LIVING BEYOND
BREAST CANCER®

# Navigating the changing landscape of early-stage breast cancer

How treatment for early-stage breast cancer has changed

# How treatment for early-stage breast cancer has changed

MARYAM LUSTBERG MD MPH

YALE CANCER CENTER

# Disclosures

- Consulting activity: Gilead, AstraZeneca, Daichi-Sanko, Novartis, Lily, Beyer, Menarini

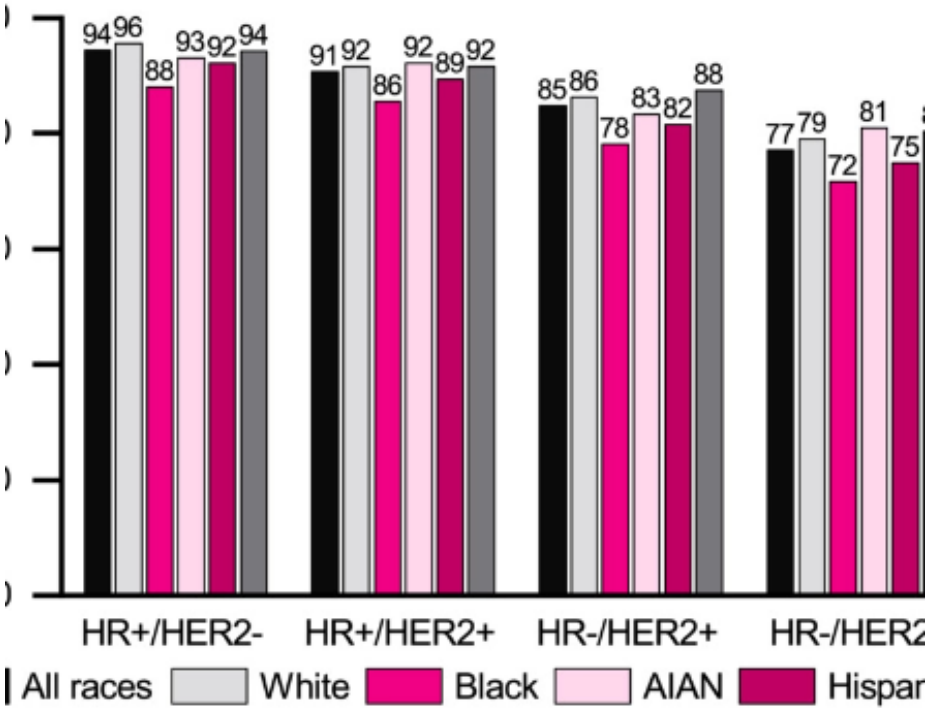
# Agenda

- Overview of new trends in early stage breast cancer
- Hormone receptor positive breast cancer
- Her2 positive breast cancer
- Triple negative breast cancer
- What about Her2 low?
- New approaches in supportive care and symptom management

# Overview of new trends in early-stage breast cancer

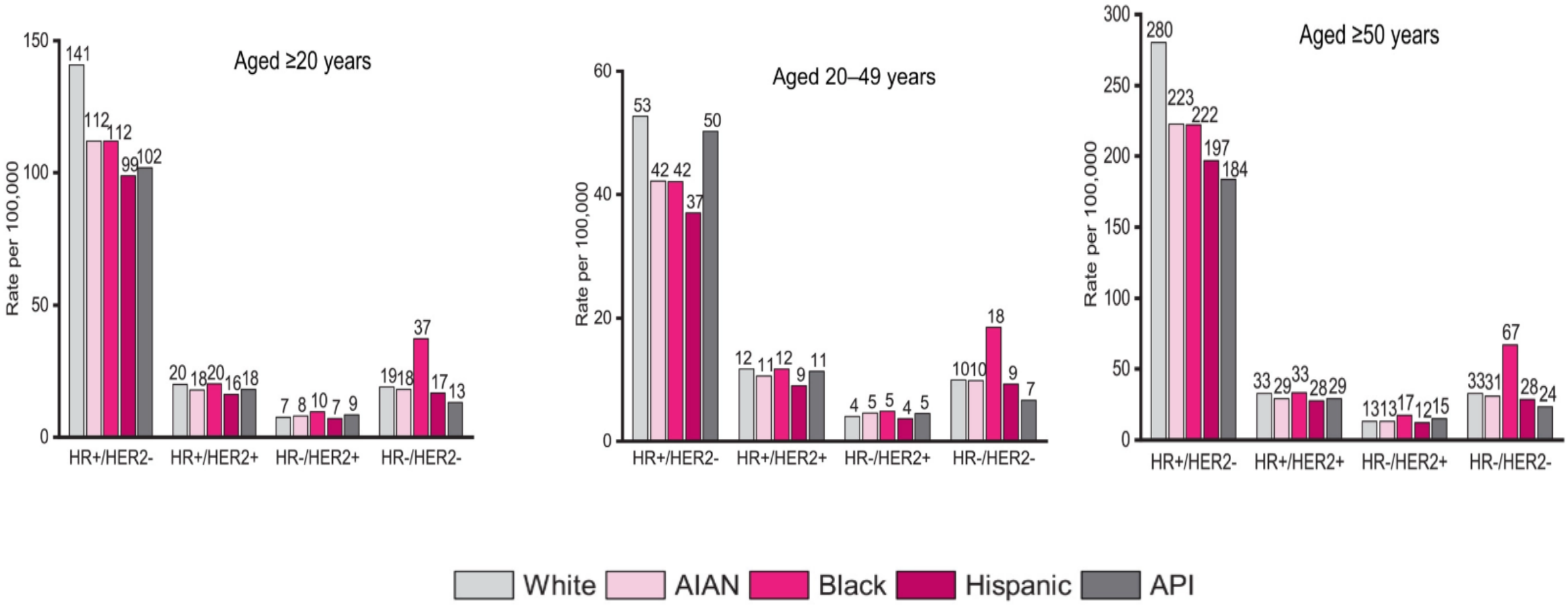
# Eary stage /non metastatic breast cancer

- Stages I-III
- Majority of breast cancers are diagnosed in these stages
- Advances in screening and treatment have improved outcomes



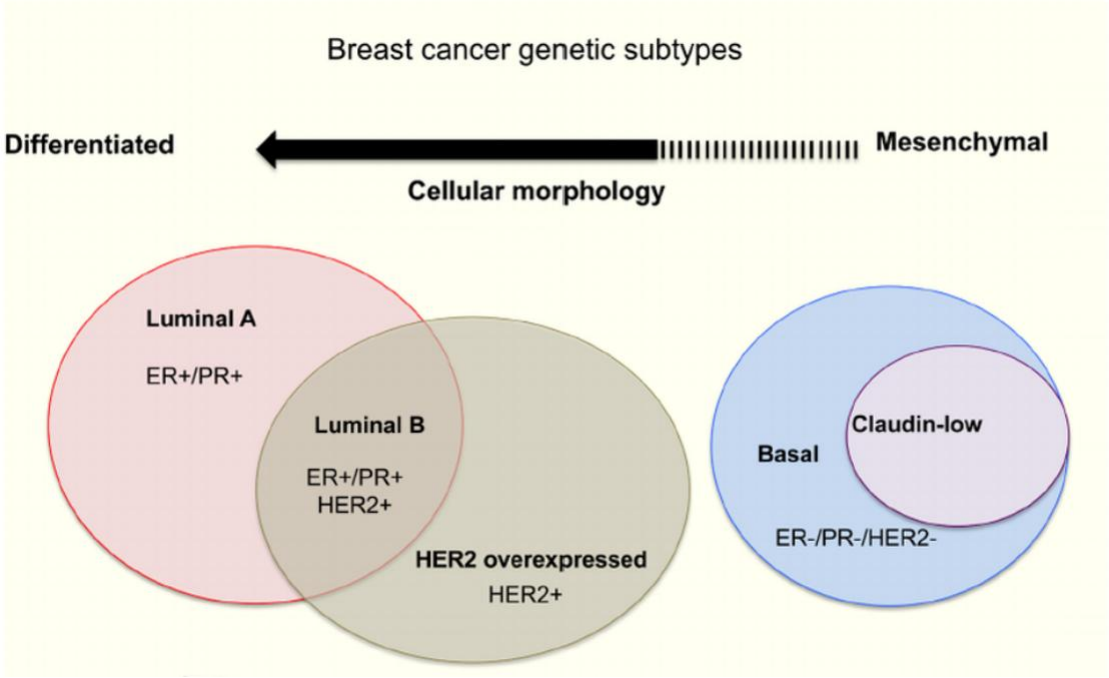

Breast Cancer Statistics, CA: A Cancer Journal for Clinicians, 202

# Female breast cancer incidence rates by subtype and race/ethnicity and age




Breast Cancer Statistics, CA: A Cancer Journal for Clinicians, 2022

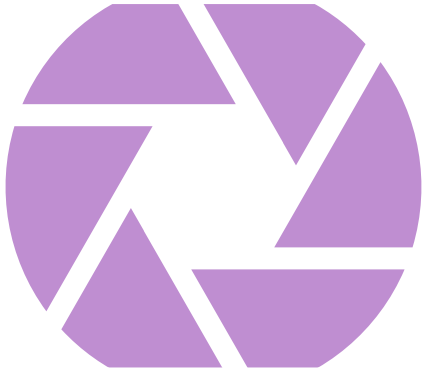
# Breast cancer is not one cancer



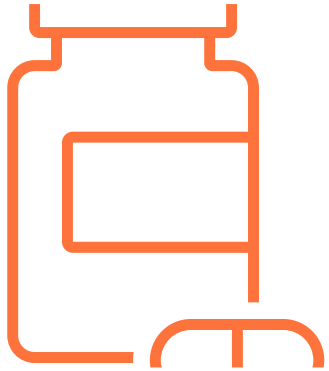
# Hormone receptor positive breast cancer

# New trends:

Less/no  chemo when not needed



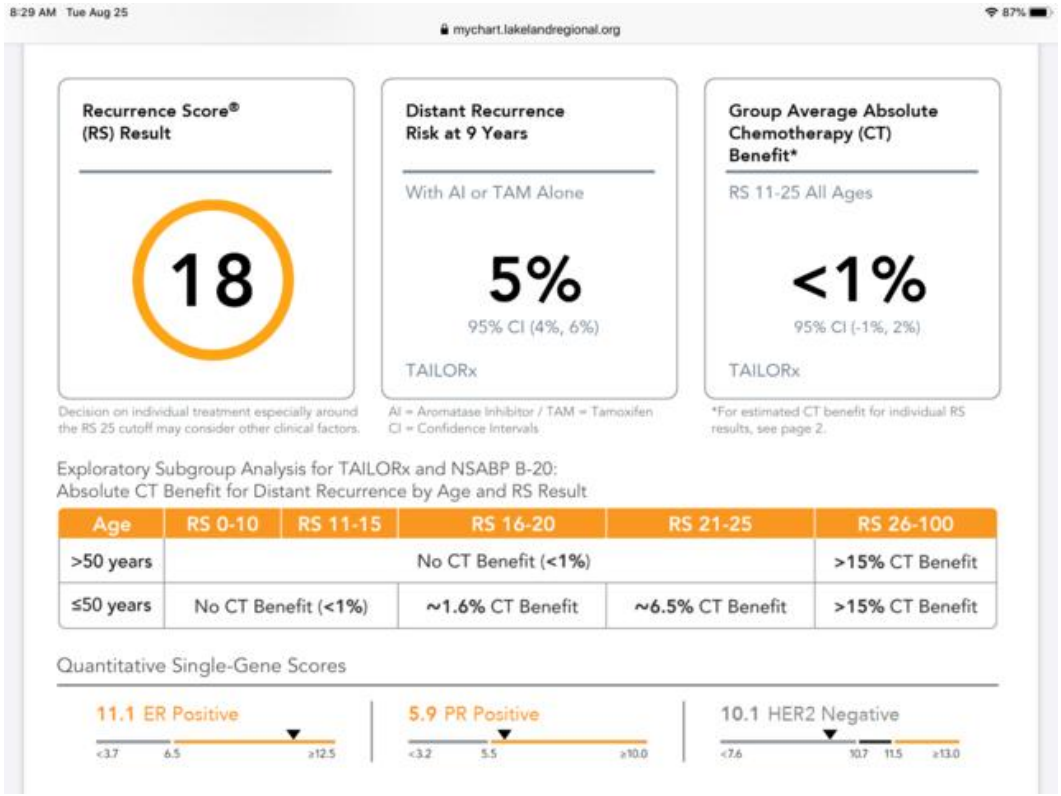
Immunotherapy for some



Helpers to endocrine therapy: CDK 4/6 inhibitors

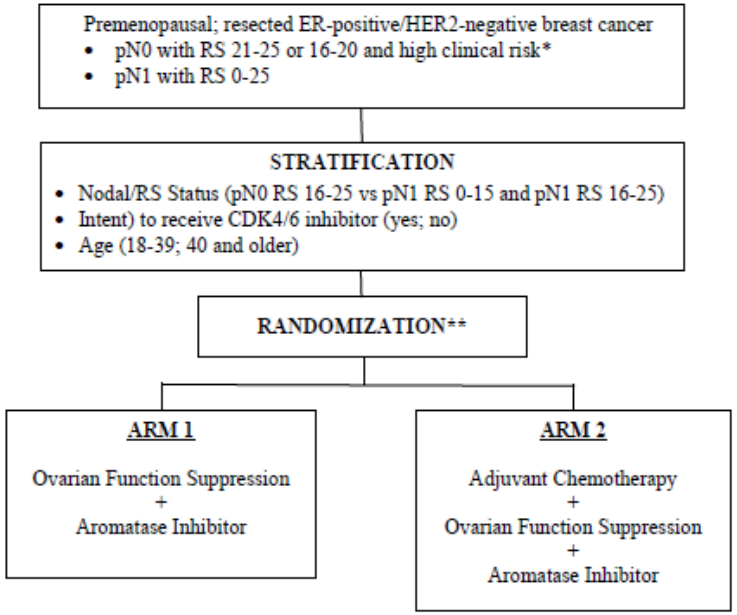
ctDNA/late recurrence studies

# Less chemo /no chemo when not needed




- Use of personalized medicine to determine who might not need chemo.
- Oncotype DX or MammaPrint are used to test tumor tissue
- Higher risk tumors are given chemo while lower risk tumors are treated with endocrine therapy plus targeted therapy.
- Has expanded to node positive disease
- Ongoing trial looking at this question in younger women  (NRG Ofset study)

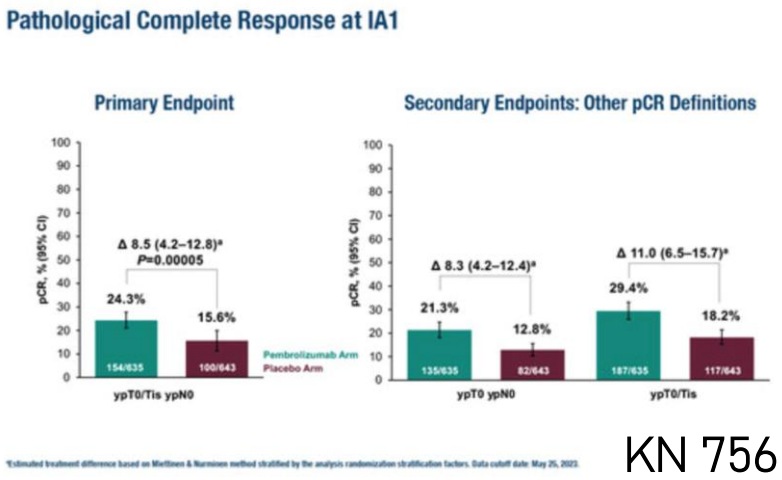
# Less chemo for premenopausal patient with favorable biology




* **High clinical risk defined as:**
1) low histologic grade with primary tumor size > 3 cm, OR
2) intermediate histologic grade with primary tumor size > 2 cm, OR
3) high histologic grade with primary tumor size > 1 cm

** Randomization is 1:1.

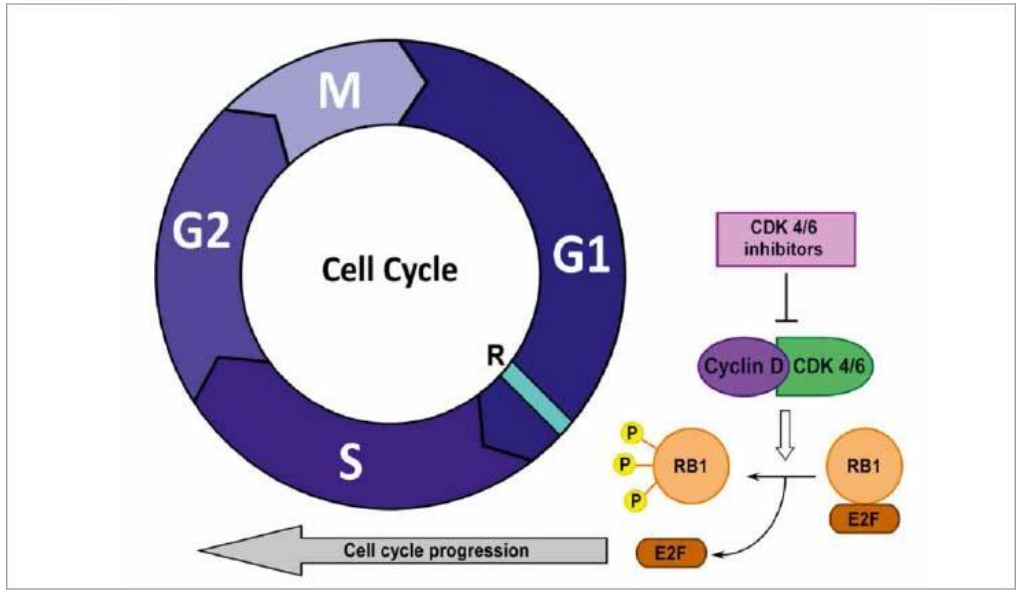
# Immunotherapy for some HR positive tumors?



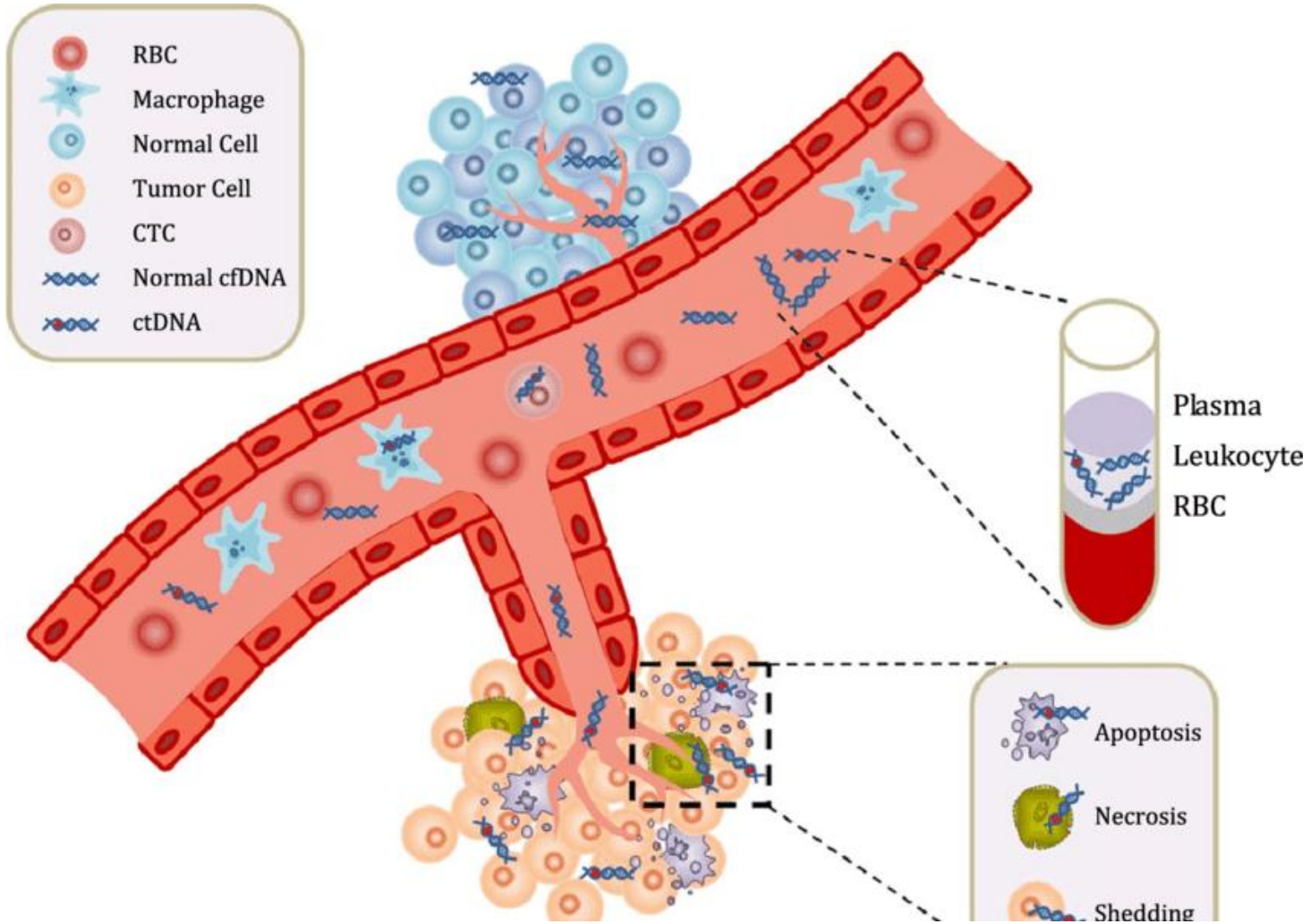

KN 756 study

- In clinical trials only so far
- In general, many hormonally driven tumors are not responsive to immunotherapy
- But some maybe be more immunogenic (about a third)
- We can use the MammaPrint assay to find High 2 (H2) tumors

# Helpers of endocrine therapy: CDK 4/6 inhibitors




- Verzenio (abemaciclib)
- Kisqali (ribociclib)

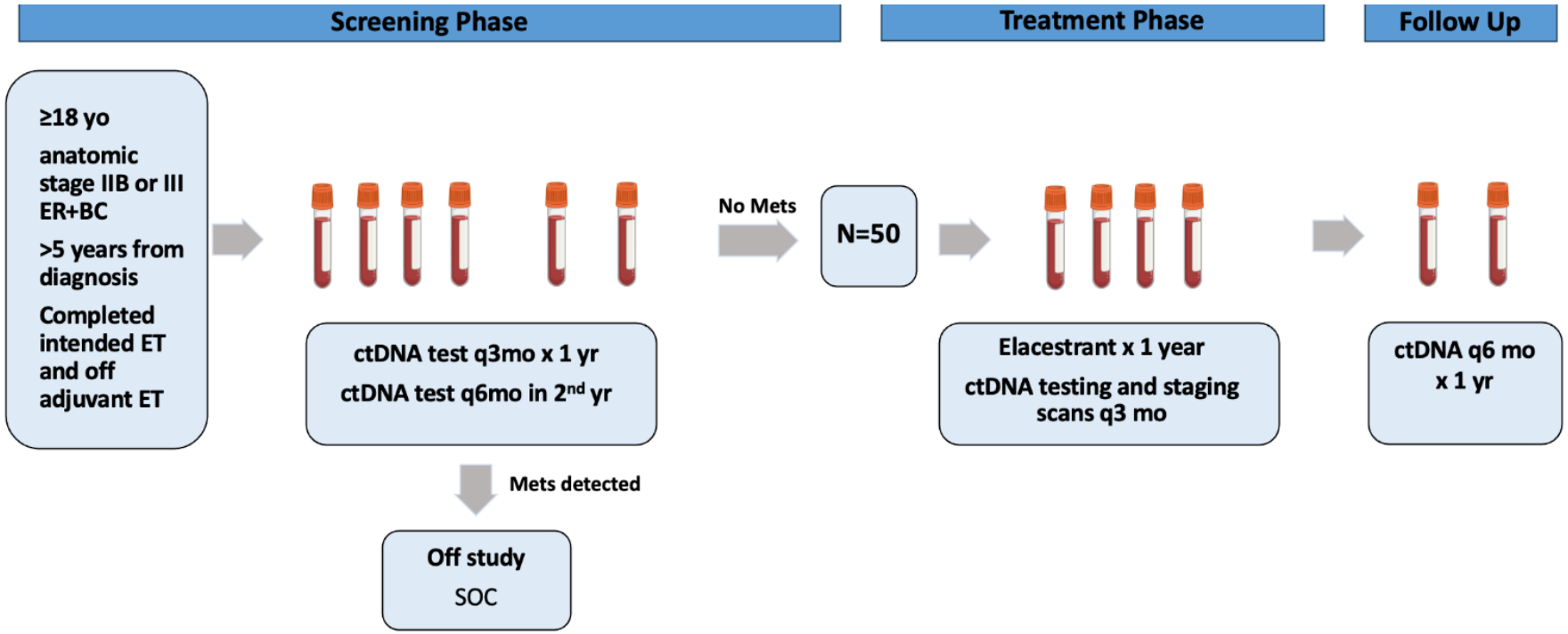



# ctDNA/late recurrence studies

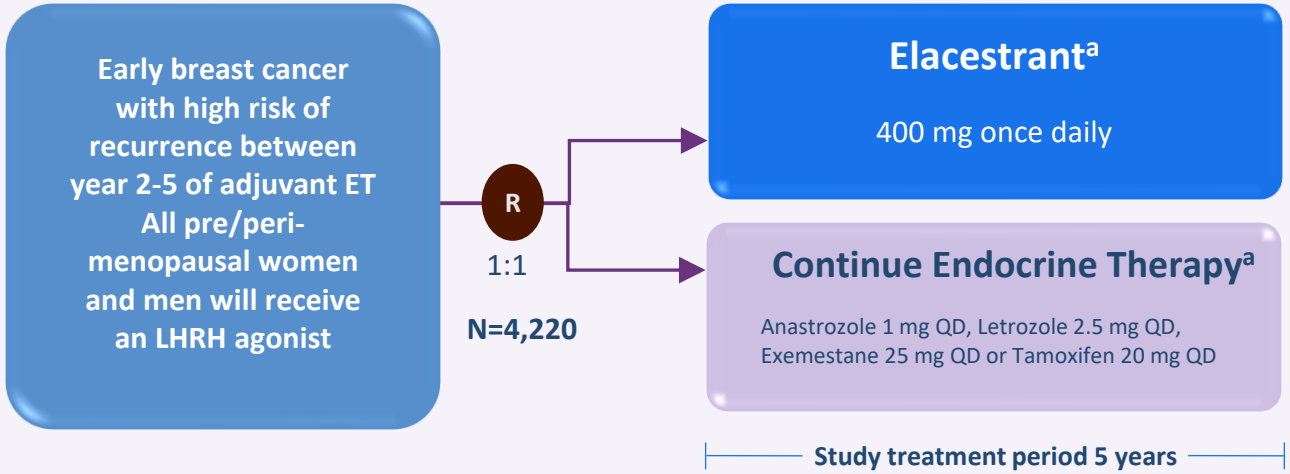
- Many patients with early stage breast cancer do well
- However, some can have recurrences years later
- We are trying to understand better way to reduce the risk of this happening.
- Many studies are looking for clues in the blood

# TBCRC 068: A single arm phase II trial of circulating tumor DNA-guided adjuvant therapy with elacestrant in ER+HER2- breast cancers at risk for late recurrence (CATE)

**Investigator Team:**
**Mariya Rozenblit MD, Wei Wei MD PhD, Ian Krop MD PhD, Eric Winer MD, Maryam Lustberg MD MPH**
**Yale University**



# ELEGANT – A Randomized Phase 3 Study of Elacestrant vs Standard Endocrine Therapy in Patients with Node-positive, Estrogen Receptor-Positive, HER2-Negative, Early Breast Cancer with a High Risk of Recurrence




## PHASE 3 OBJECTIVES

**Primary objective:** Evaluate IBCFS (Invasive breast cancer-free survival)

**Secondary objectives:** Evaluate DRFS, OS, safety, and PROs-QoL

Stratification Factors:

- Menopausal status: Post-menopausal vs. pre- or peri-menopausal
- Prior vs. No prior CDK4/6i in the adjuvant setting
- Time since curative surgery (≤48 mo vs >48 mo)

[a]Change in endocrine therapy after randomization in the control arm from an AI to another AI or to tamoxifen is allowed as per investigator's judgment

Long-term follow-up:

- Yearly for safety, survival, and recurrence
- Until end of study (approximately 5 years after last participant randomized)

- Primary objective is to evaluate IBCFS (Invasive breast cancer-free survival) with elacestrant versus SOC endocrine therapy
- Secondary Objectives are DRFS (distant relapse-free survival), IDFS, OS (overall survival), safety, and PROs-QoL

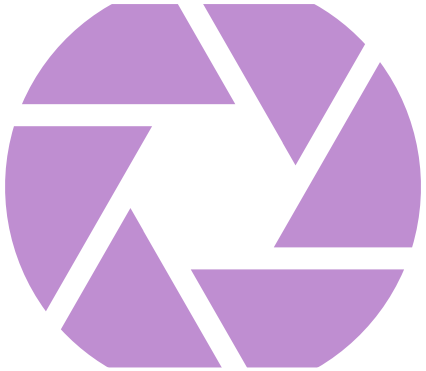
# Comparison of ongoing adjuvant oral SERD trials



| | | | ELEGANT | CAMBRIA-1 | EMBER-4 | lidERA | CAMBRIA-2 |
|---|---|---|---|---|---|---|---|
| N | | | 4220 | 4300 | 6000 | 4100 | 5500 |
| Intervention | | | elacestrant | camizestrant | imlunestrant | giredestrant | camizestrant |
| Trial design | | | Switch treatment after 2-5 years of adjuvant ET | | | Upfront adjuvant treatment | |
| Prior CDK4/6i exposure allowed | | | YES | YES | YES | NO | NO |
| Disease Stage | | T0N1 | If grade 3 | NO | If grade 3 | | |
| | IIA | T1N1 | If grade 3 | If Grade 3 or genomic high risk or Ki-67 >20% by central lab (includes N1mi) | If grade 3 | | |
| | | T2N0 | NO | NO | If grade 3 | | |
| | IIB | T2N1 | If grade 3 | If ≥2 lymph nodes positive | If tumor size 5.0cm or grade 2 | | |
| | | T3N0 | NO | YES | YES | | |
| | IIIA | | YES | YES | YES | | |
| | IIIB | T4N0 | NO | YES | If tumor size ≥5cm or 2.1-4.9cm and grade 3 | | |
| | | T4N1 | If tumor size ≥5cm or grade 3 | YES | If tumor size ≥5cm or grade 3 or 2.1-4.9cm and grade 2 | | |
| | | T4N2 | YES | YES | YES | | |
| | IIIC | | YES | YES | YES | | |

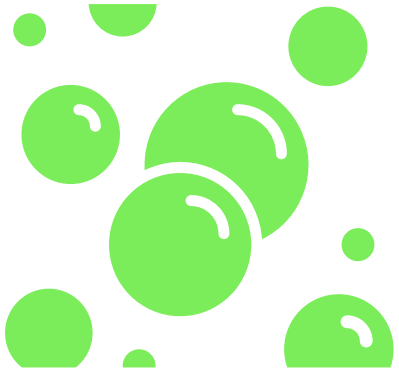
# Triple negative breast cancer

# New trends



Immunotherapy

Better drugs

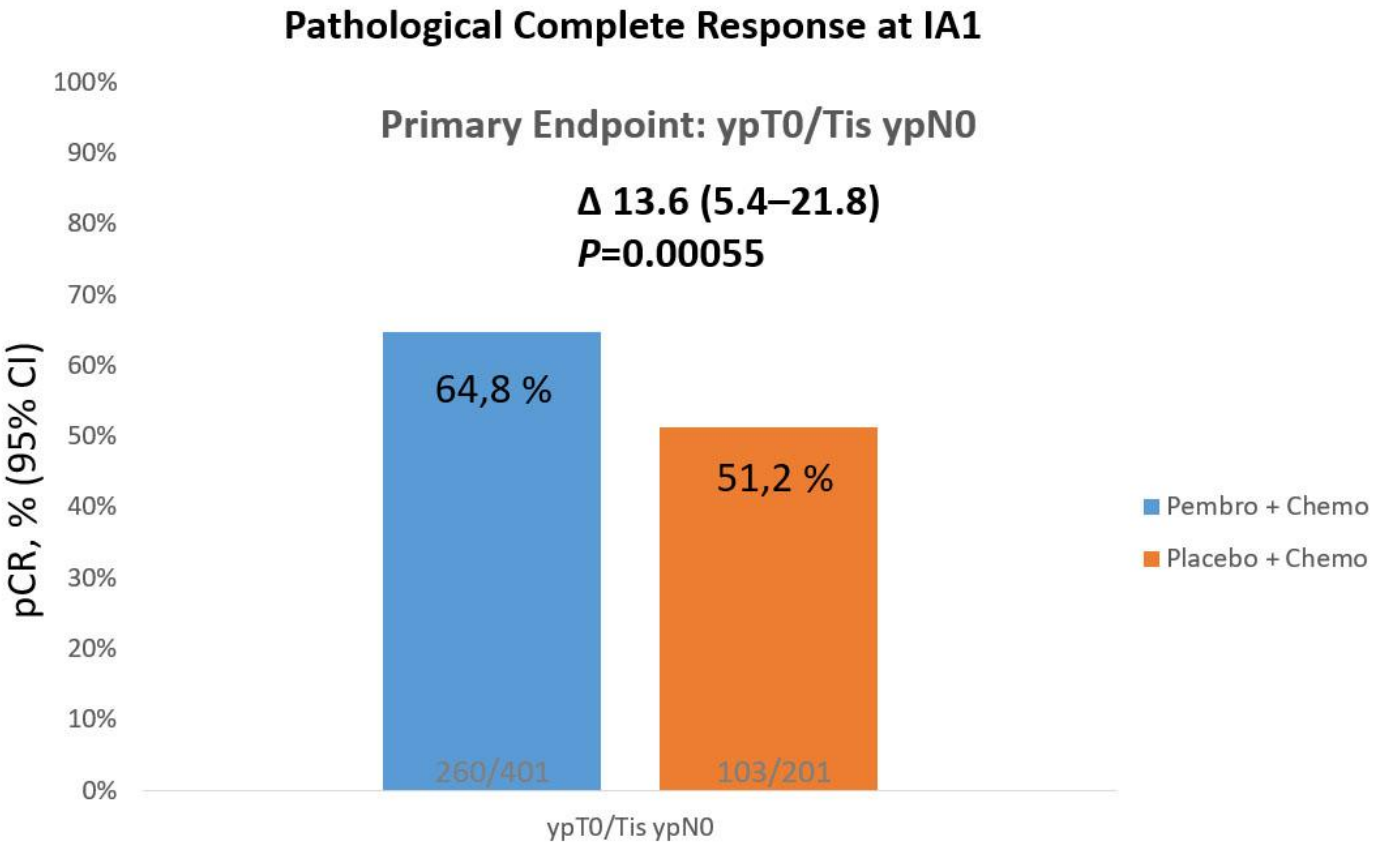


CtDNA

Less harsh treatments

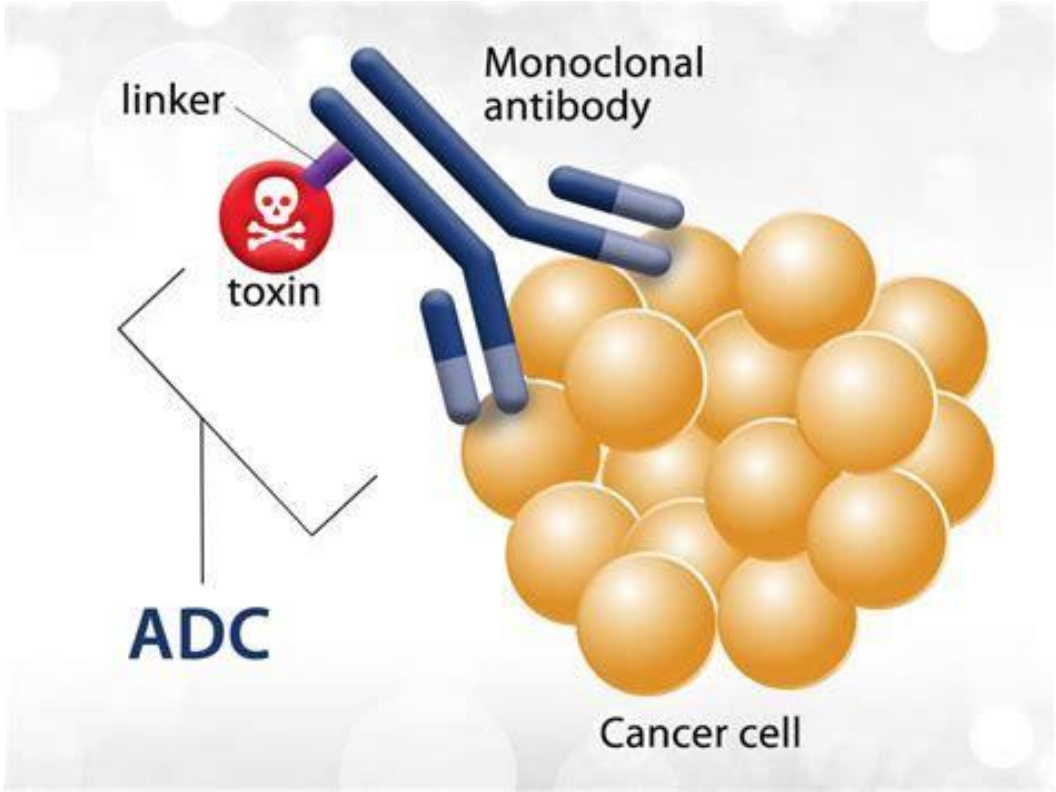
Immunotherapy (Keytruda/pembrolizumab:

first approvals in breast cancer were in triple negative tumors




Adaptiert nach: Schmid, P. et al., "KEYNOTE-522: Phase III study of pembrolizumab (pembro)+ chemotherapy (chemo) vs placebo+ chemo as neoadjuvant therapy followed by pembro vs placebo as adjuvant therapy for triple-negative breast cancer (TNBC)." (2018): TPS602-TPS602.

# Better drugs: antibody drug conjugates (ADCs)




- Using more targeted therapies in patients who do not have a complete response after neoadjuvant chemotherapy
- Several ADCs are being tested in clinical trials for this indications including Trodelvy (Sacituzumab), Sacituzumab-TMT and others

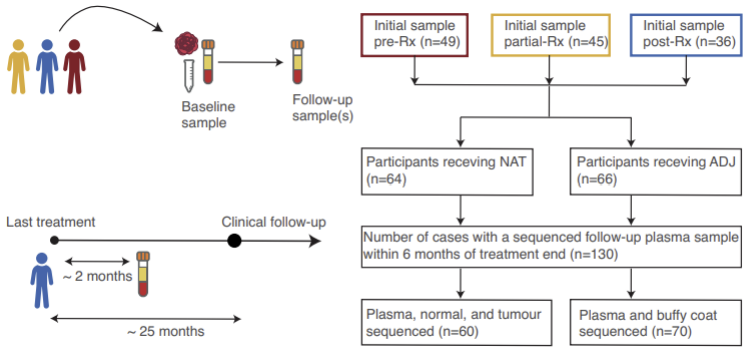
# Circulating tumor DNA (CT DNA)

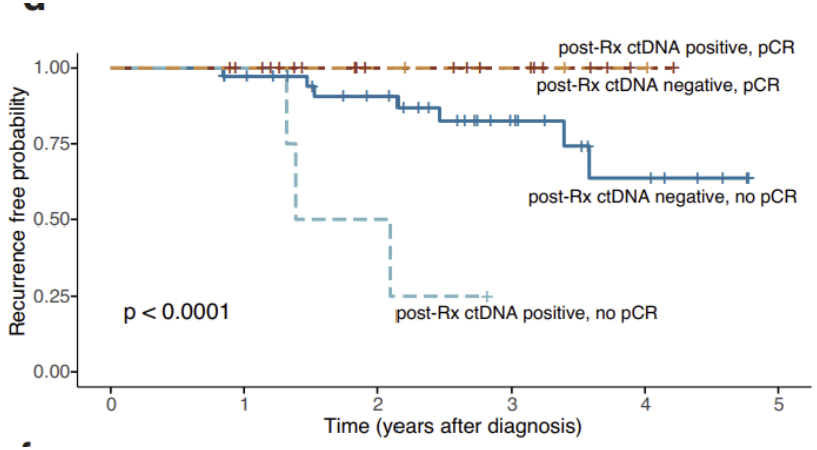
ARTICLE OPEN

Check for updates

## Circulating tumour mutation detection in triple-negative breast cancer as an adjunct to tissue response assessment

Elena Zaikova[1], Brian Y. C. Cheng[1], Viviana Cerda[1], Esther Kong[1], Daniel Lai[1], Amy Lum[1], Cherie Bates[1], Wendie den Brok[2], Takako Kono[1], Sylvie Bourque[3], Angela Chan[3], Xioalan Feng[4], David Fenton[4], Anagha Gurjal[5], Nathalie Levasseur[2], Caroline Lohrisch[2], Sarah Roberts[6], Tamara Shenkier[2], Christine Simmons[2], Sara Taylor[7], Diego Villa[2], Ruth Miller[8], Rosalia Aguirre-Hernandez[8], Samuel Aparicio[1]✉ and Karen Gelmon[2]✉



# Smarter less harsh treatments

Tumor infiltrating lymphocytes

Anthracycline sparing regimens

Avoiding chemo in very small tumors

Targeted therapies in patients with germline alterations.

Her2 positive breast cancer

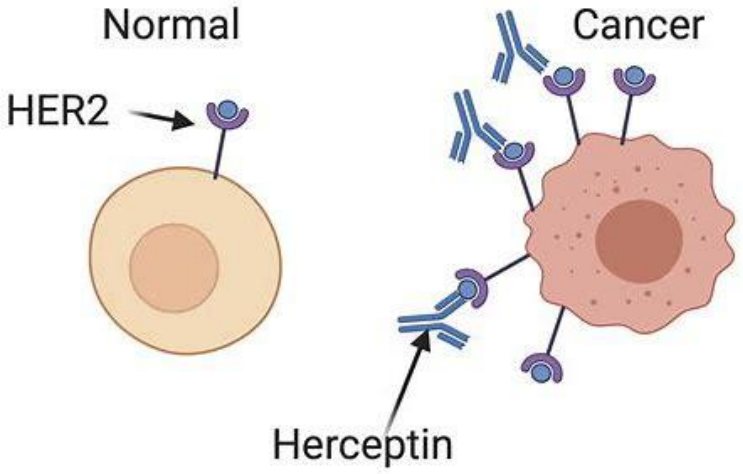
# New trends

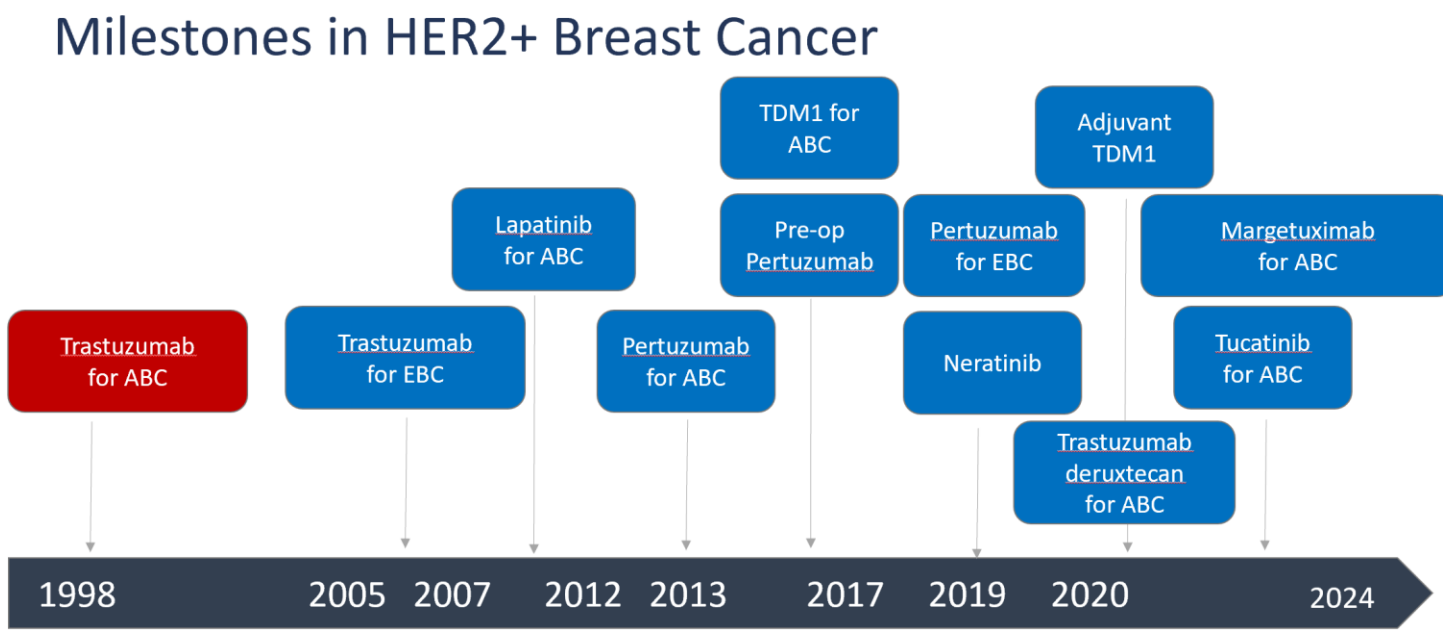
Less is more

Smarter drugs

Protection of brain

# Her2 positive breast cancer: a remarkable story of scientific discovery and personalized medicine



# Less is more

01

Less anthracyclines

02

Shorter regimens (Taxol plus Hercepin) for stage I

03

Less carbo (Taxane plus Herceptin/Perjeta)

# More is more (when needed)

If not a complete response, Kadcyla (TDM-1)

On clinical trial, addition of Tukysa (tucatinib)-COMPASS-RD

# New targeted ADC therapies are on the way

## DESTINY-Breast11 Trial Shows Enhertu Plus THP Significantly Improves Response Rates in High-Risk HER2-Positive Early Breast Cancer

May 7, 2025
By Davy James

*News* *Article*

*Topline results from the Phase III DESTINY-Breast11 trial show that Enhertu (trastuzumab deruxtecan) followed by paclitaxel, trastuzumab, and pertuzumab significantly improves pathologic complete response rates compared to anthracycline-based standard-of-care regimens in the neoadjuvant treatment of high-risk, locally advanced HER2-positive early-stage breast cancer.*

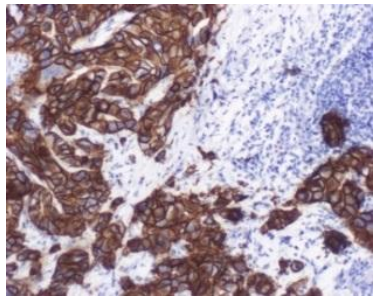
Topline results from the Phase III DESTINY-Breast11 trial (NCT05113251) show that Enhertu (trastuzumab deruxtecan; AstraZeneca and Daiichi Sankyo) followed by standard human epidermal growth factor receptor 2 (HER2)-targeted therapy produced a significant improvement in pathologic complete response (pCR) rates compared to current standard-of-care chemotherapy in patients with high-risk, locally advanced HER2-positive early-stage breast cancer.

# What about Her2 low?

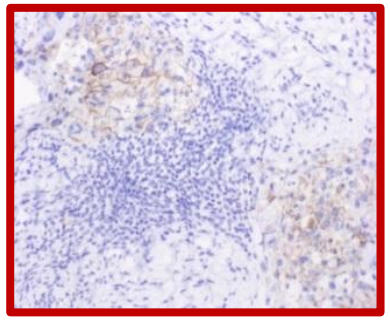
# Prevalence of HER2-low by HR-status

**HER2 IHC examples**

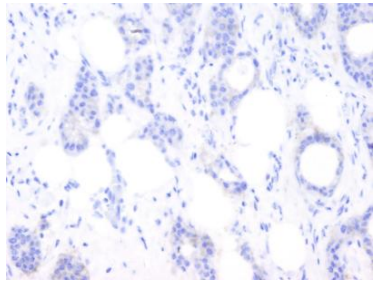
**HER2+**

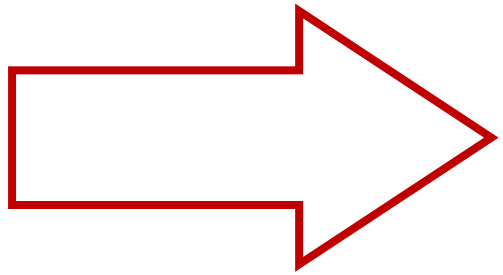


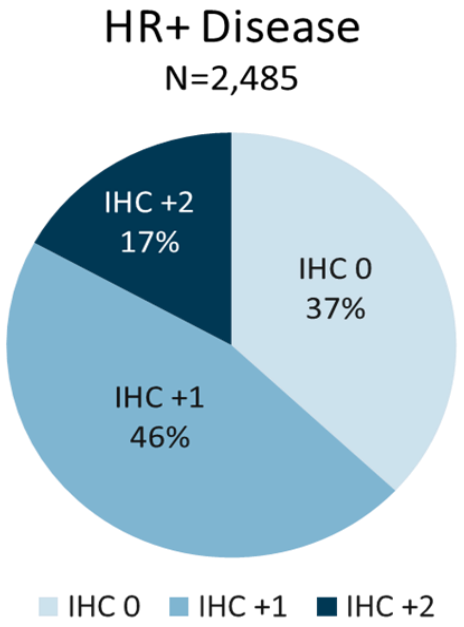
**HER2-low**



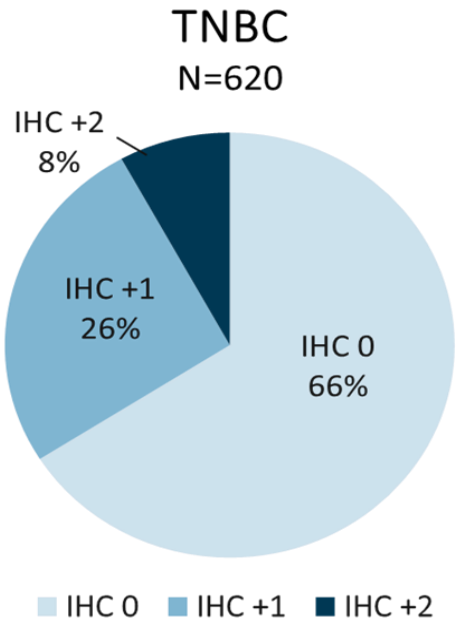
**HER2-**








63% HER2 Low




34% HER2 Low

Schettini. ESMO Breast Cancer Virtual

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# Her2 low status in early stage breast cancer

- The field is changing
- As of now, Her2 low is not used in routine care for early stage breast cancer
- Important biomarker in metastatic disease
- There are several small clinical trials investigating role of ADCs in Her2 low early stage breast cancer

# New approaches in supportive care and symptom management

# Newer approaches

Cooling/compression

Mind and body

Acupuncture

Movement/exercise

Whole person care

# The Breast Cancer Weight Loss Trial

**3180 Participants**

**Key Eligibility**

- Stage II-III breast cancer
- HER-2-
- BMI ≥ 27 kg/m2

**Randomization**

**Health Education + 2-year Telephone-based Weight Loss Intervention**

- 42 calls from health coach (**DFCI**)
- Supplemented with workbook and tools to promote weight loss
- Based on Social Cognitive Theory

**Health Education Alone**

NCT02750826

**Primary Outcome: Invasive Disease-Free Survival**

Ligibel et al. npj Breast Cancer. 2017

# MIND-BC

## Study of Food and Brain Health in women being treated for breast cancer

**Researchers at Ohio State University are seeking volunteers for a REMOTE study of nutrition and brain health**

### What Will Happen

- Randomly assigned to virtual 12-week personalized nutrition counseling or health coaching
- 8 virtual visits over 12-weeks
- Remote data collection at study start, 3 months, and 9 months
- Estimated total time commitment of 12 hours over 9 months

### Who Can Participate

- Women newly diagnosed with Breast Cancer
- Age 45 - 75, postmenopausal
- English Speaking
- Access to internet connected device

### Benefits

- Free nutrition counseling by registered dietitian nutritionist
- Free select foods during 12-week nutrition intervention
- Free Fitbit
- Fully Remote Study (No Travel Required)
- Up to $60 in gift cards

**For more information, fill out an online survey by scanning the QR code**

**Open camera on your phone and aim at the QR code.*
*A box should pop up taking you to the site.*

**Contact Information:**
**(614)-247-9270** **OrchardResearch@osu.edu**

The Ohio State University

# Food for Thought

## Study of Food and Brain Health in women being treated for Triple Negative breast cancer

**Researchers at Ohio State and Yale Universities are seeking volunteers for a REMOTE study of nutrition and brain health**

### What Will Happen

- Randomly assigned to virtual 12-week personalized nutrition counseling or health coaching
- 8 virtual visits over 12-weeks
- Remote data collection at study start, 3 months, and 9 months
- Estimated total time commitment of 12 hours over 9 months

### Who Can Participate

- Women newly diagnosed with Triple Negative Breast Cancer
- Age 40 - 65
- English Speaking
- Access to internet connected device

### Benefits

- Free nutrition counseling by a registered dietitian nutritionist
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Yale Cancer Center

The Ohio State University

The NEW ENGLAND JOURNAL of MEDICINE

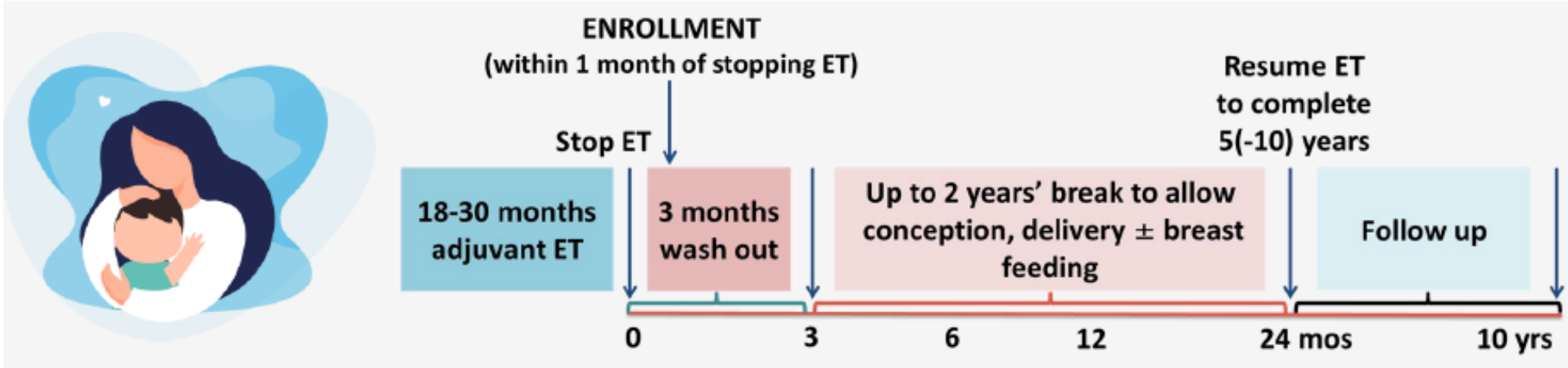


ORIGINAL ARTICLE

# Interrupting Endocrine Therapy to Attempt Pregnancy after Breast Cancer

**Authors**: Ann H. Partridge, M.D., M.P.H., Samuel M. Niman, M.S., Monica Ruggeri, Fedro A. Peccatori, M.D., Ph.D., Hatem A. Azim, Jr., M.D., Ph.D., Marco Colleoni, M.D., Cristina Saura, M.D., Ph.D., +33, for the POSITIVE Trial Collaborators† Author Info & Affiliations

Published May 3, 2023 | N Engl J Med 2023;388:1645-1656 | DOI: 10.1056/NEJMoa2212856 | VOL. 388 NO. 18

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A Comprehensive Cancer Center Designated by the National Cancer Institute

# Concluding thoughts

Q&A

# Breast Cancer Care: Personalizing Therapies


Metastasis

Diagnosis
*Over 260K new cases per year (US)*

Neoadjuvant Therapy

Surgery

Adjuvant Therapy
(endocrine, immunotherapy, radiation)

Distance recurrence
(metastasis)
over *40K deaths per year (US)*

Can we identify patients who will eventually develop metastatic disease?

Can we better mitigate toxicities and improve acute and late effects?

Can we do a better job matching patients with the most effective therapies?

***How are we involving patients as key stakeholders every step of the way?***

# Thank you!

MARYAM.LUSTBERG@YALE.EDU