Medical Education

Advances in the Standard of Care in TNBC:

Addressing Health Disparities and Integrating ADCs Into Treatment

This transcript has been edited for style and clarity and includes all slides from the presentation.

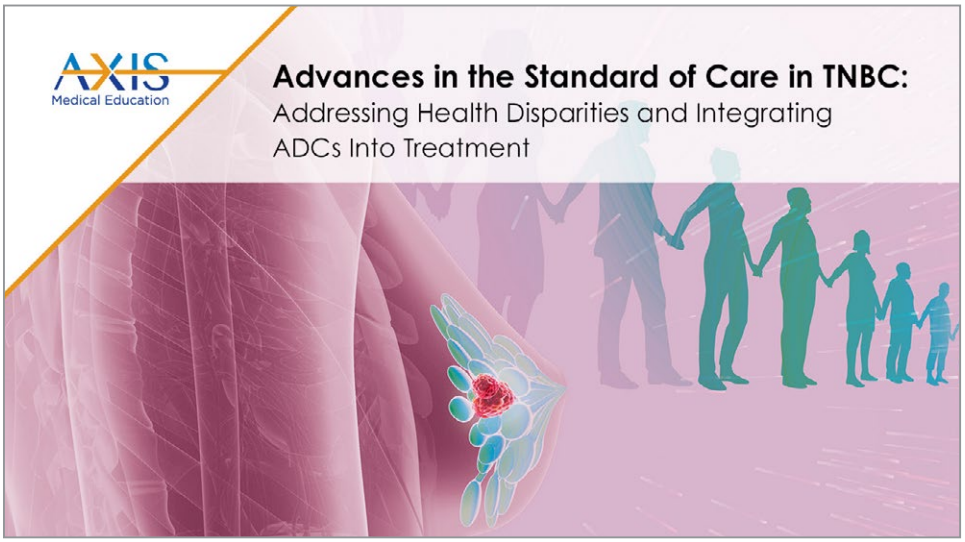
This activity is provided by

Medical Education

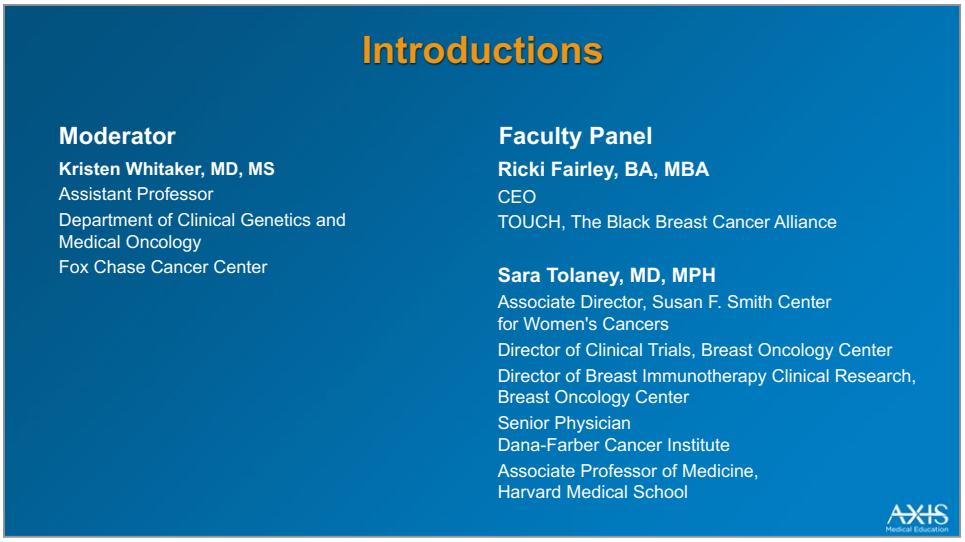
This activity is supported by an independent educational grant from Gilead.

Advances in the Standard of Care in TNBC: Addressing Health Disparities and Integrating ADCs Into Treatment

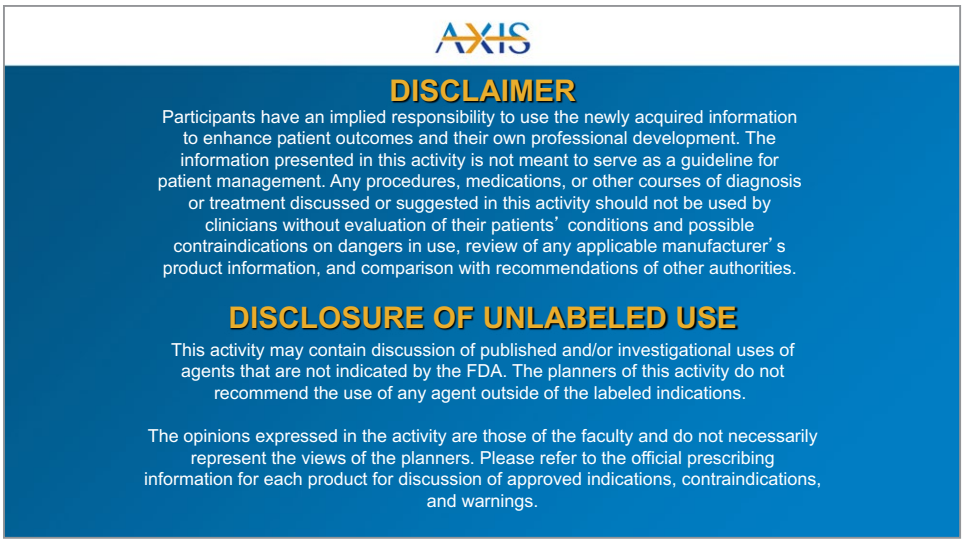
Kristen Whitaker, MD, MS, Ricki Fairley, BA, MBA & Sara Tolaney, MD, MPH



- **Kristen Whitaker, MD, MS:** Hello, and welcome to this educational activity. I am Dr. Kristen Whitaker. I'm an Assistant Professor in the Department of Clinical Genetics at Fox Chase Cancer Center where I see patients with breast cancer, as well as patients without cancer that have a high risk of breast cancer.

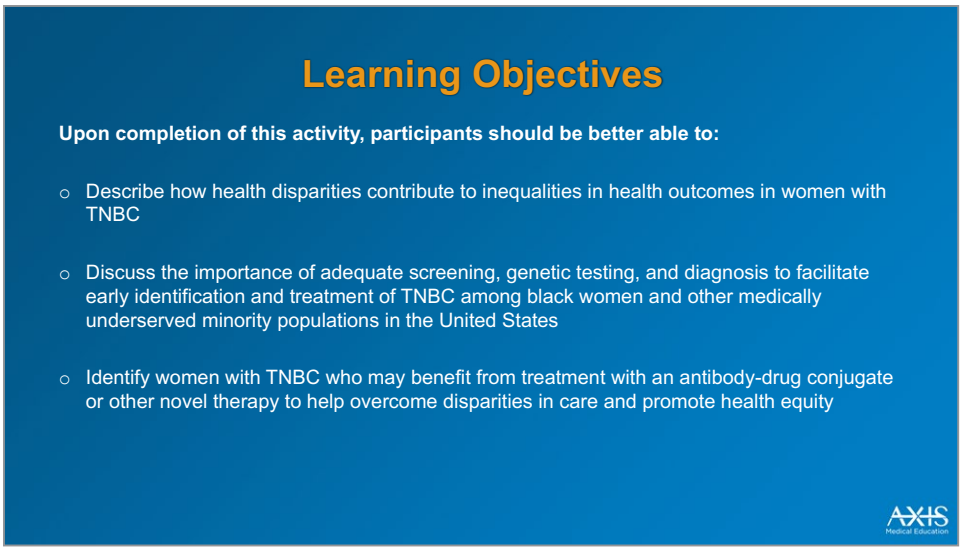


- We're joined today by two faculty panelists. Ricki Fairley, CEO of TOUCH, The Black Breast Cancer Alliance. We're also joined by Dr. Sara Tolaney, who wears many titles, but she's the Associate Director of the Women's Cancer Center, and she's at Dana-Farber Cancer Institute in Boston.

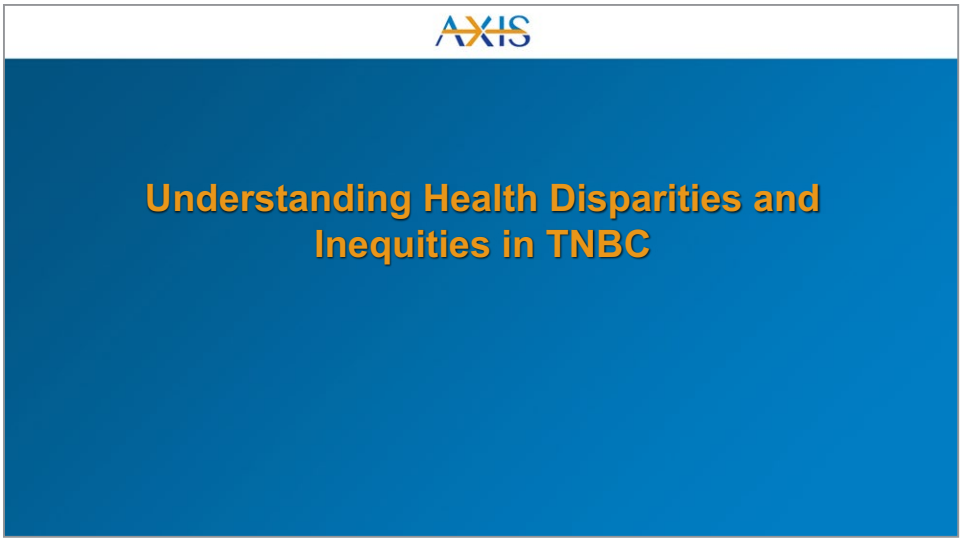


- And here's a disclaimer and a disclosure indicating that we may in fact be discussing off-label use of approved agents or agents that are in development.

- Here's our financial disclosure information.



- And I hope that this will be a very valuable session for you, and to that end we hope to achieve a few objectives.

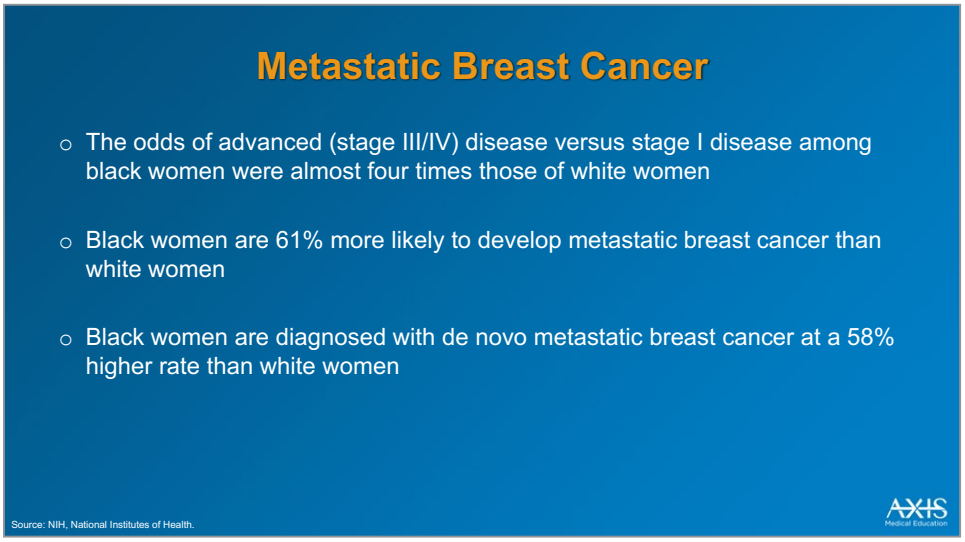


- And now, we'll have Ricki Fairley talk to you a bit more about some of these disparities and inequities in triple-negative breast cancer (TNBC).

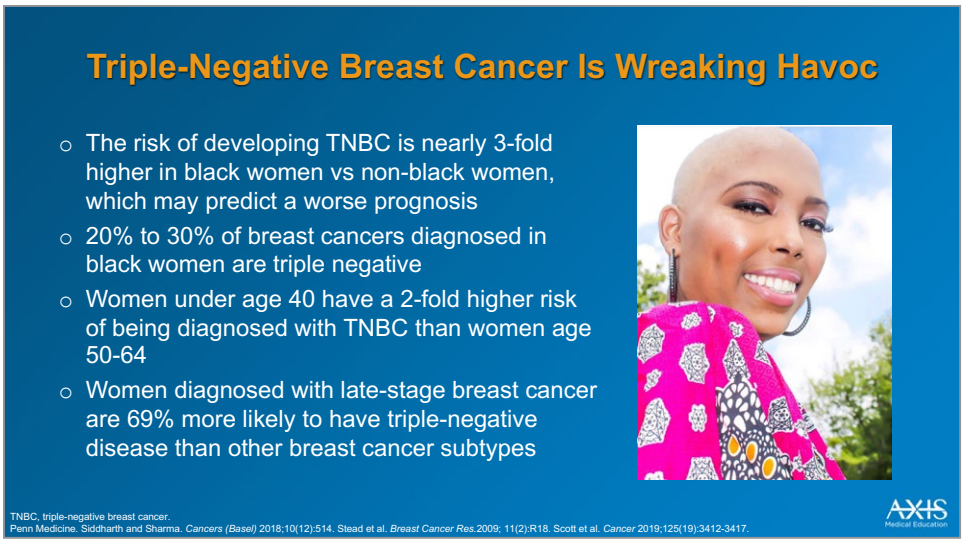
- **Ricki Fairley:** I'm Ricki Fairley, and I am a 10-year survivor of TNBC. I'm very pleased to have this talk with you today.

- Let's talk about TNBC and, really, breast cancer overall for black women. It's really a different disease state for black women. So I'm going to cover the state of black breast cancer, some key factors affecting the mortality of black women, our perception of clinical trial research, and some research that I recently did under the title Black Data Matters and how I'm working really hard to change the game on the situation.

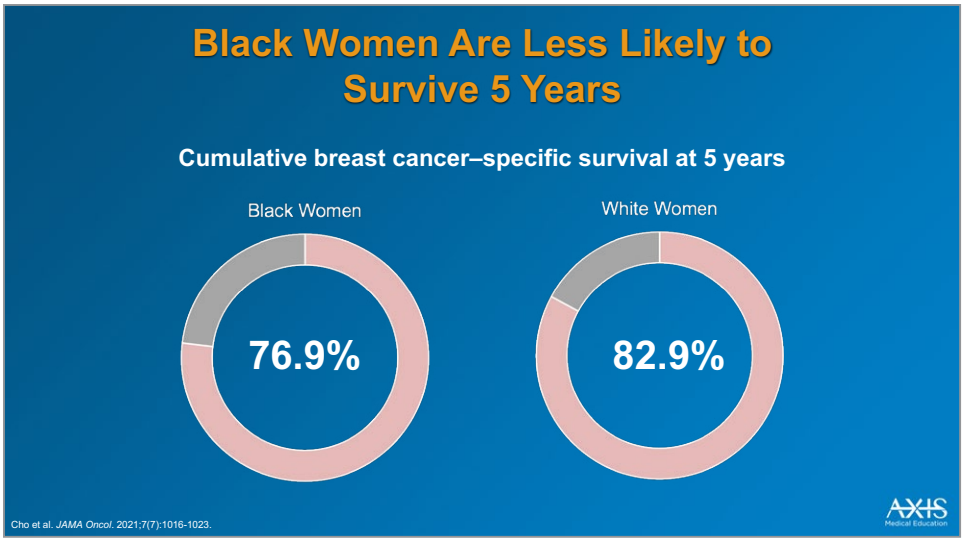
- Breast cancer is one of the most fatal health issues for black women, especially relative to white women. We are dying at a 41% higher rate than white women. Black women under 35 get breast cancer at twice the rate and die at three times the rate, well before they would have their first mammogram at age 40. Black breast cancer survivors like me have a 39% higher risk for breast cancer recurrence, compared to white women. That's really true for TNBC because we don't have a drug to prevent recurrence. TNBC is the only breast cancer subtype that doesn't have a drug to prevent recurrence, which makes us special and different and more deserving of attention from the science. Black women with breast cancer have a 52% higher risk of death than white women. These numbers are devastating and really need to be addressed.



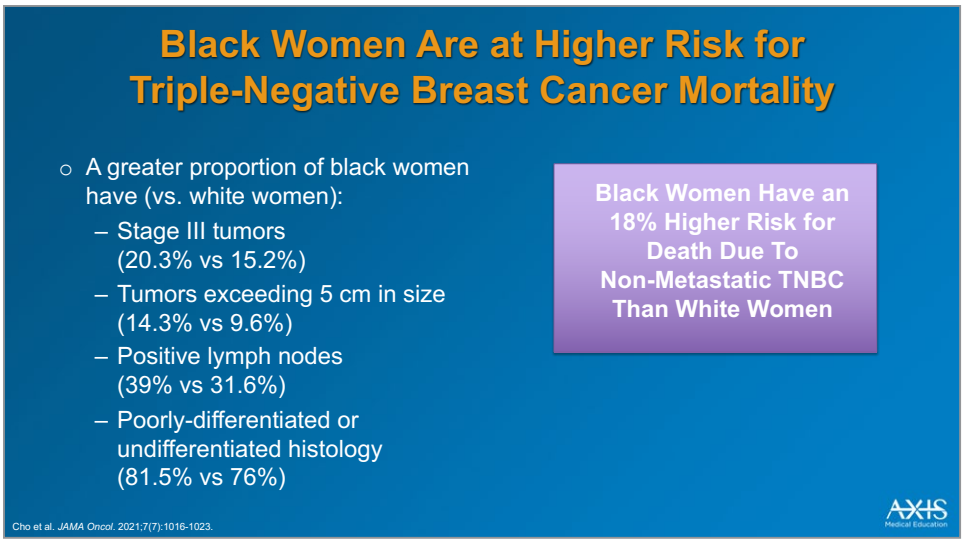
- So let's talk about metastatic breast cancer. The odds of getting stage III or IV disease versus Stage I disease among black women is almost four times that of white women. Black women are 61% more likely to develop metastatic breast cancer than a white woman. And black women are diagnosed with de novo metastatic breast cancer at a 58% higher rate than white women. This means their breast cancer diagnosis was metastatic from the beginning. And again, these numbers are astounding.



- The risk of developing TNBC is nearly threefold higher in black women versus non-black women, and we know that it has a worse prognosis. 20 to 30% of breast cancers diagnosed in black women are triple negative. And women under the age of 40 have a twofold higher risk of being diagnosed with TNBC than women ages 50 to 64. Women diagnosed with late-stage breast cancer are 69% more likely to have triple-negative disease than other breast cancer subtypes.

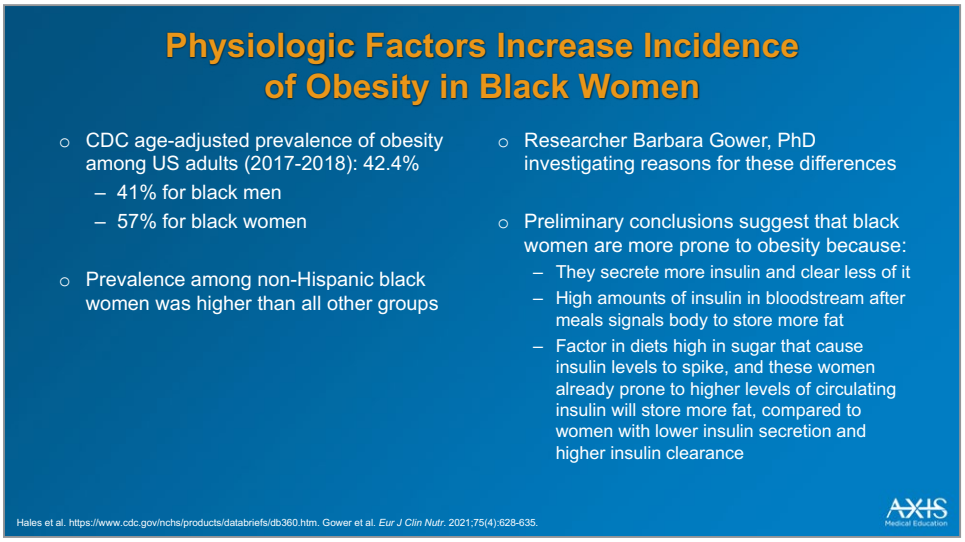


- Black women are less likely to survive 5 years: 76.9% versus 82.9% for white women.



- We don't really know why the mortality numbers are so devastating. But there are a lot of contributing factors that indicate that our bodies are different. Black bodies are different and warrant different treatment options. So let me go into those a little bit. And it really will dictate kind of the risk of breast cancer for black women.

  So black women are at higher risk for TNBC mortality. We have more stage III tumors, more positive lymph nodes, bigger tumors, and black women have an 18% higher risk of death due to nonmetastatic TNBC.



- Some other factors increase our incidence of getting breast cancer. Obesity is really a problem in black women, and this is a risk factor for breast cancer.

Obesity Is a Breast Cancer Risk Factor for Black Women

- Black women have a significantly higher mean BMI (23%) compared with white women (32 kg/m^2 vs 26 kg/m^2)
- Having a BMI >30 kg/m^2 is associated with an increased risk (HR 2.77) for TNBC and an increased risk for ER+/PR+/HER2− breast cancer in postmenopausal women

BMI, body mass index; ER, estrogen receptor; HER2, human epidermal growth factor receptor 2; PR, progesterone receptor; TNBC, triple-negative breast cancer.
Friebel-Klingner et al. *Breast Cancer Res Treat.* 2021;189(3):827-835. McCarthy et al. *Cancer Med.* 2021;10(18):6456-6467.

AXIS Medical Education

- Black women have a significantly higher BMI compared with white women. Having a BMI of greater than 30 is associated with an increased risk for TNBC and an increased risk for other breast cancers, as well, in postmenopausal women.

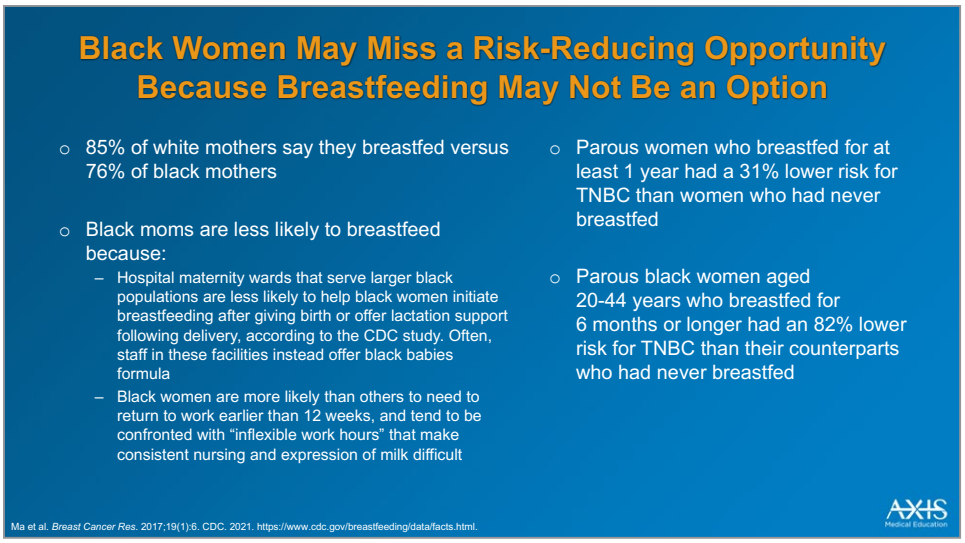
Most Black Mothers Are Single Parents

- 67.9% of all black working women are single moms, making them the primary, if not sole, economic providers for their families
- Add breast cancer to those dynamics!
- What choice will a single mom make between missing work to receive treatment versus going to work to feed her kids?

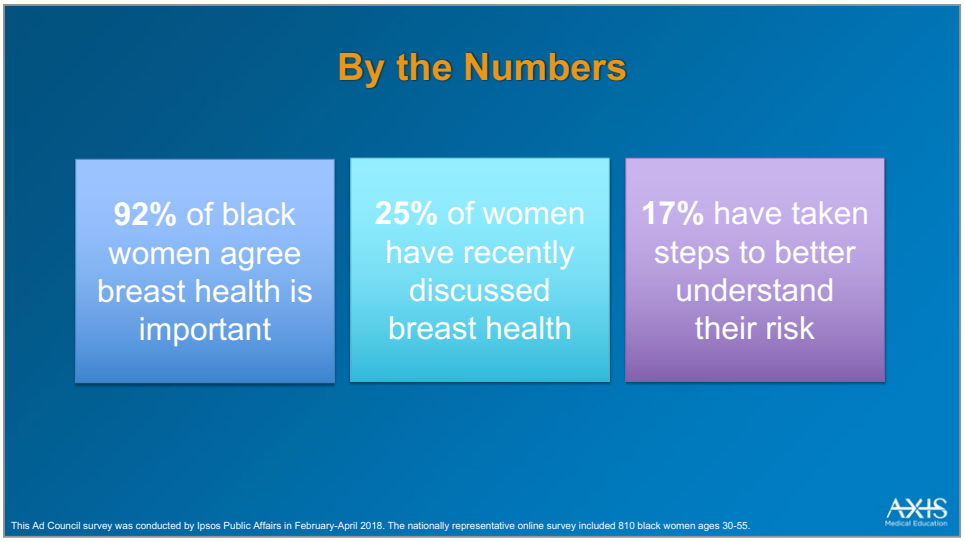
Wilson V. 2017. https://www.epi.org/blog/african-american-women-stand-out-as-working-moms-play-a-larger-economic-role-in-families/

AXIS Medical Education

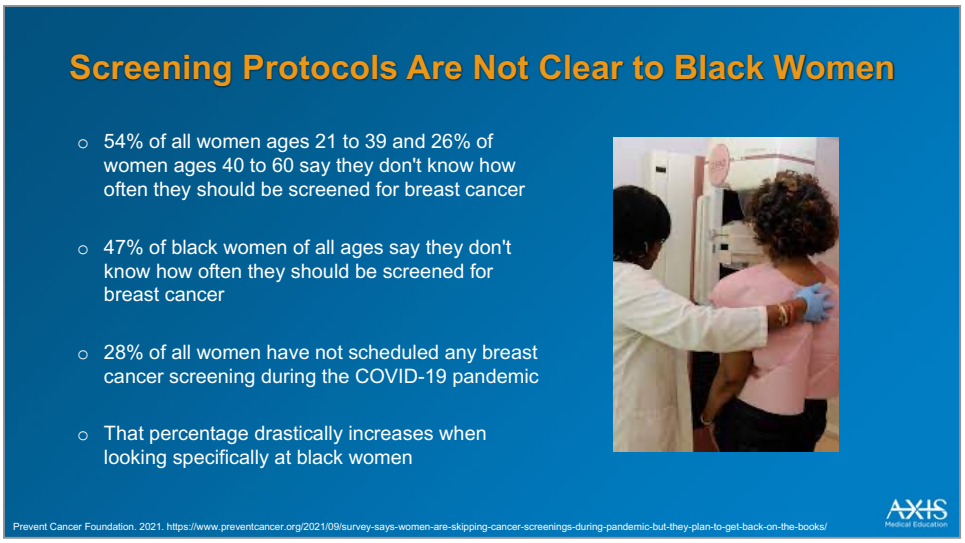
- Another factor that could impact this is that most black mothers are single parents. Almost 70% of all black working women are single moms, making them the primary, if not sole, economic providers for their households. So what does that mean? That means without disease, we are working hard to take care of our kids. They're the priority. Add breast cancer to those dynamics and what choice will a single mom make between missing work and not feeding her kids and maybe not going to treatment or not getting a mammogram? So her focus is on her kids.



- Black women may miss a risk-reducing opportunity because breastfeeding may not be an option for them. So breastfeeding is shown as a way to potentially prevent TNBC; 85% of white mothers say they've breastfed their babies versus 76% of black mothers.

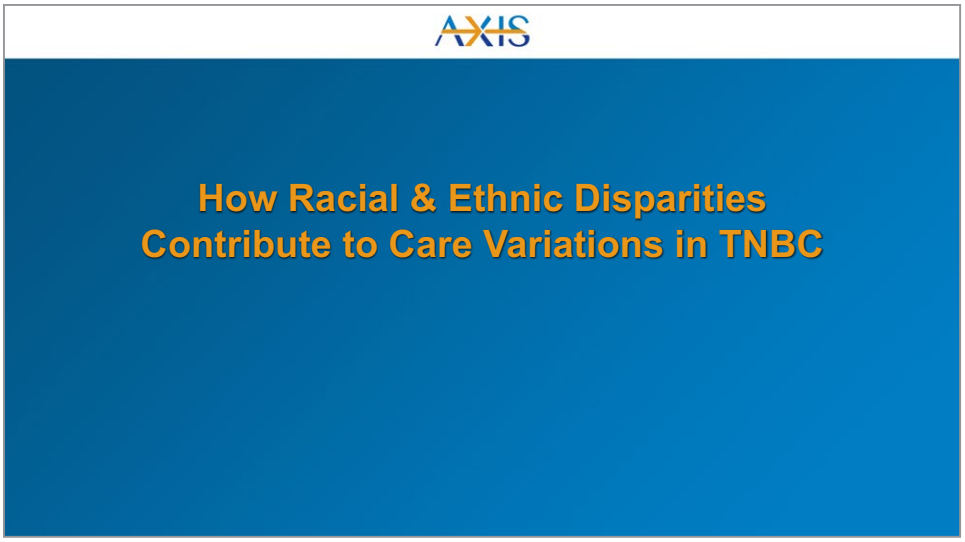


- A study was done by the Ad Council a couple of years ago, and clearly, blacks don't talk about health at the kitchen table. This study identified that 92% of black women agree that breast health is important. Only 25% of black women have recently discussed it with their friends and family, but a mere 17% have taken steps to better understand their risk. So we're not talking about it. It's not top of mind.



- A recent study also showed that screening protocols are not clear to black women. 47% of black women of all ages say they don't even know how often they should be screened for breast cancer.

  28% of all women have not scheduled any breast cancer screening during the COVID-19 pandemic that's really wreaking havoc on our community. That percentage drastically increases when you look specifically at black women. So the pandemic has had a very negative impact on screening.



- So let's talk about some of these ethnic disparities.

Black Women Experience Treatment Delays

- Black women are much more likely to delay following up with a doctor after an abnormal mammogram
- Only 69% of black women start treatment within 30 days of diagnosis compared with 83% of white women
- 20% wait more than 60 days to follow up compared with 12% of white women
- Young black women have the longest and most significant delays in care

Richardson et al. *Am J Public Health* 2010;199(9):1769-1778. Lund et al. *Breast Cancer Res Treat.* 2008;109(3):545-557.

AXIS Medical Education

- Black women also experience treatment delays. We are much more likely to delay following up with a doctor after an abnormal mammogram, and sometimes that's based on insurance, but 20% of black women wait more than 60 days to follow up with their doctor compared to 12% of white women. And only 69% of black women start treatment within 30 days of diagnosis, compared with 83% of white women. Young black women have the longest and most significant delays in care. And why is that? They could be single moms, they may have religious reasons, they may not trust their doctors. A lot of reasons for this. But these delays can cost them their life.

The Hard Truth About Clinical Research

- The unique physiology of black women has not been factored into clinical trial research
- To address the skewed mortality statistics among black women, they must be included in current and future breast cancer research

"[Inadequate minority representation in drug trials means that] we aren't doing good science... If we aren't doing good science and releasing these drugs out into the public, then we are at best being inefficient, at worst being irresponsible."

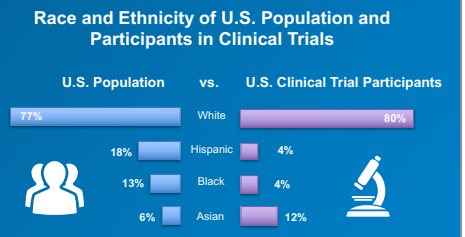
– Dr. Johnathan Jackson
Founder of Community Access
Recruitment and Engagement Center
Massachusetts General Hospital

AXIS Medical Education

- Now let's talk about clinical research. The unique physiology of black women, which we've identified as different, now, has not been factored into clinical trial research. And there's a quote that I'd like to read you from Dr. Jonathan Jackson, Founder of Community Access from Massachusetts General Hospital: "Inadequate minority representation in drug trials means that we are not doing good science. And if we're not doing good science and releasing these drugs out into the public, then we're at best being inefficient and at worst being irresponsible." So we must figure out how to get more black women included in research.

Blacks Are Significantly Underrepresented in Clinical Research

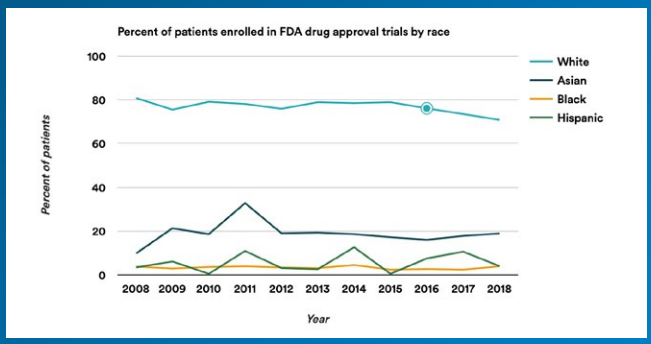
- Blacks represent 13.4% of the US population, but only 7% of clinical trial participants
- Since 2016, the FDA has approved four novel drugs for breast cancer. However, none of those clinical trials had more than 3% black participants



US Census Bureau. Camidge et al. *Future Oncol*. 2021;17(24):3271-3280.

- Blacks represent 13.4% of the US population but only 7% of clinical trial participants overall. And since 2016, the FDA has approved four novel drugs for breast cancer; however, none of those clinical trials had more than 3% black participants.

Disparity of Race Reporting and Representation in Clinical Trials Leading to Cancer Drug Approvals from 2008 to 2018



Loree et al. *JAMA Oncol*. 2019;5(10):e191870.

- The disparities are really significant in representation in clinical trials, and it's been that way for a while, and it's getting worse over time.

Black Breast Cancer and Barriers to Clinical Research

- So what are the barriers to clinical research?

Black Data Matters

- The mission of Black Data Matters is to empower black patients to directly change a research and medical system that often fails them

- Last year and earlier this year, I went out on a mission to establish a program called Black Data Matters. And I really wanted to dig into how we are different and what's driving the emotional barriers to keeping black women from participating in research.

- So I embarked upon this study, and I partnered with some partners—I knew that I couldn't do this alone.

- And together we did a study with the following goals: We wanted to really focus on increasing the participation of black women in clinical trials. What would it take so we can advance the science and save lives?

  We also want to disrupt how the breast cancer ecosystem engages black women in clinical trial research. With 3% participation, something is wrong. And this will all strive for better health equity for black women that have diagnosed with or at risk for breast cancer and help us get the best breast care possible.

Qualitative Methodology

- All digital
- 6 hour-long individual interviews
- 14 two-hour focus groups
- Participants (N = 48) included:
  - Black women with breast cancer who had never participated in a clinical trial, (n = 29)
  - Family members of black women with breast cancer (n = 10)
  - Black women at risk for breast cancer (n = 9)
- Participants ranged in age from 27-63 (mean age 42)
- Patient population included 19 patients with stage II and III breast cancer, and 10 patients with stage IV breast cancer

AXIS Medical Education

- We did 6 hour-long individual interviews, and 14 two-hour focus groups for 48 participants. The age range was 27 to 63, mean age of 42. And the patient population included 19 patients with stage II and III breast cancer and 10 patients with stage IV breast cancer. So we really tried to get the gamut of people with early-stage and late-stage breast cancer.

AXIS

"Don't do a clinical trial! You will get the sugar pill and die."

- Metastatic Patient (Stage IV)

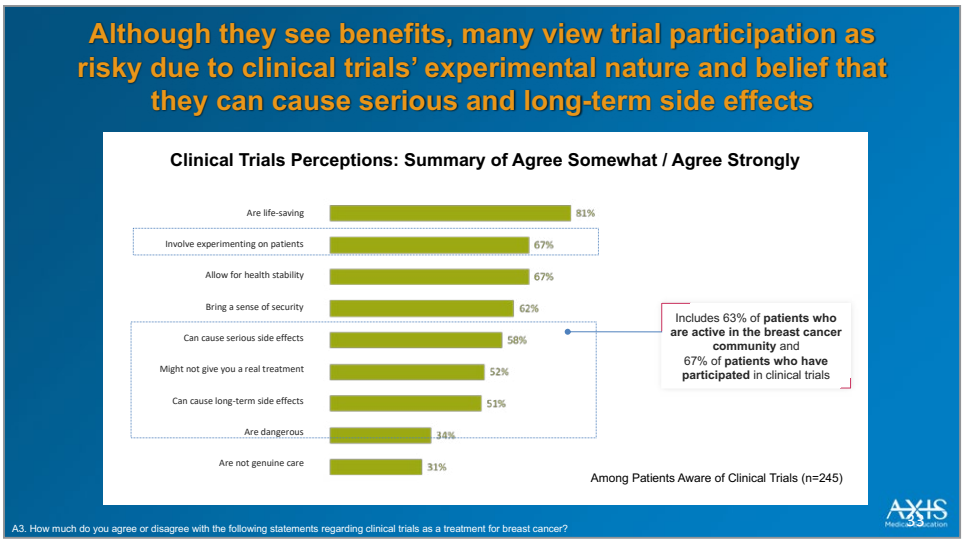
"I feel like a lot of the research is not with Black women. So if I had someone who went through it already, I trust their pain and their feedback."

- Patient Stage II

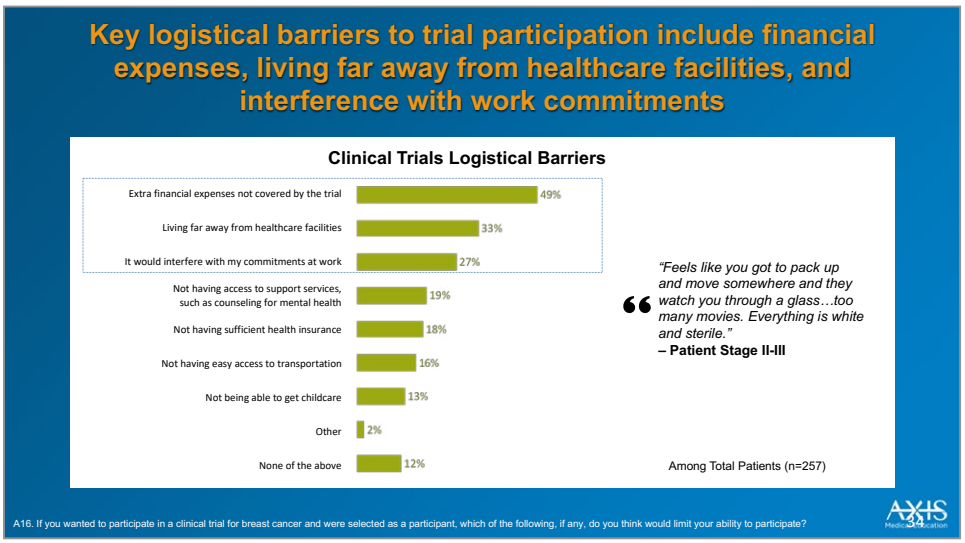
"Whenever I would hear clinical trial, I would always think experiment because it was never really broken down to me, I never considered it, and I've never been approached personally to participate. But I know with my former oncologist, I wouldn't say that I trusted him too much… he didn't really answer a lot of my questions..."

- Patient Stage II/III

- And one of the most confounding messages was coming from a 'Breastie,' "Don't do a clinical trial, you'll get the sugar pill and die." And that was from a metastatic breast cancer patient, a black woman. So when I say as a Breastie, when a Breastie says something, it's a credible thing to another Breastie. So we what we found in the research was that our Breasties were giving incorrect information to other Breasties because of their own personal fears and biases.

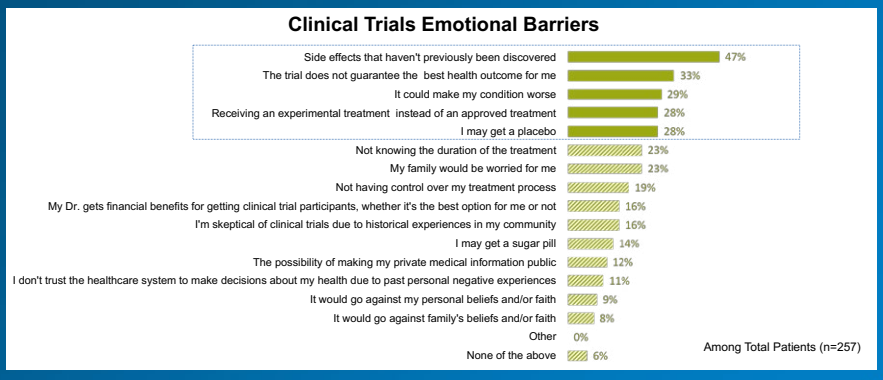


- Although they see benefits, many view trial participation as risky because of the clinical trials' experimental nature, and they believe they could cause serious and long-term side effects.



- There are also logistical barriers to trial participation, including: Am I going to have to pay for it? Is it far away from my home? Is it going to interfere with my work?

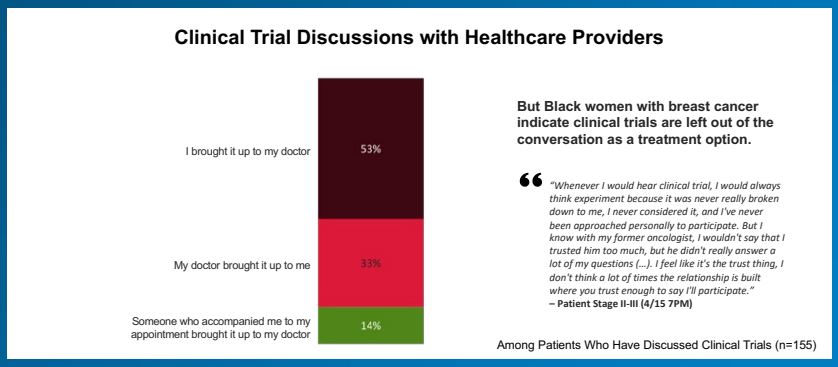
Uncertainty shapes patients' emotional barriers to trial participation



A17. Which of the following, if any, are concerns you have about participating in clinical trials for breast cancer?

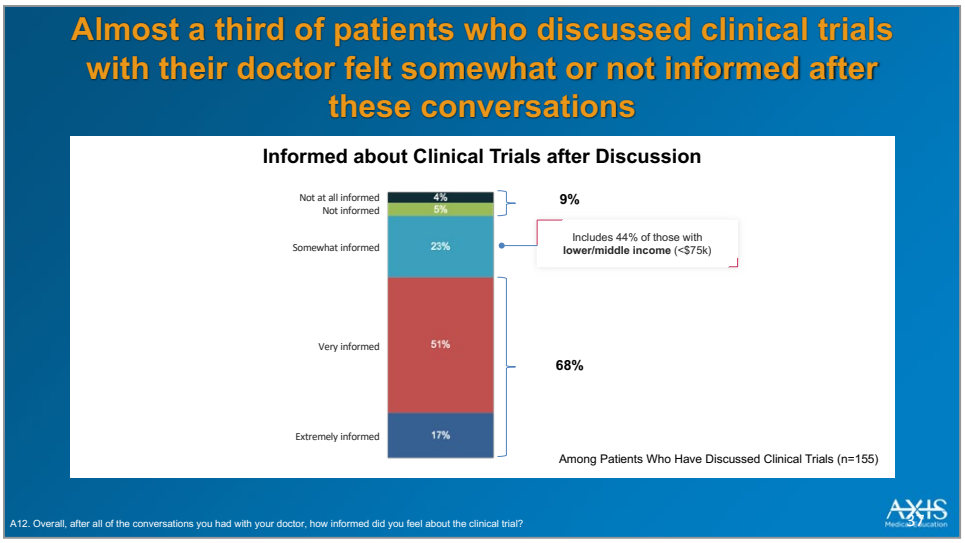
- Also, uncertainty shapes our emotional barriers of trial participation.

Almost two-thirds of patients have discussed clinical trials with their doctor, but it's the patient who is more likely to initiate this conversation

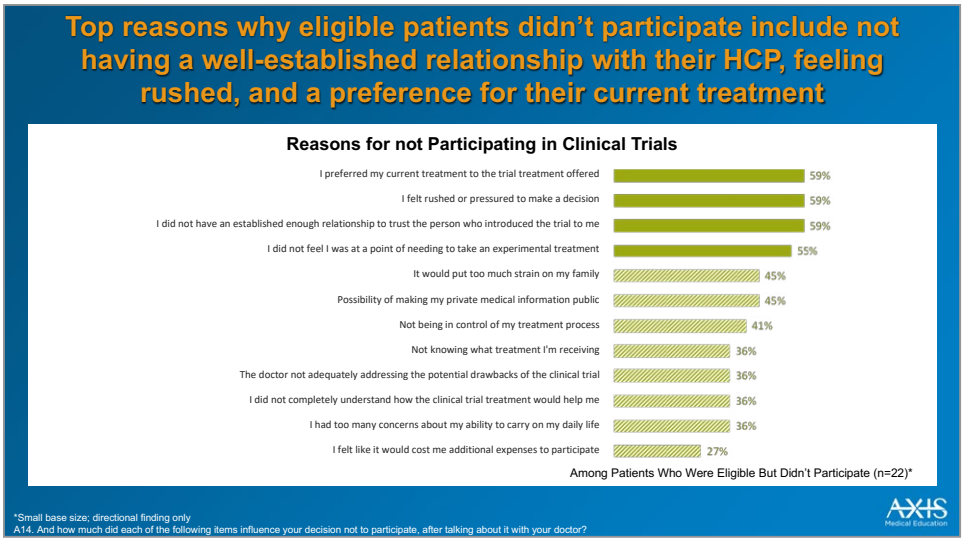


A6. How many times have you talked to your doctor about possibly participating in a clinical trial for breast cancer?
A7. During the **first** time you talked to your doctor about possibly participating in a clinical trial for breast cancer, who brought it up?

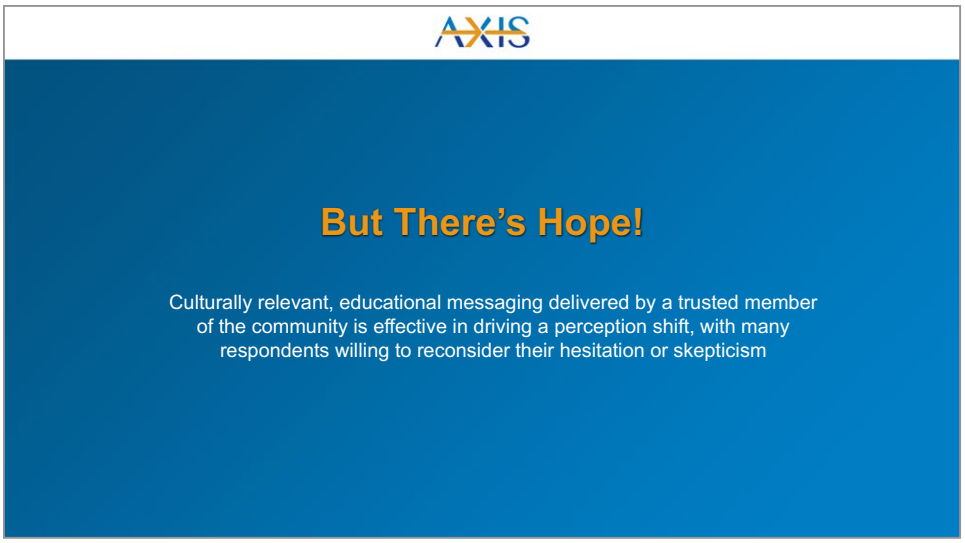
- Almost two-thirds of the patients in our study have actually discussed a clinical trial with their doctor, but it's the patient who was more likely to initiate the conversation.



- Almost a third of the patients we talked to who discussed clinical trials with their doctor felt somewhat or not informed after the conversations.



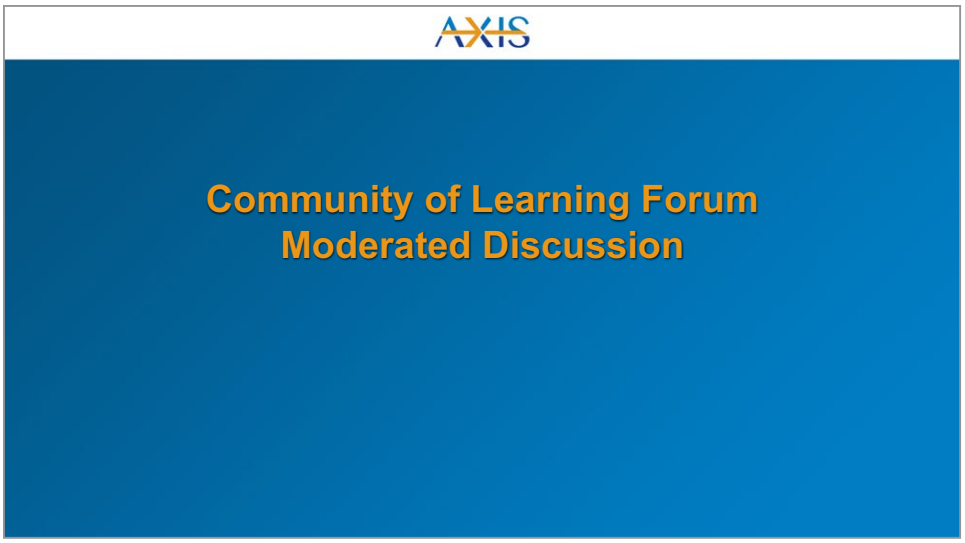
- The top reasons why eligible patients didn't participate include not having a well-established relationship with their HCP, feeling rushed in the conversation, and a preference for their current treatment just because they were somewhat comfortable with it. So those are some of the fears.



- But the good news, though, is that there's hope.

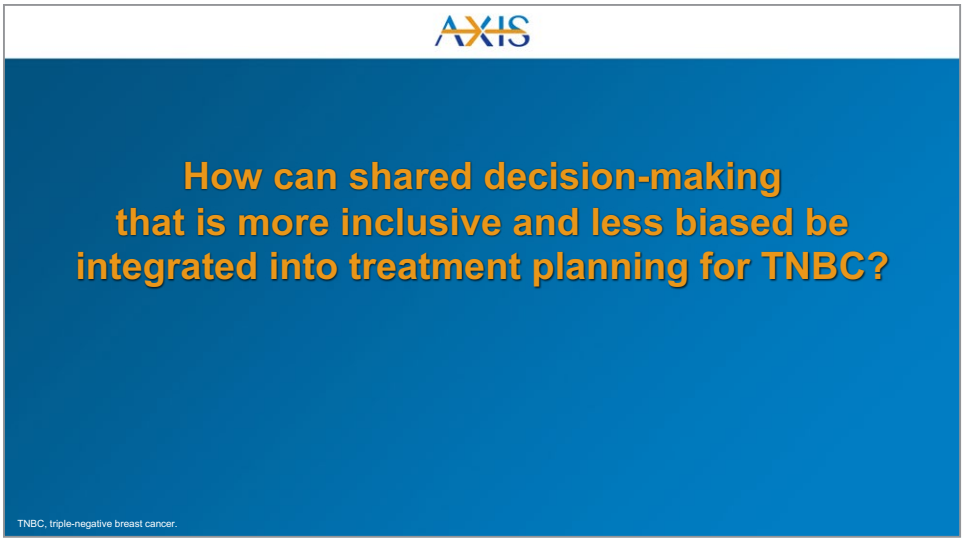
- And what I learned in talking to these Breasties, that if we have culturally relevant and educational messaging from a trusted member of the community, a 'Breastie,' it's effective in driving a perception shift, with many of the respondents willing to reconsider their hesitation or skepticism, once they talk to a Breastie with very simple messaging.

  But the most compelling messaging that really worked with this audience was do it for your daughter, do it for your granddaughter, think about your community, think about your family.



Whitaker: Thank you so much, Ricki, for that really informative talk on disparities in TNBC.

Now we're going to move on to a few questions that are relevant to this topic, and our faculty panel will address these questions.



The first question—and Ricki, I'm going to start with you: How can shared decision-making that is more inclusive and less biased be integrated into treatment planning for TNBC?

Fairley: It really is shared decision-making, because it's really a family decision. But we have to provide an outlet for black women to be able to really understand the basics of clinical trial research. We have to make sure that they are equipped with information, and that is ground zero. And right now, the literacy around this is very, very low.

So even before they can talk about making a decision about it, we need to educate them. And that should come from every place that it can—from the provider, from the health institution, from whoever they interact with, so that when they go home and talk about it, they feel good about

being able to even explain it to their family. But it really is, even before they can get to making a decision, it's about education.

Whitaker: Education is so important. We see that definitely is the case with improving clinical trial enrollment.

Dr. Tolaney, what is your take on this? I know you're at the Dana-Farber Institute where you have a lot of resources and probably support for clinical trials. What has been your experience in terms of trying to improve the shared decision-making?

Sara Tolaney, MD, MPH: Ricki did a wonderful job discussing the challenges that we face with clinical trial enrollment. One of the things you highlighted so nicely is that it is really a discussion between the patient and physician. And sometimes there are patient barriers to clinical trial enrollment, but sometimes there are physician barriers to enrollment. One of the things you brought up really nicely is sometimes it's a patient who's coming to the doctor asking for the trial rather than the doctor offering the trial to the patient, which is such an important point.

Sometimes there are challenges that physicians face with getting patients into trials. And in fact, our group did a survey of physicians about what they felt were barriers to clinical trial enrollment for them, one of which was it's hard for them to keep track of all the trials that are available for patients and to figure out how to match patients to trials. There needs to be better systems in place for that. And in fact, our group created a matching system on a website so the physician can just plug in a couple key factors, and then it spits out the trials that are available at our institution, just to make them aware, so that they can match the patient to the trial.

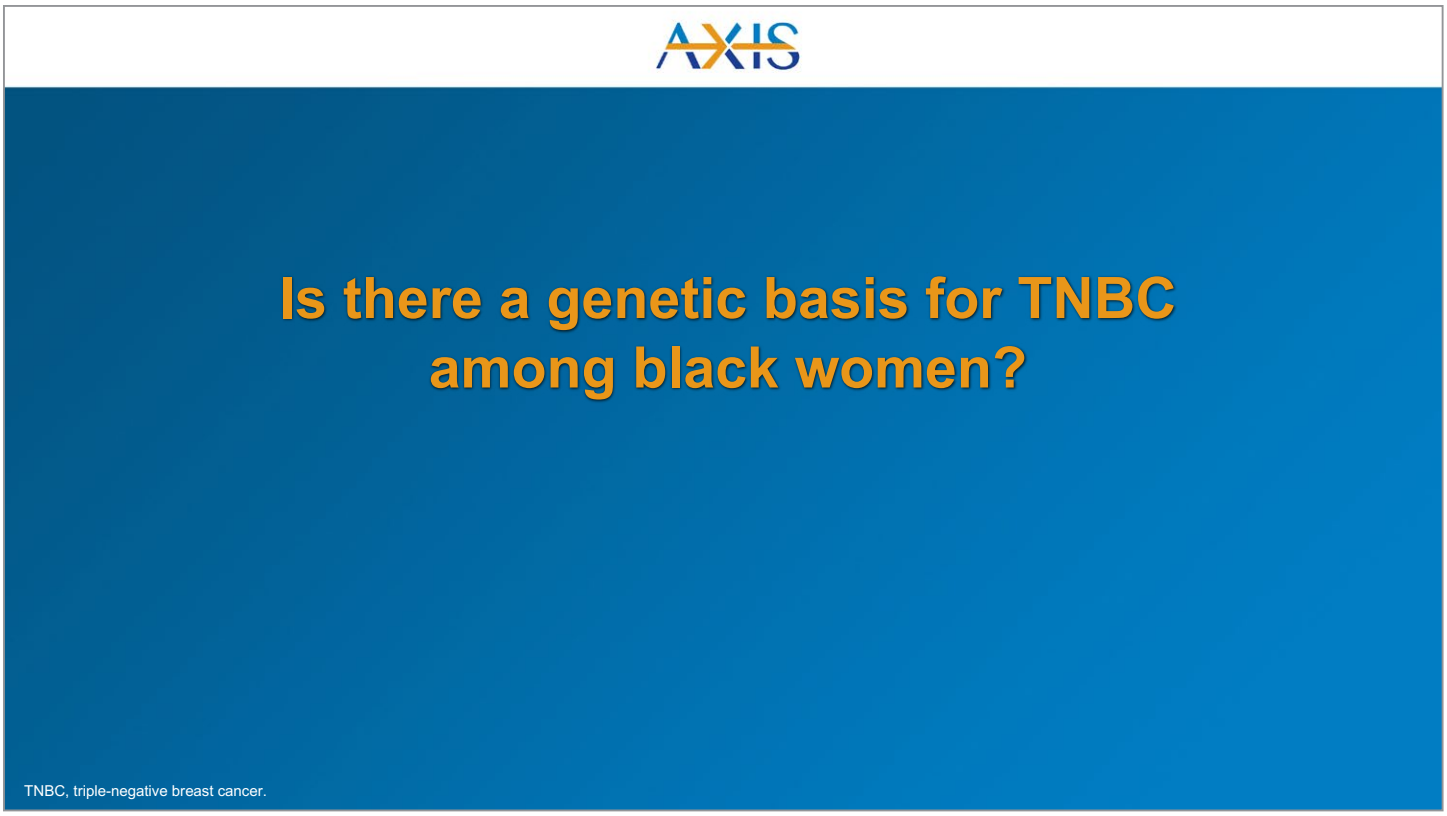
But again, it's getting more and more complex, as there are more nuances, like more genomic alterations you need to take into account when trying to figure out if a trial would make sense. There's just a lot of pieces of information for physicians to keep note of, and better technological systems to help with that would be important. It also takes time in clinic to have a discussion; that shared decision-making process is not a quick one and needs to be dealt with carefully, with an informed process between the physician and the patient.

I think physicians feel pressured and rushed because they have a certain number of patients they have to get to in clinic. That plays a role in terms of part of this decision-making process.

There are challenges on both ends of it. We all need to do better, because clinical trials are the path to not only allowing patients to get access to new drugs in a timely manner, but also for us to be able to make dramatic improvements in care. And so, lots of systematic changes are needed to make this process better.

Whitaker: This issue of implicit bias is a real one in terms of clinical trials. There have been studies that have demonstrated that black patients get offered clinical trials less, but when they're offered clinical trials, they tend to accept clinical trial participation similar to non-black patients.

So, we absolutely have to make sure that all members of the research team, whether that be the physician or the research assistant, trial coordinators, have that implicit bias training so that we're not automatically writing off patients that definitely need to be in these trials and probably would be willing to participate under the right kind of informed discussion.



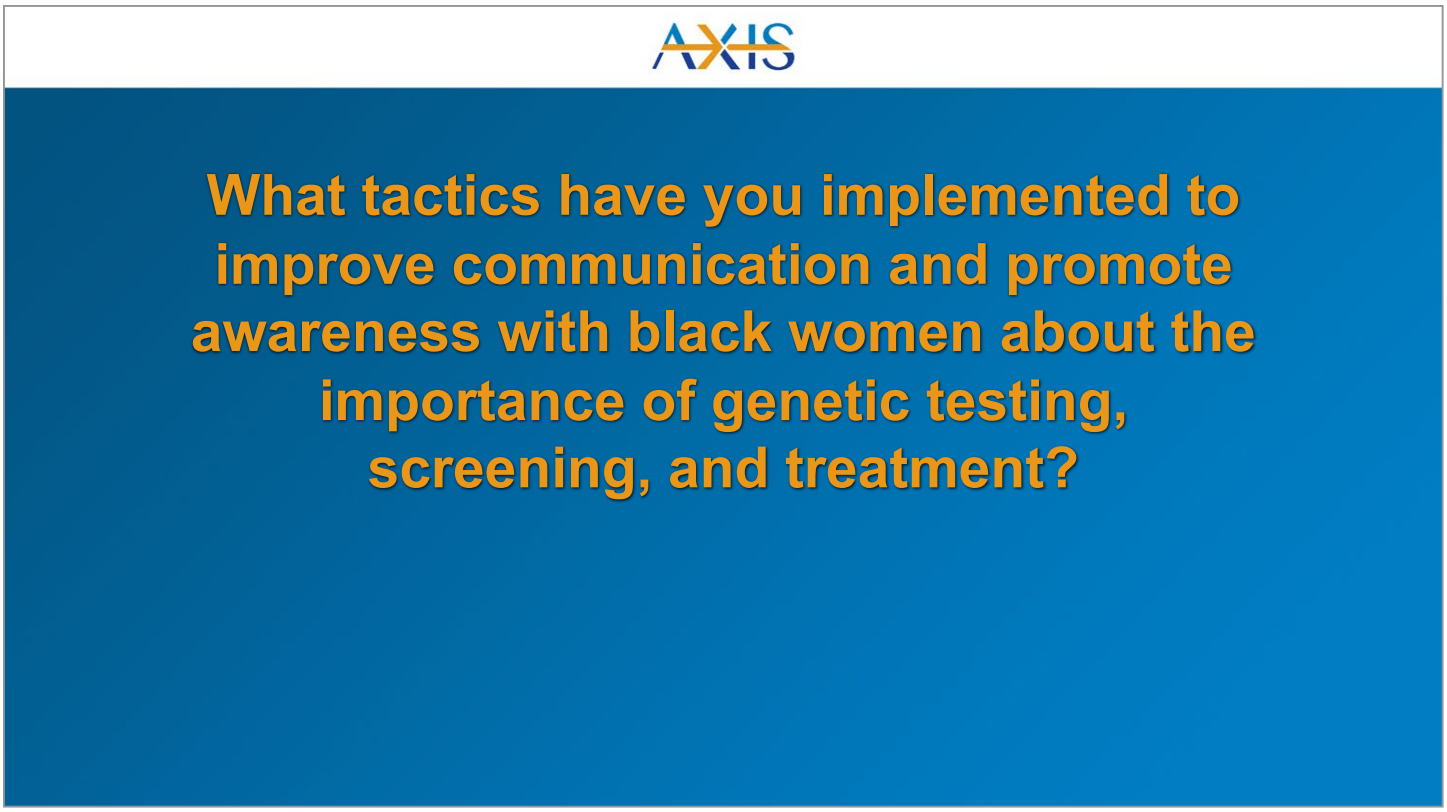
So, we can move on to the next question, which asks: Is there a genetic basis for TNBC among black women? And because I do so much talking about genetics as part of my practice, I'll start with this question. So it's a great question, and it's an important point to make. Of all the breast cancer subtypes, we know that TNBC is the most likely type of breast cancer to have a genetic basis. As we continue to study TNBC, we're getting a better idea of how common is to have a genetic etiology for your breast cancer.

So, you know, in your kind of run-of-the-mill breast cancer, that's not TNBC; for example, hormone receptor–positive HER2-negative breast cancer, you're going to see about 5% of patients have a genetic cause for their breast cancer. In TNBC, we have studies showing that that number could be as high as 20%; most studies show somewhere about 15% to 17% of people with TNBC will have a genetic mutation.

What is really important to emphasize is that we actually don't have good estimates in terms of the prevalence of genetic mutations in black TNBC patients, as opposed to white TNBC patients. Unfortunately, much of the genetics research we have was conducted in non-Hispanic, white patient populations. We just now are starting to see racial and ethnic diversity in our research studies in patients undergoing genetic testing. So right now, I don't think we have the answer in terms of whether or not there's a difference in the genetic basis. But I would say certainly black women have a genetic etiology beyond their TNBC that's probably pretty similar to other races, if not more contributed to genetics.

Dr. Tolaney, did you have anything you wanted to add?

Tolaney: It's a great question, but as you point out, we don't have great data about differences between black and white women, for example, and genetic risk. But there's got to be something with genetic risk, just given the high rates of TNBC among the black community.



Whitaker: So we'll ask this question. Ricki, we can start with you. What tactics have you implemented to improve communication and promote awareness with black women about the importance of genetic testing, screening, and treatment?

Fairley: We have started an education campaign to really educate black women about the importance of these important things. And one of the things that we're doing is we have an HBCU internship program. They're all pre-med students, pre-health career students, and what we ask them to do is do an interview with their moms at the beginning of their internship, and then also do a poll on their Instagram accounts to see how many of their friends actually are aware of breast health. And when they start out, it's zero. None of their friends can talk about breast self-exams, about screening, about anything.

And guess what? Those conversations with their moms are really the first time that they've actually talked to their mom about breast health. And then they work for 10 weeks, they post on social media, we give them a lot of content. And by the end of the internship, they can show that, 85% of my friends now know how to do a self-exam. And so we're finding great, great, you know, insight from these young women not only being an educator of their peers, but also starting those important conversations at the kitchen table with their moms and their aunties and their grandmas.

So it's so important to educate them when they're young, before they have risk of cancer and before they – actually, they're at risk even at that age, black women, but also before they, you know, have to even think about trying to do a clinical trial. So that's so important.

The other thing is that we do a lot of education, through what I call our Breastie Choir talking to breast cancer patients about the importance of screening, the importance of knowing your treatment options.

Whitaker: Great, Ricki.

What about you, Dr. Tolaney, is there anything that you guys are doing at Dana-Farber, initiatives to improve genetic testing or screening in minority patient populations?

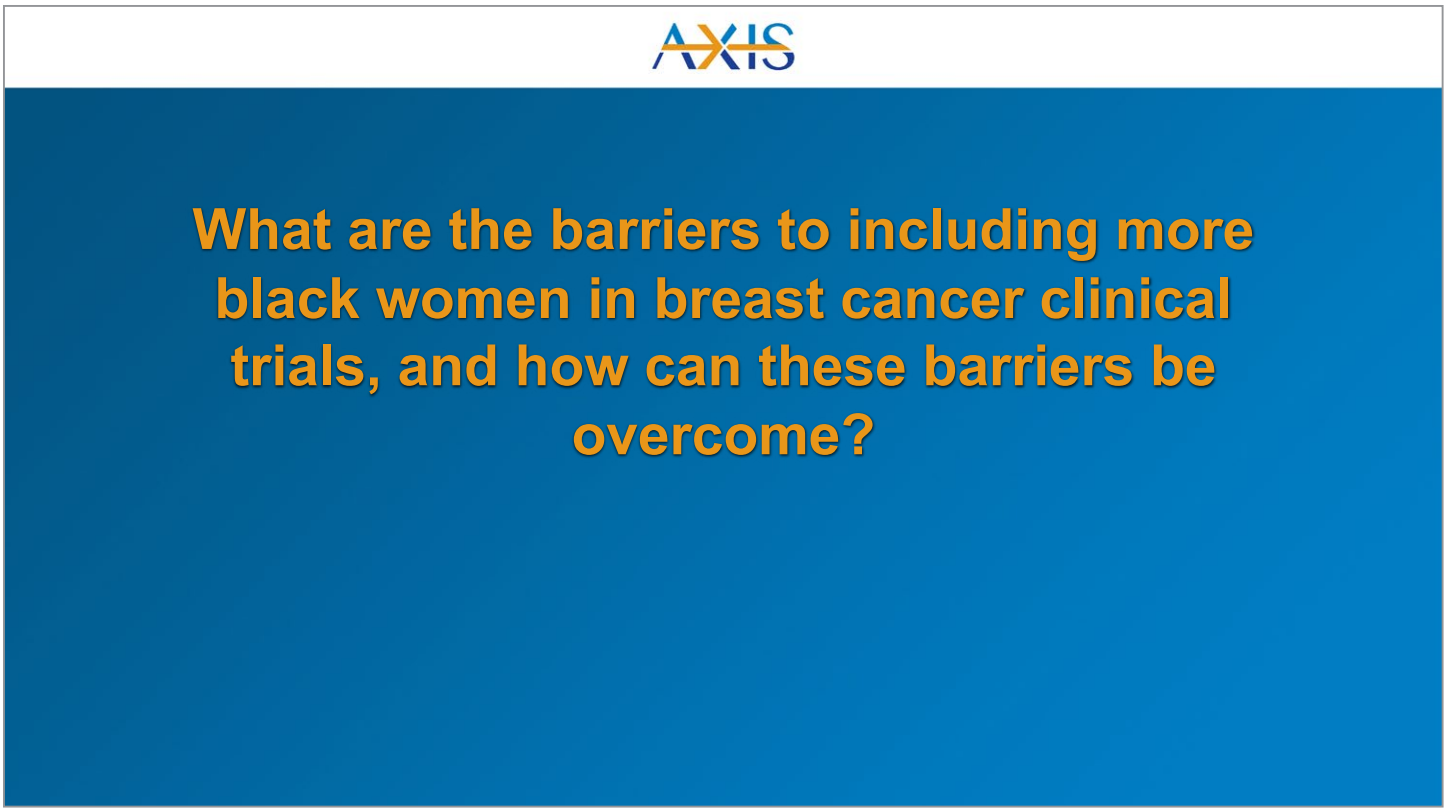
Tolaney: We've learned that genetic testing is becoming more and more critical in all breast cancer patients, regardless of race, ethnicity, or even breast cancer subtype, because what we're learning is that there are drugs, actually, that can work in patients who have breast cancer, who have genetic mutations. But we won't know if they're candidates for those drugs if we don't know if they have a

mutation. And so really, there needs to be a movement toward more universal testing for patients who've developed breast cancer, and that is a movement that our group has been working toward.

One of the challenges is access to genetic counselors. So, one of the big areas of interest that our group has had is trying to get genetic counselors into the communities. Certainly we're at a very privileged institution where we have genetic counselors available, but this isn't a common thing in many community locations. And so, you know, one of the great things about virtual technology is that you can do telehealth consult for genetics, you can send someone to swab themselves at home and mail it back. It's making genetic testing and counseling so much more accessible.

We need to really move this into the community more, and that has been an area of outreach for our group. And certainly I'm in a different position because most of my patients already have breast cancer, right? I am a breast oncologist, so I don't get into the community from a prevention standpoint, which is also equally important.

Whitaker: Dr. Tolaney, that's great. When I think about care and improving disparities, we have to definitely adapt to this mindset of taking the care to where the patients are, and this idea of going into the community and using telegenetics and things like that, it's really a great way to try to move in that direction.



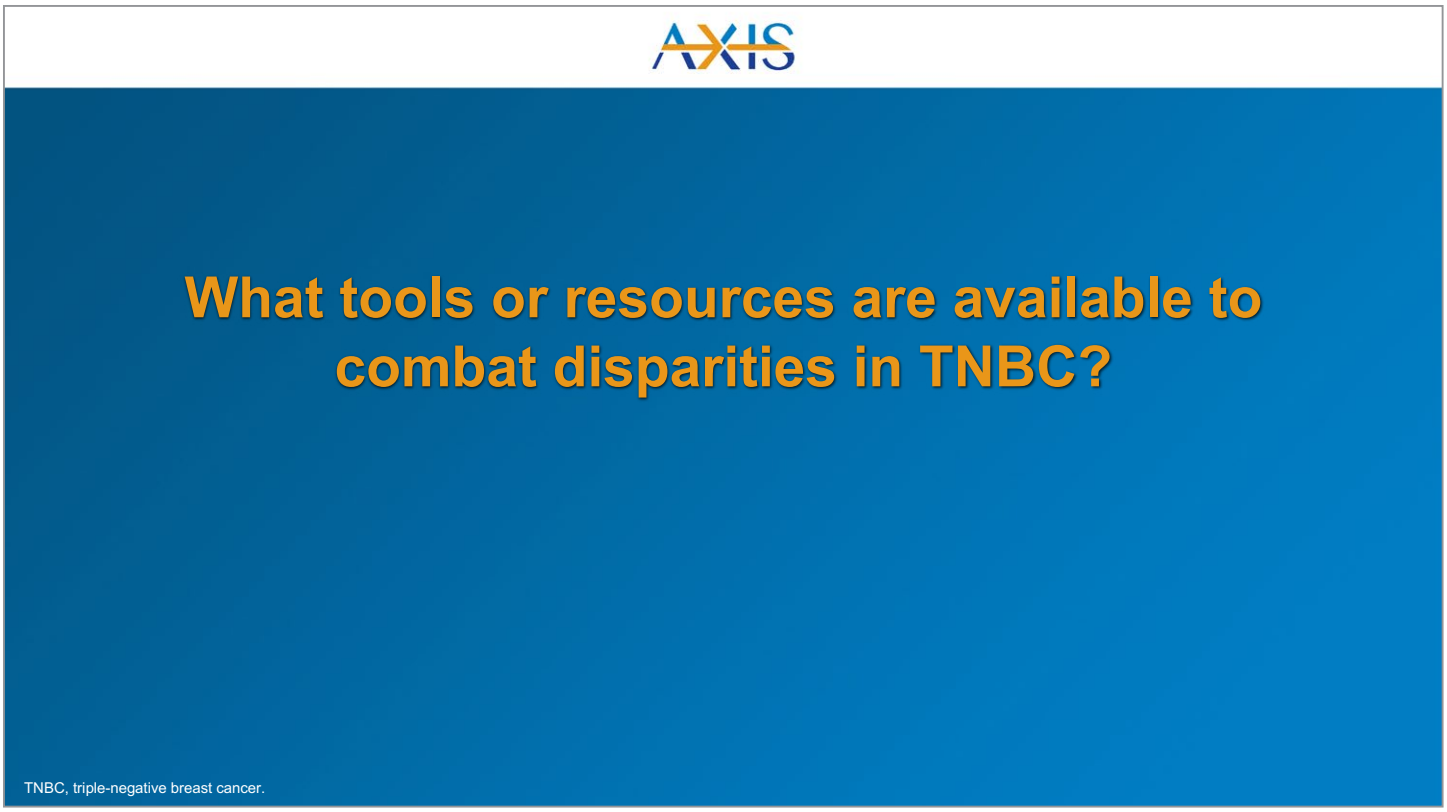
- Ricki, you talk so much about this; I'm going to direct this one at you to start with. What are the barriers to including more black women in breast cancer clinical trials, and how can these barriers be overcome?

Fairley: It's fear. It's just fear. From history, from perceptions, from, you know, I'm going to get the sugar pill, I think it's all the things that I spoke about earlier. But it's also we're taking away her power. You know, black women are these powerful, amazing women that take care of everybody at the expense of themselves.

Whitaker: Dr. Tolaney, do you have other thoughts about this question?

Tolaney: It's interesting, because education about treatment and trials is part of the critical nature to taking away that fear. Right? And it does mean that whether it's the black community, the Hispanic community, whatever ethnicity, we need to be making sure we continue to educate and continue to earn that trust, which I think is such a critical part of the shared decision-making process and coming to a good plan moving forward.

Whitaker: Yeah, that's definitely true. And, you know, I think the only thing I'll add is that in these situations with clinical trials, there is so much medical mistrust because of history. So, it's important to emphasize to patients when we talk about clinical trials, there now are protections that are in place for clinical trial participants, because I think that's something that, your everyday person is not going to realize. Well, Tuskegee happened, and then the Tuskegee syphilis report happened, and then we designed these protections of human rights for research subjects, rules and regulations. So there are some protections. I think that's important to emphasize when you talk with black patients about clinical trials.



- Ricki, this is probably a great question for you.

  What tools or resources are available to combat disparities in TNBC?

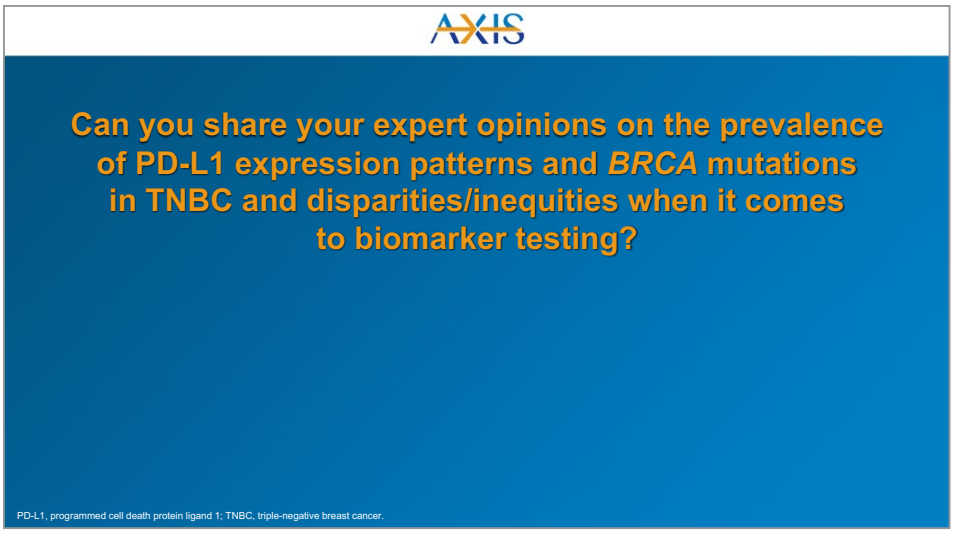
  Fairley: Well, you know, I serve on the board of the Triple Negative Breast Cancer Foundation and our website, tnbcfoundation.org has incredible resources for anyone with TNBC, no matter your color. And we've worked really hard for it to be kind of a place of information, kind of the go-to place for information, support, resources, science, just even having a support group with women with TNBC. We really try to make that available.

  Also within my foundation, TOUCH, we have a virtual support group about once a month. And we talk about other things besides TNBC, but whereas the TNBC Foundation has women with only TNBC, our foundation has resources for black women with all kinds of breast cancer. So just having that platform to provide communication and, again, the voice of creditability as a Breastie. So I know I can talk about breast cancer and TNBC in a different way than a doctor can. And so providing this outlet for conversation and just giving a hug and making people feel comfortable that they could ask anything is really important.

  I think the one thing that really kind of is frustrating to TNBC survivors is, normally the support groups that you go to for breast cancer are predominantly white women over 50 or 60. And we're usually younger, and we can't take tamoxifen. And they're complaining about tamoxifen and, you know, and getting hot flashes. And so just to have a place that's relevant about TNBC for women that look like us is really, really important. So making those tools available.

  We also have some tools on our website, touchbbca.org. And frankly, I answer the phone every day. I know this is my purpose. You know, my doctor gave me 2 years to live, and I'm on 10. And this is my purpose. I do it every day, I fight like a girl every day to help have these conversations and provide tools and resources for black women. So call me. Tweet me.

  Whitaker: Yeah, we'll have to remember Ricki's name. She's really doing very powerful work here for the TNBC community, especially.



So, the next question, Dr. Tolaney: Can you share your expert opinions on the prevalence of PD-L1 expression patterns and BRCA mutations in TNBC and then potentially comment a little bit on whether there are any known disparities or inequities when it comes to biomarker testing?

Tolaney: In general, we test patients who have TNBC. We test their tumors for PD-L1, if they have metastatic triple-negative disease. We don't need to do that in someone with early-stage TNBC. And the reason we do this is because there are data to suggest in metastatic triple-negative disease that if the tumor has the PD-L1 receptor on it, that patients with that kind of TNBC will benefit from the use of immunotherapy, specifically, with the benefit of checkpoint inhibition with chemotherapy. So it really is a critical part of making treatment decisions for our patients with metastatic TNBC.

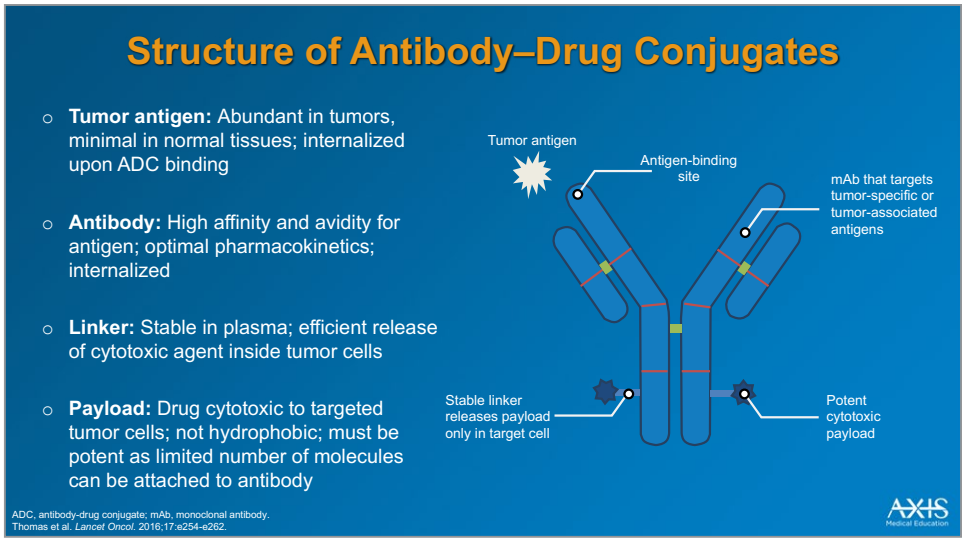
And similarly for genetic testing, we do want to know if someone has a BRCA mutation to understand if they could be a candidate for a drug called a PARP inhibitor. So you know, these two pieces of biomarker testing are really quite critical when trying to make treatment decisions for patients with, particularly, metastatic disease. And now even with early-stage triple-negative disease, understanding if someone has a BRCA mutation can impact treatment recommendation.

So really again, very critical, we know that about 40% of patients with metastatic TNBC will have a tumor that is PD-L1 positive. We know that about 10% to 15% of patients with triple-negative disease will have a BRCA mutation. So, these aren't rare findings and are critical to understand.

In truth, we don't have great data about differences according to different ethnicities or racial patterns. I think much to Ricki's point, a lot of this is because of a lot of research that has been done involves very few minorities. If you look at the major registration trials that led to approval, for example for pembrolizumab, as Ricki pointed out, there are very few patients who are, for example, black or Hispanic. And so getting data from large registration trials is even challenging, even though there are 1,100 patients, for example, in KEYNOTE-522, you're still going to have very limited data on differences by ethnicity and race. And that's a challenge. Again, it shows that this is an area where we really need to do better.

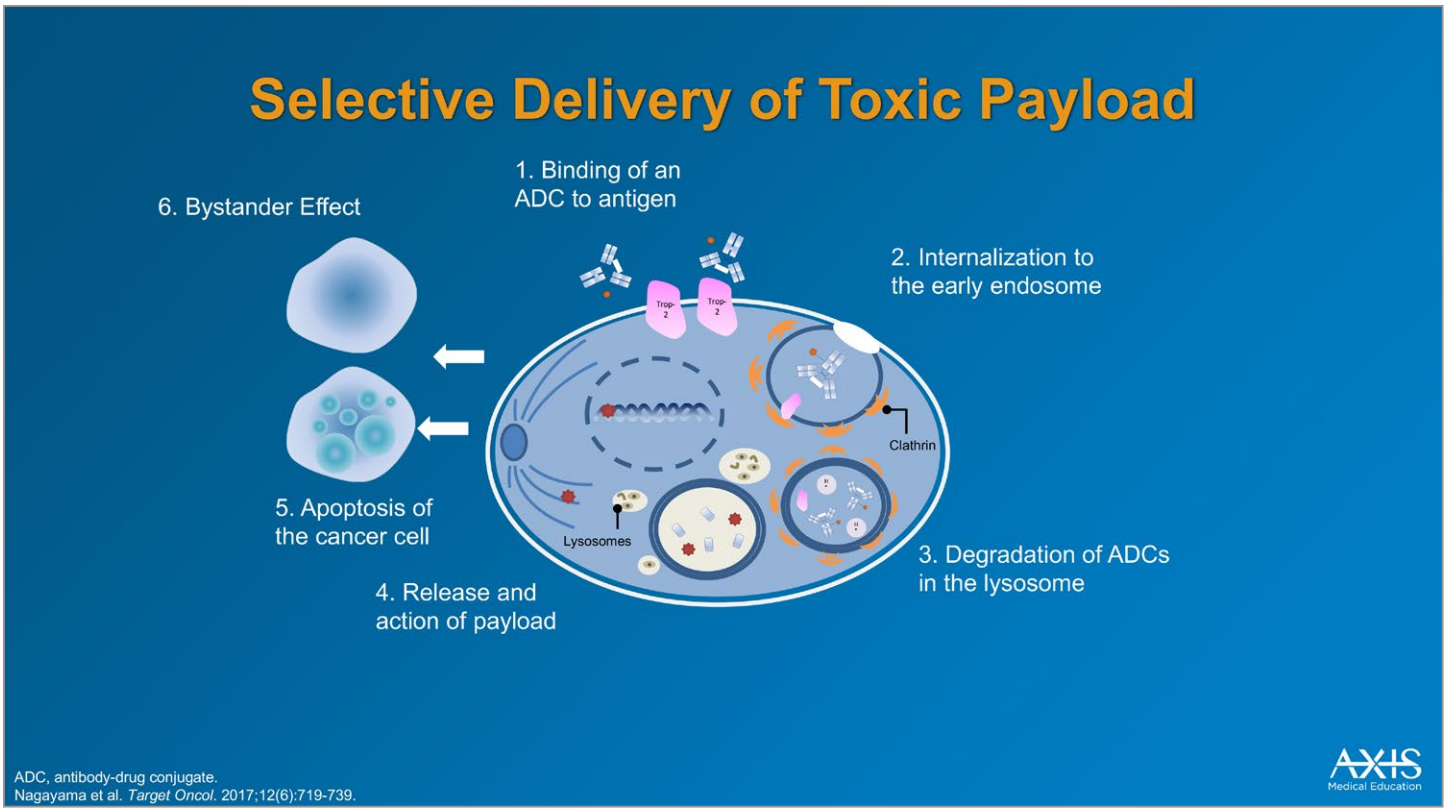
Whitaker: We've talked so much about the aggressive nature of TNBC, we've talked about how we don't have any kind of drugs to prevent recurrence, as Ricki pointed out in her talk. And we know that these patients tend to have the worst prognosis of any breast cancer subtypes. So with that, we can easily say there's a critical need to expand treatment options for all patients with TNBC.

Dr. Tolaney, can you comment on some of the newer developments in the triple-negative space over the past couple of years?



Tolaney: I think it's been a really exciting time, because we have seen new approvals for TNBC.

And particularly, I think one area that is of great interest is development of what we call antibody-drug conjugates. So this really means that we take an antibody that is designed to target a particular receptor on a cancer cell and link it to very potent chemotherapy. And then that antibody binds to the receptor that's on that cancer cell. It gets taken into the cancer cell and releases its chemotherapy into the cell. A lot of people think of these as smart bombs or targeted delivery of chemotherapy. It's pretty ingenious, because it allows you to give drugs that are normally very toxic drugs that we couldn't just normally infuse but can now when we link it to an antibody, and we can deliver high doses into a cancer cell.



And I think one other clever trick about some of the newer models of antibody-drug conjugates is that once that chemo drug gets into the cancer cell, it can actually diffuse through the cell membrane into a neighboring cancer cell and kill it. And the reason that is sometimes critical is because not all cancer cells are the same. Sometimes we see heterogeneity within a tumor where we see, for example, that not all the cancer cells have the same receptors on them. And so let's say you had an antibody-drug conjugate that was targeting TROP2, and the TROP2 was only expressed on one cell but not on the neighboring cell. Well then, if an antibody drug conjugate didn't have chemotherapy that was being delivered that could diffuse into neighbors, then it wouldn't work in that neighboring cell, right? Being able to have what we call bystander effect and get your drug into the neighboring cell, sometimes can be quite critical in overcoming tumor heterogeneity. These newer antibody-drug conjugates have been developed with that in mind.

FDA-Approved ADCs in Breast Cancer

Drug Name	Target	Indication	FDA Approval
Trastuzumab emtansine	HER2	As a single agent, is indicated for the adjuvant treatment of patients with **HER2-positive early breast cancer** who have residual invasive disease after neoadjuvant taxane and trastuzumab-based treatment	05/2019
		As a single agent, is indicated for the treatment of patients with **HER2-positive, metastatic breast cancer** who previously received trastuzumab and a taxane, separately or in combination	02/2013
Trastuzumab deruxtecan	HER2	Adults with unresectable or **metastatic HER2+ breast cancer** who have received ≥2 prior anti-HER2 based regimens	12/2019
Sacituzumab govitecan	TROP-2	Adult patients with unresectable, locally advanced or **metastatic TNBC** who have received ≥ 2 prior therapies (at least 1 in metastatic setting)	04/2020 (accelerated) 4/2021 (regular)

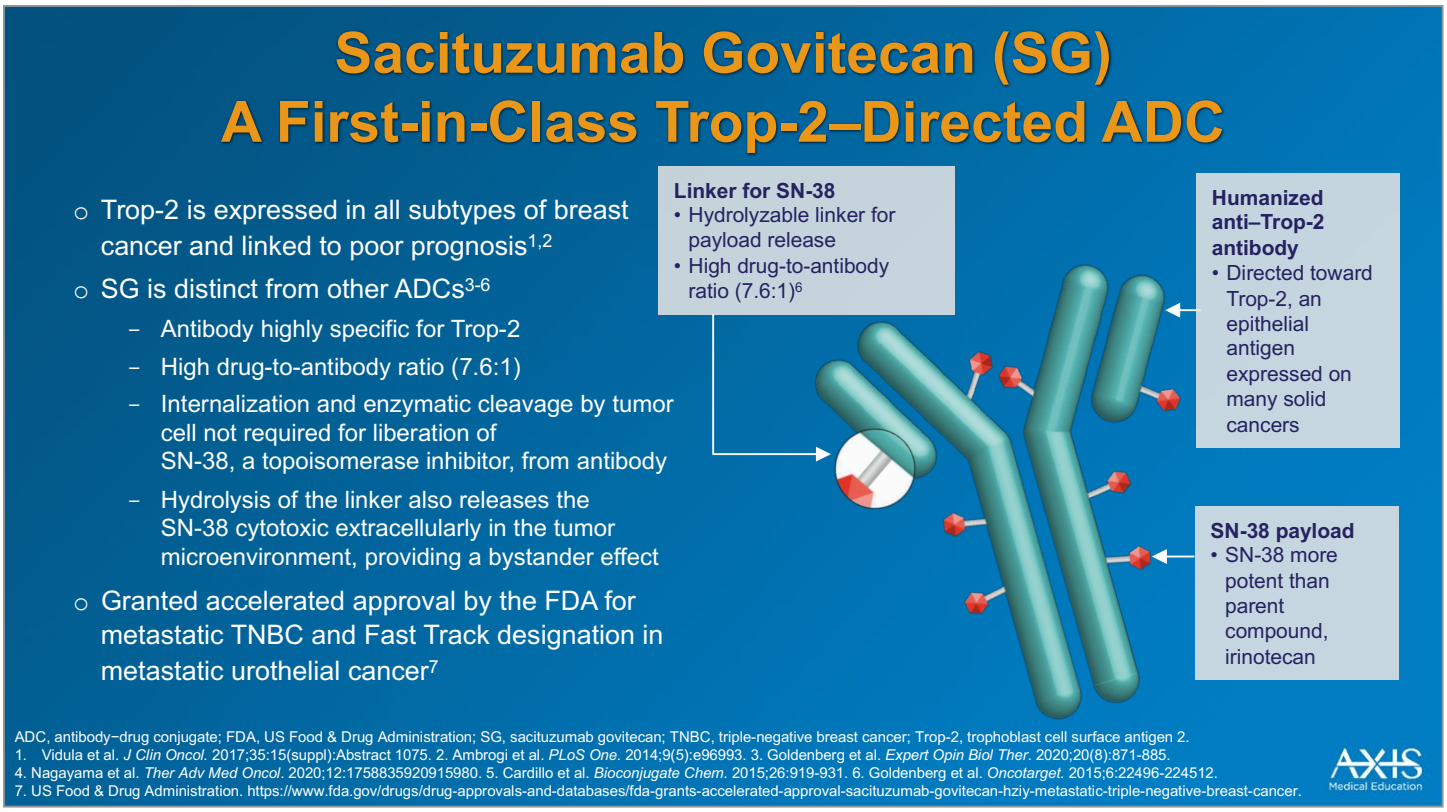
ADCs, antibody-drug conjugates; FDA, US Food & Drug Administration; HER2, human epidermal growth factor receptor 2; TNBC, triple-negative breast cancer; TROP-2, trophoblast cell surface antigen 2.
FDA, 2013, 2019, 2020, 2021.

AXIS Medical Education

- The very first antibody-drug conjugate that was approved in breast cancer was a drug we call T-DM1 or trastuzumab emtansine that was FDA approved for HER2-positive disease and is a standard drug that we use both in early-stage and metastatic HER2-positive breast cancer. That was developed with a bit of an older technology, so that drug cannot function by bystander effect. It has a non-cleavable linker, and the payload or the chemotherapy that's being delivered does not diffuse through the cell membrane.

  However, the newer drugs that have been developed, such as a drug called trastuzumab deruxtecan also known as T-DXd, which is FDA approved for metastatic HER2-positive disease, does function by bystander effect. It delivers very high doses of chemotherapy into the cell. And sacituzumab govitecan, which is approved in TNBC, also can function by bystander effect.

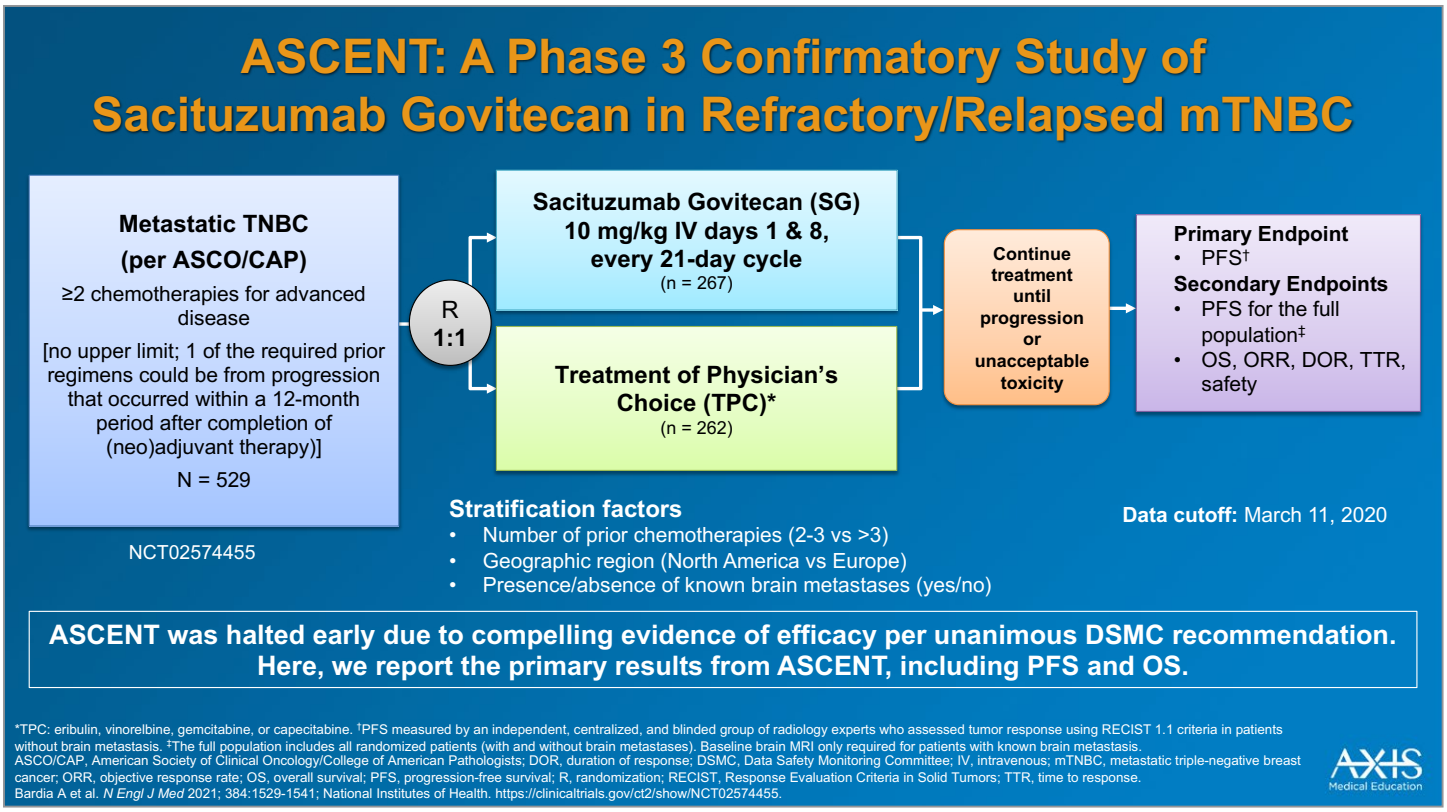
  So, again, nice to see these new technologies that are making antibody-drug conjugates even more effective because of their new ability to deliver high doses of chemo and function by bystander effect.



The drug that was FDA approved for triple-negative disease, again, is sacituzumab govitecan. Sometimes I call it "sassy" for short.

Interestingly, again, it's targeting TROP2. It's confusing for patients sometimes, because we just told them they have a TNBC that doesn't have estrogen, progesterone, or HER2. And so they're like well why do you think there's this other receptor on the cancer cell? But it turns out that TNBC truthfully is a very bad name, because it doesn't mean that there aren't other receptors on cancer cells. In fact, TROP2 is actually very prevalent in the vast majority of TNBCs and actually is also on hormone receptor–positive breast cancer cells.

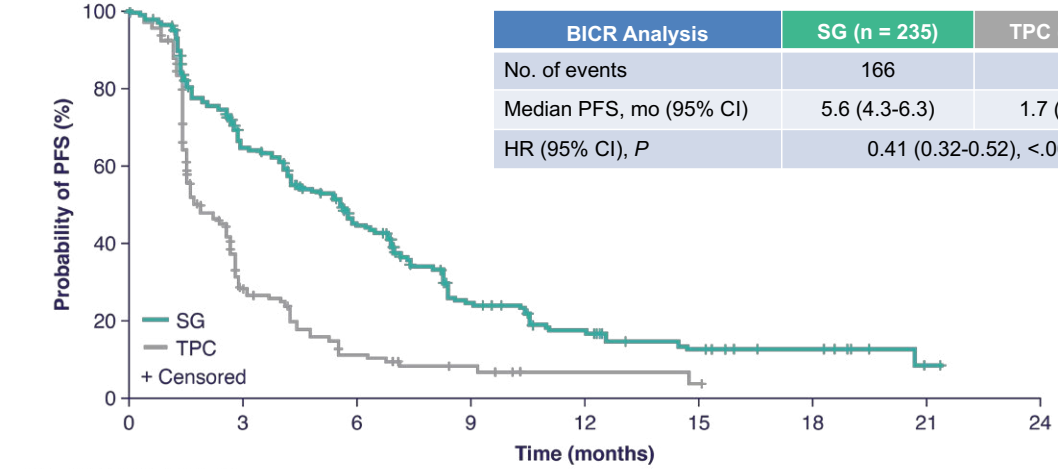
It's a clever way to target the cancer cell when you know that that receptor is there. Sacituzumab is targeting the TROP2 receptor, and it's linked to a chemo drug, which is called SN-38. On each antibody, there are almost eight different molecules of chemotherapy attached to the antibody. So it's able to deliver a ton of chemotherapy, much more than we ever could by just infusing a standard chemotherapy drug.



This drug was tested originally in early-phase studies, but it looked so promising, that it led to a randomized trial called the ASCENT study, which took patients who have metastatic TNBC and randomized them to receive sacituzumab or to receive what we call treatment of physician's choice therapy. So the doctor could choose from a bucket of different chemo drugs for which one to administer. And this was a trial that was really developed for patients who have pretreated metastatic disease. So they had to have had two lines of prior chemotherapy. So this was really a third line or beyond trial.

The eligibility is a little interesting, though, because if you had a treatment for early-stage disease, and you relapsed within a year of that treatment, that counted as a line of treatment. In fact, there were some patients in this trial that did receive sacituzumab as their second treatment for their metastatic TNBC.

ASCENT: Progression-Free Survival (BICR Analysis) Brain Metastases-negative Population



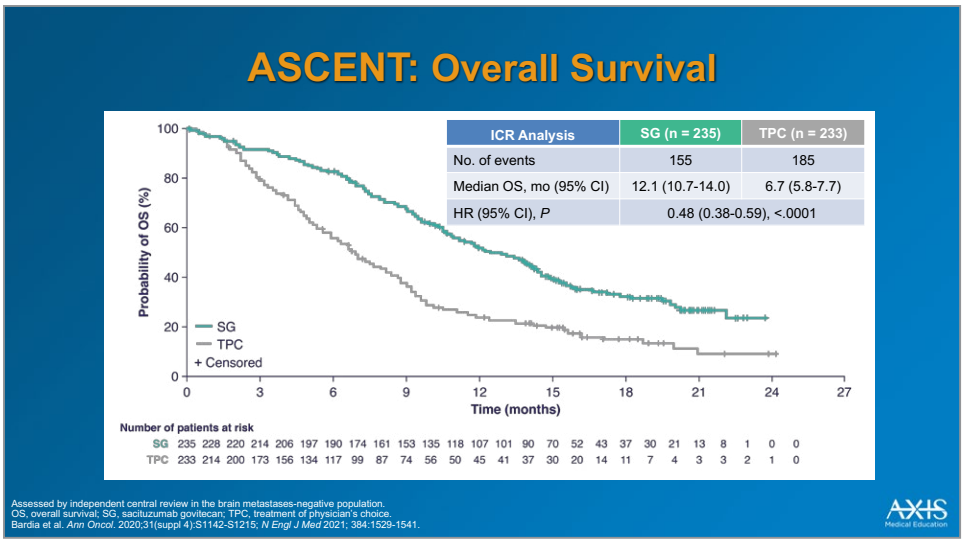
BICR Analysis	SG (n = 235)	TPC (n = 233)
No. of events	166	150
Median PFS, mo (95% CI)	5.6 (4.3-6.3)	1.7 (1.5-2.6)
HR (95% CI), *P*	0.41 (0.32-0.52), <.0001	

Primary endpoint (PFS) assessed by independent central review in the brain metastases-negative population, as pre-defined in the study protocol.
Secondary endpoint (PFS) assessed in the full population (brain metastases-positive and -negative) and PFS benefit was consistent (HR 0.43 [0.35-0.54], *P* < .0001).
BICR, blinded independent central review; PFS, progression-free survival; SG, sacituzumab govitecan; TPC, treatment of physician's choice.
Bardia et al. *Ann Oncol*. 2020;31(suppl 4):S1142-S1215; *N Engl J Med* 2021; 384:1529-1541.

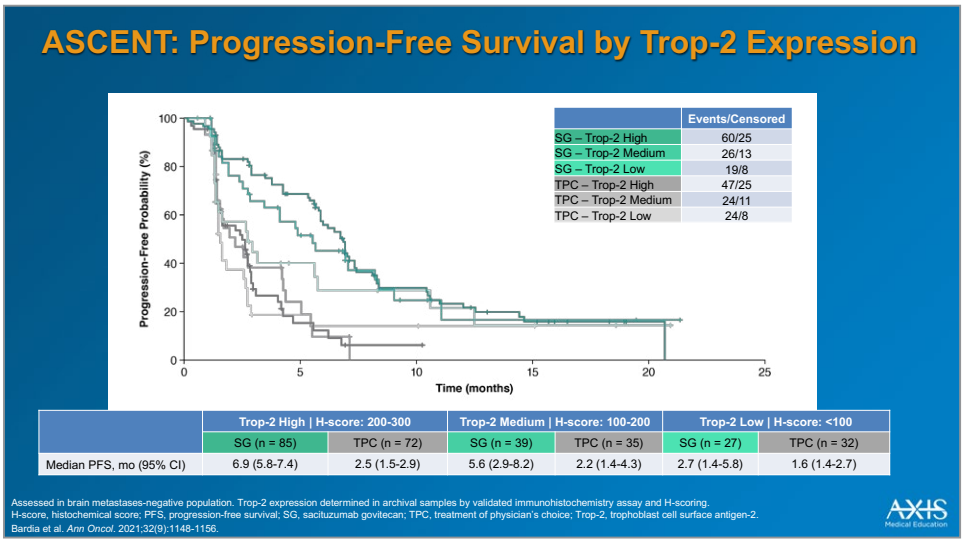
AXIS Medical Education

We saw very impressive results because what happened was that the duration of time patients had their cancer controlled or the progression-free survival was dramatically better with sacituzumab compared to treatment of physician's choice therapy. So it's 5.6 months for sacituzumab compared to 1.7 months for the treatment of physician's choice therapy.

These data tells us a couple things: One is, unfortunately, in pretreated, metastatic TNBC, standard chemotherapy drugs honestly don't work that well, right? We're seeing a median progression-free survival that's under 2 months. This shows us that we really need to do much better. But at least we find now a new drug with sacituzumab that is able to do much better, again, achieving a progression-free survival of almost 6 months, and importantly, is allowing patients to live longer.



So overall survival was almost doubled from about 6.7 months to 12 months, again, showing that the sacituzumab is able to keep disease control longer but also able to allow patients to live longer with their metastatic triple-negative disease.



One question that we all had when we saw these data, well, is: If it's targeting TROP2, wouldn't you think that if someone had more TROP2 expression on their cancer cell, that they would derive greater benefit from sacituzumab compared to someone, for example, who had a lower expression of TROP2 or no expression, even, of TROP2?

So the study did look at this. They did it in a retrospective manner, though. They took archival tissue that's been sitting around. This wasn't necessarily a biopsy that was done immediately prior to going onto the trial. There are some challenges with the data. We don't have TROP2 expression on all patients. It wasn't from, again, a baseline biopsy in all patients but did provide some interesting data that suggested that all patients, regardless of level of TROP2 expression, did do better with sacituzumab compared to standard chemotherapy.

These data suggested that we don't need to be testing patients for TROP2 to figure out who's going to benefit from treatment. It is interesting though, that the patients who had intermediate-to-high levels of TROP2 expression did derive even greater benefit from sacituzumab compared to the physician's choice therapy. So the differences were larger in the higher expressers.

There are interesting data here but, again, not enough to suggest we need to test patients for TROP2 expression to select those who are going to benefit, since all did benefit.

ASCENT: TRAEs (All Grade, >20%; Grade 3/4, >5% of Patients)

		SG (n = 258)			TPC (n = 224)		
TRAE*		All grade %	Grade 3, %	Grade 4, %	All grade, %	Grade 3, %	Grade 4, %
Hematologic	Neutropenia†	63	46	17	43	27	13
	Anemia‡	34	8	0	24	5	0
	Leukopenia§	16	10	1	11	5	1
	Febrile neutropenia	6	5	1	2	2	<1
Gastrointestinal	Diarrhea	59	10	0	12	<1	0
	Nausea	57	2	<1	26	<1	0
	Vomiting	29	1	<1	10	<1	0
Other	Fatigue	45	3	0	30	5	0
	Alopecia	46	0	0	16	0	0

- Key Grade ≥3 TRAEs (SG vs TPC): neutropenia (51% vs 33%), diarrhea (10% vs <1%), leukopenia (10% vs 5%), anemia (8% vs 5%), and febrile neutropenia (6% vs 2%)
  - G-CSF usage was 49% in the SG arm vs 23% in the TPC arm
  - Dose reductions due to TRAEs were similar (22% SG vs 26% TPC)
- No severe cardiovascular toxicity, no grade >2 neuropathy or grade >3 interstitial lung disease with SG
- No treatment-related deaths with SG; 1 treatment-related death (neutropenic sepsis) with TPC
- AEs leading to treatment discontinuation were low for SG and TPC: 4.7% and 5.4%
- Patients received a median of 7 treatment cycles of SG, with a median treatment duration of 4.4 months

*Patients may report more than 1 event per preferred term. AEs were classified according to the MedDRA systems of preferred terms and system organ class and according to severity by NCI CTCAE v4.03.
†Combined preferred terms of 'neutropenia' and 'decreased neutrophil count'.
‡Combined preferred terms of 'anemia' and 'decreased hemoglobin'.
§Combined preferred terms of 'leukopenia' and 'decreased white blood cell count'.
G-CSF, granulocyte-colony stimulating factor; SG, sacituzumab govitecan; TPC, treatment of physician's choice; TRAEs, treatment-related adverse events.
Bardia et al. *Ann Oncol*. 2021;32(9):1148-1156.

But of course, then, comes the question about what's the cost? So what are the toxicities of the drug? This is an antibody-drug conjugate. It is chemotherapy, right? You are still delivering chemotherapy, and we do see chemotherapy toxicities. So all my patients, for example, lose their hair. Alopecia is very common with this drug.

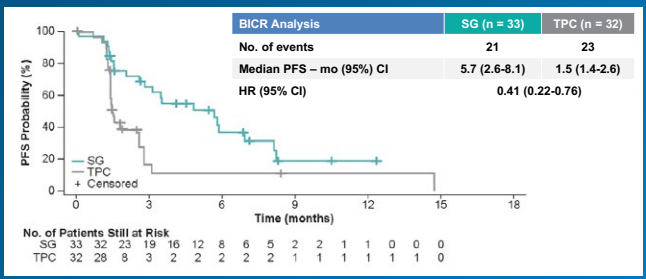
And it does cause neutropenia, and about half of the patients in the trial actually did require using growth-factor support. So that's important. And that the neutropenia is significant enough that many patients do require growth factor to keep their blood cell counts up enough to keep on schedule.

It can cause diarrhea. Usually, the diarrhea, however, is a low-grade diarrhea, so this isn't something where you need to take prophylactic anti-diarrheal therapy. Usually patients only need to use anti-diarrheal therapy as needed. And for me that has worked very well for the majority of my patients.

Generally speaking, major toxicities are hair loss, neutropenia, diarrhea, and fatigue. So again, things that do need to be monitored in patients.

Assessment of Sacituzumab Govitecan in Patients with Prior Neoadjuvant/Adjuvant Chemotherapy in the Phase 3 ASCENT Study in Metastatic TNBC: Second-line Patients

Progression-Free Survival



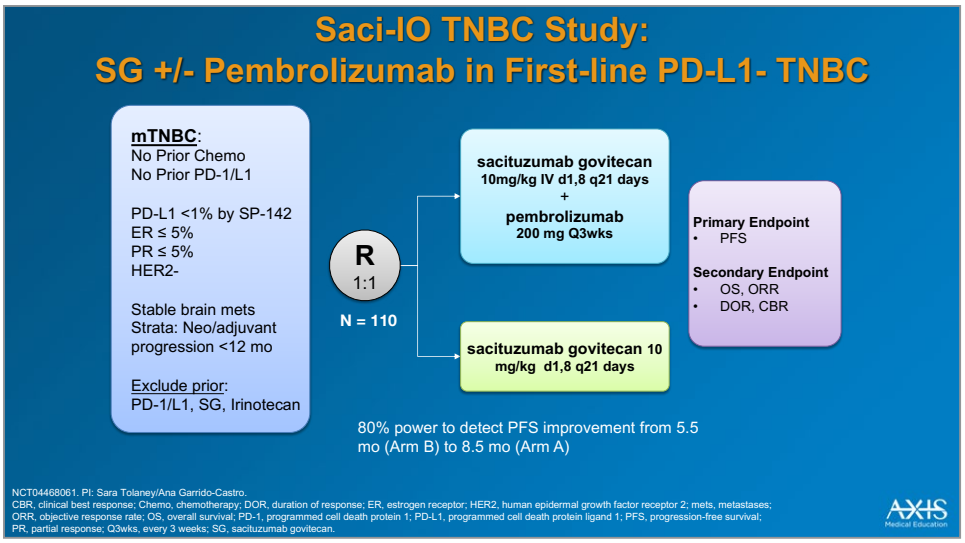
BICR Analysis	SG (n = 33)	TPC (n = 32)
No. of events	21	23
Median PFS – mo (95% CI)	5.7 (2.6-8.1)	1.5 (1.4-2.6)
HR (95% CI)	0.41 (0.22-0.76)	

FDA approved for mTNBC patients with ≥2 systemic therapies, at least one of them for metastatic disease

Assessed by independent central review in the BM-negative population who recurred ≤12 months after (neo)adjuvant chemotherapy and received 1 line of therapy in the metastatic setting prior to study enrollment.
BICR, blinded independent central review; BM_{NEG}, brain metastases negative; CBR, clinical benefit rate; CI, confidence interval; HR, hazard ratio; mDOR, median duration of response; mOS, median overall survival; mPFS; median progression-free survival; ORR, overall response rate; RECIST, Response Evaluation Criteria in Solid Tumors; R/R, relapsed/refractory; SG, sacituzumab govitecan; TNBC, triple negative breast cancer; TPC, treatment of physician's choice.
Carey et al. *J Clin Oncol*. 2021;39(15):1080.

Another question, I think, that arose was, if you remember, we said that the eligibility was a little interesting that it did allow some patients who could have been second line if they had relapsed within a year of their adjuvant therapy. And so they did look at outcomes specifically for those second-line patients and did find that they did similarly to the overall population in the trial. So they did better with sacituzumab compared to chemotherapy, with a progression-free survival of around 5.7 months compared to 1.5 months in the control arm.

This drug now has FDA approval as a second-line and beyond treatment, which has been really critical for our patients to be able to get access to the drug earlier, which was great to have that second-line cohort of patients.

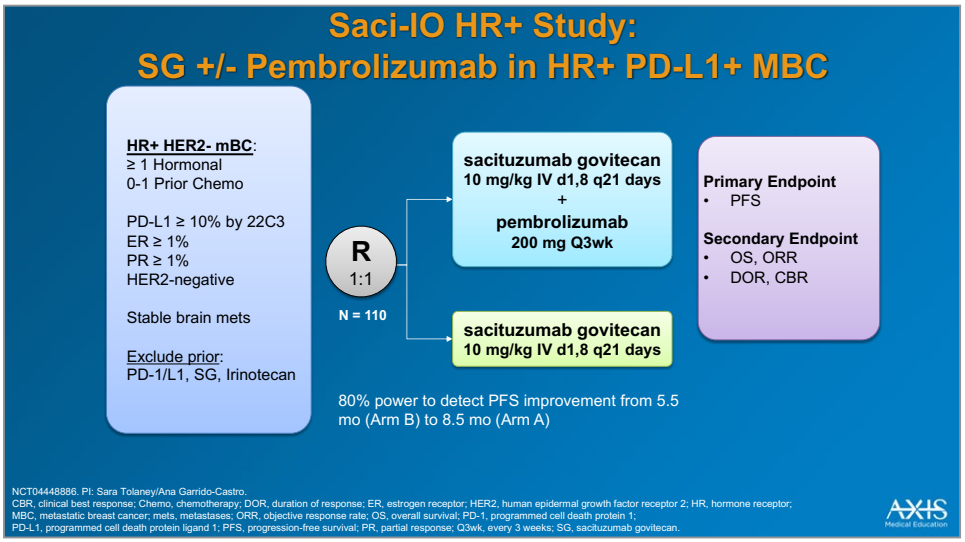


- There's certainly interest in trying to do better. Can we move sacituzumab, for example, to the first-line setting? We all want to have data about the benefits of sacituzumab earlier.

Our group is running a trial that's specifically looking at the question: Can we add immunotherapy to sacituzumab in the first-line setting and make it work better but, really interestingly, in a PD-L1–negative population? It is standard of care to give immunotherapy to a PD-L1–positive triple-negative patient. We have not seen benefit to immunotherapy in the PD-L1–negative patients with chemotherapy.

But the question is: If you use an antibody-drug conjugate that is delivering so much more chemo into the cancer cell, can you get more antigen release from the cancer cell and potentially allow for better synergistic activity with immunotherapy?

This particular trial called the Saci-IO study in triple-negative diseases, randomizing first-line triple-negative metastatic patients to get sacituzumab alone or to get it with pembrolizumab if they have PD-L1–negative triple-negative disease.



- And we're also doing a study in hormone receptor–positive disease with a similar randomization of sacituzumab with or without pembrolizumab to see if we see benefits in other subtypes of disease, as well, with the combination.

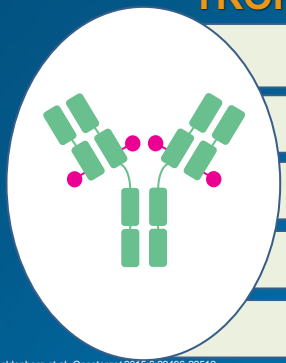
Combination Trials In TNBC

- MORPHEUS-TNBC, a phase 1b/2 study that includes a cohort of PD-L1-positive patients receiving sacituzumab govitecan combined with atezolizumab (NCT03424005)
- Combination of sacituzumab govitecan plus durvalumab (Syed, 2020)
- Phase 3 trial of sacituzumab govitecan plus pembrolizumab vs chemotherapy plus pembrolizumab as a first-line treatment for patients with locally advanced or metastatic TNBC

AXIS Medical Education

- There are also lots of other combinations that are ongoing. There's a trial one of my colleagues is running at Mass General combining sacituzumab with talazoparib, it's a PARP inhibitor, looking for that synergistic activity. And again there are also other trials, combining it with immunotherapy. So we're going to see a lot more from sacituzumab to come potentially in earlier lines and other combinations.

Datopotamab Deruxtecan (DS-1062): TROP2 ADC In Development



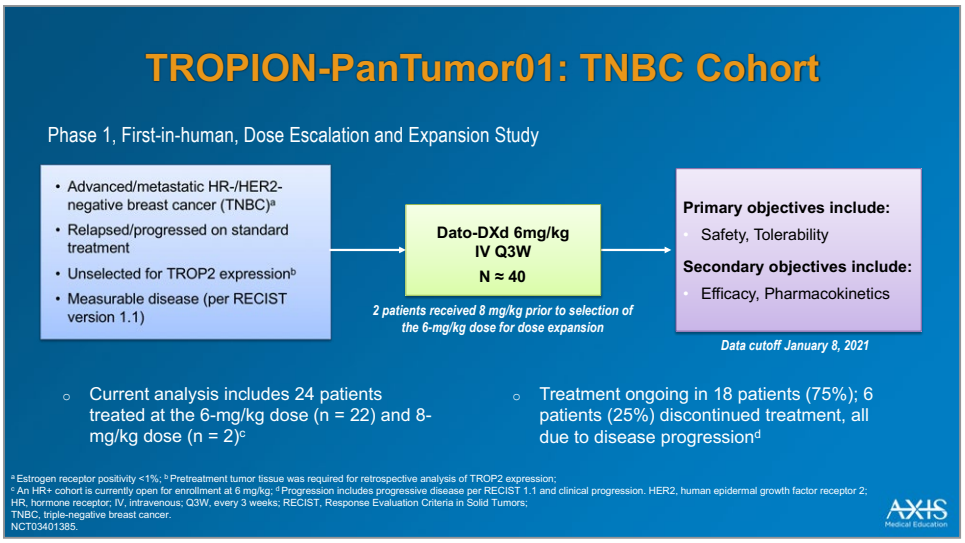
- Circulating free payload is negligible due to high stability of the linker, thereby limiting systemic exposure or nontargeted delivery of the payload[1]
- High-potency membrane-permeable payload (DXd; topoisomerase inhibitor) that requires TROP2-mediated internalization for release[2]
- DS-1062 has a DAR of 4 for optimized therapeutic index[2]
- DS-1062 has a substantially **longer half-life** than SG (≈ 5 days vs 11-14 hours), enabling a more optimal dosing regimen[3]
- SG's DLT is neutropenia, while DS-1062's DLTs are maculopapular rash and stomatitis/mucosal inflammation[4-6]

1. Goldenberg et al. *Oncotarget* 2015;6:22496-22512.
2. Ogitani et al. *Clin Cancer Res* 2016;22(20):5097-5108.
3. Ocean et al. *Cancer*. 2017;123:3843-3854.
4. Bardia et al. *J Clin Oncol* 2017;35:2141-2148.
5. Lisberg et al. *J Clin Oncol* 2020;38(15):9619.
6. Heist et al. Oral presentation at: WCLC; September 7-10, 2019; Barcelona, Spain.

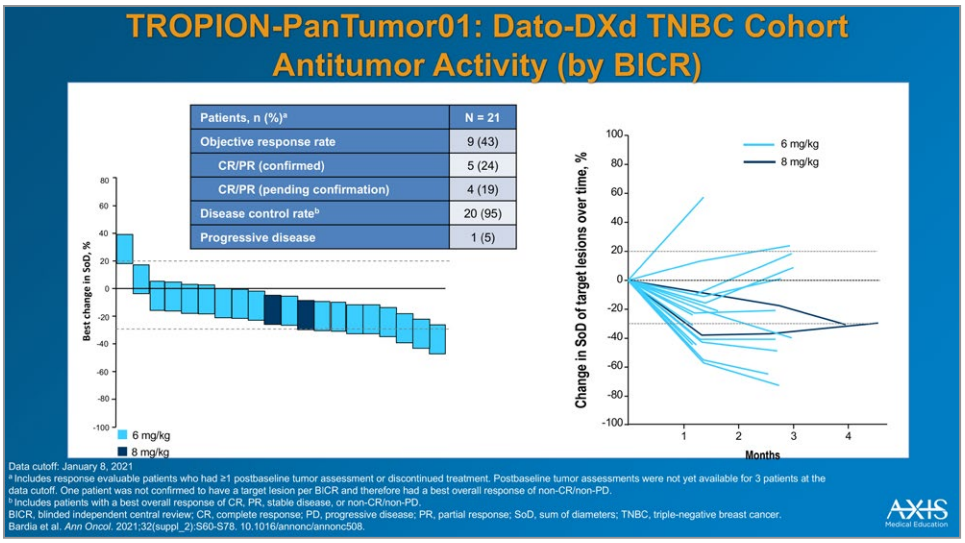
DAR, drug-to-antibody ratio; DLT, dose-limiting toxicity; SG, sacituzumab govitecan.

AXIS Medical Education

- But what about other antibody-drug conjugates in development for triple-negative disease? I think one really interesting drug is called datopotamab deruxtecan, also known as Dato-DXd or DS-1062. This drug is interestingly also targeting TROP2. So the same receptor that sacituzumab is targeting. And it's also delivering a topoisomerase-1 payload. The payload is a little different. It's not exactly SN-38 like we see in sacituzumab. It is deruxtecan, so it's the payload that's also used in trastuzumab deruxtecan. And this drug also can function by bystander effect.



- And we saw some very interesting early data that emerged from the use of Dato-DXd in metastatic triple-negative disease,



- where in fact I saw a response rate that was over 40% in pretreated triple-negative patients.

TROPION-PanTumor01: Dato-DXd TNBC Cohort
Majority of Patients Were Heavily Pretreated

Patient Characteristics	N = 24
Age, median (range), y	57.0 (32-82)
Country, n (%)	
US	18 (75)
Japan	6 (25)
ECOG PS, n (%)	
0	8 (33)
1	16 (67)
De-novo metastatic disease, n (%)	
Yes	9 (38)
No	15 (63)

Patient Characteristics	N = 24
Brain metastases, n (%)	2 (8)
Prior therapies, median (range), n[a]	4 (1-9)
≥2 prior lines of therapy, n (%)[a]	21 (88)
Previous systemic treatment, n (%)[a]	
Taxanes	20 (83)
Platinum-based chemotherapy	12 (50)
Immunotherapy	8 (33)
Sacituzumab govitecan	2 (8)
PARPi	1 (4)

[a] Includes prior lines of therapy in the (neo)adjuvant and/or metastatic setting.
Data cutoff: January 8, 2021
ECOG PS, Eastern Cooperative Oncology Group performance status; PARPi, poly (ADP-ribose) polymerase inhibitor; TNBC, triple negative breast cancer.
Bardia et al. *Ann Oncol*. 2021;32(suppl_2):S60-S78. 10.1016/annonc/annonc508.

AXIS Medical Education

- That being said, it was from a small cohort of patients, only 24 patients, but it's very impressive data, suggesting that this drug does have robust activity.

TROPION-PanTumor01: Dato-DXd TNBC Cohort
Dato-DXd Demonstrated a Manageable Safety Profile

Patients, n (%)	N = 24	
	Any grade	Grade ≥3
TEAEs	24 (100)	8 (33)
Treatment related	24 (100)	4 (17)
Serious TEAEs[a]	3 (13)	3 (13)
Treatment related	0	0
Fatal TEAEs	0	–
Treatment related	0	–

- Dose reductions due to AEs occurred in 6 patients (25%) and were most commonly due to stomatitis (3 patients [13%]) and mucosal inflammation (2 patients [8%])
- No patients discontinued treatment due to AEs

Data cutoff: January 8, 2021
[a] A serious TEAE was defined as any untoward medical occurrence that at any dose results in death, is life-threatening, requires inpatient hospitalization or prolongation of existing hospitalization, or results in persistent or significant disability/incapacity or is a congenital anomaly/birth defect or is an important medical event.
AE, adverse event; TEAE, treatment-emergent adverse event; TNBC, triple-negative breast cancer.
Bardia et al. *Ann Oncol*. 2021;32(suppl_2):S60-S78. 10.1016/annonc/annonc508.

AXIS Medical Education

- When we looked at the toxicity profile for this agent, generally speaking, it's been pretty well tolerated. I've used this drug in several patients to date on clinical trials and also have found it pretty well tolerated. It is every 3 weeks, which is nice, compared to the sacituzumab, which was 2 weeks on, 1 week off.

  It does cause mouth sores. So the rates of stomatitis were pretty high in this trial. Our group has tried using dexamethasone mouthrinse for prevention, which I have found to be quite beneficial to many patients.

TROPION-PanTumor01: Dato-DXd TNBC Cohort Manageable, Predominantly Nonhematologic AEs

- Predominantly grade 1 or 2 (67%) and nonhematologic
- No cases of grade ≥3 diarrhea or neutropenia
- No cases adjudicated as drug-related ILD were observed

Preferred Term, n (%)[a]	N = 24	
	Any grade	Grade ≥3
TEAEs	24 (100)	8 (33)
Stomatitis	15 (63)	3 (13)
Nausea	15 (63)	0
Fatigue	10 (42)	1 (4)
Vomiting	10 (42)	0
Alopecia	6 (25)	–
Cough	5 (21)	0
Pruritus	5 (21)	0
Anemia	4 (17)	1 (4)
Headache	4 (17)	0
Constipation	4 (17)	0

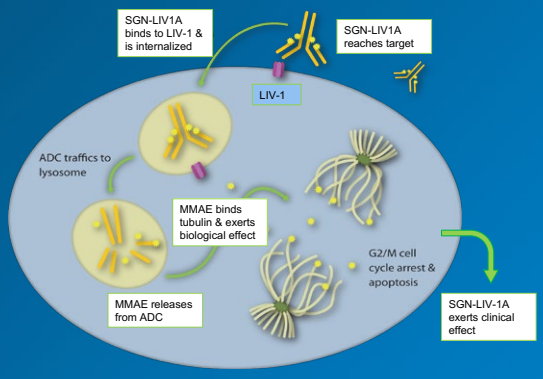
[a] TEAEs observed in ≥15% of patients.
Data cutoff: January 8, 2021
AEs, adverse events; ILD, interstitial lung disease; TEAEs, treatment-emergent adverse events; TNBC, triple-negative breast cancer.
Bardia et al. *Ann Oncol*. 2021;32(suppl_2):S60-S78. 10.1016/annonc/annonc508.

AXIS Medical Education

- But it doesn't really cause much in the way of neutropenia, so very different from sacituzumab with regards to neutropenia, and also doesn't cause the diarrhea like we've seen with sacituzumab.

  It does have nausea and fatigue, and so again, you have different toxicities with these different agents. But again, very robust early data for response. We're all eagerly looking forward to seeing more data for this drug to see, again, look at progression-free survival in larger numbers of patients.

Ladiratuzumab Vedotin (SGN-LIV1A) Mechanism of Action

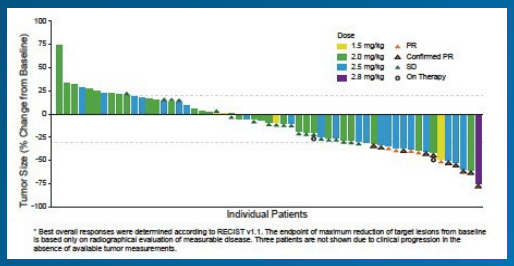


ADC, antibody-drug conjugate; MMAE, monomethyl auristatin E.
Sussman et al. *Mol Cancer Ther*. 2014 Dec; 13(12):2991-3000.

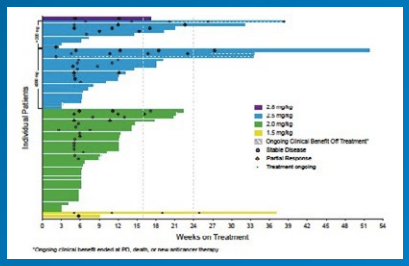
AXIS Medical Education

- Another antibody-drug conjugate in development is by the SGN group, which is targeting LIV1A. This ADC is targeting the LIV1A receptor and is linked to an MMAE payload, so a different cytotoxic drug that's a microtubule inhibitor.

Ladiratuzumab Vedotin (SGN-LIV1A)



* Best overall responses were determined according to RECIST v1.1. The endpoint of maximum reduction of target lesions from baseline is based only on radiographical evaluation of measurable disease. Three patients are not shown due to clinical progression in the absence of available tumor measurements.



Median 3 prior chemo for MBC
TNBC n = 63
ORR = 25%

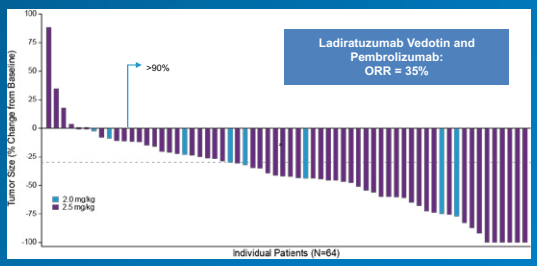
Median PFS = 11.6 weeks

MBC, metastatic breast cancer; ORR, objective response rate; PFS, progression-free survival; TNBC, triple-negative breast cancer.
Modi et al. SABCS 2017. Abstract PD3-14.

- This drug has had nice activity in pretreated metastatic triple-negative disease with an objective response rate of around 25%.

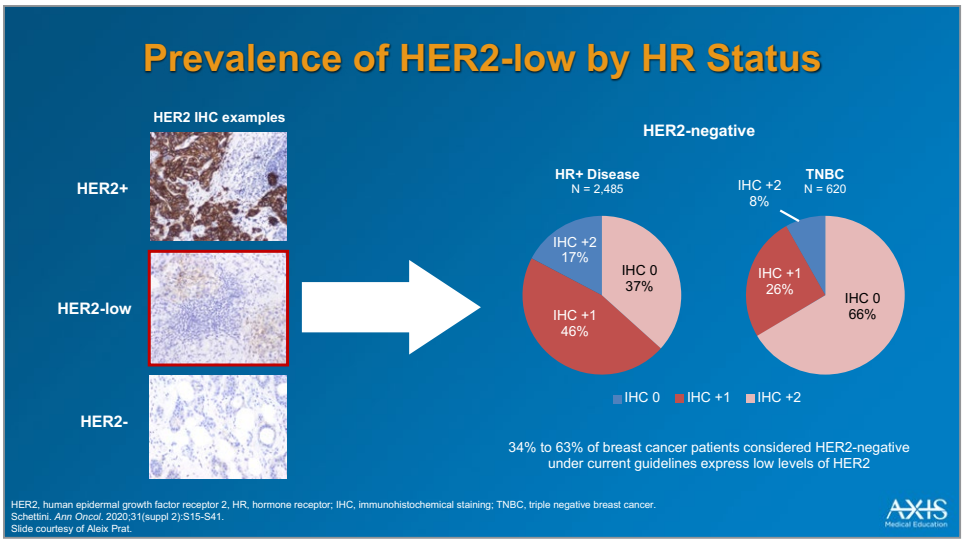
Combination of Ladiratuzumab (ADC targeting LIV1 linked to MMAE) and Immunotherapy

- The efficacy evaluable population includes all treated subjects with at least one evaluable post-baseline assessment according to RECIST v1.1 or those off study (N = 69)
- Of the efficacy evaluable population, 5 subjects did not have evaluable response assessments before study discontinuation

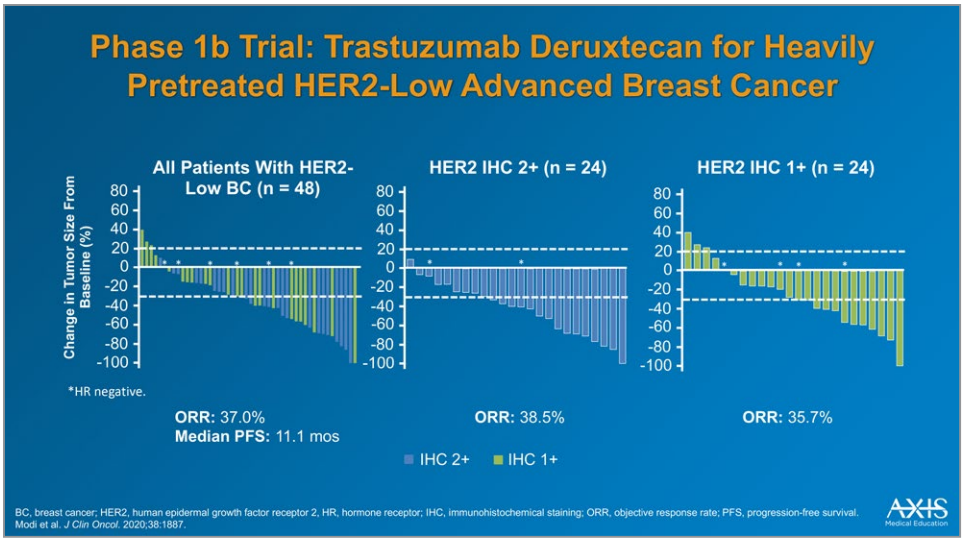


ADC, antibody-drug conjugate; MMAE, monomethyl auristatin E; ORR, objective response rate.
Han et al. *J Clin Oncol*. 2019;37(15):TPS1110.

- And in fact, they've done some work combining it with immunotherapy, suggesting robust activity with even higher response rates of around 35%. So more work is ongoing with this particular ADC.

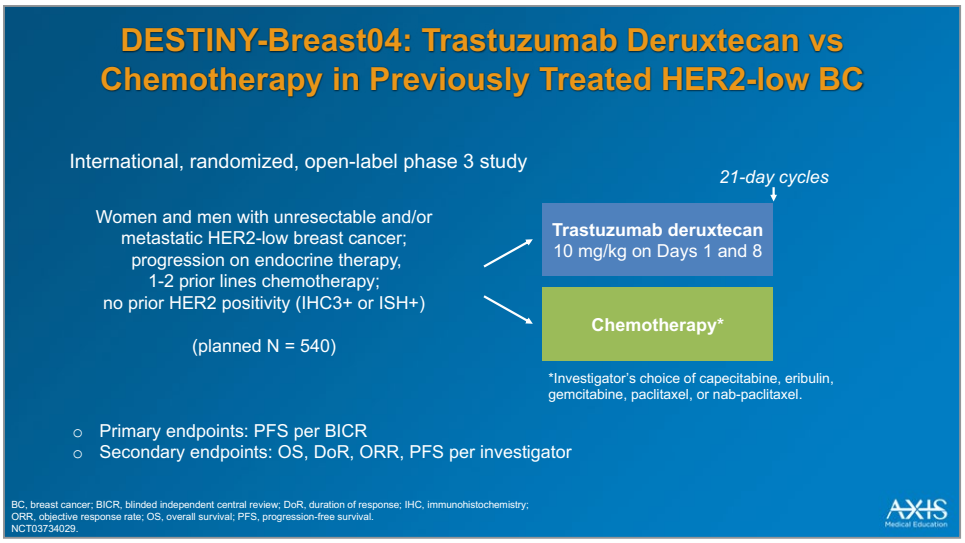


- One thing I think that is important for TNBC patients to realize is, again, that there are receptors on TNBC cells. We talked about TROP2, but interestingly, even though TNBC patients have a HER2-negative cancer, you can still see a little bit of HER2 expression in some TNBC cells. So about 25% to 30% of TNBCs will actually be HER2-low-positive, meaning that they have 1+ or 2+ expression of HER2 and are not FISH amplified. So they have a little bit of receptor there.



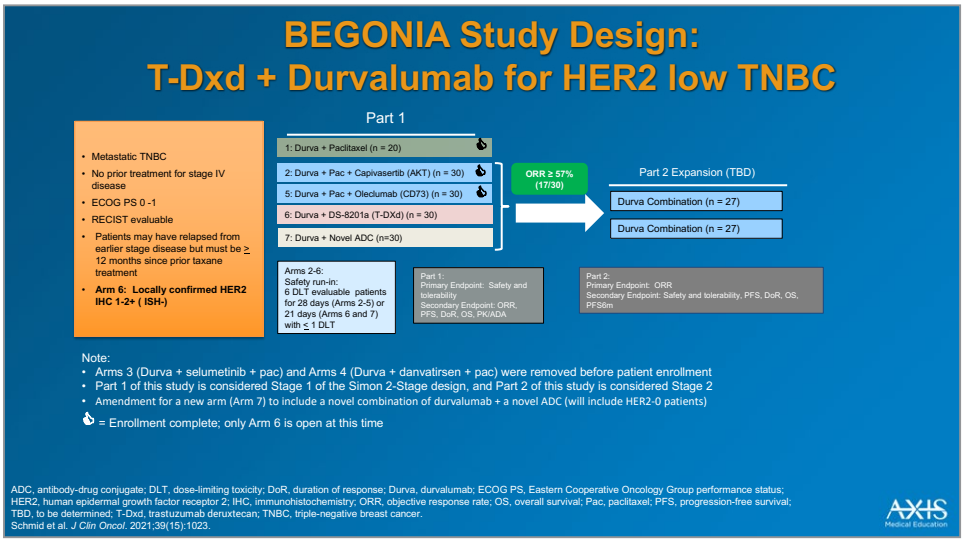
- And so the thought would be is: If some of these triple-negative cancers have some HER2 expression, can we use that receptor as that anchor to get an antibody-drug conjugate to bind to the cell and deliver its chemotherapy?

  And so, interestingly enough, trastuzumab deruxtecan, which again, is FDA approved in HER2-positive breast cancers, has been tested in HER2-low-positive cancers, and has had very nice efficacy where, in fact, we've seen response rates that are just under 40% with T-DXd in HER2-low-positive disease.



- There was a registration trial that was conducted comparing T-DXd to physician's choice chemotherapy in HER2-low-positive metastatic breast cancer. This trial has been fully enrolled. It's called DESTINY-Breast04 and will be reported, likely, in 2022.

  And so the thought is if that trial is positive, so T-DXd is better than chemotherapy, then we could get a new approval for T-DXd in HER2-low-positive cancers. And that could really change things because, again, for triple-negative disease, that's almost one third of patients who could have access to get another antibody-drug conjugate. It'll make us have lots of questions about how to think about sequencing of antibody-drug conjugates, but again, would be tremendous for patients.

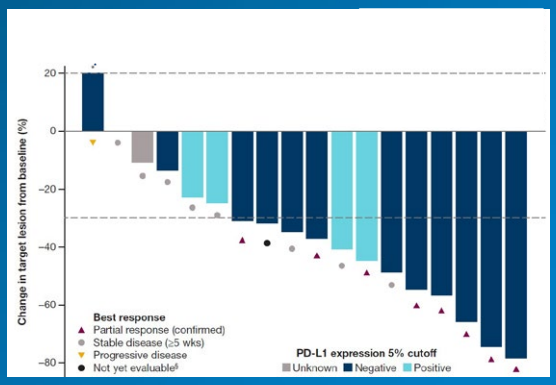


- There's work being done combining T-DXd with other agents, specifically with immunotherapy in triple-negative disease. The BEGONIA trial had investigated T-DXd with durvalumab in the first-line metastatic triple-negative setting for patients who have HER2-low-positive triple-negative disease. The data included small numbers of patients but very dramatic data with almost an over 70% response rate. Really something...we almost never see such a high response rate.

T-Dxd+ Durvalumab: Efficacy

Responses observed in both PD-L1–positive (confirmed ORR 1/1 [100%]) and PD-L1–negative (confirmed ORR 7/10 [70.0%]) groups

Parameter	D+T-DXd
Patients who completed at least 1 on-treatment assessment, n	18
Response evaluable analysis set, n	12
Confirmed ORR, n (%) 95% CI Complete response, n Partial response, n	8/12 (66.7) 41.0, 86.7 0 8
Stable disease, n	8
Progressive disease, n	1

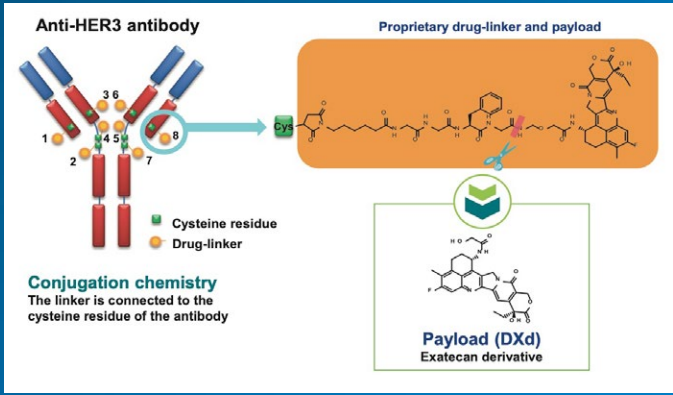


Will there be a role for TDxd+ Durvalumab in 1L HER2-low TNBC?
And will activity be greater than TDxd alone even in PD-L1-negative patients?

D, durvalumab; HER2, human epidermal growth factor receptor 2; ORR, objective response rate; PD-L1, programmed cell death protein ligand 1; T-Dxd, trastuzumab deruxtecan; TNBC, triple-negative breast cancer.
Schmid et al. *J Clin Oncol*. 2021;39(15):1023.

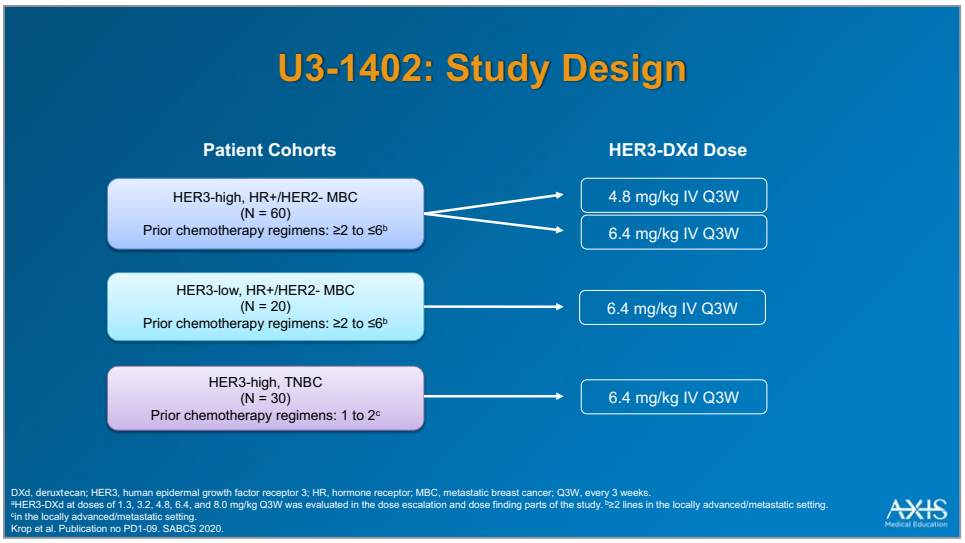
- So there's definitely interest in better understanding the benefits of the combination and whether or not the combination is truly benefiting PD-L1–negative patients equally to PD-L1–positive patients. Again, numbers here are so small, I don't think we can conclusively say that it's the synergy of the combination-driving benefit in PD-L1–negative patients. But again, what we have to learn more and so really exciting to see the potential for not only single-agent ADC but also potentially with immunotherapy.

Patritumab Deruxtecan (U3-1402): HER3 ADC



ADC, antibody-drug conjugate; HER3, human epidermal growth factor receptor 3.
Krop et al. Publication no PD1-09. SABCS 2020.

- And another antibody-drug conjugate in development targets HER3. This is U3-1402 or patritumab deruxtecan. And this agent has been studied both in hormone receptor–positive as well as triple-negative disease.



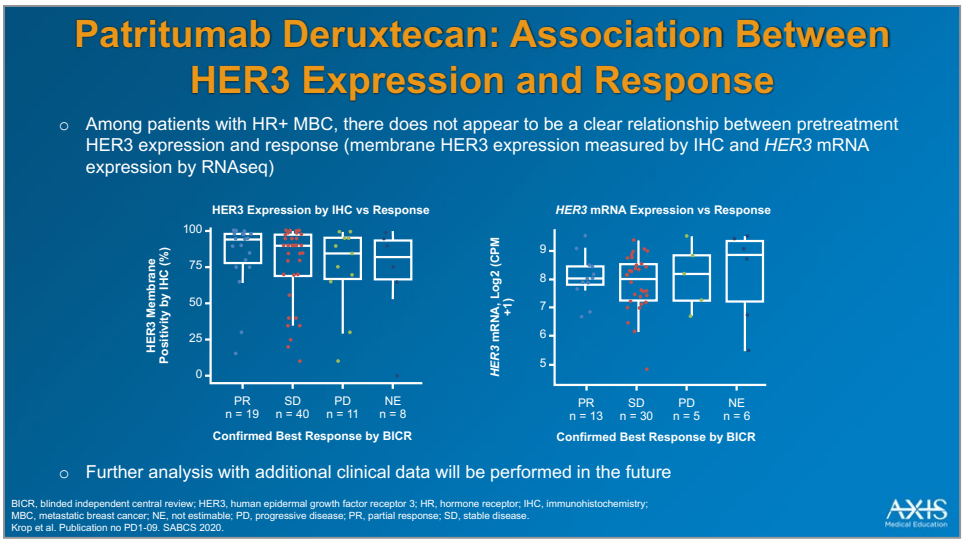
- They actually studied it in patients who had HER3 high and low expression.

U3-1402: Results

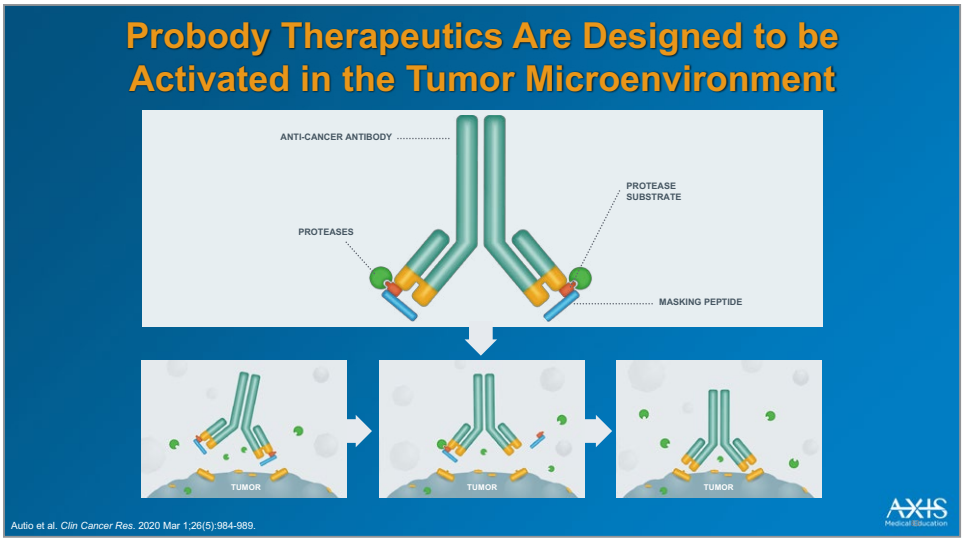
Efficacy by BICR	HER3-high, HR+/HER2- MBC		HER3 low, HR+/HER2- MBC	HER3-high TNBC
Dose	4.8 mg/kg (n=33)	6.4 mg/kg (n=31)	6.4 mg/kg (n=21)	6.4 mg/kg (n=31)
Follow-up, median, months	16.8	20.4	18.7	7.4
Confirmed ORR, %	30.3	12.9	33.3	16.1
PR	30.3	12.9	33.3	16.1
SD	60.6	61.3	33.3	67.7
PD	6.1	22.6	14.3	9.7
NE	3.0	3.2	19.0	6.5
DCR, %	90.9	74.2	66.7	83.9
Median DOR, months	5.0	7.2	5.3	NR
Median PFS, months	8.4	2.8	5.8	5.5
Median OS, months	14.3	9.7	9.2	NR

BICR, blinded independent central review; DCR, disease control rate; DOR duration of response; NE, not evaluable; NR, not reached; ORR, objective response rate; OS, overall survival; PD, progressive disease; PFS progression-free survival; PR, partial response; SD, stable disease.
Adapted from Krop et al. Publication no PD1-09. SABCS 2020.

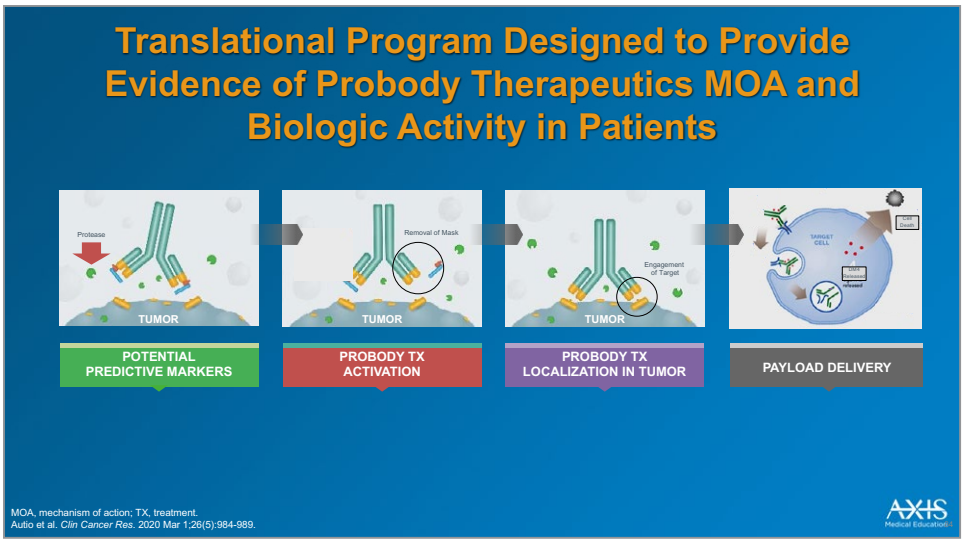
- Specifically in triple-negative disease in the HER3 high expressers, we did see about a 16% response rate. So there were some responses in this subgroup.



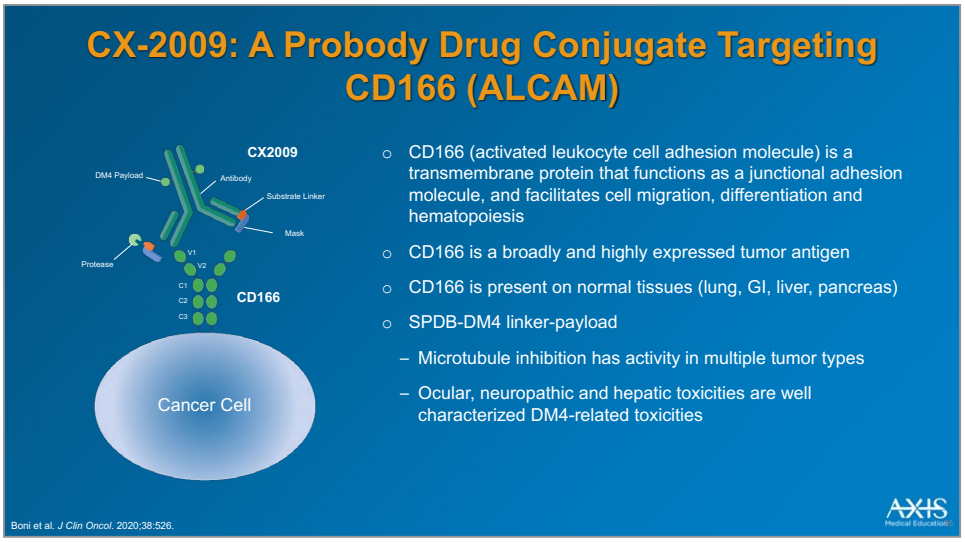
- Interestingly, it seems like activity is not necessarily dependent on degree of HER3 expressionAgain, more work is needed to better understand the activity in triple-negative disease, because numbers are still small, but exciting to see, again, potential for other antibody-drug conjugates.



- Another class of drugs that is emerging and quite early in development are what we call Probodies. And so if you think about antibody-drug conjugates, they're trying to target a receptor that is uniquely on the cancer cell, but not on a healthy cell, right, because you're trying to target delivery of a payload into the cancer cell and spare the normal healthy cells. But what if the target is both on the healthy cell and on the cancer cell? Well, you don't want the chemo to get delivered into the healthy cell.



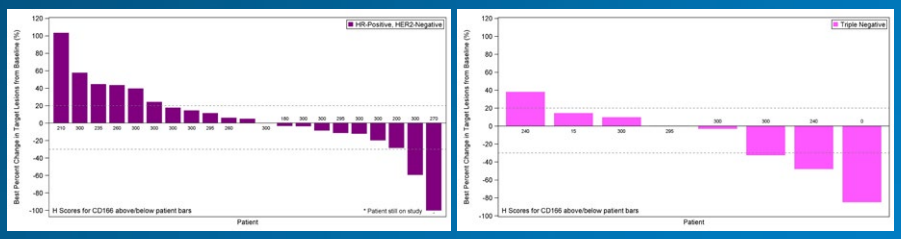
- And so some smart people figured out, well, we could put a mask on the antibody that only comes off in the cancer cell but doesn't come off when it hits a normal cell. And so these probodies were very smartly developed to do that, so that they can just deliver the chemotherapy into the cancer cell and spare the normal cells because the mask only comes off via enzymatic cleavage in the cancer cell itself.



- An example of such a drug is called CX-2009. It is targeting CD166, which is present both on normal cells and cancer cells, but again, because of the mask, that mask only gets taken off in the cancer cells. So then you only get delivery of the payload into the impacted malignant cell.

Observed Clinical Activity in Breast Cancer With CX-2009 (Doses ≥4 mg/kg Q3W)

Breast cancer patients with measurable disease who received ≥ 4 mg/kg CX-2009 and had a post-baseline assessment



Parameter	Evaluable* Breast Cancer Patients		
	Overall (n = 32)	HR+/HER2- (n = 22)	TNBC (n = 10)
CBR16	13 (41%)	9	4
CBR24	9 (28%)	5 (2 cPR)	4 (3 uPR)

*Includes those with non-measurable but evaluable (eg, bone-only) disease

CBR16, clinical benefit rate at 16 weeks; CBR24, clinical benefit rate at 24 weeks; cPR, confirmed partial response; HER2, human epidermal growth factor receptor 2; HR, hormone receptor; uPR, unconfirmed partial response; TNBC, triple-negative breast cancer.
Liuet al. *Cancer Res* 2021;81(4 Suppl):Abstract nr PS11-07.

- This agent looks very promising, based on some very early data, both in hormone receptor–positive, as well as within TNBC, where we've seen responses of both subtypes.

CX-2009 Breast Cancer Phase 2 Study Design

Monotherapy (7 mg/kg Q3W) and Combination with Pacmilimab (CX-072; anti-PD-L1) In Advanced, HER2 non-Amplified Breast Cancer

Key Eligibility

Ocular prophylaxis required
- Treated/stable brain metastases allowed
- No active corneal disease
- Measurable disease required

HR+/HER2 non-amplified
- 0 – 2 prior cytotoxics for advanced disease
- Prior CDK4/6i required

TNBC
- CD166 High
- ≥ 1 and ≤ 3 priors for advanced disease
- **Arm C exclusion criteria:**
  - PD-L1 negative/unknown
  - I/O refractory
  - History of or active autoimmune condition

Breast Cancer SubType

Arm A
HR+/HER2 non-amp (n~40)
CX-2009

Arm B
TNBC (n~40)
CX-2009

Arm C
TNBC (n~40)
CX-2009 + CX-072

Endpoints

Primary: Overall response rate by central review

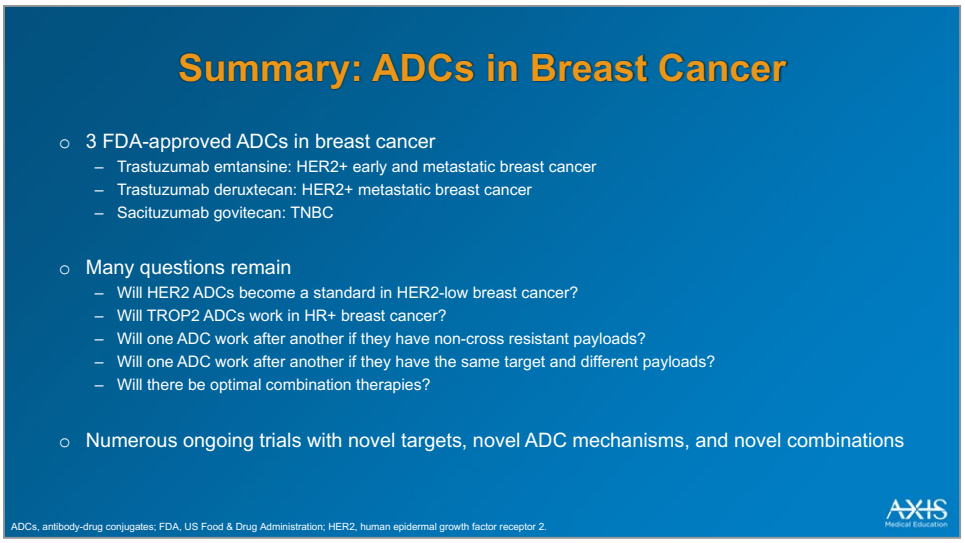
Secondary: ORR (Inv), PFS, DCR, CBR24, DoR, OS, Safety, PK, ADA

Exploratory: Biomarker correlation with outcome

Readout: Initial data expected Q4 2021

DCR, disease control rate; DoR, duration of response; HER2, human epidermal growth factor receptor 2; HR, hormone receptor; OS, overall survival; PD-L1, programmed cell death protein ligand 1; PFS, progression-free survival; Q3W, every 3 weeks; TNBC, triple-negative breast cancer.
NCT04596150; Miller et al. *Cancer Res* 2021;81(4 Suppl):Abstract nr OT-03-08.

- There is a phase 2 study that is enrolling patients getting CX-2009 either with hormone receptor–positive or triple-negative disease, and, in fact, is also looking at combination therapy with immunotherapy for metastatic triple-negative disease.

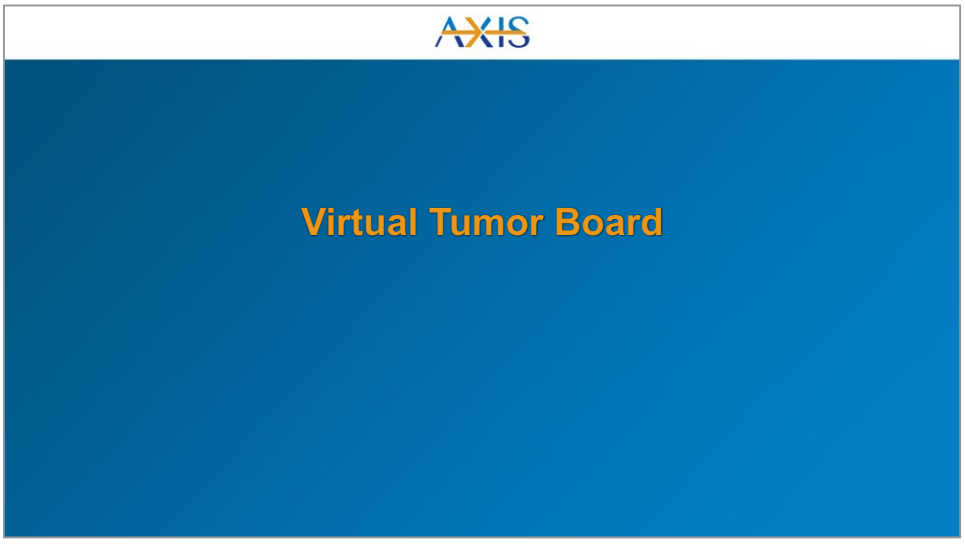


- This is a really exciting time where years ago, we only had chemotherapy for metastatic TNBC, and now we have immunotherapy, PARP inhibitors, antibody-drug conjugates, and many other really exciting drugs in development.

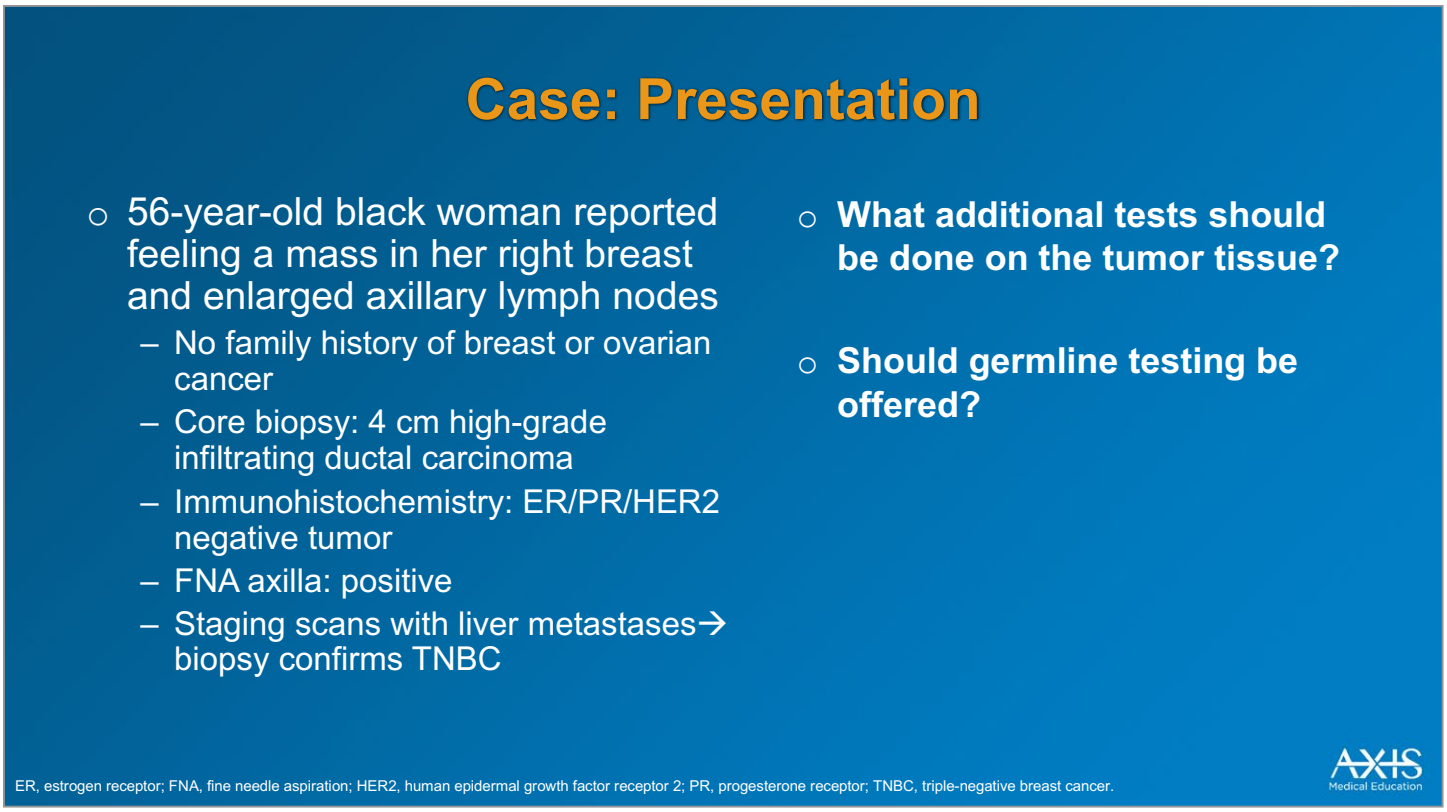
  It's very nice to see us finally making headway for TNBC. I'm definitely very excited about the new path ahead with many of these new antibody drug conjugates that appear to be very promising, and also excited about the combinations that are being studied with the really impressive early data that's emerging.

  So I am hopeful that we are going to continue to see new drugs emerge. And hopefully we will continue to make headways in improving outcomes for our patients with metastatic TNBC.

  So thank you, again, for the opportunity to review some of these data. But maybe it'd be nice to think about some cases to put these data into perspective. So Kristen, I'll pass it back to you.



- **Whitaker:** So now we can go on and move on to a case presentation. So here is a case that we'll discuss today.



A 56-year-old black woman reported feeling a mass in her right breast and enlarged axillary lymph nodes. She had no family history of breast or ovarian cancer. She also ended up undergoing a core biopsy of the breast mass that revealed a 4-centimeter high-grade infiltrating ductal carcinoma. We looked at her immunohistochemistry, which showed that her ER was negative, her PR was negative, and her HER2 was negative, consistent with what we call TNBC. She had an fine needle aspiration of the axillary node, which was positive for metastatic infiltrating ductal carcinoma. Unfortunately, at the time of her diagnosis, we were concerned about the potential for having distant disease, so we got a CT of her chest, abdomen, and pelvis, and she had a lesion shown in her liver which underwent biopsy and ultimately came back showing TNBC that had already metastasized to the liver.

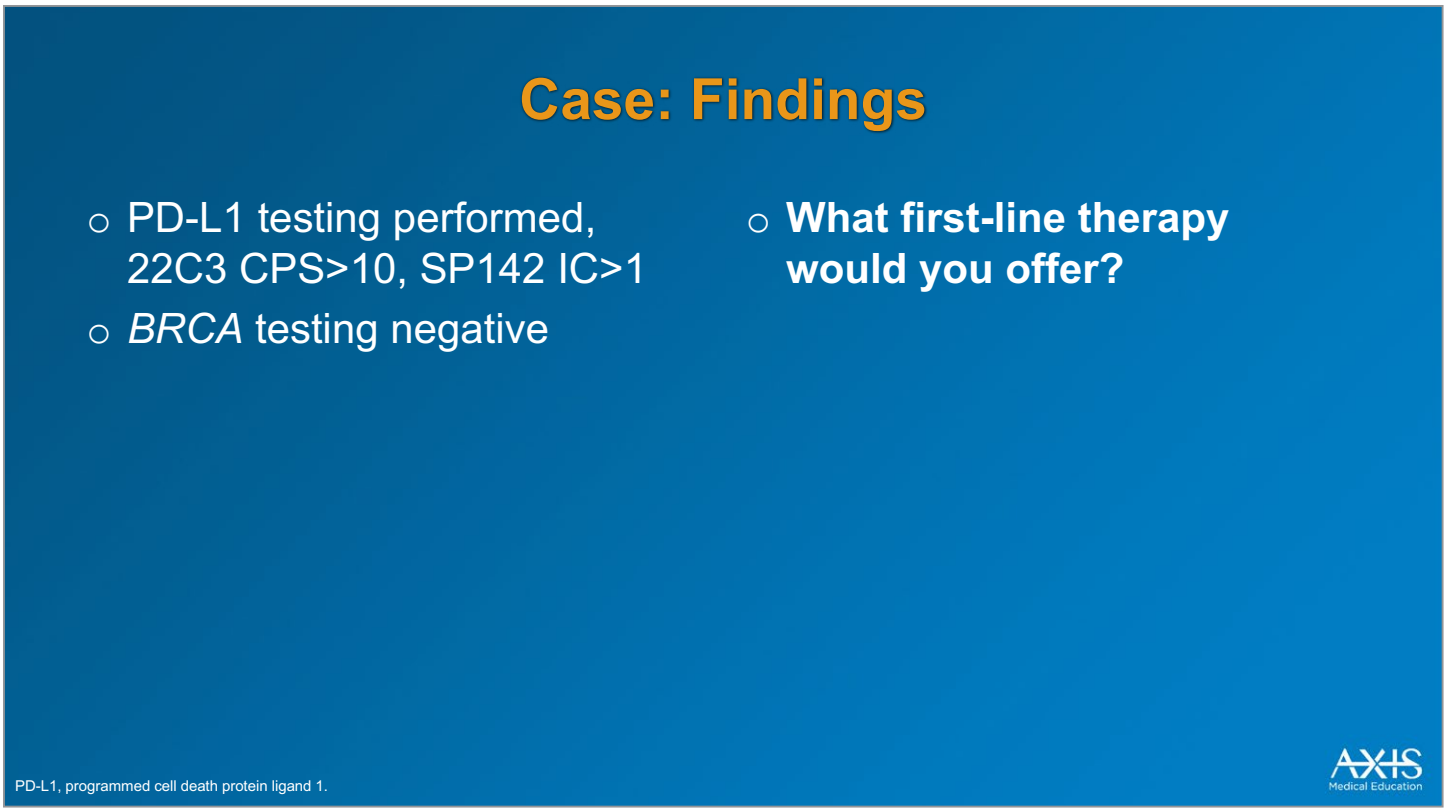
Dr. Tolaney, what additional tests should be done on her tumor now?

Tolaney: Great question. So this comes back to the discussion we were having surrounding biomarkers. Because for triple-negative metastatic disease, it is critical to know if someone has a PD-L1 receptor on their cancer. So, we do know that if someone has PD-L1-positive TNBC, we would consider offering immunotherapy. I would recommend testing this patient for PD-L1 using 22C3, and if the CPS is greater than or equal to 10, you would declare that person having a PD-L1–positive TNBC.

We also should consider BRCA testing. Again, we did discuss the importance of genetic testing here. Certainly it has implications for that patient and their family, but also has implications for treatment. Because we do know that having a BRCA mutation means that use of a PARP inhibitor is actually superior to standard chemotherapy, based on randomized trials in terms of progression-free survival. So really critical to get PD-L1 testing on the tumor and to offer that patient germline genetic testing.

I will say that many of us also consider next-generation sequencing on the tumor. That being said, those findings from, you know, genomic testing of the tumor are not quite actionable at this time. There are very few actionable findings. One would be high tumor mutation burden (TMB). But the PD-L1 and BRCA are the most critical components of biomarker testing for this patient.

Whitaker: Great information, Dr. Tolaney. We get that take-home that you absolutely should be doing PD-L1 testing, BRCA testing your new diagnosis of TNBC.



For this patient, after she had her liver biopsy, we did this PD-L1 testing on her, and we saw that her 22C3 CPS score was greater than 10. And then her SP142 IC was greater than 1. She also had genetic testing, and she was negative for a BRCA mutation.

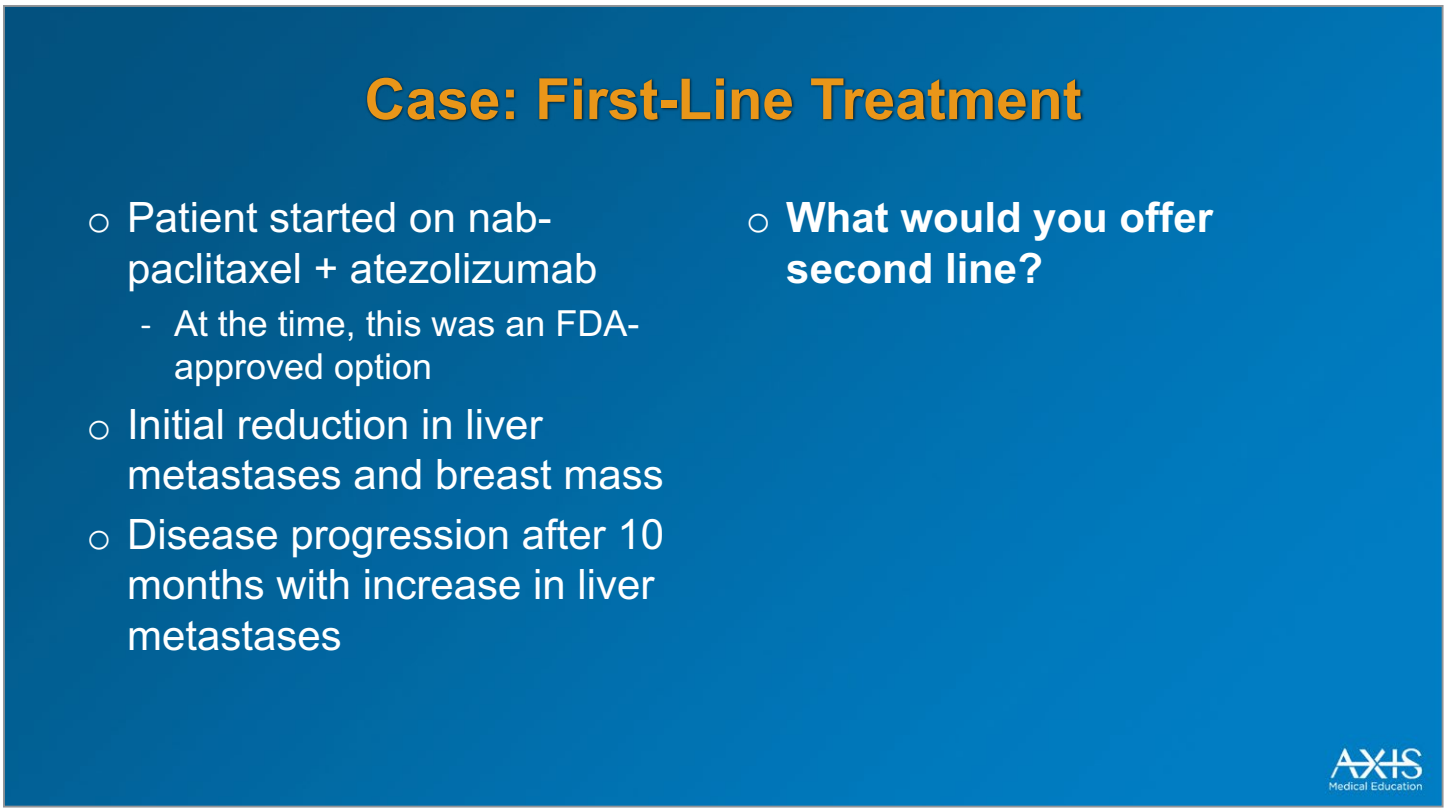
And so, Dr. Tolaney, what would you now offer her as first-line therapy?

Tolaney: Because she has a PD-L1–positive tumor, we generally would like to use chemotherapy with a checkpoint inhibitor, since we know that the combination is associated not just with progression-free survival benefit but also overall survival benefit.

And so, prior to a few months ago, we had access to two different checkpoint inhibitors: atezolizumab or pembrolizumab in combination with chemotherapy. However, there has been withdrawal of atezolizumab's approval in the United States.

So that means that at this time we could only offer this patient chemotherapy with pembrolizumab. Obviously, prior to a couple months ago, this patient could have gotten atezolizumab. So in truth, I would have been comfortable with either approach. I generally would use a taxane with a checkpoint inhibitor in this de novo metastatic patient. So in this case, probably paclitaxel/pembrolizumab with a CPS greater than 10. But a couple months ago, again, you could have given nab-paclitaxel/atezolizumab, so either one of those would have been appropriate.

Whitaker: Thanks, Dr. Tolaney. That's really important information and clarification for everyone to know about these different PD-L1 agents.

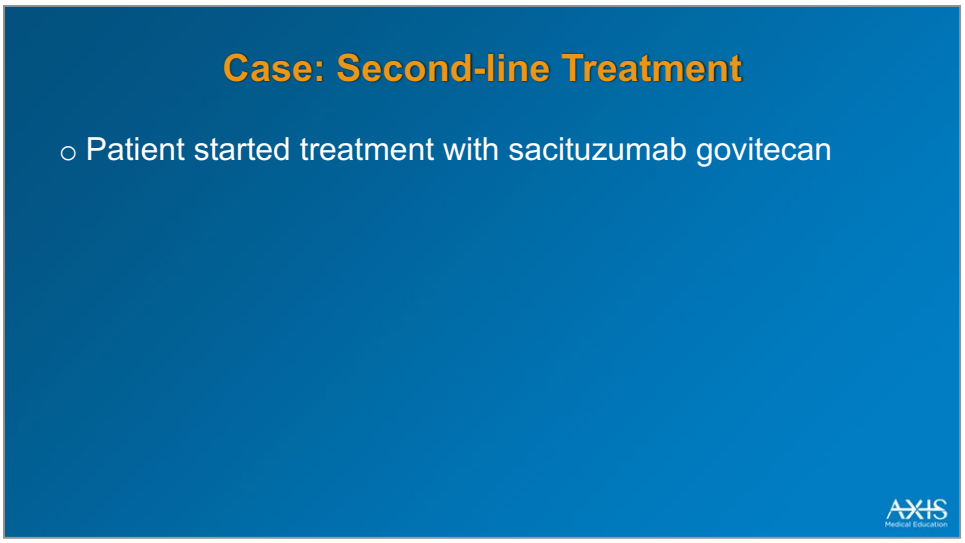


So returning back to our case. This patient, in this case, received nab-paclitaxel and atezolizumab. She initially had disease control for about 10 months, but then she had some progression of her breast cancer in the liver.

So then returning to you, Dr. Tolaney, now we have this patient who has had immunotherapy plus chemo as her first-line treatment but progressed in about 10 months on that treatment. What would you offer her now?

Tolaney: That's a good question. So remember, this patient does not have a BRCA mutation. So PARP would not be an option for this patient.

So really, you're thinking about standard chemotherapy or sacituzumab. And so remember, sacituzumab technically has a second-line indication, you know, based on the ASCENT trial, and so it is accessible in the second-line setting. And because it performed so much better than chemotherapy, I generally do like to use sacituzumab as early as possible. And so in the second-line setting is when I typically will administer it. And so for me, I would use sacituzumab here.



- **Whitaker:** That's a really great point about sacituzumab because a lot of times, we're thinking that we have to save it for kind of later lines, but you make an excellent point of clarification.

- I hope that you leave today's educational seminar with a better understanding of some of these health disparities and inequities in TNBC, both related to diagnosis and treatment.

  Dr. Tolaney, you did an absolutely fabulous job of covering where we're at with current approvals related to antibody-drug conjugates, but also the future of antibody-drug conjugatesfor breast cancer.

  And then I hope you also leave with the take-home that it is critical that we incorporate shared decision-making without the implicit bias that we talked about a lot of times to lead us towards this path of more inclusive care for TNBC and better outcomes for our patients. Thank you so much for participating in this activity.

REFERENCES

Ambrogi F, Fornili M, Boracchi P, et al. Trop-2 is a determinant of breast cancer survival. *PLoS One* 2014;9(5):e96993.

Autio KA, Boni V, Humphrey 3 RW, et al. Probody therapeutics: an emerging class of therapies designed to enhance on-target effects with reduced off-tumor toxicity for use in immuno-oncology. *Clin Cancer Res.* 2020;26(5):984-989.

Bardia A, Mayer IA, Diamond JR, et al. Efficacy and safety of anti-Trop-2 antibody drug conjugate sacituzumab govitecan (IMMU-132) in heavily pretreated patients with metastatic triple-negative breast cancer. *J Clin Oncol* 2017;35:2141-2148.

Bardia A, Tolaney SM, Loirat D, et al. ASCENT: a randomized phase III study of sacituzumab govitecan (SG) vs treatment of physician's choice (TPC) in patients (pts) with previously treated metastatic triple-negative breast cancer (mTNBC). *Ann Oncol.* 2020;31(suppl 4):S1142-S1215.

Bardia A, Hurvitz SA, Tolaney SM, et al. Sacituzumab govitecan in metastatic triple-negative breast cancer. *N Engl J Med* 2021;384:1529-1541.

Bardia A, Tolaney SM, Punie K, et al. Biomarker evaluation in the phase 3 ASCENT study of sacituzumab govitecan versus chemotherapy in patients with metastatic triple-negative breast cancer. *Ann Oncol.* 2021;32(9):1148-1156.

Bardia A. Datopotamab deruxtecan (Dato-DXd), a TROP2-directed antibody-drug conjugate (ADC), for triple-negative breast cancer (TNBC): Preliminary results from an ongoing phase 1 trial. *Ann. Oncol*. 2021;32(suppl_2):S60-S78.

Black women have higher risk of recurrence than other ethnicities. *Oncology Times* 2019;41(1):24.

Boni V, Burris HA, Liu JF, et al. CX-2009, a CD166-directed probody drug conjugate (PDC): Results from the first-in-human study in patients (Pts) with advanced cancer including breast cancer (BC). *J Clin Oncol*. 2020;38:526.

Camidge DR, Park H, Smoyer KE, et al. Race and ethnicity representation in clinical trials: findings from a literature review of Phase I oncology trials. *Fut Oncol.* 2021;17(24):3271-3280.

Cardillo TM, Govindan SV, Skarkey TM, et al. Sacituzumab govitecan (IMMU-132), an anti-Trop-2/SN-38 antibody-drug conjugate: characterization and efficacy in pancreatic, gastric, and other cancers. *Bioconjugate Chem*. 2015;26:919-931.

Carey LA, Loirat D, Punie K, et al. Assessment of sacituzumab govitecan (SG) in patients with prior neoadjuvant/adjuvant chemotherapy in the phase 3 ASCENT study in metastatic triple-negative breast cancer (mTNBC). *J Clin Oncol.* 2021;39(15):1080.

Center for Disease Control. 2021. Key breastfeeding indicators. https://www.cdc.gov/breastfeeding/data/facts.html

Cho B, Han Y, Lian M, et al. Evaluation of racial/ethnic differences in treatment and mortality among women with triple-negative breast cancer. *JAMA Oncol*. 2021;7(7):1016-1023.

Friebel-Klingner TM, Ehsan S, Conant EF, et al. Risk factors for breast cancer subtypes among Black women undergoing screening mammography. *Breast Cancer Res Treat*. 2021;189(3):827-835.

Goldenberg DM, Cardillo TM, Govindan SV, et al. Trop-2 is a novel target for solid cancer therapy with sacituzumab govitecan (IMMU-132), an antibody-drug conjugate (ADC). *Oncotarget* 2015;6:22496-22512.

Goldenberg DM, Sharkey RM. Sacituzumab govitecan, a novel, third-generation, antibody-drug conjugate (ADC) for cancer therapy. *Expert Opin Biol Ther.* 2020;20(8):871-885.

Gower BA, Pearson K. Bush N, et al. Diet pattern may affect fasting insulin in a large sample of black and white adults. *Eur J Clin Nutr.* 2021;75(4):628-635.

Hales CM, Carroll MD, Fryar CD, Ogden CL. Prevalence of obesity and severe obesity among adults: United States, 2017-2018. NCHS Data Brief, no 360. Hyattsville, MD: National Center for Health Statistics. 2020. https://www.cdc.gov/nchs/products/databriefs/db360.htm

Han HS, Alemany CA, Brown-Glaberman UA, et al. SGNLVA-002: Single-arm, open label phase Ib/II study of ladiratuzumab vedotin (LV) in combination with pembrolizumab for first-line treatment of patients with unresectable locally advanced or metastatic triple-negative breast cancer. *J Clin Oncol.* 2019;37(15):TPS1110.

Han H, Diab S, Alemany C, et al. Abstract PD1-06: Open label phase 1b/2 study of ladiratuzumab vedotin in combination with pembrolizumab for first-line treatment of patients with unresectable locally-advanced or metastatic triple-negative breast cancer. *Cancer Res.* 2020;80(4 Supplement):PD1-06-PD1-06.

Heist et al. First-in-human phase 1 study of DS-1062a (TROP2 antibody-drug conjugate) in patients with advanced non-small cell lung cancer. Abstract 3854. Mini Oral Session at the IASLC 2019 World Conference on Lung Cancer (WCLC); September 7-10, 2019; Barcelona, Spain.

Krop I, Yonemori K, Takahashi S, et al. Safety and efficacy results from the phase 1/2 study of U3-1402, a human epidermal growth factor receptor 3 (HER3)-directed antibody drug conjugate (ADC), in patients with HER3-expressing metastatic breast cancer (MBC). Presented at the 2020 San Antonio Breast Cancer Virtual Symposium; December 8-11, 2020; San Antonio, Texas

Lisberg AE, Sands J, Shimizu T, et al. Dose escalation and expansion from the phase I study of DS-1062, a trophoblast cell-surface antigen 2 (TROP2) antibody drug conjugate (ADC), in patients (pts) with advanced non-small cell lung cancer (NSCLC). *J Clin Oncol* 2020;38(15):9619.

Liu JF, Zein IA, Dang T, et al. Intratumoral activation and phase 1/2 clinical activity of CX-2009, a probody drug conjugate (PDC) targeting CD166. *Cancer Res.* 2021;81(4 Suppl):PS11-07.

Loree JM, Anand S, Dasari A, et al. Disparity of race reporting and representation in clinical trials leading to cancer drug approvals from 2008 to 2018. *JAMA Oncol.* 2019;5(10):e191870.

Lund MJ, Brawley OP, Ward KC, et al. Parity and disparity in first course treatment of invasive breast cancer. *Breast Cancer Res Treat*. 2008;109(3):545-557.

Ma H, Ursin G, Xu X, et al. Reproductive factors and the risk of triple-negative breast cancer in white women and African-American women: a pooled analysis. *Breast Cancer Res*. 2017;19(1):6.

McCarthy AM, Friebel-Klinger T, Ehsan S, et al. Relationship of established risk factors with breast cancer subtypes. *Cancer Med.* 2021;10(18):6456-6467.

Miller K, et al. A Phase 2, open-label study to evaluate the safety and efficacy of the probody therapeutic (Pb-Tx) CX 2009 in metastatic HR-positive/HER2-negative breast cancer (mHR+/HER2– BC) and of CX-2009 as monotherapy and in combination therapy with CX-072 in metastatic triple-negative breast cancer (TNBC). *Cancer Res.* 2021;81(4 Suppl):OT-03-08.

Modi S, Pusztai L, Forero A, et al. Phase 1 study of the antibody-drug conjugate ladiratuzumab vedotin (SGN-LIV1A) in patients with heavily pretreated triple-negative metastatic breast cancer. Abstract PD3-14. Presented at the 2016 San Antonio Breast Cancer Symposium; December 5-9, 2017; San Antonio, Texas.

Modi S, Park H, Murthy RK, et al. Antitumor activity and safety of trastuzumab deruxtecan in patients with HER2-low–expressing advanced breast cancer: results from a phase Ib study. *J Clin Oncol.* 2020;38:1887.

Nagayama A, Ellisen LW, Chabner B, Bardia A. Antibody-drug conjugates for the treatment of solid tumors: clinical experience and latest developments. *Target Oncol.* 2017;12(6):719-739.

REFERENCES

Nagayama A, Vidula N, Ellisen, et al. Novel antibody-drug conjugates for triple negative breast cancer. *Ther Adv Med Oncol.* 2020;12:1758835920915980.

National Institutes of Health. NCT02574455. Trial of sacituzumab govitecan in participants with refractory/relapsed metastatic triple-negative breast cancer (ASCENT). https://clinicaltrials.gov/ct2/show/NCT02574455.

National Institutes of Health. NCT04468061. Sacituzumab govitecan +/- pembrolizumab in metastatic TNBC. https://clinicaltrials.gov/ct2/show/NCT04468061.

National Institutes of Health. NCT04448886. Sacituzumab govitecan +/- pembrolizumab in HR+ / HER2 – MBC. https://clinicaltrials.gov/ct2/show/NCT04448886.

National Institutes of Health. NCT03424005. A study evaluating the efficacy and safety of multiple immunotherapy-based treatment combinations in patients with metastatic or inoperable locally advanced triple-negative breast cancer (Morpheus-TNBC). https://clinicaltrials.gov/ct2/show/NCT03424005.

National Institutes of Health. NCT03401385. First-in-human study of DS-1062a for advanced solid tumors (TROPION-PanTumor01). https://clinicaltrials.gov/ct2/show/NCT03401385.

National Institutes of Health. NCT03734029. Trastuzumab deruxtecan (DS-8201a) versus investigator's choice for HER2-low breast cancer that has spread or cannot be surgically removed [DESTINY-Breast04]. https://clinicaltrials.gov/ct2/show/NCT03734029.

National Institutes of Health. NCT04596150. Study to evaluate the safety and antitumor activity of CX-2009 monotherapy and in combination with CX-072 in advanced breast cancer. https://clinicaltrials.gov/ct2/show/NCT04596150.

Ocean AJ, Starodub AN, Bardia A, et al. Sacituzumab govitecan (IMMU-132), an anti-Trop-2-SN-38 antibody-drug conjugate for the treatment of diverse epithelial cancers: safety and pharmacokinetics. *Cancer* 2017;123:3843-3854.

Ogitani Y, Aida T, Hagihara K, et al. DS-8201a, a novel HER2-targeting ADC with a novel DNA topoisomerase I inhibitor, demonstrates a promising antitumor efficacy with differentiation from T-DM1. *Clin Cancer Res*. 2016;22(20):5097-5108.

Prevent Cancer Foundation. September 1, 2021. Survey says: women are skipping cancer screenings during pandemic, but they plan to get 'back on the books. https://www.preventcancer.org/2021/09/survey-says-women-are-skipping-cancer-screenings-during-pandemic-but-they-plan-to-get-back-on-the-books/.

Richardson LC, Henley SJ, Miller JW, et al. Patterns and trends in age-specific black-white differences in breast cancer incidence and mortality – United States, 1999–2014. *MMR Weekly*. 2016;65(40):1093-1098.

Richardson LC, Royalty J, Howe W, Helsel W, Kammerer W, Benard VB. Timeliness of breast cancer diagnosis and initiation of treatment in the national breast and cervical cancer early detection program, 1996–2005. *Am J Public Health* 2010;199(9):1769-1778.

Roche News Release. February 22, 2013. FDA approves Roche's Kadcyla (trastuzumab emtansine), the first antibody-drug conjugate for treating HER2-positive metastatic breast cancer. https://www.roche.com/media/releases/med-cor-2013-02-22.htm

Schettini F. Clinical, pathological and gene expression features of HER2-low breast cancer. *Ann Oncol.* 2020;31(suppl 2):S15-S41.

Schmid P, Im S-A, Armstrong A, et al. BEGONIA: Phase 1b/2 study of durvalumab (D) combinations in locally advanced/metastatic triple-negative breast cancer (TNBC)—Initial results from arm 1, d+paclitaxel (P), and arm 6, d+trastuzumab deruxtecan (T-DXd). *J Clin Oncol.* 2021;39(15):1023.

Scott LC, Mobley LR, Kuo TM, et al. Update on triple-negative breast cancer disparities for the United States: A population-based study from the United States Cancer Statistics database, 2010 through 2014 *Cancer* 2019;125(19):3412-3417.

Siddharth S, Sharma D. Racial disparity and triple-negative breast cancer in African-American women: a multifaceted affair between obesity, biology, and socioeconomic determinants. *Cancers* (Basel) 2018;10(12):514.

Sparano JA, Gray RJ, Makower DF, et al. Clinical outcomes in early breast cancer with a high 21-gene recurrence score of 26 to 100 assigned to adjuvant chemotherapy plus endocrine therapy. *JAMA Oncol.* 2020;6(3):367-374.

Sussman D, Smith LM, Anderson ME, et al. SGN-LIV1A: a novel antibody-drug conjugate targeting LIV-1 for the treatment of metastatic breast cancer. *Mol Cancer Ther.* 2014 Dec; 13(12):2991-3000.

Stead LA, Lash TL, Sobieraj JE, et al. Triple-negative breast cancers are increased in black women regardless of age or body mass index. *Breast Cancer Res*. 2009;11(2):R18.

Syed YY. Sacituzumab govitecan: first approval. *Drugs* 2020:1-7. doi:10.1007/s40265-020-01337-5

Thomas A, Teicher BA, Hassan R. Antibody-drug conjugates for cancer therapy. *Lancet Oncol.* 2016;17(6):e254-e262.

US Census Bureau. https://www.census.gov/quickfacts/fact/table/US/PST045219

US Food & Drug Administration. May 3, 2019. FDA approves ado-trastuzumab emtansine for early breast cancer. https://www.fda.gov/drugs/resources-information-approved-drugs/fda-approves-ado-trastuzumab-emtansine-early-breast-cancer.

US Food & Drug Administration. December 20, 2019. FDA approves fam-trastuzumab deruxtecan-nxki for unresectable or metastatic HER2-positive breast cancer. https://www.fda.gov/drugs/resources-information-approved-drugs/fda-approves-fam-trastuzumab-deruxtecan-nxki-unresectable-or-metastatic-her2-positive-breast-cancer.

US Food & Drug Administration. April 22, 2020. FDA grants accelerated approval to sacituzumab govitecan-hziy for metastatic triple negative breast cancer. https://www.fda.gov/drugs/drug-approvals-and-databases/fda-grants-accelerated-approval-sacituzumab-govitecan-hziy-metastatic-triple-negative-breast-cancer.

US Food & Drug Administration. April 7, 2021. FDA grants regular approval to sacituzumab govitecan for triple-negative breast cancer. https://www.fda.gov/drugs/resources-information-approved-drugs/fda-grants-regular-approval-sacituzumab-govitecan-triple-negative-breast-cancer.

Vidula N, Yau C, Rugo HS. Trop2 gene expression (Trop2e) in primary breast cancer (BC): correlations with clinical and tumor characteristics. *J Clin Oncol.* 2017;35(suppl 15):1075.

Wilson V. May 11, 2017. African American women stand out as working moms play a larger economic role in families. https://www.epi.org/blog/african-american-women-stand-out-as-working-moms-play-a-larger-economic-role-in-families/.

About AXIS Medical Education, Inc.

AXIS Medical Education, Inc. is a full-service continuing education company that designs and implements live, web-based, and print-based educational activities for healthcare professionals. AXIS provides convenient opportunities to engage learners based on their individual learning preferences through a full spectrum of educational offerings.

The executive leadership of AXIS combines 75 years of experience in adult learning theory, curriculum design/implementation/assessment, continuing education accreditation standards, and medical meeting planning and logistics. Our team has a deep understanding of the governing guidelines overseeing the medical education industry to ensure compliant delivery of all activities. AXIS employs an experienced team of medical and scientific experts, medical writers, project managers, meeting planners, and logistics professionals. This team is dedicated to meeting the unmet educational needs of healthcare professionals, with the goal of improving patient outcomes.

AXIS believes that partnerships are crucial in our mission to deliver timely, relevant, and high-quality medical education to healthcare professionals. To that end, AXIS partners with other organizations and accredited providers to offer added expertise and assist in expanding access to our educational interventions. AXIS also partners with numerous patient advocacy organizations to provide recommended patient education and caregiver resources in specific disease areas. AXIS finds value in these partnerships because they complement our core clinical curriculum with validated and relevant supplemental resources for busy clinicians and their patients.

The mission of AXIS is to enhance the knowledge, skills, competence, and performance of the interprofessional healthcare team to ensure patients receive quality care, resulting in improved patient outcomes. We engage healthcare professionals in fair-balanced, scientifically rigorous, expert-led certified educational activities designed to foster lifelong learning that is applicable to clinical practice and patient-centered care.

To learn more and to see our current educational offerings, visit us online at www.AXISMedEd.com.

AXIS
Medical Education