Confidence: 0.858326927333333
01:11:48.975 --> 01:11:50.650 this Platten to standard chemotherapy
NOTE Confidence: 0.858326927333333
01:11:50.650 --> 01:11:53.493 and it wasn’t much of a difference in
NOTE Confidence: 0.858326927333333
01:11:53.493 --> 01:11:55.293 terms of pathological complete response.
NOTE Confidence: 0.858326927333333
01:11:55.300 --> 01:11:57.910 For just just that comparison.
NOTE Confidence: 0.858326927333333
01:11:57.910 --> 01:11:59.926 So it’s still a question that’s up
NOTE Confidence: 0.858326927333333
01:11:59.926 --> 01:12:01.986 in the air whether to incorporate
NOTE Confidence: 0.858326927333333
01:12:01.986 --> 01:12:03.866 it into the early stage.
NOTE Confidence: 0.7494846625
01:12:06.690 --> 01:12:08.748 There’s a probably a question maybe
NOTE Confidence: 0.7494846625
01:12:08.748 --> 01:12:10.975 for Andrew, but also others in the
NOTE Confidence: 0.7494846625
01:12:10.975 --> 01:12:13.230 chat box from our fellow Angelique.
NOTE Confidence: 0.7494846625
01:12:13.230 --> 01:12:15.552 Has there been any reduction of
the disparities in outcomes between minority races and white women in the last two or three decades?

And maybe expanding on some of the exciting work and research that you've been doing here at home?

An advocacy that you've been doing here in Connecticut. We do a lot better in Connecticut than in rest of the country.

Some of the disparities in terms of outcomes, certainly in terms of screening and access to care, are better in this state than many others, and there is still a huge disparity. Partially because white women are
doing better, which it increases.

But the difference between races and I think.

We've got a long way to go.

There is a question in the chat box from Professor Rim and Merriam.

Do you want to 'cause I can't even pronounce half the drugs that you guys can put out the transducer map I get, but the others are tougher.

Yeah, it's great. Great question, so I think I think what you're pointing at is, I think our poor man's definition of what's triple negative and what's to her two positive. I think it's going to change a lot.
in the coming years because of these antibody drug conjugate therapies. Drugs like this have shown to have remarkable activity even in what we would consider normally hurting negative, but just a little bit of her to her too low signal. Is associated with significant outcomes. So I do agree with you Doctor Ram that I, I suspect, as these trials are finalized, I think we will be looking at different standards or care for this purchase subgroup.
teak sent he can make all low.

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Her two patients targets

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for this sort of therapy.

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And will this change the

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triple negative category so?

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So, so it’s like, yeah, I think

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obviously we need to wait for additional.

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You know, phase three data for that category,

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but so far the results are very,

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very promising. I think there may

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be additional Adcs that maybe safer.

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But with this particular drug,

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the higher, higher risk of interstitial

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lung disease is a concern.

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But but, but I, I really think

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we’re going to have a lot more.
ABC’s in the next few years, and they seem to be very effective class of drugs.

So maybe a question for all three of you. You know, I guess, how do you know in your leadership positions and when you go to advocate for these drug therapy trials to be developed, you know how do you convince drug companies and pharmaceuticals to deescalate when so much of their work is based on giving more so that they can make more money for themselves and shareholders and that kind of that. Challenge that you know that we all we all
01:15:40.927 --> 01:15:43.808 face in in this in these discussions.
NOTE Confidence: 0.87893873
01:15:47.570 --> 01:15:49.260 No simple answer, I'm sure.
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01:15:49.270 --> 01:15:52.348 think there is such a mark.
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01:15:52.350 --> 01:15:53.988 I live in a market because
NOTE Confidence: 0.82416936666667
01:15:53.988 --> 01:15:55.080 these are human lives,
NOTE Confidence: 0.82416936666667
01:15:55.080 --> 01:15:58.496 but there there there is so much need.
NOTE Confidence: 0.82416936666667
01:15:58.500 --> 01:16:02.451 For additional therapeutic that
NOTE Confidence: 0.82416936666667
01:16:02.451 --> 01:16:04.226 sadly there is a market to have
NOTE Confidence: 0.82416936666667
01:16:04.230 --> 01:16:06.085 new drugs that address things.
NOTE Confidence: 0.82416936666667
01:16:06.085 --> 01:16:07.782 But one thing if we were talking
NOTE Confidence: 0.82416936666667
01:16:07.782 --> 01:16:09.480 is what happens in breast cancer?
NOTE Confidence: 0.82416936666667
01:16:09.480 --> 01:16:11.532 Is if an agent is shown to be effective
NOTE Confidence: 0.82416936666667
01:16:11.532 --> 01:16:13.536 in the metastatic setting then we move
NOTE Confidence: 0.82416936666667
01:16:13.536 --> 01:16:15.560 it forward to the earlier stages.
NOTE Confidence: 0.82416936666667
01:16:15.560 --> 01:16:17.380 Untested and early state setting.
So just take the CD 46 inhibitors or even some of these Adcs. I think the market will expand and they will be tested in these earlier stage cancers with the goal of improving outcomes so. I don’t, I think they’ll do fine. I think they’ll be OK. And I guess I would add the drug looks the best when it has the best outcome and the drugs have the best outcome when they are used in the population for which they there is really the benefit for them.
with respect to disparities, that if more people who had chronic conditions from different backgrounds were in the clinical trials, they would better be able to evaluate is more better for everyone. What happens with the diabetic obese patient? Maybe more isn’t better for them, and because so many of these patients are excluded from trials. We’re able to say more, maybe better for the healthy, wealthy and wise patients, but not necessarily for other patients. And maybe that points to the kind of the low resource countries,
because a lot of this has been focused on, you know, discussions, and what happens here in the United States and you know, many of the audience you know are in or watching from overseas and a low resource settings. And you know some of the challenges they may face not having the access of the same drug therapies that we do here in the US. Yeah, so the the World Health Organization has launched a new global Breast health initiative.
and there are actually looking for interested members to apply to be part of these committees.

Looking at different pillars and that includes diagnostics. That’s one area where if you can’t even determine her two results reliably, you know how can you even determined a good therapies. So there’s a pillar. There’s a pillar. Focus on Diagnostics, which includes supportive care and symptom management. So I think there are some exciting developments in diagnostics so that we can at least have a better
understanding of the subtype of breast cancer and then further working with pharma companies to form collaboration. So so for those who are interested WHO is now accepting applications to these committees, and if you need if you want to be in touch, I'm happy to put you in touch. I'm also encouraged at Yale seeing younger physicians who are very, very interested in lower resource nations and devoting their academic careers to finding some solutions. Excellent and any parting words. Merriam, Andrea, Michael.
I just wanted to thank Doctor Gauchan for organizing the series of best breast care is really truly multidisciplinary and I think Next up will be radiation oncology, correct? And I’ll say that you asked about the difficulty of getting patients on some of our other clinical trials, and I’ll say clinical trials is also the best care. Absolutely. And I was just going to conclude by saying I’m lucky to be able to work with the colleagues that I can because we really do have a breadth of experience. And thank you very much for having me here.
Thank you everyone and would like to thank all the participants you know, calling either from the office or from overseas. This is a lot of fun. Thanks so much.