GAIL breast cancer CME series.

Really excited and fortunate to have three phenomenal speakers in our medical oncology colleagues in this session.

We’re going to first start off with Doctor Maryam Lustberg, who is our incoming breast program director, packing her bags, and on our way from Ohio State to Yale in the next couple of weeks.

She’s going to be talking about a really interesting area of change and controversy on when do we...
deescalate and when do we escalate for breast oncology therapies?

Then we'll go to. Doctor Michael D. Geovanna is going to be discussing recent advances in systemic therapy for breast cancer, and you know each year whether it’s at ASCO, ESMO or San Antonio. There’s so many really exciting developments in drug therapy that come out and it’ll be great to to hear about those and certainly last but not least is Doctor Andrea Silber discussing really super important topic.
00:01:11.310 --> 00:01:14.395 of breast cancer epidemiology in 2021.
NOTE Confidence: 0.836859365789474
00:01:14.395 --> 00:01:15.765 Risk factors,
NOTE Confidence: 0.836859365789474
00:01:15.765 --> 00:01:19.190 and specifically in our vulnerable
NOTE Confidence: 0.836859365789474
00:01:19.190 --> 00:01:19.875 population.
NOTE Confidence: 0.836859365789474
00:01:19.880 --> 00:01:21.924 We're going to leave some time at
NOTE Confidence: 0.836859365789474
00:01:21.924 --> 00:01:24.258 the end to answer any questions,
NOTE Confidence: 0.836859365789474
00:01:24.260 --> 00:01:26.871 but please feel free to put in
NOTE Confidence: 0.836859365789474
00:01:26.871 --> 00:01:29.076 questions either into the chat box
NOTE Confidence: 0.836859365789474
00:01:29.076 --> 00:01:31.435 or to the question and answer box.
NOTE Confidence: 0.836859365789474
00:01:31.440 --> 00:01:33.648 It will try to answer some of those
NOTE Confidence: 0.836859365789474
00:01:33.648 --> 00:01:35.810 in real time and then at the end
NOTE Confidence: 0.836859365789474
00:01:35.810 --> 00:01:38.310 leave time for some discussion
NOTE Confidence: 0.836859365789474
00:01:38.310 --> 00:01:40.810 with our three esteemed colleagues.
NOTE Confidence: 0.836859365789474
00:01:40.810 --> 00:01:41.764 And with that,
NOTE Confidence: 0.836859365789474
00:01:41.764 --> 00:01:43.672 I’d like to turn the podium
NOTE Confidence: 0.836859365789474
00:01:43.672 --> 00:01:45.720 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 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 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 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 RX study 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, when it preceded undergone 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
00:06:22.752 --> 00:06:24.717 scores actually came up study.
NOTE Confidence: 0.86163117
00:06:24.720 --> 00:06:27.670 Receive standard of care chemotherapy.
NOTE Confidence: 0.86163117
00:06:27.670 --> 00:06:30.376 Close to 5000 patients were enrolled.
NOTE Confidence: 0.86163117
00:06:30.380 --> 00:06:31.820 And as you can see,
NOTE Confidence: 0.86163117
00:06:31.820 --> 00:06:34.370 there was no significant difference in
NOTE Confidence: 0.86163117
00:06:34.370 --> 00:06:36.560 invasive disease free survival with
NOTE Confidence: 0.86163117
00:06:36.560 --> 00:06:38.260 additional chemotherapy for those
NOTE Confidence: 0.86163117
00:06:38.260 --> 00:06:40.820 with requests for between zero to 25.
NOTE Confidence: 0.86163117
00:06:40.820 --> 00:06:43.424 After immediate follow up of five years,
NOTE Confidence: 0.86163117
00:06:43.430 --> 00:06:48.590 so this is obviously practice changing and.
NOTE Confidence: 0.86163117
00:06:48.590 --> 00:06:51.313 A wonderful set of data for us
NOTE Confidence: 0.86163117
00:06:51.313 --> 00:06:54.294 to reassure our patients with not
NOTE Confidence: 0.86163117
00:06:54.294 --> 00:06:56.590 positive disease with favorable
NOTE Confidence: 0.86163117
00:06:56.590 --> 00:06:58.808 features on gentleman profiling.
NOTE Confidence: 0.86163117
00:06:58.808 --> 00:07:03.080 But again, similar to the Taylor RX study,
NOTE Confidence: 0.86163117
00:07:03.080 --> 00:07:06.328 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,

arm actually had a variance.

Regression therapy administered

and only 3% in the chemotherapy

arm had a variance oppression.

Straight so so where do we go from here?

How do we synthesize these data

and how do we?

How do we approach that younger

patients with no positive disease?

And I think the data are

continuing to evolve,

and it’s important to also highlight

some new data that represented

also in the last time Junior

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 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,

can be better tailor our therapies in this endocrine responsive group that had this lower post Ki 67 levels after a short pre operative in therapy at the data I just showed you in the previous slide tend to do relatively well.

I did a nice job summarizing these data as a discussion in the last thing Antonio,

and as I mentioned, these data are continuing to evolve.

What we know for sure is that we do need 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 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 anther

site plans since her to direct the

therapies carried cardio toxicity risk.

And as you enter cyclins,

looking at whether we can safely

eliminate anthracyclines in in

So this was one of the first studies that

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
00:10:40.427 --> 00:10:42.609 in outcomes between the two groups,
00:10:42.610 --> 00:10:46.060 but certainly higher toxicity with
00:10:46.060 --> 00:10:49.920 increased cardiac toxicity as well as.
00:10:49.920 --> 00:10:53.330 Secondary malignancies with anthracite news.
00:10:53.330 --> 00:10:55.635 But this numerical difference still
00:10:55.635 --> 00:10:57.940 was unsettling for some oncologists,
00:10:57.940 --> 00:11:00.946 and I think many of us had continued to
00:11:00.946 --> 00:11:04.310 use anthracite playing for very high risk.
00:11:04.310 --> 00:11:06.818 Her two positive disease and inflammatory
00:11:06.818 --> 00:11:09.340 breast cancer and said that the
00:11:09.340 --> 00:11:11.300 after cycling news has persisted.
00:11:11.300 --> 00:11:13.407 But just in the last month the
00:11:13.407 --> 00:11:15.265 results of the perspective train
00:11:15.265 --> 00:11:17.465 two study were reported out.
00:11:17.470 --> 00:11:19.078 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 two positive cases, what about staging won her two 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. I would like to just highlight that it’s a nice combination of both escalation, 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
And we always need chemotherapy
I think there is an opportunity to potentially look at imaging biomarkers
by Rosen Connelly and this 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

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, 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
00:15:54.612 --> 00:15:56.946 this coming as still coming up.
NOTE Confidence: 0.847098561428571
00:15:56.950 --> 00:15:59.036 So we talked a lot about Deescalation,
NOTE Confidence: 0.847098561428571
00:15:59.040 --> 00:15:59.694 but obviously.
NOTE Confidence: 0.847098561428571
00:15:59.694 --> 00:16:02.310 We need to just kind of touch on
NOTE Confidence: 0.847098561428571
00:16:02.382 --> 00:16:04.747 some of the escalation approaches.
NOTE Confidence: 0.847098561428571
00:16:04.750 --> 00:16:07.165 Certainly we’ve made a lot of progress,
NOTE Confidence: 0.847098561428571
00:16:07.170 --> 00:16:09.606 but we still have over 40,000
NOTE Confidence: 0.847098561428571
00:16:09.606 --> 00:16:11.230 individuals with breast cancer
NOTE Confidence: 0.847098561428571
00:16:11.305 --> 00:16:13.610 dying from advanced breast cancer,
NOTE Confidence: 0.847098561428571
00:16:13.610 --> 00:16:17.010 so it goes without saying that our current
NOTE Confidence: 0.847098561428571
00:16:17.010 --> 00:16:19.518 strip strategies have significant gaps.
NOTE Confidence: 0.847098561428571
00:16:19.520 --> 00:16:22.640 So one of the great successes of escalation,
NOTE Confidence: 0.847098561428571
00:16:22.640 --> 00:16:23.852 in my opinion,
NOTE Confidence: 0.847098561428571
00:16:23.852 --> 00:16:26.796 has been the the introduction of the CD.
NOTE Confidence: 0.847098561428571
00:16:26.800 --> 00:16:30.940 46 inhibitors 222 minus static breast cancer.
NOTE Confidence: 0.847098561428571
00:16:30.940 --> 00:16:33.586 That’s’s, ER, positive that they have led
to improved progression free survival.

Anne continued more and more overall survival data are maturing and will be presented in this year’s ASCO, so you can look at it as an escalation approach, but also deescalation approach because.

What the data to show also is at work for a long time to initiation of chemotherapy in patients with metastatic breast cancer. 

Three studies have been reported out, but only monarchy with Emoci club has

What about escalating argument underground therapy in early stage?

Breast cancer.
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.

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, while Penelope B and Palace were not an?

There’s a very nice presentation coming looking at the composition of tumors that actually derive benefit and Penelope and they tend to be of the luminal before iety,
So I think kind of the biology of these chambers. Whether we can kind of phenotype, the tumors that are more likely to benefit from agile and taxi for 1600. Happy, I think it’s the next step. Brain metastases are huge gap and inverted climb with an important study and as the basis of adjutant to catnip that I mentioned in the compass study coming up. And I will wrap up with escalation of our preoperative chemotherapy regiments 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, they 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? 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 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, team science and collaborations.
are the path forward.

Thank you so much for your attention.

Thank you Doctor Lustberg that was really fantastic and I know I have a bunch of questions for you at the end and hopefully our audience, whether they're locally here in Connecticut or internationally, will put some questions in the chat box for you.

Next, we're going to move on to Doctor Michael D. Geovanna and discussing recent advances of systemic therapy for breast cancer.

Thank you doctor Cubana.

Sorry for the technical problems,
00:21:58.980 --> 00:22:01.446 thank you for having me and for all of
00:22:01.446 --> 00:22:04.020 the attendees being on the conference.
00:22:04.020 --> 00:22:06.449 I will hit some highlights and advances
00:22:06.449 --> 00:22:09.136 in therapy for each of the types of
00:22:09.136 --> 00:22:11.466 breast cancer and I’ll start with her
00:22:11.466 --> 00:22:13.867 two positive breast cancer we now have.
00:22:13.870 --> 00:22:15.960 Eight different targeted drugs for
00:22:15.960 --> 00:22:18.550 treating her two positive breast cancer,
00:22:18.550 --> 00:22:20.075 so it’s been wonderful progress
00:22:20.075 --> 00:22:22.369 in this field and of these eight,
00:22:22.370 --> 00:22:24.578 there’s actually been five new FDA
00:22:24.578 --> 00:22:27.109 approvals in just the last two years.
00:22:27.110 --> 00:22:28.790 Those are the ones that I’ve
00:22:28.790 --> 00:22:29.910 highlighted in red here,
00:22:29.910 --> 00:22:32.381 and that does not even include FDA
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 complete 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 analysis. 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 getting neoadjuvant therapy. An of those who entered the trial with clinical stage one disease and still had residual disease. Those who got switched to TDM one 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.

For those who don’t get a path CR.

The next drug I wanted to talk about is to cotton.
00:26:33.816 --> 00:26:35.160 tyrosine kinase inhibitor.

00:26:35.160 --> 00:26:36.728 We now have three.

00:26:36.728 --> 00:26:41.446 Her two tyrosine kinase inhibitors to choose from and low to captain.

00:26:41.446 --> 00:26:47.218 If unlike the other two is highly selective just for her two without hitting the other members of the her two receptor family,

00:26:47.218 --> 00:26:49.679 Let Patton in has an Nurettin.

00:26:49.679 --> 00:26:51.974 you can see here that there’s no activity against the EGF receptor.

00:26:53.968 --> 00:26:55.569 They both have equivalent activity against the EGF receptor interaction.

00:26:55.570 --> 00:26:58.150 Let Patton in has an Nurettin.

00:26:58.150 --> 00:27:00.200 They both have equivalent activity against the EGF receptor interaction.

00:27:00.200 --> 00:27:04.870 the receptors in this family.
So the HER two 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. 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
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,
00:27:56.142 --> 00:27:59.040 almost half of the patients entered
00:27:59.139 --> 00:28:01.110 with brain metastases.
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%.

An 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,

and it 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 TDM 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.
00:30:25.790 --> 00:30:27.890 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. So if there is heterogeneity of the 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 14.15% 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
physicians choice in a phase three setting.

With these options, the Destiny 03 is comparing this after first line therapy head to head against TDM one.

So it’s just using web touristy can versus TDM.

One in second line.

The Destiny 04 trial is looking at her two low breast cancer patients because I showed you in phase one.

Trials responses in those patients.

So this is just using map touristy can versus chemotherapy of physicians choice,

and in Destiny 05 it’s actually

being compared to TDM one in the
in the post neoadjuvant setting.

As per the Catherine trial where patients who get into management therapy and have residual disease will be randomized to TDM one or try D’souza Mabdi rixty cat. So being tested in all of these different settings.

Another her two targeting drug that was just recently approved is margetuximab, and this is actually a derivative of her of trastuzumab that has the FC Gamma portion replaced by another Gamma alteration that has a higher affinity for activating FC.
Gamma receptor and a lower affinity for inhibitory FC Gamma receptor. And this is based on the fact that we know that trastuzumab is not only a targeted signal transduction. That does recruit the immune system, and so it was thought by making transducer maps more able to actively recruit the immune system. It may give it enhanced activity, and so this was tested in the Sophia trial, which was a phase three trial of transducer Med 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

58
La Pata nibt 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.
metastatic disease patients. In the first line, therapy should have pertuzumab, trastuzumab, and taxane because of the remarkable overall survival benefit seen in the Cleopatra trial TDM, one is still considered the second line therapy as per the Amelia trial and we now can consider a third line therapy. Being just do some AB capeside it being into cotton if since we have seen an improvement in overall survival in the her two climb study and this is especially
of course attractive for patients who may already have brain metastases from their 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 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. They had a remarkable high response rate to single agent carboplatin about a 60% response rate for germline.
00:37:50.790 --> 00:37:53.955 carriers and that is applies to not
NOTE Confidence: 0.837415576470588
00:37:53.955 --> 00:37:56.445 only triple negative disease but any
NOTE Confidence: 0.837415576470588
00:37:56.445 --> 00:37:59.017 germ line BRCA mutation carriers.
NOTE Confidence: 0.837415576470588
00:37:59.020 --> 00:38:01.990 So in terms of immunotherapy,
NOTE Confidence: 0.837415576470588
00:38:01.990 --> 00:38:04.630 we have two positive results in
NOTE Confidence: 0.837415576470588
00:38:04.630 --> 00:38:05.950 the metastatic setting.
NOTE Confidence: 0.837415576470588
00:38:05.950 --> 00:38:08.092 I think the results aren’t as
NOTE Confidence: 0.837415576470588
00:38:08.092 --> 00:38:09.882 enormously impressive as they are
NOTE Confidence: 0.837415576470588
00:38:09.882 --> 00:38:11.646 in some other types of cancer,
NOTE Confidence: 0.837415576470588
00:38:11.650 --> 00:38:14.630 like Melanoma or lung cancer,
NOTE Confidence: 0.837415576470588
00:38:14.630 --> 00:38:16.430 but they are positive results,
NOTE Confidence: 0.837415576470588
00:38:16.430 --> 00:38:18.902 and so we now have these that we
NOTE Confidence: 0.837415576470588
00:38:18.902 --> 00:38:21.955 can use in the IMPASSION 130 trial
NOTE Confidence: 0.837415576470588
00:38:21.955 --> 00:38:24.976 atisa lism AB versus placebo was
NOTE Confidence: 0.837415576470588
00:38:24.976 --> 00:38:26.960 added to nab paclitaxel,
NOTE Confidence: 0.837415576470588
00:38:26.960 --> 00:38:30.019 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, 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 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, 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 --> 00:40:01.814 I suspect nabbed paclitaxel
00:40:01.814 --> 00:40:03.446 that it would make this difference?
00:40:03.446 --> 00:40:04.000 but is it really so much of an edge
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 Papaxol 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. Then in order to have a statistical significance though, there was very high stringency for what the P value would need to be and 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 4 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, the 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,
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, 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 an 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
patient population?

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,

NOTE Confidence: 0.888861496206897

and at the four year follow-up Timepoint,

NOTE Confidence: 0.888861496206897

essentially no difference between the arms.

NOTE Confidence: 0.888861496206897

When we look at the monarchy

NOTE Confidence: 0.888861496206897

with abemaciclib,

NOTE Confidence: 0.888861496206897

which appears to be a positive trial so far.

NOTE Confidence: 0.888861496206897

The treatment duration is 2 years,

NOTE Confidence: 0.888861496206897

but the follow up so far is

NOTE Confidence: 0.888861496206897

only 19 months and so it may be

NOTE Confidence: 0.888861496206897

that we see some effect of these

NOTE Confidence: 0.888861496206897

while the therapy is going on.

NOTE Confidence: 0.888861496206897

But once the therapy is completed over time,

NOTE Confidence: 0.888861496206897

the difference between the

NOTE Confidence: 0.888861496206897

two arms might go away.

NOTE Confidence: 0.888861496206897

So we need more study,

NOTE Confidence: 0.888861496206897

more follow up and we need to
00:48:31.931 --> 00:48:33.870 see the results of the Natalie

00:48:33.870 --> 00:48:35.910 trial which is using recycled for

00:48:35.910 --> 00:48:38.018 three years in high risk disease.

00:48:38.020 --> 00:48:39.680 That’s my last slide.

00:48:40.850 --> 00:48:41.898 One thing I wanted

00:48:41.910 --> 00:48:43.688 to say once again getting back to

00:48:43.688 --> 00:48:45.351 dealing with the person to sitting

00:48:45.351 --> 00:48:47.043 in front of you question arises.

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

00:48:49.800 --> 00:48:51.172 It’s not FDA approved.

00:48:51.172 --> 00:48:53.576 We really don’t know if this is

00:48:53.576 --> 00:48:55.784 going to hold up in the long term,

00:48:55.790 --> 00:48:57.914 but I will tell you that I have brought

00:48:57.914 --> 00:48:59.657 this up sometimes with patients.

00:48:59.660 --> 00:49:02.748 So I recently had a patient who had
12 nodes positive and was starting her regimen therapy and I discussed with her whether to add Emoci clip because it’s enormously high risk to have. Well, no, it’s positive and I prescribed with Emoci 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 --> 00:49:57.576 but we have Professor Andreas Silvers.

00:49:59.620 --> 00:50:00.980 Gonna really give us a exciting

00:50:02.900 --> 00:50:06.200 update on breast cancer

00:50:08.200 --> 00:50:10.966 epidemiology for risk factors,

00:50:11.069 --> 00:50:12.986 especially in our vulnerable populations so.

00:50:14.970 --> 00:50:16.218 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.

It's my conflict of interest.

Breast cancer in the United States is extremely common. It's the most common cancer one season women.

But it is 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.
actually can change in up to 25% of patients when they metastasize.

Their breast cancer has changed subtype and the most common change that one sees is going from luminal,

And here’s the breakdown of breast cancer by subtype,

but hormone receptor positive breast cancer,

is the most common type,

regardless of age or race,

and it’s six times more common than the triple negative breast cancer.

Let’s move ahead and talk about risk factors.

I think from my previous slide,
you can tell one of the risk factors is being female and another is being older, but those are non-modifiable risk factors. Personal history of invasive or non-invasive breast cancer predisposes to both contralateral and ipsilateral primaries. Benign breast disease with atypia. Family history and this is regardless of whether there’s a mutation for women with family history. Only 5 to 6% have identifiable mutations, and when you look at known mutations that comprise less than 10% of all breast cancers. Breast density I will get into that.
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 an 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. An risk factors vary by subtype. Greater parity was associated with a lower risk of hormone receptor positive breast cancer, but it is an increased risk for...
00:56:40.094 --> 00:56:42.040 triple negative breast cancer.
NOTE Confidence: 0.770337186666667
00:56:42.040 --> 00:56:44.656 Breastfeeding can cut the risk for
NOTE Confidence: 0.770337186666667
00:56:44.656 --> 00:56:47.170 triple negative breast cancer by 50%.
NOTE Confidence: 0.770337186666667
00:56:47.170 --> 00:56:49.970 Well, that’s not true for
NOTE Confidence: 0.770337186666667
00:56:49.970 --> 00:56:52.210 receptor positive breast cancer.
NOTE Confidence: 0.872638806363636
00:56:54.720 --> 00:56:57.534 So these two women on the cover
NOTE Confidence: 0.872638806363636
00:56:57.534 --> 00:56:59.210 of Good Housekeeping show.
NOTE Confidence: 0.872638806363636
00:56:59.210 --> 00:57:02.594 How are modern women are more likely to
NOTE Confidence: 0.872638806363636
00:57:02.594 --> 00:57:06.155 have risk factors for hormone receptor
NOTE Confidence: 0.872638806363636
00:57:06.155 --> 00:57:09.435 positive breast cancer by delaying
NOTE Confidence: 0.872638806363636
00:57:09.435 --> 00:57:11.825 childbearing having fewer children
NOTE Confidence: 0.872638806363636
00:57:11.825 --> 00:57:15.107 and those things increase the risk.
NOTE Confidence: 0.872638806363636
00:57:15.110 --> 00:57:16.730 As a matter of fact,
NOTE Confidence: 0.872638806363636
00:57:16.730 --> 00:57:20.498 breast cancer is more common in
NOTE Confidence: 0.872638806363636
00:57:20.498 --> 00:57:23.522 areas like the I-95 corridor,
NOTE Confidence: 0.872638806363636
00:57:23.522 --> 00:57:25.786 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.
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 World wide, you can see a very different story. The five year survival in the United States is 95%. 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. When you look at some of the SEER data,
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 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. Top of this slide.

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 get 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 disproportionally
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 for breast cancer is the communities that people grew up in.

And thank you for your attention, and I always like to mention those that I seen with breast cancer or...
01:05:58.096 --> 01:06:00.736 have been affected by the disease.
01:06:03.880 --> 01:06:05.506 Thank you doctor.
01:06:05.506 --> 01:06:09.176 So that was fantastic and you know,
01:06:09.180 --> 01:06:10.614 thank you for all three of
01:06:10.614 --> 01:06:11.880 our speakers for you know,
01:06:11.880 --> 01:06:13.744 three really phenomenal presentations
01:06:13.744 --> 01:06:16.540 that you know show the breadth
01:06:16.613 --> 01:06:18.150 of the care and services that
01:06:18.150 --> 01:06:20.765 we provide here at Yale.
01:06:19.550 --> 01:06:20.765 But more importantly,
01:06:20.765 --> 01:06:23.195 you know the the options and
01:06:23.195 --> 01:06:25.135 therapies that are available to
01:06:25.135 --> 01:06:27.325 women and some of the challenges
01:06:27.394 --> 01:06:29.338 that we have moving forward in
01:06:29.338 --> 01:06:31.802 terms of not only screening but
01:06:31.802 --> 01:06:34.707 treatment of our more vulnerable.

NOTE Confidence: 0.82665481

01:06:34.710 --> 01:06:36.480 Populations there were a couple of

NOTE Confidence: 0.82665481

01:06:36.480 --> 01:06:38.554 questions in the chat box and hopefully

NOTE Confidence: 0.82665481

01:06:38.554 --> 01:06:40.507 others will come in in the question

NOTE Confidence: 0.82665481

01:06:40.566 --> 01:06:42.358 and answer until we get some more.

NOTE Confidence: 0.82665481

01:06:42.360 --> 01:06:44.866 I wanted to start with a question

NOTE Confidence: 0.82665481

01:06:44.866 --> 01:06:47.216 to for Doctor Lustberg and the

NOTE Confidence: 0.82665481

01:06:47.216 --> 01:06:49.434 others on D escalation of therapy,

NOTE Confidence: 0.82665481

01:06:49.434 --> 01:06:52.671 and I guess how do you approach that

NOTE Confidence: 0.82665481

01:06:52.671 --> 01:06:55.216 question to patients when you’re,

NOTE Confidence: 0.82665481

01:06:55.220 --> 01:06:56.844 you know, trying to offer a trial?

NOTE Confidence: 0.82665481

01:06:56.850 --> 01:06:59.386 That’s going to do less rather than more,

NOTE Confidence: 0.82665481

01:06:59.390 --> 01:07:00.878 especially for that anxious

NOTE Confidence: 0.82665481

01:07:00.878 --> 01:07:02.366 patient who’s you know,

NOTE Confidence: 0.82665481

01:07:02.370 --> 01:07:05.359 main concern is living and survival and.

NOTE Confidence: 0.82665481

01:07:05.360 --> 01:07:08.446 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. Doctor goes on, I think. 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.

I think it opens up the dialogue for potentially an additional trials down the road just to get them comfortable.

about the clinical trial process, how these concepts are vetted so carefully and that we would never.

Consciously give a therapy that is known to be so far.
Angel yeah. 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

And maybe a little bit about

the difference between kinetic

I'm, well, Connecticut was one of the

first states to pass a wonderful law

mandating that women are identified

as having dense breasts and making

sure that there is insurance

coverage for additional testing

either an ultrasound or an MRI.

An Carolyn, you bring up a great point.

Many states have signed on to this.

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,
01:10:33.500 --> 01:10:36.650 or is it still something that were?
NOTE Confidence: 0.788246111666667
01:10:36.650 --> 01:10:39.422 You know struggling through case by
NOTE Confidence: 0.788246111666667
01:10:39.422 --> 01:10:41.868 case and differences maybe between
NOTE Confidence: 0.788246111666667
01:10:41.868 --> 01:10:45.800 bracca specific T NBC versus sporadic.
NOTE Confidence: 0.858326927333333
01:10:46.760 --> 01:10:48.713 It’s a good question and we still
NOTE Confidence: 0.858326927333333
01:10:48.713 --> 01:10:50.560 do struggle with it an it’s we it.
NOTE Confidence: 0.858326927333333
01:10:50.560 --> 01:10:53.038 I think it’s fair to say it’s
NOTE Confidence: 0.858326927333333
01:10:53.038 --> 01:10:54.769 still not standard of care.
NOTE Confidence: 0.858326927333333
01:10:54.770 --> 01:10:57.010 There are a number of trials that that
NOTE Confidence: 0.858326927333333
01:10:57.010 --> 01:10:59.266 have shown that when it’s incorporated
NOTE Confidence: 0.858326927333333
01:10:59.266 --> 01:11:00.898 into the neoadjuvant setting,
NOTE Confidence: 0.858326927333333
01:11:00.900 --> 01:11:02.480 it improves the pathological
NOTE Confidence: 0.858326927333333
01:11:02.480 --> 01:11:03.665 complete response rate.
NOTE Confidence: 0.858326927333333
01:11:03.670 --> 01:11:06.160 So if you are of the mind that the goal
NOTE Confidence: 0.858326927333333
01:11:06.233 --> 01:11:08.501 of treating early stage triple negative
NOTE Confidence: 0.858326927333333
01:11:08.501 --> 01:11:11.359 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,
so it may be worth incorporating it in that standpoint, although there was an early stage trial that compared. Yes, this Platten to standard chemotherapy and it wasn’t much of a difference in terms of pathological complete response. For just that comparison. So it’s still a question that’s up in the air whether to incorporate it into the early stage. There’s a probably a question maybe for Andrew, but also others in the chat box from our fellow Angelique. 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 here at home?

I’m. 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, but there is still a huge disparity.
01:12:58.040 --> 01:13:01.957 doing better, which it increases.
NOTE Confidence: 0.850145492142857
01:13:01.957 --> 01:13:08.360 But the difference between races and I think.
NOTE Confidence: 0.850145492142857
01:13:08.360 --> 01:13:10.628 You know, we’ve got a long way to go.
NOTE Confidence: 0.837891923076923
01:13:13.840 --> 01:13:17.128 There is a question in the chat box
NOTE Confidence: 0.837891923076923
NOTE Confidence: 0.837891923076923
01:13:19.350 --> 01:13:21.870 Do you want to ’cause I can’t even
NOTE Confidence: 0.837891923076923
01:13:21.870 --> 01:13:23.984 pronounce half the drugs that you guys
NOTE Confidence: 0.837891923076923
01:13:23.984 --> 01:13:26.290 can put out the transducer map I get,
NOTE Confidence: 0.837891923076923
01:13:26.290 --> 01:13:28.130 but the others are tougher.
NOTE Confidence: 0.872252413333333
NOTE Confidence: 0.872252413333333
01:13:30.330 --> 01:13:32.486 Great question, so I think I
NOTE Confidence: 0.872252413333333
01:13:32.486 --> 01:13:34.130 think what you’re pointing at is,
NOTE Confidence: 0.872252413333333
01:13:34.130 --> 01:13:37.140 I think our our poor man’s definition
NOTE Confidence: 0.872252413333333
01:13:37.140 --> 01:13:39.430 of what’s triple negative and
NOTE Confidence: 0.872252413333333
NOTE Confidence: 0.872252413333333
01:13:41.710 --> 01:13:43.342 I think it’s going to change a lot
117
in the coming years because of these antibody drug conjugate therapies.

Drugs like this have shown 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. And for those who couldn’t see the question, it will be trousers some outdoor.
teak sent he can make all low.

Her two patients targets

And will this change the triple negative category so?

So, obviously we need to wait for additional. You know, phase three data for that category, but so far the results are very, very promising. I think there may be additional Adcs that maybe safer.

But with this particular drug, the higher, higher risk of interstitial lung disease is a concern.

But but, but I, I really think 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 their 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. I
NOTE Confidence: 0.82416936666667
01:15:49.270 --> 01:15:52.348 think there is such a mark.
NOTE Confidence: 0.82416936666667
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 --> 01:15:59.912 For additional therapeutic that
NOTE Confidence: 0.82416936666667
01:15:59.912 --> 01:16:02.451 sadly there is a market to have
NOTE Confidence: 0.82416936666667
01:16:02.451 --> 01:16:04.226 new drugs that address things.
NOTE Confidence: 0.82416936666667
01:16:04.230 --> 01:16:06.085 But one thing if we were talking
NOTE Confidence: 0.82416936666667
01:16:06.085 --> 01:16:07.782 about the business model of things
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. And I was going to say,
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 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 Focus on Diagnostics, an access to therapeutic. 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 for those who are interested WHO is now accepting applications to these committees, and if you need 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.
01:19:28.390 --> 01:19:30.735 I just wanted to thank Doctor
NOTE Confidence: 0.91841394
01:19:30.735 --> 01:19:32.880 Gauchan for organizing the series
NOTE Confidence: 0.801163685625
01:19:32.950 --> 01:19:35.056 of best breast care is really,
NOTE Confidence: 0.801163685625
01:19:35.060 --> 01:19:39.608 truly multidisciplinary and I think
NOTE Confidence: 0.801163685625
01:19:39.608 --> 01:19:41.780 up will be radiation oncology, correct?
NOTE Confidence: 0.865352983684211
01:19:43.100 --> 01:19:44.820 And I'll say that you asked about the
topConfidence: 0.865352983684211
01:19:44.820 --> 01:19:46.052 difficulty of getting patients on
NOTE Confidence: 0.865352983684211
01:19:46.052 --> 01:19:47.570 some of our other clinical trials,
NOTE Confidence: 0.865352983684211
01:19:47.570 --> 01:19:48.830 and I'll say clinical trials
NOTE Confidence: 0.865352983684211
01:19:48.830 --> 01:19:50.090 is also the best care.
NOTE Confidence: 0.93961334
01:19:51.540 --> 01:19:52.530 Absolutely.
NOTE Confidence: 0.905919320333333
01:19:53.660 --> 01:19:55.884 And I was just going to conclude by
NOTE Confidence: 0.905919320333333
01:19:55.884 --> 01:19:58.572 saying I'm lucky to be able to work with
NOTE Confidence: 0.905919320333333
01:19:58.572 --> 01:20:00.581 the colleagues that I can because we
NOTE Confidence: 0.905919320333333
01:20:00.581 --> 01:20:02.540 really do have a breadth of experience.
NOTE Confidence: 0.905919320333333
01:20:02.540 --> 01:20:05.780 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 next door or from overseas. This is a lot of fun. Thanks so much.