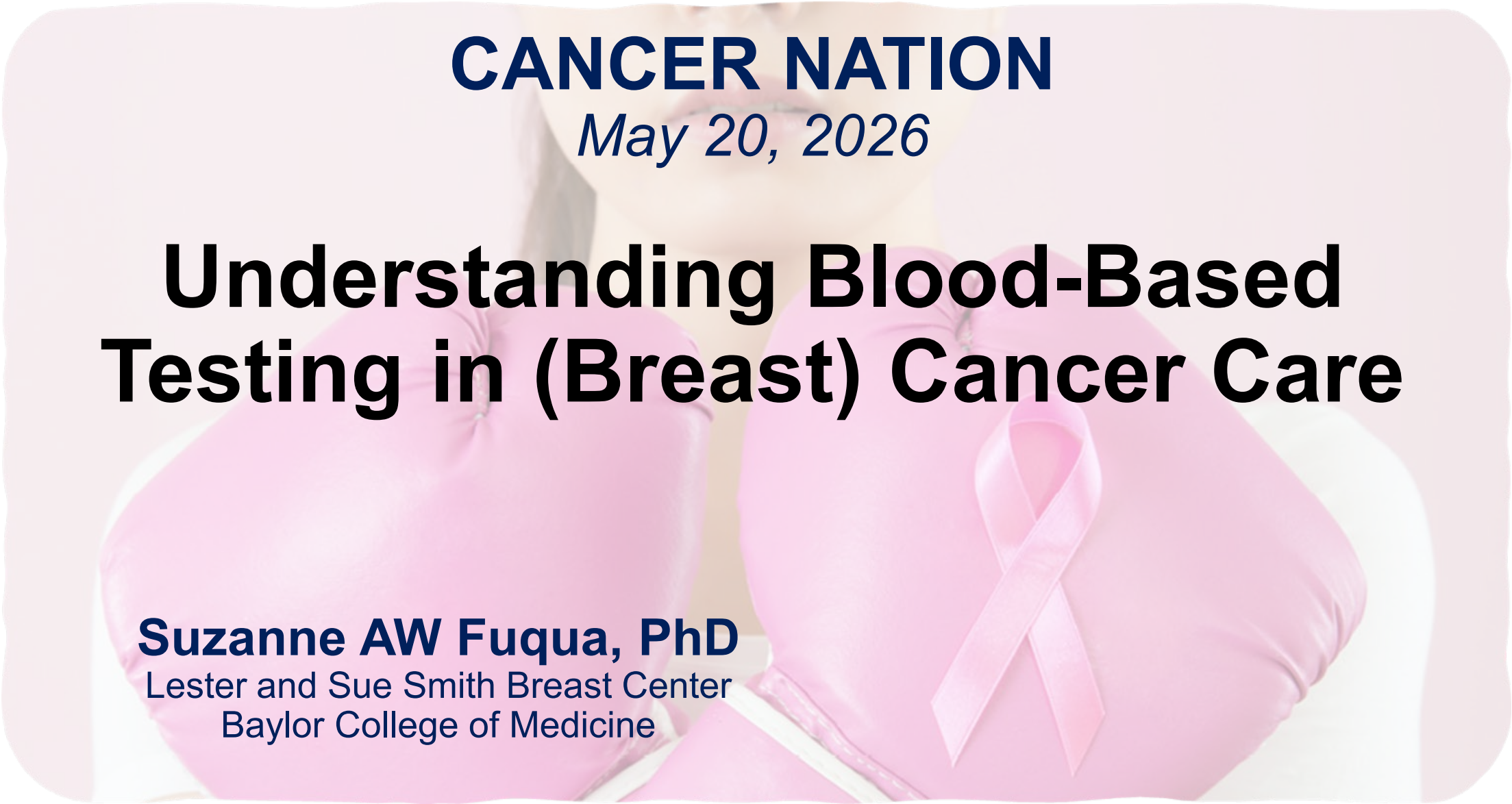


CANCER NATION

May 20, 2026

Understanding Blood-Based Testing in (Breast) Cancer Care

Suzanne AW Fuqua, PhD
Lester and Sue Smith Breast Center
Baylor College of Medicine

Blood Based Testing in Cancer

A simple blood test for cancer clues

- Clues are tiny fragments of tumor DNA (ctDNA) in bloodstream
- Can also detect whole tumor cells (CTCs) and proteins

Lets us watch cancer over time with less invasiveness

- Provides up to date snapshots of cancer spread
- Less invasive than tissue biopsy

Adds to, does not replace, tissue biopsy and scans

- Complements, doesn’t replace traditional diagnostic tools
- Provides additional information to guide treatment

What Liquid Biopsy Can Do Today

Screen for cancer before it happens

- Used to investigate abnormalities detected on imaging exams

Find evidence cancer is coming back

- MRD can go deep (low levels) & see if cancer if gone or back

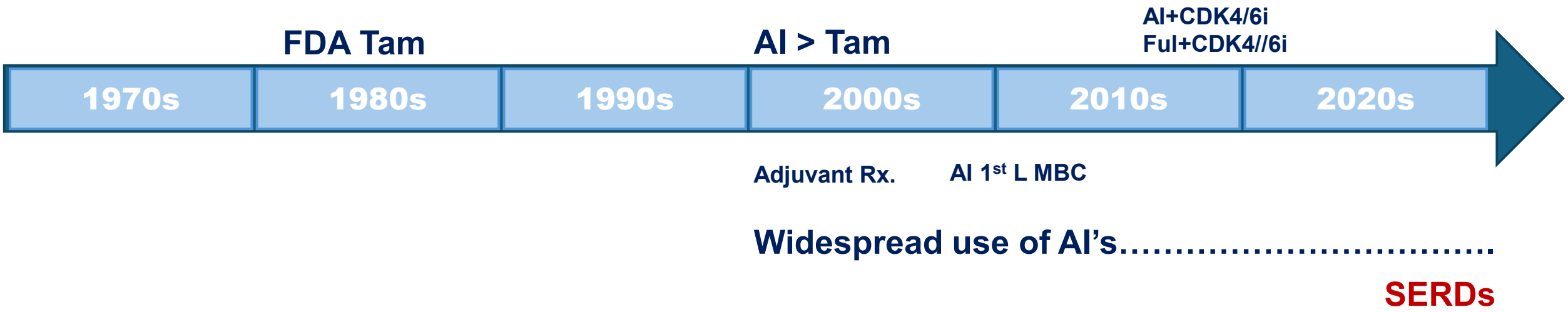
Find targets to guide therapy

- Detect mutations in cancer driving genes like PIK3CA to help guide targeted treatments and personalize therapy

Reveal resistance after targeted or hormone therapy

- As tumors evolve, can uncover new mutations that confer resistance to drugs, like mutated estrogen receptor (*ESR1*m)

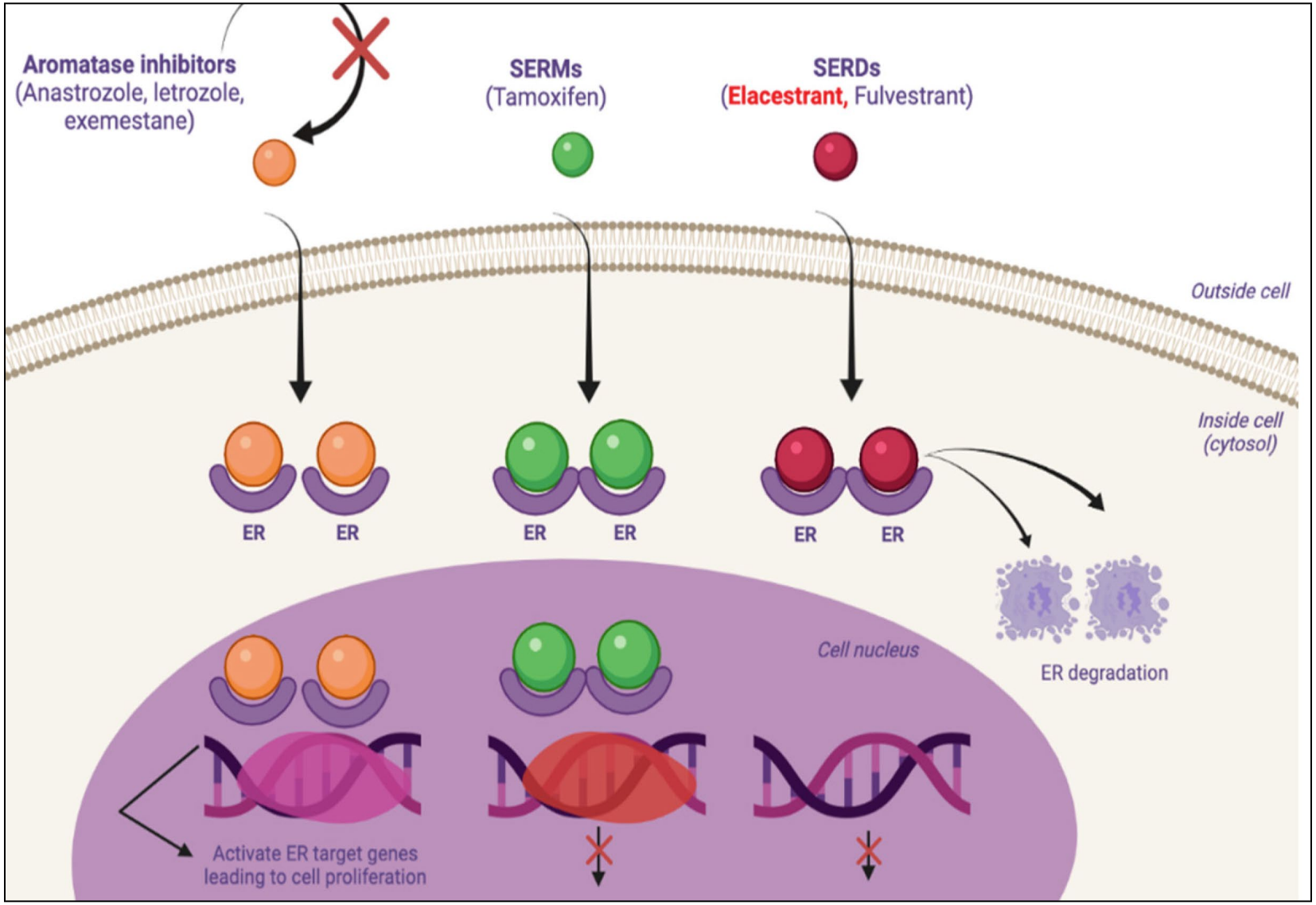
Background: Standard of Care for ER+ BC



- ESR1m evolve on AI and emerge in MBC
- Blood based ctDNA monitoring can spot ESR1m months before scans
- Switching to SERDs based on ctDNA can extend time before cancer starts growing again (PFS)

"Current 1st line SOC is causing, facilitating, or selecting for the emergence of *ESR1* mutations (*ESR1*m) which are the major cause of resistance and metastatic progression."

Treatment for *ESR1*m: What is a SERD? (Selective Estrogen Receptor Degrader)



ESR1m Emerge with SOC Endocrine Therapy Combinations

Trial	Study Treatment	*ESR1* mutation frequency	
Monarch 2* 2017	Fulvestrant+/- Abemaciclib	59.3%	PFS: 20.7 mo
BOLERO-2 2013	Exemestane +/- Everolimus	28.8%	OS: D538G 26 mo Y537S 20 mo Both 15 mo
FERGI 2016	Fulvestrant +/- Pictilisb	37%	NS
PALOMA-3 2017	Fulvestrant +/- Palbociclib	25.3%	PFS: 9.4 mo
SOFeA 2013	Fulvestrant +/- Anastrozole	39.1%	PFS: 5.7 mo

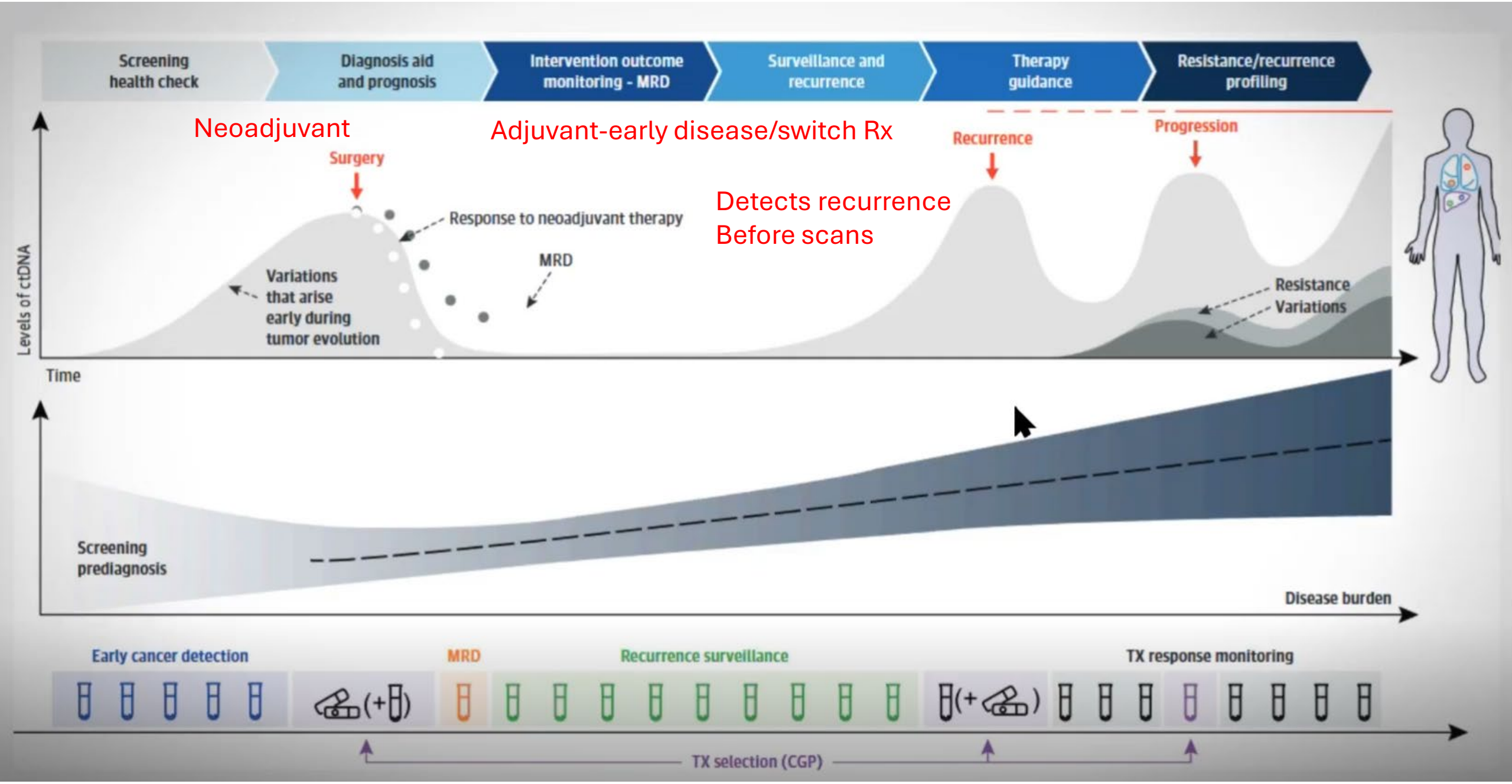
My quote from 1997: “If present in other metastatic breast tumors, this naturally occurring ER mutant may contribute to breast cancer progression and/or hormone resistance.” Unfortunately, my prediction became true…

FDA Approved Oral SERDs for MBC

Elacestrant (Orserdu):
- Approved for *ESR1*m+ MBC after progression on ET+ CDK4/6 therapy
- SERM & SERD properties

Imlunestrant (Inluriyo):
- Approved for Pre/Postmenopausal, 1st/2nd line MBC therapy
- More of a "pure" ER antagonist and degrader
- EMBER-3: Imlun + Abema- Improved PFS (10.9mos); OS (34.5mos, NS)

Vepdegestrant (Veppanui):
- Approved for *ESR1*m+ MBC after progression on ET+ CDK4/6, along with ctDNA test (Guardant360CDx)
- VERITAC-2: Improved PFS (3mos); OS immature


Screening health check
Diagnosis aid and prognosis
Intervention outcome monitoring - MRD
Surveillance and recurrence
Therapy guidance
Resistance/recurrence profiling
Neoadjuvant
Adjuvant-early disease/switch Rx
Surgery
Recurrence
Progression
Response to neoadjuvant therapy
MRD
Variations that arise early during tumor evolution
Detects recurrence
Before scans
Resistance Variations
Levels of ctDNA
Time
Screening prediagnosis
Disease burden
Early cancer detection
MRD
Recurrence surveillance
TX response monitoring
TX selection (CGP)

TWO TESTING STYLES FOR MRD

Guardant360CDx

Tumor-agnostic: one panel for everyone

This type of test does not require information about your specific tumor. It is good for broad cancer screening or monitoring.

Signatera

Tumor-informed: customized to your tumor

This test is built based on the specific mutations found in your tumor. It is great for detecting minimal residual disease (MRD) after treatment.

Trade-off: convenience vs sensitivity

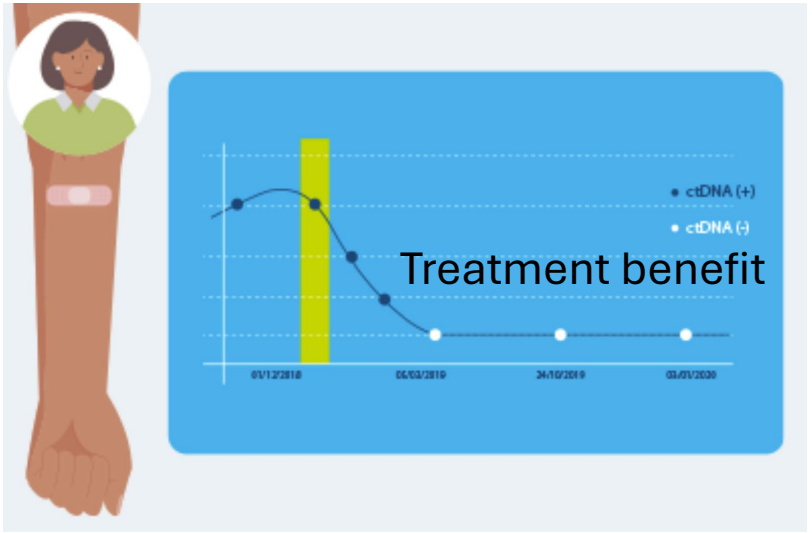
Tumor-agnostic tests are quicker and more convenient, while tumor-informed tests are more sensitive but take more time to develop.

The choice between a tumor-agnostic or tumor-informed liquid biopsy test involves balancing speed and convenience with increased sensitivity and personalization.

Example: Signatera™

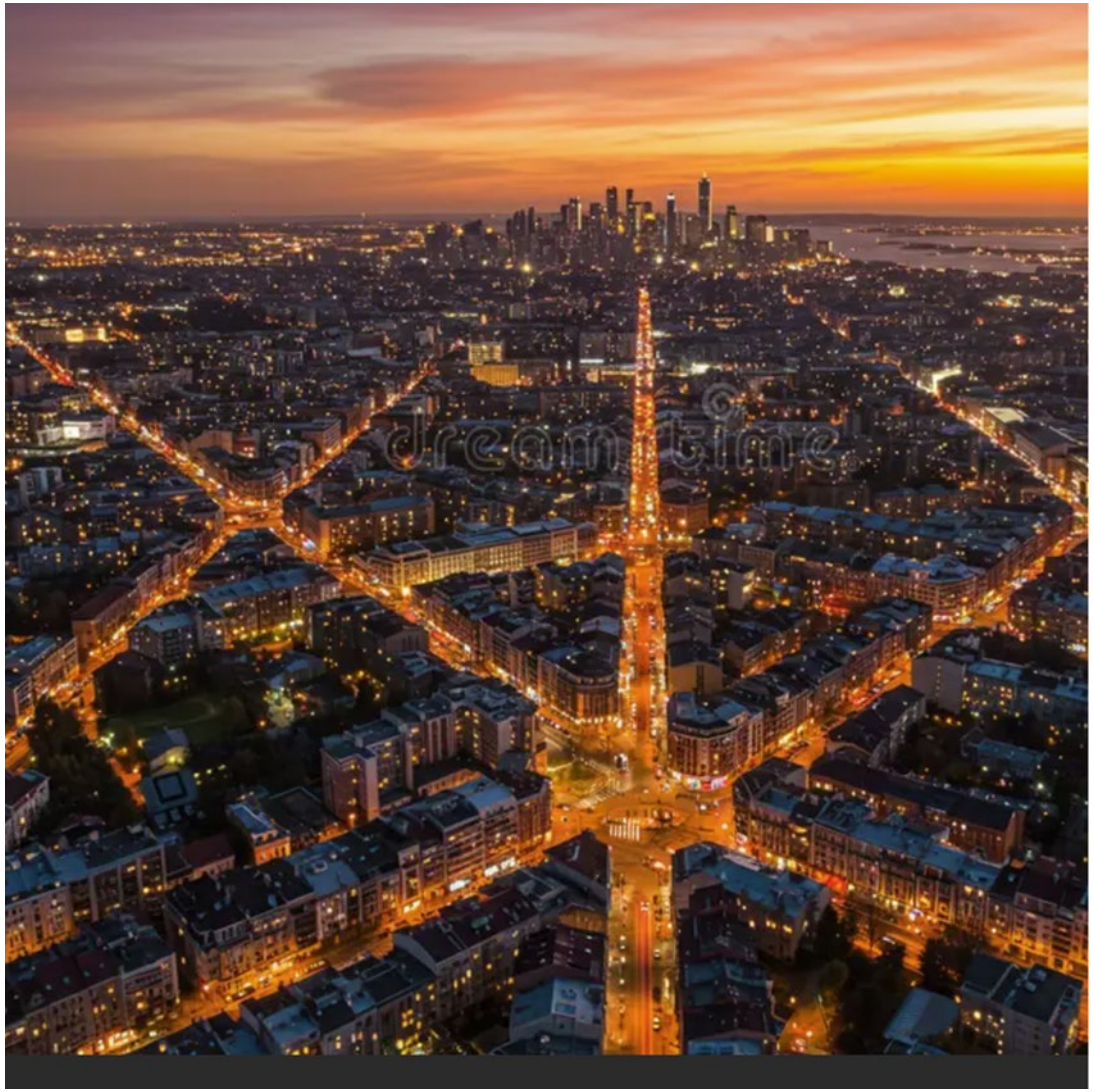
- Monitoring neoadjuvant setting (MRD)
- Monitoring response to immunotherapy
- **Monitoring response to adjuvant therapy**

Signatera™ Residual Disease Test

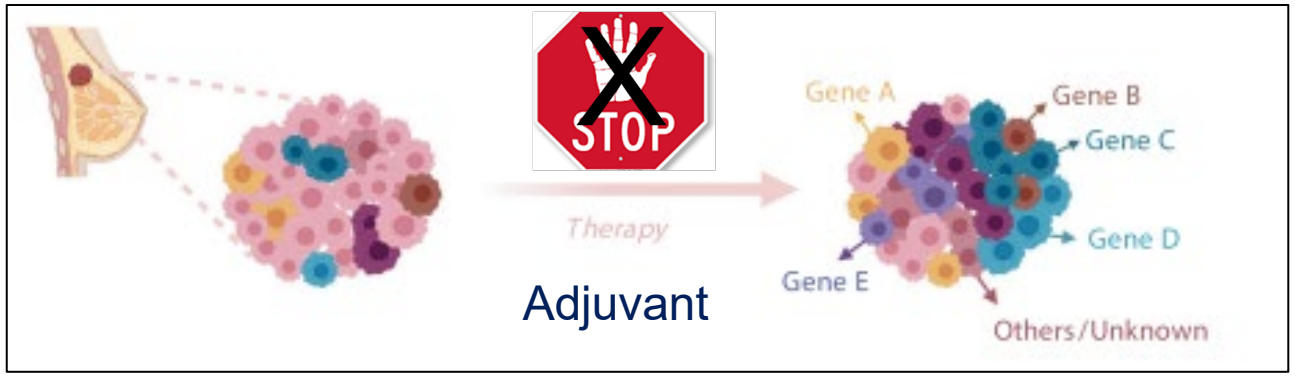


- Custom built blood test after sequencing of your tumor
- Con: Increased anxiety if positive result
- Pro: Earlier treatment intervention
- Pro-active: Not just waiting for your cancer to come back

ET is Rapidly Evolving and We're at a Crossroads for Earlier Interventions



Clonal Evolution During Treatment



Adapted from npjBC 2021

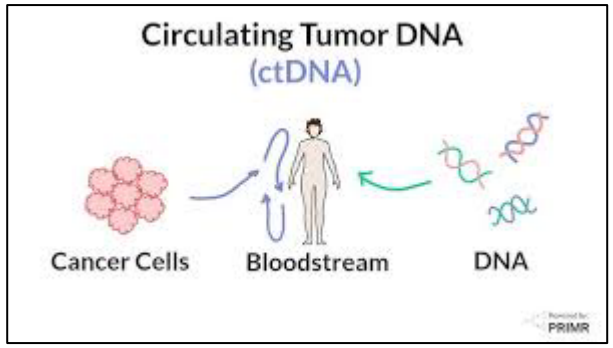
Adjuvant SERD Giredestrant Demonstrated Superiority to SOC ET (AIs and Tamoxifen)

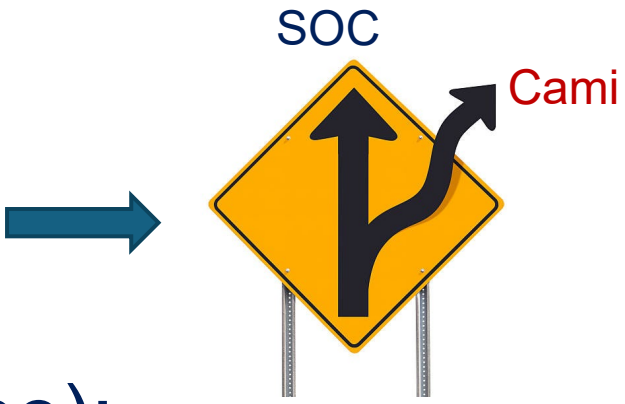
lidERA Adjuvant Trial (SABCS 2025):

- Significantly better iDFS (32 mos)
- 30% less likely to develop metastatic progression
- Study's limitation: Limited follow-up and immature OS

"Practice Changing"

SERENA6: Switching Trial of Camizestrant Ahead of Disease Progression in MBC





SERENA-6 Trial (*NEJM*, June):

- Reduced progression by 56%
- Reduced deterioration of QOL by 47%

My views as a cancer researcher for 40 years and breast cancer patient advocate:

✓ FDA voted 6-3 against ctDNA-guided switching strategy
✓ Is the bar different when intervention is guided by blood test?
✓ Absence of crossover? Isolates the effect of timing and contamination of arms
✓ Is resistance monitoring being held to a standard that radiologic progression has not been?

Acknowledgements

Holding Hands With Your BC

Funding Sources:

NIH National Institutes of Health R01 CA072038-22

Eli Lilly

BCRF Breast Cancer Research Foundation

KENDRA SCOTT

Kendra Scott Award for Holley Rothell KItchen

Thank you to patients who participate in clinical trials and donate tissue for research!