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Informed Therapy for Black Women with Triple-Negative Breast Cancer:
Meeting Them Where They Are and Moving Toward Better Outcomes

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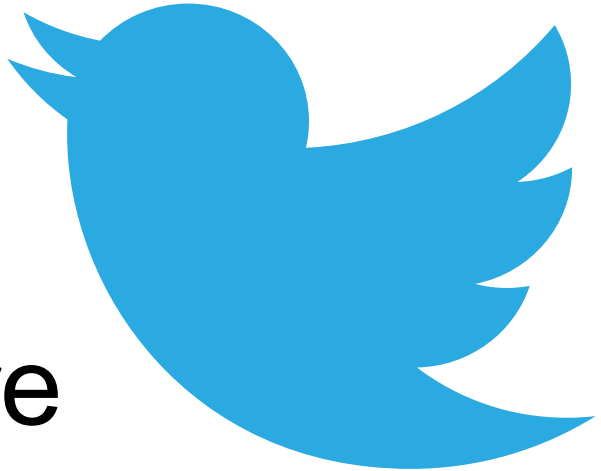

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Learning Objective 1

Evaluate the changing landscape of treatment options for high-risk TNBC to inform therapy plans

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Learning Objective 2

Recognize the disparate impact of TNBC in Black women

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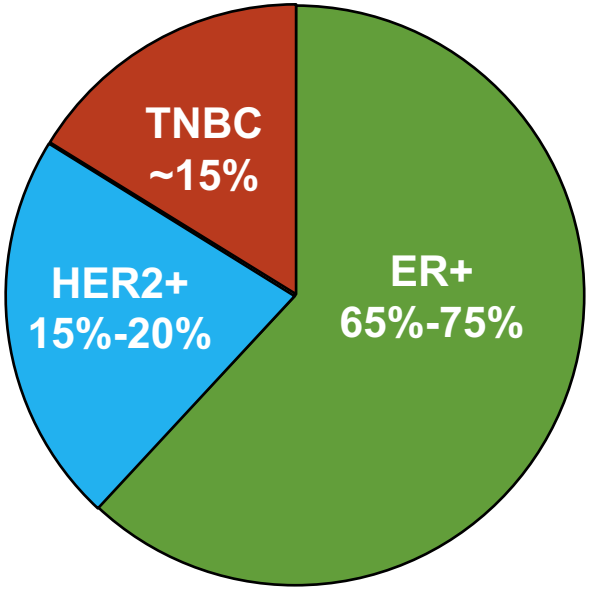
Learning Objective 3

Engage to empower Black women regarding mammography screenings, treatment decisions, and participation in clinical trials

Triple-negative Breast Cancer (TNBC)

- TNBC lacks estrogen and progesterone hormone receptors (ER and PR), and does not exhibit overexpression of human epidermal growth factor receptor 2 (HER2)
- TNBC accounts for ~15% of breast cancers
- Patients with TNBC have poorer overall survival vs other forms of metastatic breast cancer (median OS = ~18 months)
- More aggressive disease course
  - Higher risk of both local and distant recurrence
  - Recurrences typically occur within the first 5 years of diagnosis
- Historically, limited treatment options



TNBC = triple-negative breast cancer.

Saha P, Nanda R. *Ther Adv Med Oncol.* 2016; Lebert JM, et al. *Curr Oncol.* 2018.

Biomarker-directed Treatment of Metastatic Breast Cancer

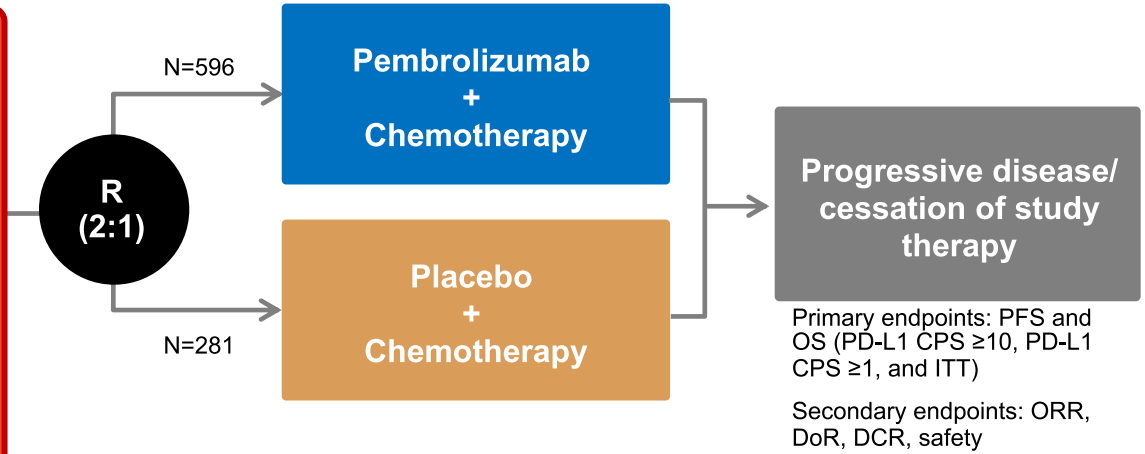
Breast Cancer Subtype	Biomarker	Detection	FDA-approved Agents	NCCN Category of Evidence	NCCN Category of Preference
Any	*BRCA1* mutation *BRCA2* mutation	Germline sequencing	Olaparib Talazoparib	Category 1 Category 1	Preferred Preferred
HR-positive/ HER2-negative	*PIK3CA* mutation	PCR (blood or tissue block if blood negative), molecular panel testing	Alpelisib + fulvestrant	Category 1	Preferred second-line therapy
HR-negative/ HER2-negative	PD-L1+ (CPS ≥10)	IHC	Pembrolizumab + Chemotherapy	Category 2A	Preferred
Any	*NTRK* fusion	FISH, NGS, PCR (tissue block)	Larotrectinib Entrectinib	Category 2A Category 2A	Useful in certain circumstances Useful in certain circumstances
Any	MSI-H/dMMR	IHC, PCR (tissue block)	Pembrolizumab	Category 2A	Useful in certain circumstances

NCCN Guidelines. Breast Cancer. Version 3.2022.

KEYNOTE-355: Study Design

Key Eligibility Criteria

- Central determination of TNBC and PD-L1 expression
- Previously untreated locally recurrent inoperable or metastatic TNBC
- Completion of treatment with curative intent ≥6 months prior to first disease recurrence
- ECOG performance status 0 or 1



Stratification Factors

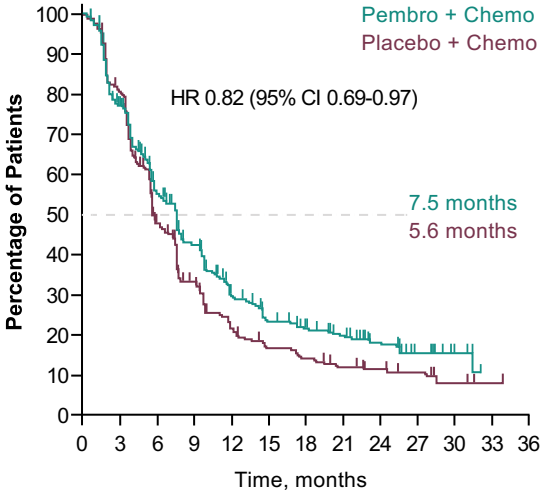
- Chemotherapy on study (taxane vs gemcitabine/carboplatin)
- PD-L1 tumor expression (CPS ≥1 vs CPS <1)
- Prior treatment with same class chemotherapy in the neoadjuvant or adjuvant setting (yes vs no)

Pembrolizumab, in combination with chemotherapy, is indicated for the treatment of patients with locally recurrent unresectable or metastatic TNBC whose tumors express PD-L1 (CPS ≥10) as determined by an FDA-approved test.

Cortes J, et al. ASCO 2020. Abstract 1000.

KEYNOTE-355: Primary Outcome (PFS)

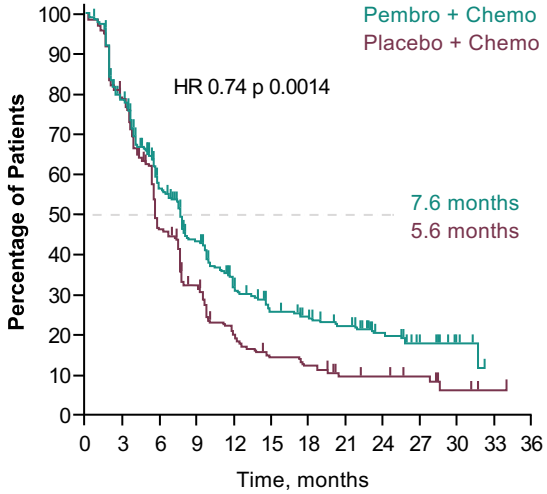
ITT



Statistical significance was not tested due to the prespecified hierarchical testing strategy.

PD-L1 CPS ≥1

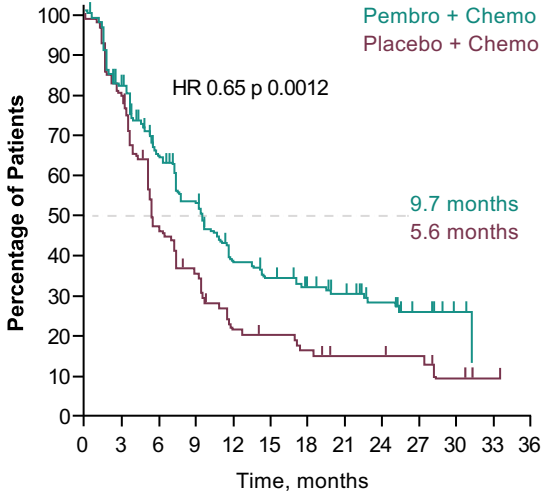
75% of patients



Prespecified *P* value boundary of 0.00111 **not** met.

PD-L1 CPS ≥10

38% of patients

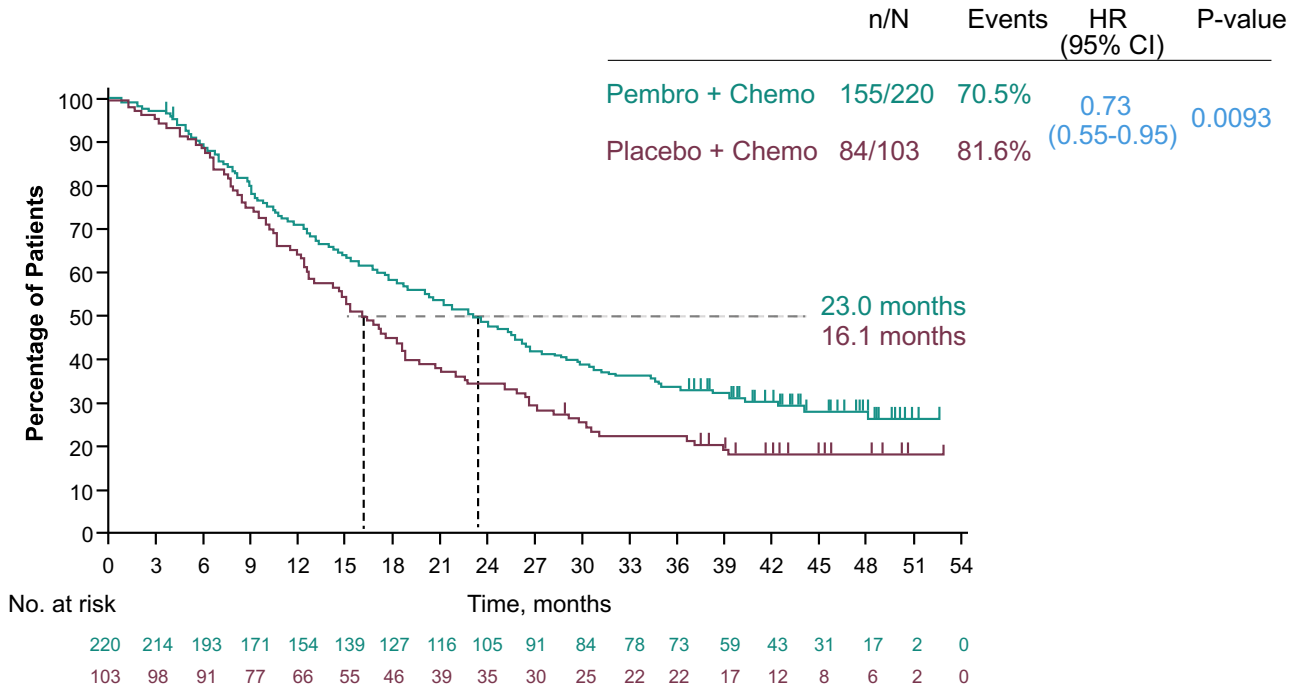


Prespecified *P* value boundary of 0.00411 met.

Pembrolizumab, in combination with chemotherapy, is indicated for the treatment of patients with locally recurrent unresectable or metastatic TNBC whose tumors express PD-L1 (CPS ≥10) as determined by an FDA-approved test.

Cortes J, et al. ASCO 2020. Abstract 1000.

KEYNOTE-355: OS for CPS ≥10

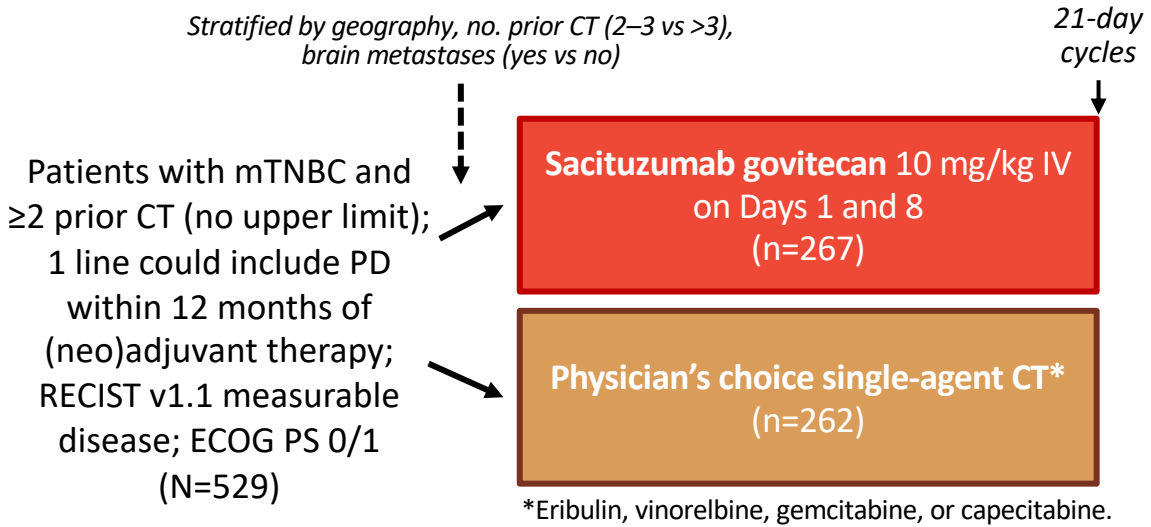


Pembrolizumab, in combination with chemotherapy, is indicated for the treatment of patients with locally recurrent unresectable or metastatic TNBC whose tumors express PD-L1 (CPS ≥10) as determined by an FDA-approved test.

Rugo H, et al. ESMO Congress 2021. Abstract LBA16.

ASCENT: Sacituzumab Govitecan vs Single-agent CT in Metastatic TNBC after ≥2 Previous CT Regimens

- Randomized, open-label phase III trial



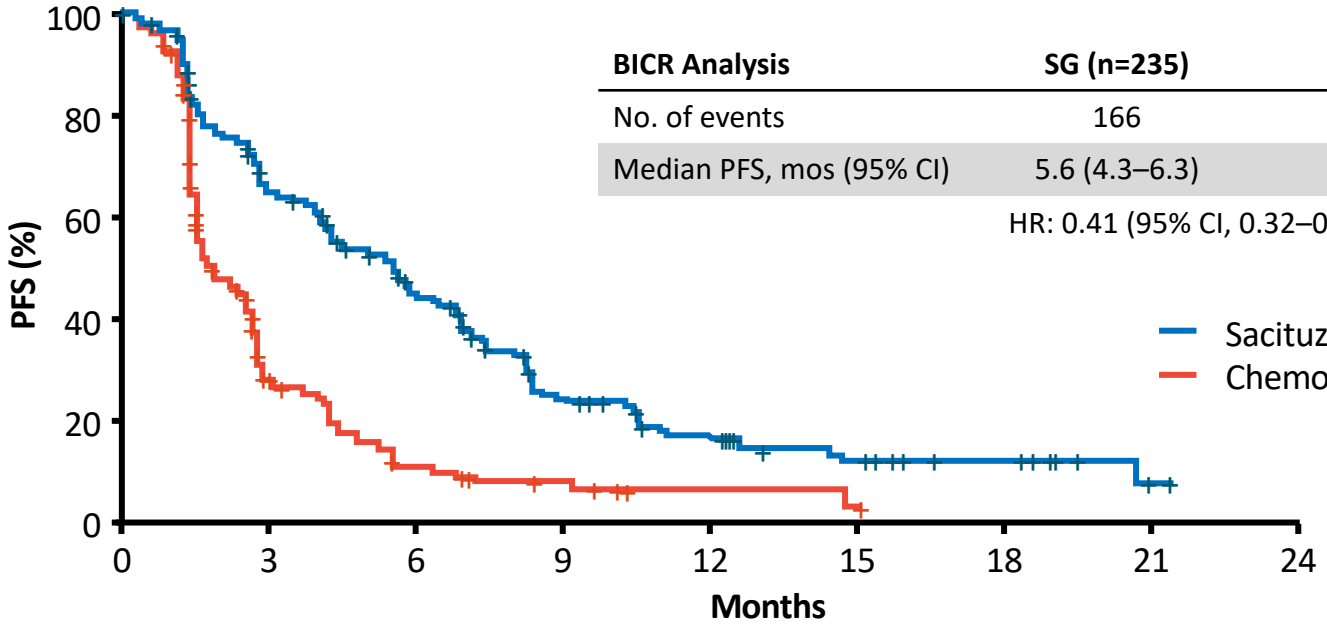
- Primary endpoint: PFS by IRC in patients without brain metastases
- Secondary endpoints: PFS (full population), OS, ORR, DoR, TTR, safety

- Trial halted early based on efficacy per unanimous independent DSMC recommendation

CT, chemotherapy; DoR, duration of response; DSMC, data and safety monitoring committee; ECOG, Eastern Cooperative Oncology Group; IRC, independent review committee; mTNBC, metastatic triple negative breast cancer; PD, progressive disease; PS, performance status; RECIST, Response Evaluation Criteria in Solid Tumors; TTR, time to response.

Bardia A, et al. *N Engl J Med*. 2021.

ASCENT: PFS by BICR (Primary Outcome)

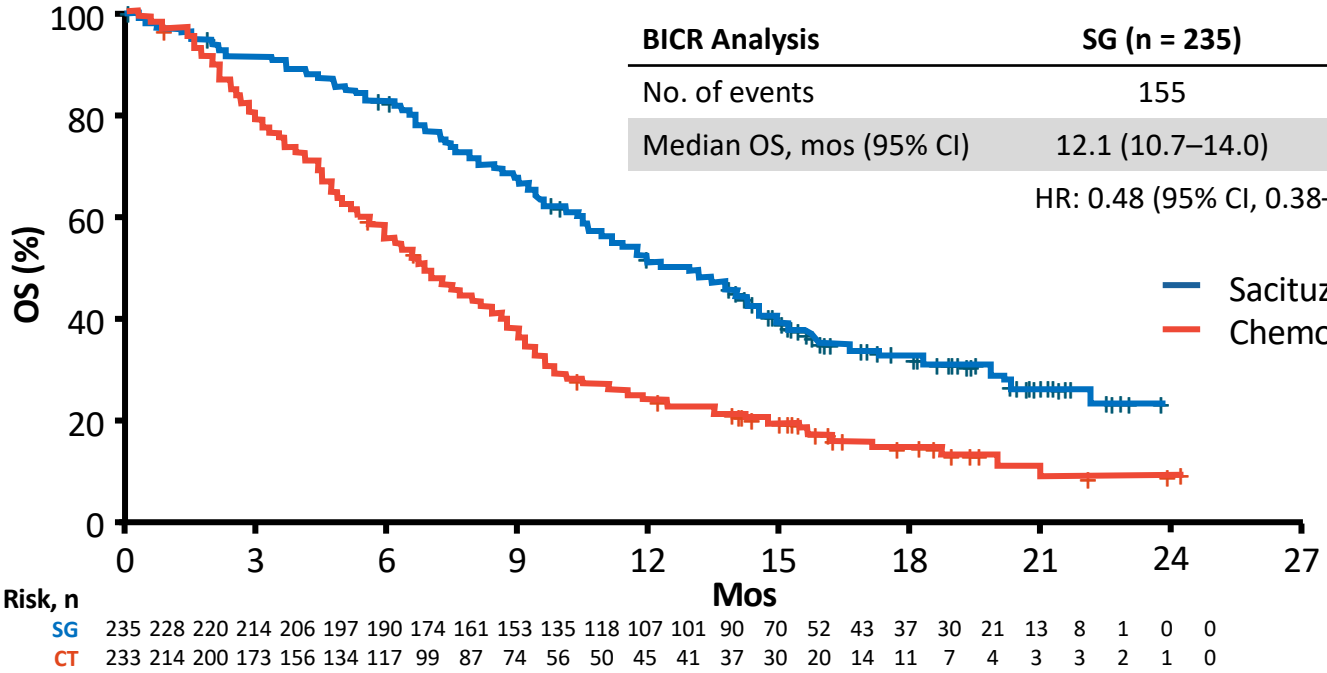


BICR Analysis	SG (n=235)	CT (n=233)
No. of events	166	150
Median PFS, mos (95% CI)	5.6 (4.3–6.3)	1.7 (1.5–2.6)

HR: 0.41 (95% CI, 0.32–0.52; *P*<0.0001)

Bardia A, et al. N Engl J Med. 2021;384(16):1529-1541

ASCENT: Overall Survival

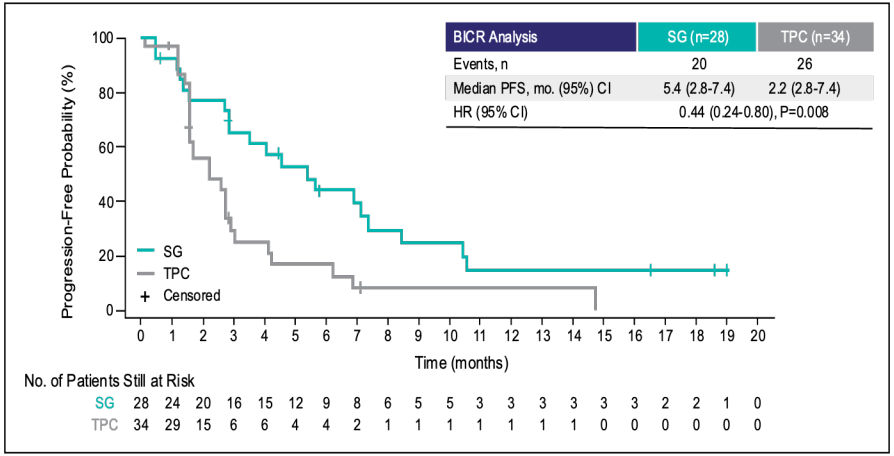


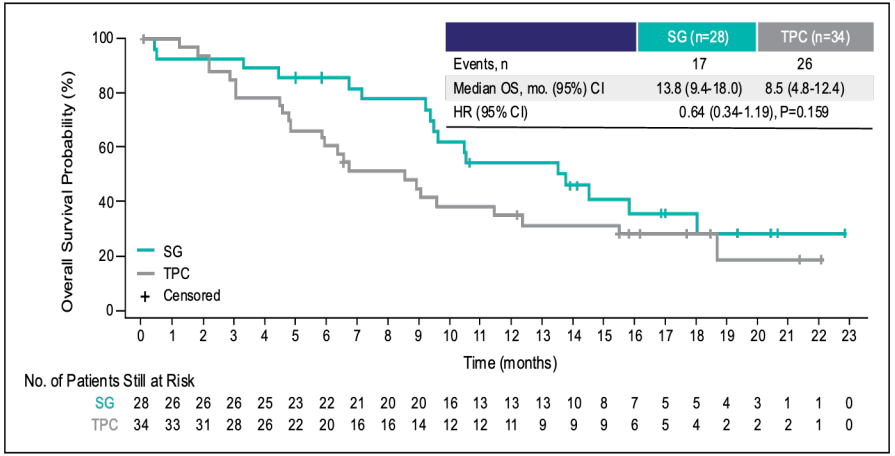
BICR Analysis	SG (n = 235)	CT (n = 233)
No. of events	155	185
Median OS, mos (95% CI)	12.1 (10.7–14.0)	6.7 (5.8–7.7)

HR: 0.48 (95% CI, 0.38–0.59; *P*<0.0001)

Bardia A, et al. N Engl J Med. 2021;384(16):1529-1541

Phase 3 ASCENT: Efficacy in ITT Population, Stratified for Black Patients

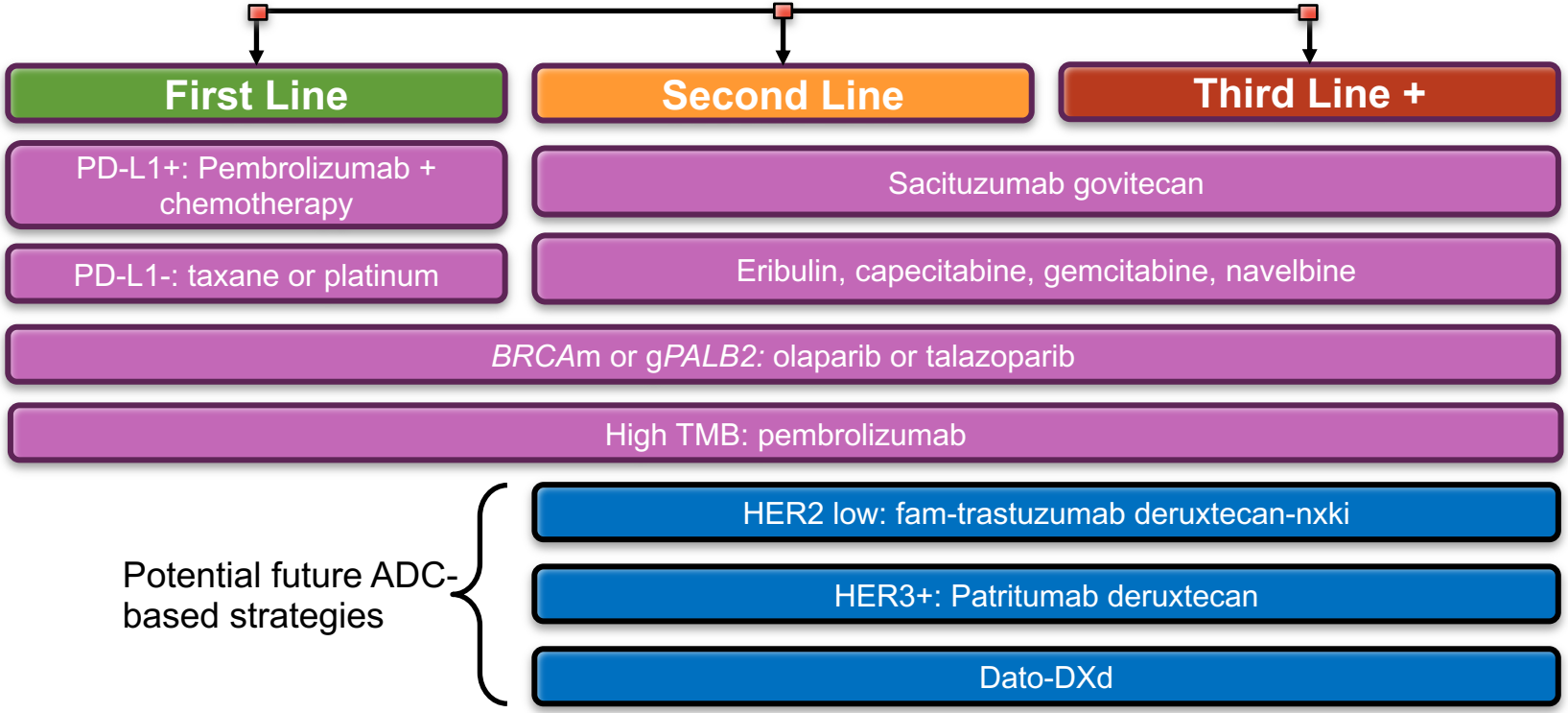




- 62/529 pts enrolled in ASCENT were black (12%; 28 SG vs 34 TPC)
- Black patients derived similar benefit in PFS and OS as overall population
- The safety profile of SG in this subgroup was consistent with the full trial population

Carey L, et al. 2021 SABCS Annual Meeting. Poster P05-16-07.

Approach to Therapy for Metastatic TNBC

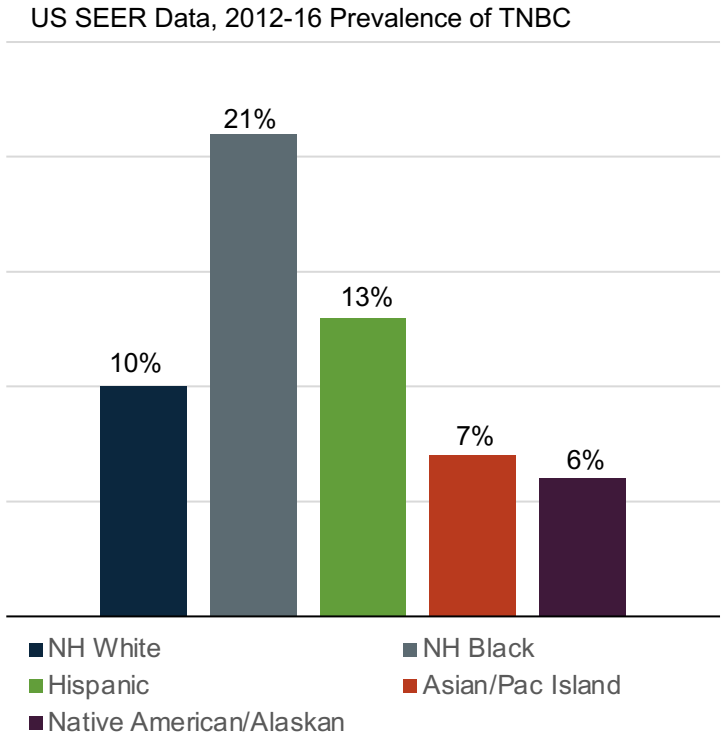


NCCN guidelines. Breast cancer. Version 3.2022.

And yet, disparities among Black women with TNBC persist

Higher Incidence of TNBC in Black Women

- TNBC is more prevalent in Black women than other ethnicities
  - Worldwide, highest rates found in US and West African Black women (~24%)
  - Contributes to excess BC-related mortality among Black women, but not sole explanation
- Incidence of TNBC is twofold higher for Black women compared to White Women
- TNBC disproportionately affects younger, premenopausal women
- Pathogenic variant frequency in 21 cancer-associated genes:
  - White: 7.8% BRCA1/BRCA2, 6.2% non-BRCA
  - Black: 9.0% BRCA1/BRCA2, 5.6% non-BRCA



NH = NonHispanic; Pac Island = Pacific Islander.

American Cancer Society. https://www.cancer.org/research/cancer-facts-statistics/breast-cancer-facts-figures.html. Accessed Nov. 1, 2021. Dietze. *Am J Pathol.* 2018;188:280. Foulkes. *N Engl J Med.* 2010;363:1938. Howard. Cancer J. 2021;27:8. Prakash. Front Public Health. 2020;8:576964. Sharma. Oncologist. 2016;21:1050. National Cancer Institute. Genetics of Breast and Gynecologic Cancers (PDQ®)–Health Professional Version. https://www.cancer.gov/types/breast/hp/breast-ovarian-genetics-pdq#_2723_toc. Published April 20, 2022. Accessed May 26, 2022.

Genetics of TNBC

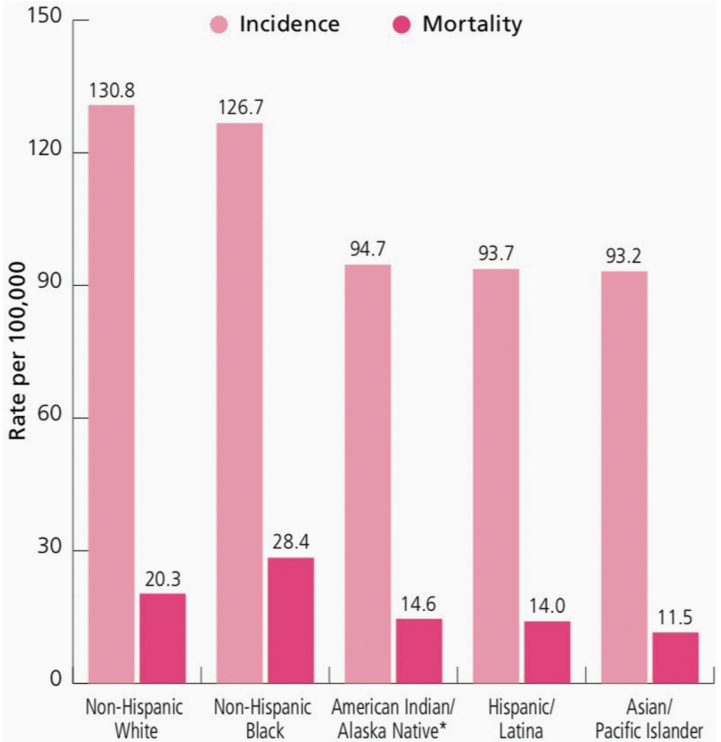
- CARRIERS study: A population-based, multicenter study that examined the prevalence of germline mutations in 12 breast cancer susceptibility genes among 3946 Black women and 25, 287 White women with breast cancer
  - 75% of mutations seen in TNBC were in *BRCA1, BRCA2*, or *PALB2* genes
  - The overall prevalence of germline mutations were the same in Black vs White Women
    - 9.28% in Black women vs. 8.08% in White women(P=0.28)
  - *PALB2* was the only gene found at higher rates in Black patients than White patients (2.79% vs. 1.23%; P=0.05)

Domchek SM, et al. *JAMA Oncol*. 2021;7(7):1045-1050.

Higher Mortality for Black Women With TNBC

- Median age at death due to breast cancer
  - 68 yrs all women
  - 70 yrs White women
  - 63 yrs Black women

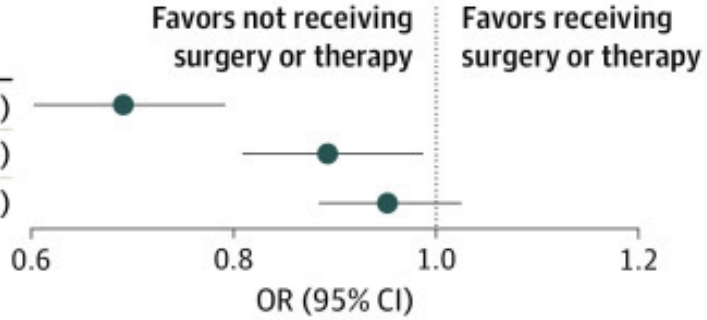
Female breast cancer incidence (2012–2016) and death (2013–2017) rates by race/ethnicity in the US



Rebner M and Pai VR. *Journal of Breast Imaging*. 2020;2(5):416-421

Black Women Less Likely to Receive Surgery and Chemotherapy

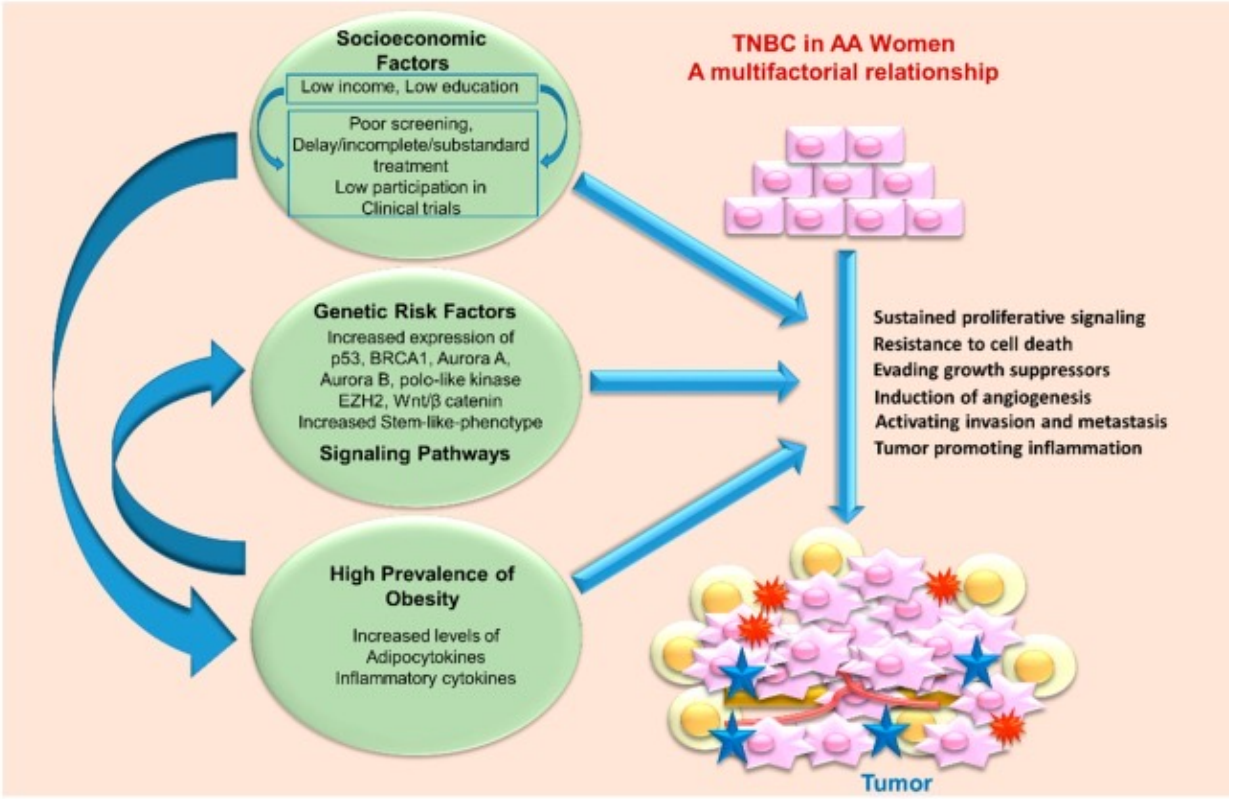
	White women, %	African American women, %	OR (95% CI)
Receipt of surgery	94.1	93.3	0.69 (0.60-0.79)
Receipt of chemotherapy	73.2	78.3	0.89 (0.81-0.99)
Receipt of radiotherapy	51.1	54.3	0.95 (0.88-1.03)



- Black patients had lower odds of receiving surgery and chemotherapy compared with White patients, after adjustment for sociodemographic, clinicopathological, and neighborhood covariables
- Radiation therapy not significantly different

Cho B, et al. *JAMA Oncol*. 2021;7(7):1016-1023.

Biological and Socioeconomic Causes of Disparities



Siddharth S and Sharma D. *Cancers (Basel)*. 2018;10(12):514.

Disparities in Diagnosis and Treatment

- Modifiable risk factors for TNBC may be more prevalent in certain at-risk groups
- Low SES and less-generous insurance associated with diagnosis at advanced stage for all women
- Outcomes in Black women influenced by underlying disease characteristics as well as SES and patterns of care
  - Low SES Black women more likely to receive inadequate treatment vs. higher SES NHW

Risk Factors for TNBC	
Early menarche (<12 y) and/or later menopause	Obesity (>30 kg/m^2) in premenopausal women
African-American and Hispanic ancestry	Moderate/high alcohol consumption
Underlying *BRCA1* mutation	Low physical activity
Family history	Exogenous hormone use
	Young age at 1st pregnancy

NHW = non-Hispanic white; SES = socioeconomic status

Asad. *J Natl Compr Canc Netw*. 2020;19:797. Prakash. *Front Public Health*. 2020;8:576964. Howard. *Cancer J*. 2021;27:8. Silber. *Milbank Q*. 2018;96:706.

The Experiences and Perceptions of Black Women with TNBC

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Polling Question

Have you personally witnessed bias in cancer care by fellow clinical staff (Drs, RNs, NPs, PAs, pharmacists, office staff, patient navigators) in the past year?

A. Yes, but only once or twice in the past year
B. Yes, more than once per month
C. Yes, more than once per week
D. Yes, seems like daily
E. No, never

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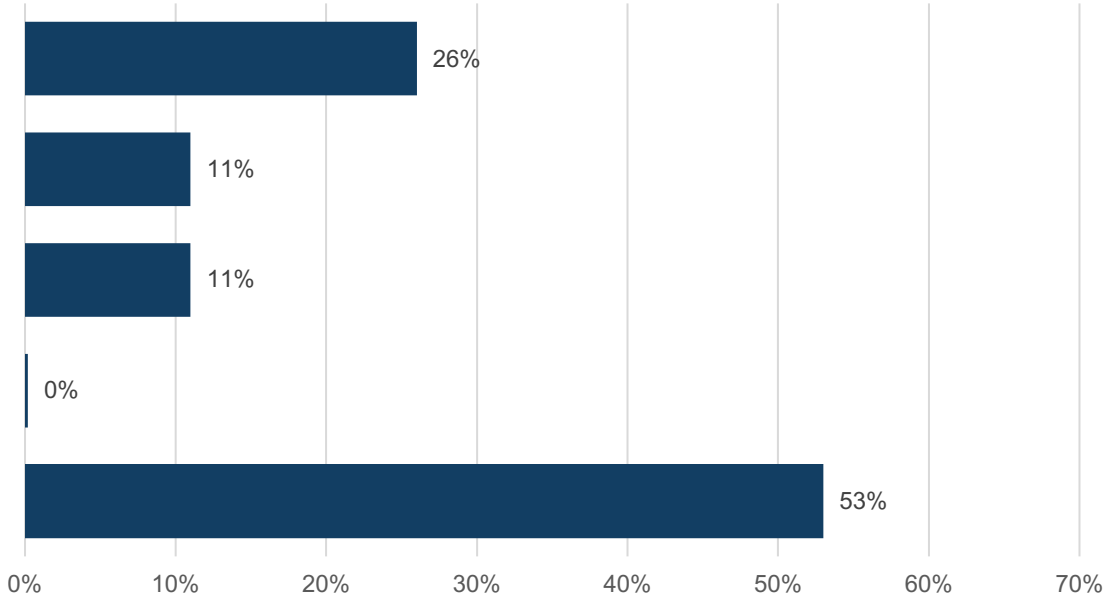

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- How important is the race of the physician to the quality of care you receive?

I believe that race can and is sometimes a factor in care. My oncologist happens to be a person of color, although he is not African American, but I prefer being treated by those individuals that are of color. And I think that sometimes they have a better connection with a patient who is of color and that the patient feels more confident and the patient feels like they have the ability to be heard and understood. **There's certainly cultural things that go along with being African American that I believe only an African American physician and/or a person of color would be in tune to and recognize that it could have a bearing on care.**

I absolutely feel that the race of the oncologist affects the cancer care.

The race of the physician isn't really an important factor in the quality of care that I receive, but at the same time meeting a Black physician would definitely increase my level of comfortability and the treatment that I'm getting. But generally the race of the physician does not affect the care I receive.

Does Race of Oncologist Matter?

- Health care mistrust
  - Long history in US of unethical experimentation and research on Black women without consent[1]
- Some women are more confident in the care they receive, if their doctor is Black or non-White
  - Others do not think it makes a difference

1. Washington HA. Medical Apartheid: The Dark History of Medical Experimentation on Black Americans from Colonial Times to the Present. New York, NY: Doubleday Books: 2007.

- Prior to receiving a diagnosis of breast cancer, did your primary care physician talk to you about breast cancer screening?

Yes. **My physician actually spoke to me about breast cancer screenings lots of times. I would say that I was careless …** [W]hen I was diagnosed, I didn't have all those [textbook symptoms]. So it came as a shock. So I must say that my doctor did speak to me about screenings, but I was very careless in my approach to it, but I know better now.

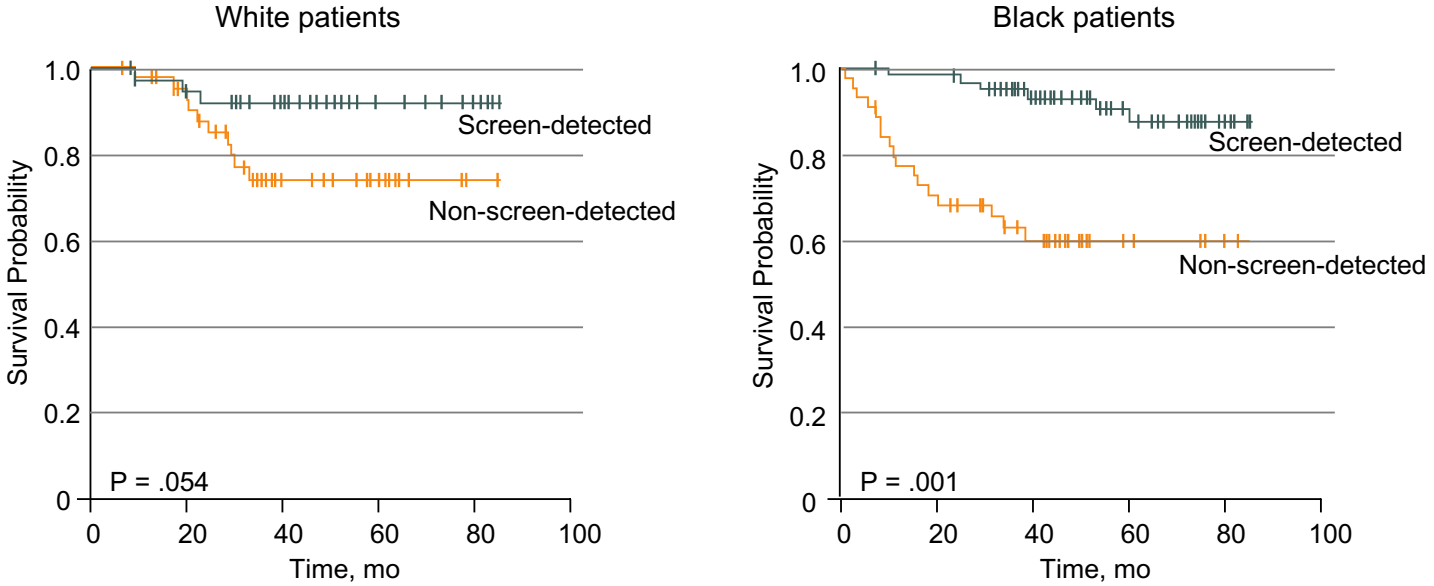
Oh God. Yes. My primary care physicians stress breast cancer, of checking yourself, being screened and everything, and I value them with helping find the cancer in the stage that it was. And they were earlier stage because of the care that they gave.

[My doctor] did not talk to me about it, but that is because I was under 40. So it was only when I turned 35, and I was having really weird symptoms, and I actually went to her and said, "Is there a way that I can get a cancer screening early because my mother had ovarian cancer when she was pregnant with me." And so the fact that the laws state that you have to be 40 in order to get a preventative mammogram that's covered by insurance, I was at 35, but I was able to get it covered by insurance because my mother had ovarian cancer. **But if I hadn't brought it up, it never would've been brought to my attention** which is sad.

Screening Hesitancy

- Outcomes improve with guideline-recommended screening

Overall Survival Probability for With TNBC, Comparing Mammography Screening–Detected and Non–Screening-Detected Cases[1]



Chen Y, et al. JAMA surgery. 2020;155(5):440-442.

Screening and Diagnosis Recommendations

- Consider BC screening at earlier ages for Black women[1]
  - Avoid delayed follow-up of mammograms
  - Rapid tumor growth/prevalence in younger women complicate diagnosis on mammography: MRI is more sensitive for early detection and diagnosis
- Suspect TNBC in premenopausal breast cancer and Black women[2]
- Ensure accurate assessment of HR/HER2 status, PD-L1 expression, and BRCA1/2 status to guide optimal treatment decisions in TNBC[2]
- Avoid delays in treatment[2]
  - Follow recommended regimens for CT and other treatments for all patients

1. Rebner M, et al. Journal of Breast Imaging. 2020;2(5):416-421. 2. NCCN Guidelines. Breast Cancer. Version 3.2022.

- After your diagnosis, did you feel that your oncologist involved you in treatment decisions or talked to you about participating in clinical trials?

I really felt that she talked to me rather than with me. The first time I met my oncologist in the same breath she said you need 16 rounds of chemo and do you want to freeze your egg? All I heard in that sentence was chemo. So to this day I really struggle with that because I was single at the time, single now and I will never have children. So that was really hard. **They never mentioned clinical trials, which would've been ideal for me because my body is intolerant of all the current medications to help prevent a recurrence.**

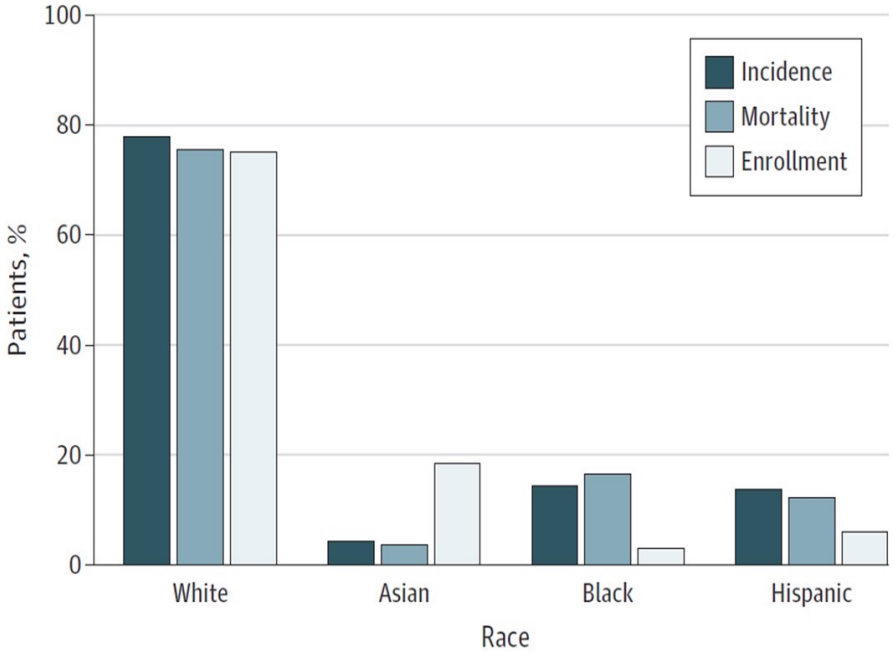
I feel my oncologist lumped you in a category. If you were African-American, you had this type of breast cancer, whatever, this was your treatment. As far as clinical trials, I was involved in a clinical trial, but I think … **I happened to be the person that they needed for the trial. It wasn't so much that he wanted to give that to me. But I could still be in a box.**

After my diagnosis, the oncologist made mention of these [trials]. I think my oncologist valued my perspective

Clinical Trial Participation

- Trial participation is lowest among Black patients
- In a survey of 358 trials, Black people represented
  - 12.1% of total cancer population
  - 9.0% of participations in SWOG trials
  - 2.9% of participants in pharmaceutical company sponsored trials

Relative proportion among US patients with cancer compared with trial participants in FDA approval trials between July 2008 and June 2018.

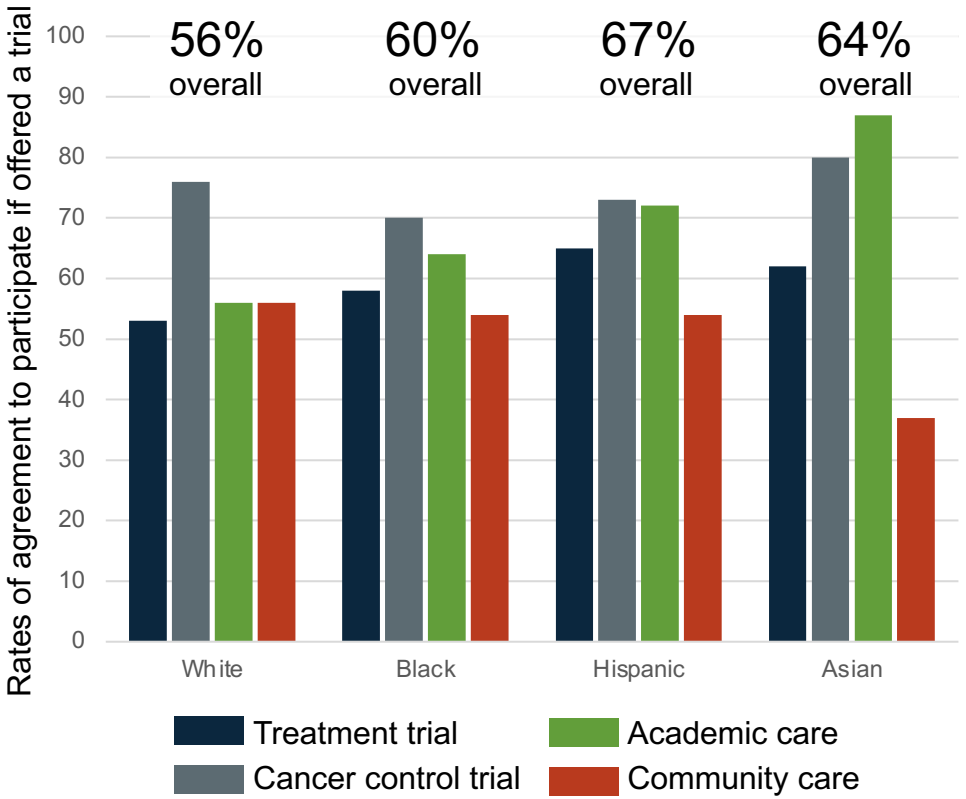


SWOG = Southwest Oncology Group

Unger JM, et al. *JNCI Cancer Spectrum*. 2020;4(4).

"If They Are Offered the Opportunity"

- Meta-analysis (35 studies, 9759 patients, all cancer types)
  - > Half of patients participate in clinical trials, **if they are offered the opportunity**
  - No difference by race
- The main reasons for nonparticipation were treatment choice or lack of interest
  - 24% desire for other treatment
  - 20% not interested in trial participation
  - 8% passive refusal
  - 8% fear of side effects
  - 7% financial
  - 7% dislike being part of experiment



Unger JM, et al. *JNCI: Journal of the National Cancer Institute*. 2020;113(3):244-257.

- Generally, what are the greatest **personal challenges** that Black individuals face in receiving prompt and high-quality health care, particularly as it relates to cancer?

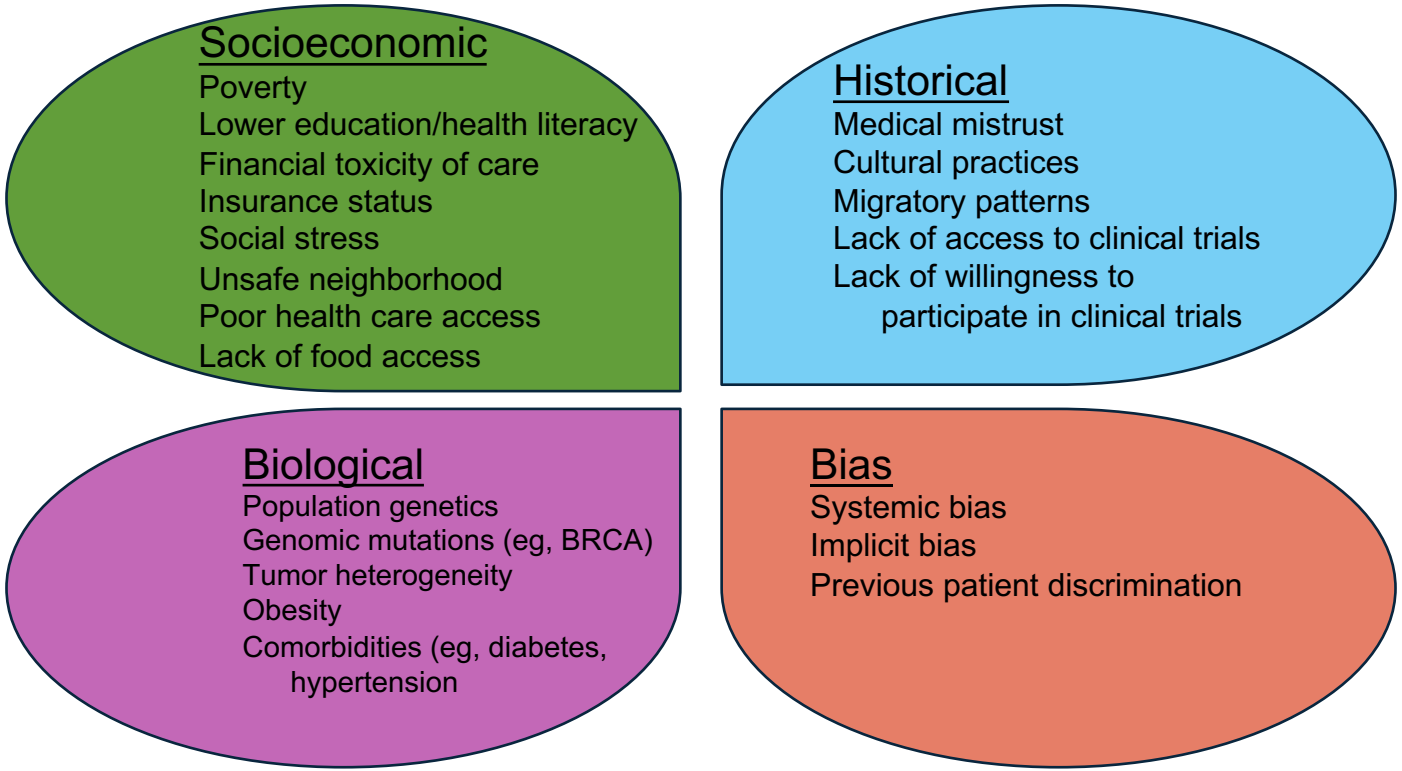
[M]any of them went into depression and … not having psychosocial tools to take care of their mental issues. Many went into a very dark place during their cancer treatments. And so trying to get them out of that abyss it becomes very difficult.

it's really devastated me spiritually, because I just don't understand why I have to keep going through so many things … the way [White women] felt dismissed was not the way I felt dismissed, because I know it was specifically due to the color of my skin … I really don't trust the medical community … **It's like no one wants to believe that Black patients are treated differently.**

Logistical challenges, as an example, clinical trials. Well, if those clinical trials are not close, where the individual could stay home and travel back and forth to those clinical trials, it becomes challenging. … There's a lot of stress, just general day-to-day living stress. And then you add that stress to the stress of a diagnosis and it becomes astronomical and almost insurmountable.

Most of the black people I know who have breast cancer do complain about the cost of treatment, the finance of getting quality care and treatment

Challenges That Increase Disparities



1. Wang F, et al. Cancer Research. 2021;81(4):1163-1170. 2. Prakash O, et al. Front Public Health. 2020;8:576964. 3. Hossain F, et al. Front Public Health. 2019;7:18. 4. Newman LA. Ann Surg Oncol. 2017;24(10):2869-2875. 5. Penner LA, et al. Soc Sci Med. 2017;191:99-108. 6. Penner LA, et al. J Health Care Poor Underserved. 2016;27(3):1503-1520.

- Generally, what are the greatest **health system challenges** that Black individuals face in receiving prompt and high-quality health care, particularly as it relates to cancer?

You have to now try to find a doctor or hospital that will guide you through the maze because healthcare system is a maze in the United States. [W]hen I first started, the first oncologist that I was referred to refused my insurance until I got my blood sent to second oncologist that actually took care of me from diagnosis to survivorship.

The greatest challenge they face currently is about the insurance carrier. A lot of them complain about the cost. Most of them complain about the physicians.

I think whether you have insurance or not, or the type of insurance that you have does make a difference in the care that you receive.

So many times, African Americans are close-lipped about chronic diseases, especially cancer. I think that one of the things we as a community need to address is our ability to share information about our health situations with our family, with our friends, and with the greater community, if at all possible.

Addressing Disparities

How do we improve care for Black women with TNBC?

Improving Breast Cancer Care for Black Patients

- Increased efforts aimed at early detections of breast cancer
  - Reviewing family history of cancer prior to a breast cancer diagnosis to
    1) Identify women eligible for genetic testing or high risk breast cancer screening (to include breast MRI and mammogram) or
    2) Identify women eligible for earlier age of initiation of breast cancer screening with mammogram
- Provide guideline concordant care for all patients regardless of race (including chemotherapy, radiation, surgery, etc).
- Avoid treatment delays (work-up of abnormal imaging, time to surgery or radiation, initiation of chemotherapy)
- Ensure accurate assessment of HR, HER2, and BRCA1/2 status, PD-L1 expression, and genetic testing, to facilitate biomarker-guided treatment decisions
  - Outcomes are improved when treatments are selected according to the results of biomarker testing

Patel MI, et al. JCO. 2020;38(29):3439-3448.

Addressing Disparities in Access to Care

- Ensure equitable access to high-quality care[1]
  - Improve medical insurance access and reduce financial toxicity
  - Medicaid expansion: Cancer outcomes improved in Medicaid expansion states and worsened in states that chose not to expand.[2]
- Ensure equitable access to research[1]
  - Use recruitment strategies that ensure adequate representation of populations afflicted with the disease being studied
- Address structural barriers[1]
  - Promote access to socially, culturally, and linguistically appropriate, respectful, and high-quality cancer care
  - Address implicit and explicit institutional biases
  - Diversify work force
  - Address social determinants of health (SDoH)

1. Patel MI, et al. JCO. 2020;38(29):3439-3448. 2. Adamson BJS, et al. JCO. 2019;37(18_suppl):LBA1.

Summary

- TNBC disproportionately affects Black women with higher incidence, higher stage at diagnosis, and higher mortality
- New approvals have expanded the therapeutic options
- Many Black women perceive their care to be different than their White peers
- Many Black women do not have access to clinical trials
- There continues to be a need to
  - Ensure equitable access to high-quality care
  - Ensure equitable access to research
  - Address structural and institutional barriers

SMART Goals

Specific, Measurable, Attainable, Relevant, Timely

- Deliver high-quality care to every patient
- Listen to your patients and consider their concerns
- Remember that some patients may need extra help overcoming cancer care hurdles
- Speak up when you see intentional or unintentional biases affecting cancer care
- Take part in community outreach projects that address access to care

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