

Biomarker Panel

Biomarkers: what are they and how to use them

Moderator: Kelly Shanahan

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Guardant Health



Stage IV Stampede & Summit 2026



Agenda

01 What is a biomarker? How do we test for them? Tameron Harvell, MSN, FNP-BC, Guardant Health



02 When to test for biomarkers? How they guide treatment decisions. Jenna Canzoniero, MD, Johns Hopkins



03 Living with MBC and experience with biomarker testing: Megan O'Neil, METAvivor board member



Jake Messier,
@theguywithstage4breastcancer



04 Panel discussion/Q&A

Understanding Biomarkers and Cancer Testing

Tameron Harvell is a nurse practitioner based in Huntsville, Alabama, with more than 20 years of experience in oncology and breast health. Her career has included providing community breast cancer education, leading a hospital-based breast care program, and caring for patients as a nurse practitioner in a large community oncology practice. She earned her Master of Science in Nursing from Vanderbilt University and has completed advanced training in hereditary cancer risk assessment through City of Hope and in cancer genomics and precision oncology through Harvard Medical School. Today, she is part of the Medical Affairs team at Guardant Health, where she collaborates with clinicians to help make the rapidly evolving science of cancer genomics meaningful and applicable to patient care.

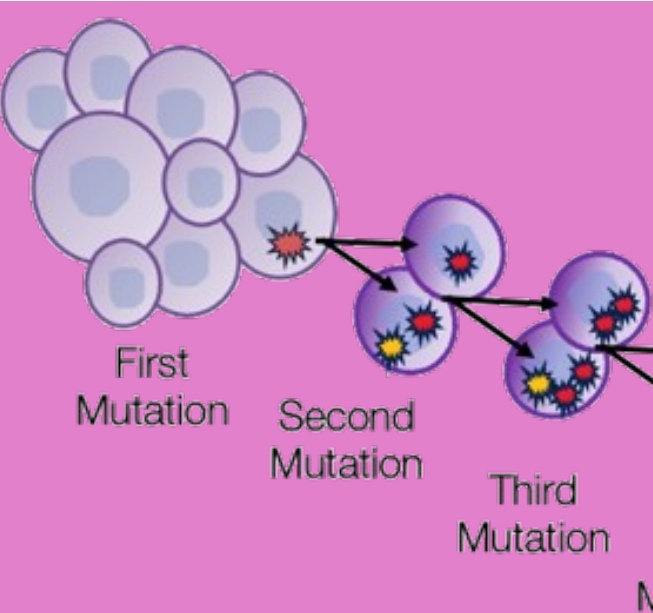


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METAVIVOR
Metastatic Breast Cancer | Research | Advocacy | Support

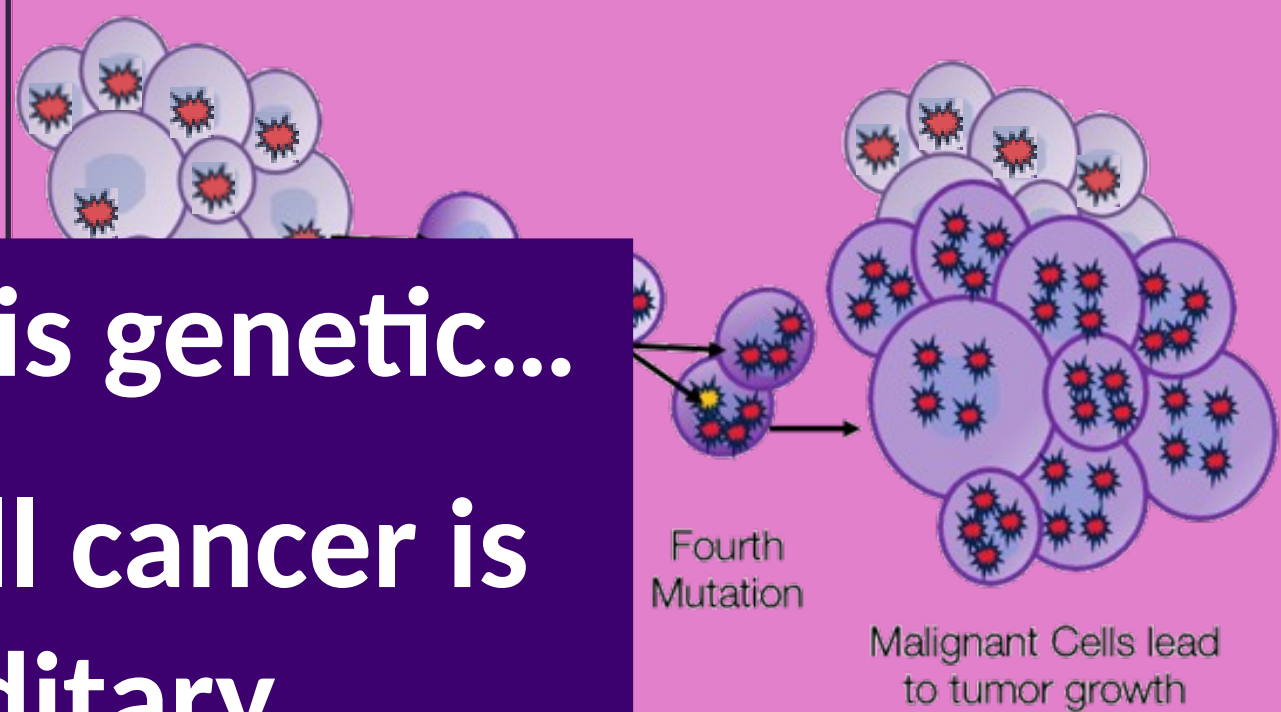
Somatic Alterations



**All cancer is genetic...
but not all cancer is
hereditary.**

- Majority of cancers are sporadic
- Acquired over a lifetime
- Present in tumor cells only
- Not inheritable
- **Mutation only in affected area**
(PIK3CA mutation present in breast cancer tumor cells)

Germline Alterations



- Up to 10% of all cancers
- Present from birth
- Present in all cells (including egg and sperm)
- Inheritable
- **Entire organism carries mutation**
(Germline BRCA2 mutation)

Driver Mutations

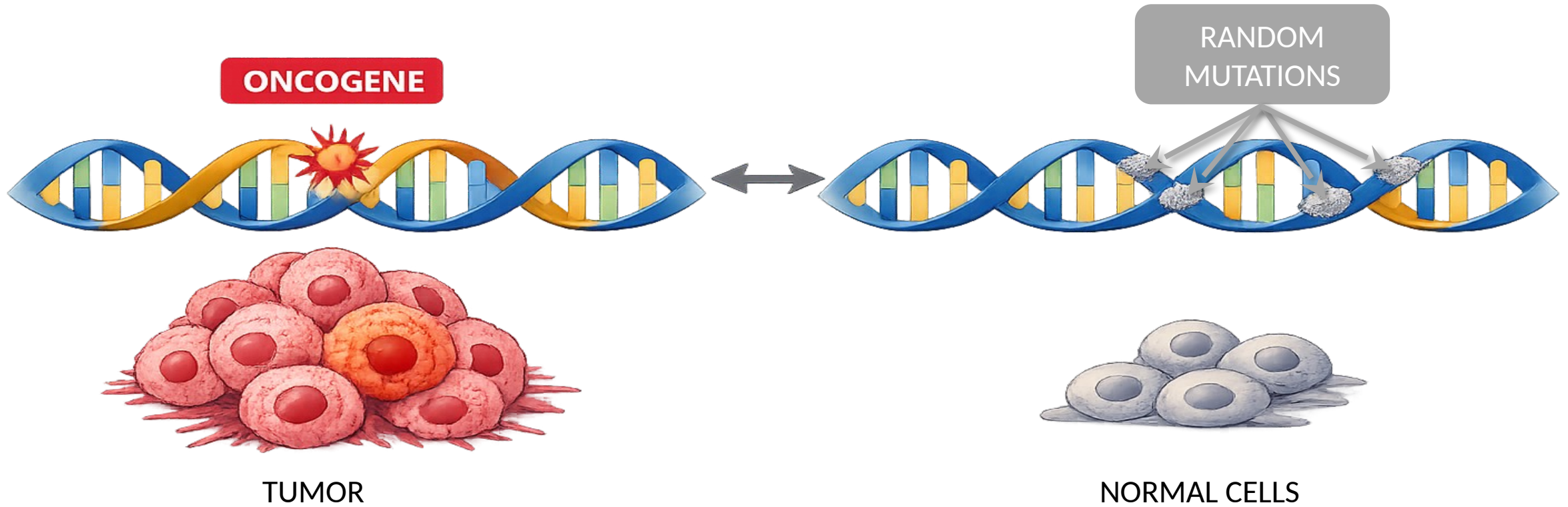
- ✓ Promote Tumor Growth
- ✓ Frequently Recurrent Mutations
- ✓ Provide Selective Advantage



VS.

Passenger Mutations

- ✓ No Impact on Tumor Growth
- ✓ Random, Neutral Mutations
- ✓ Along for the Ride



TWO MAIN SOURCES OF BIOMARKER TESTING

- Also called genomic profiling, molecular testing, next generation sequencing

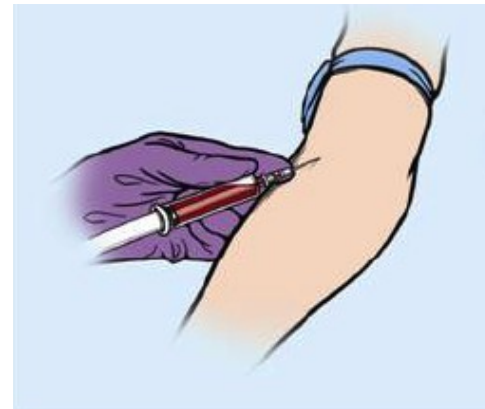
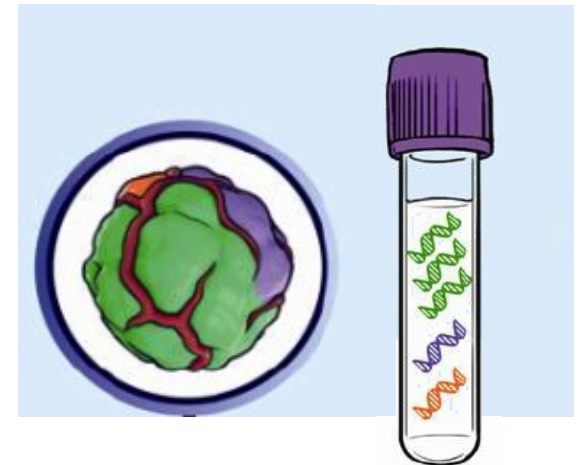
Tissue

- Requires biopsy
- ER, PR, HER2, PD-L1, Ki-67



Liquid (plasma)

- Evaluates ctDNA in blood
- ESR1



Why metastatic breast cancer testing may need to evolve over time

Tumor biology can change across treatment lines and across disease sites, while tissue access may limit what can be tested.

Informative biomarkers

Breast cancer

ESR1

ATK1

PIK3CA

PTEN

ERBB2 (HER2)

BRCA1

BRCA2

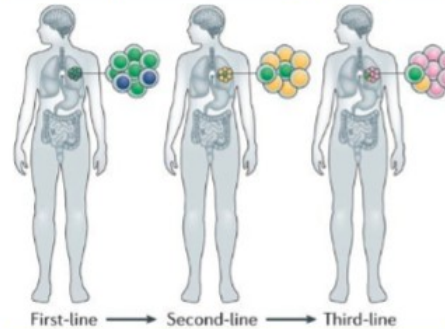
PALB2

TMB-High
MSI-High
PD-L1

NTRK fusions
RET fusions

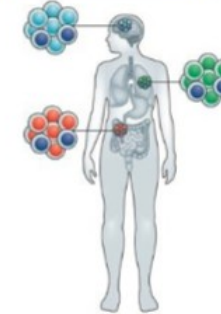
Cancer biology changes by time and site

Temporal Heterogeneity

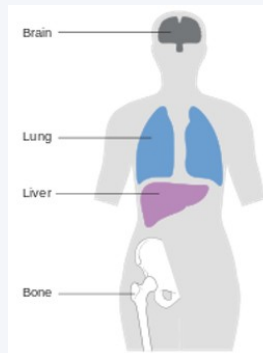


New alterations can occur in a tumor as it evolves over lines of therapy

Spatial Heterogeneity



Different alterations can occur in the various sites of disease



Some metastatic sites are difficult to biopsy.

Bone samples may not always provide enough tumor material for testing.

ESR1 detection can create an earlier treatment decision point

Therapy choices differ depending on whether ESR1 is detected after progression or before radiographic progression.

Treatment pathway after ESR1 detection

AI + CDK4/6 inhibitor

ESR1 detected

After clinical progression

- Efacestrant
- Imlunestrant
- Vepdegestrant

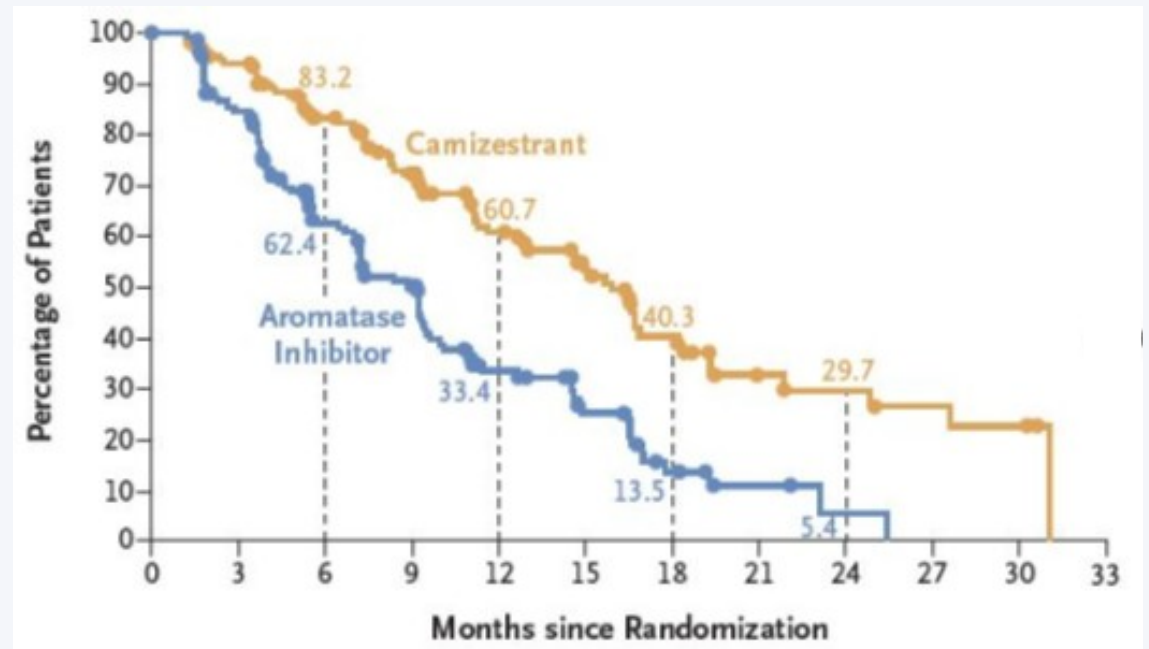
Before radiographic progression

- Camizestrant

SERENA-6 evidence

Switching to camizestrant after ESR1 detection reduced risk versus remaining on aromatase inhibitor therapy.

56% lower risk of progression or death



Clinical Use of Biomarkers for Breast Cancer

A Medical Oncologist's Perspective

Jenna Canzoniero is a breast medical oncologist and a translational researcher focused on the use of liquid biopsies to guide breast cancer care. She is the liquid biopsy leader for the molecular tumor board and leads the precision oncology initiative for the breast and gyn cancers program at Johns Hopkins.



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When should testing be performed?

Depends on the type of test!

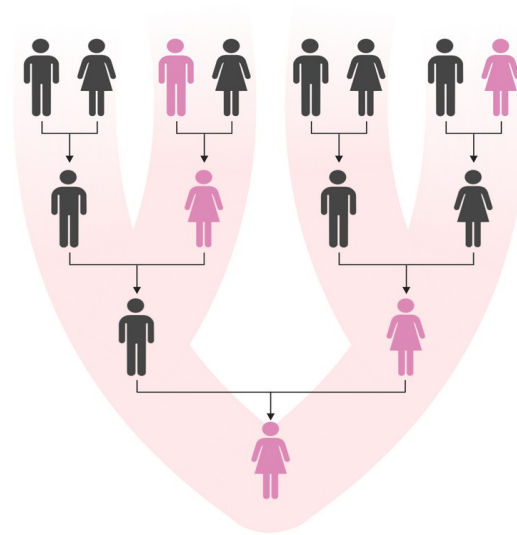
1. Germline Genetic Testing

- Looks for inherited mutations that increase risk for developing breast and other cancers
- Relevant in some Early-Stage Breast Cancer and Metastatic Breast Cancer

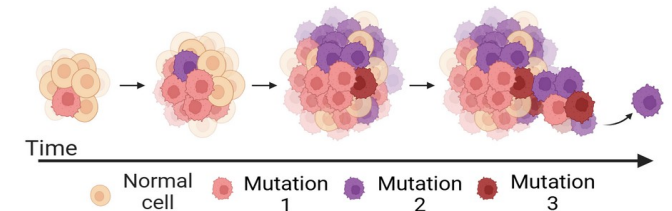
2. Somatic Genetic Testing

- Looks for mutations in the tumor that explain how the cancer transformed from normal cell into cancer
- Currently only relevant in Metastatic Breast Cancer

Germline Testing Looks for Inherited Mutations that Increase Risk for Developing Cancer



Somatic Testing Looks for Mutations in the Tumor that Changed it from Normal to Cancer (NOT Inherited)



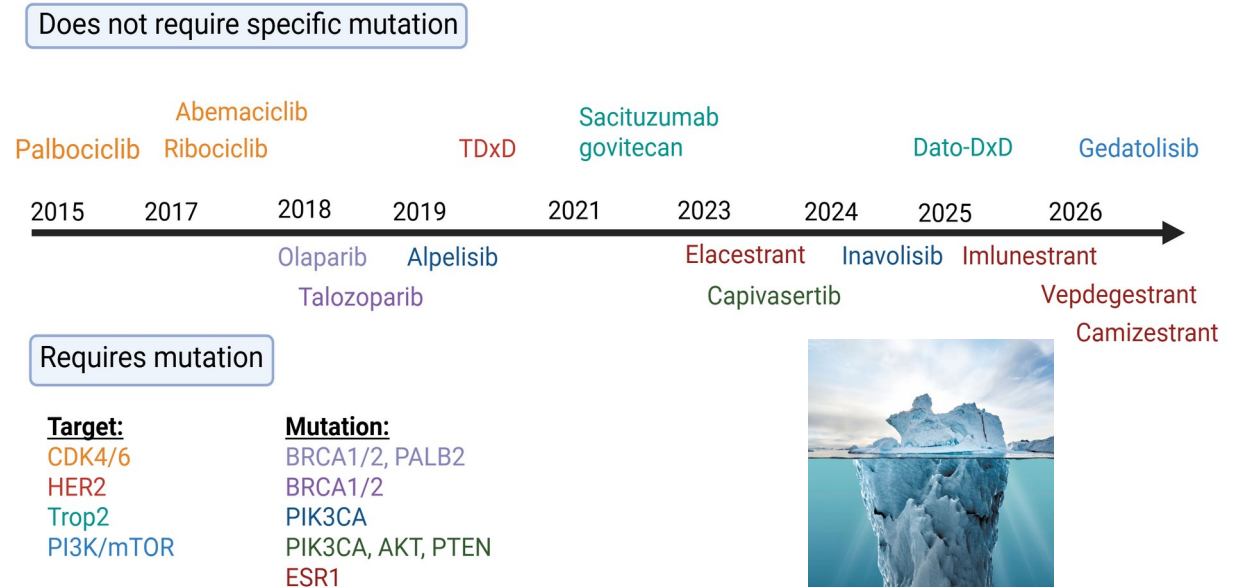
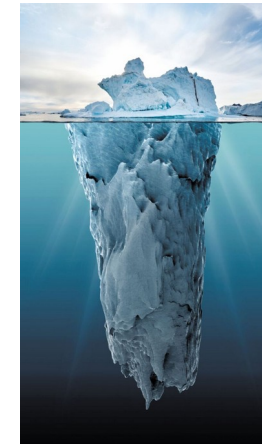
Germline Genetic Testing – Inherited Risk

- Genetic testing finds underlying cause in only ~10% of patients
- Early-Stage Breast Cancer
 - Testing recommended for patients at high risk: Age <50, Triple negative, Strong family history
 - Can inform decision about risk-reducing surgery (i.e. mastectomy)
 - Surveillance for breast/other cancer based on risk
 - Triple negative breast cancer with BRCA1/2 – adjuvant olaparib
 - Family testing
- Metastatic Breast Cancer
 - All patients with MBC (often germline mutations can also be detected as part of somatic testing)
 - HER2 negative MBC with BRCA1/2 or PALB2 – olaparib
 - Family testing

Somatic Testing – Tumor Tissue or Liquid Biopsy

- Relevant for metastatic breast cancer
- More and more breast cancer treatments (yay!)
- Treatment becoming increasingly complex and more targeted
- Decisions depend on tumor-specific mutations as well as receptors (ER, PR, and HER2)

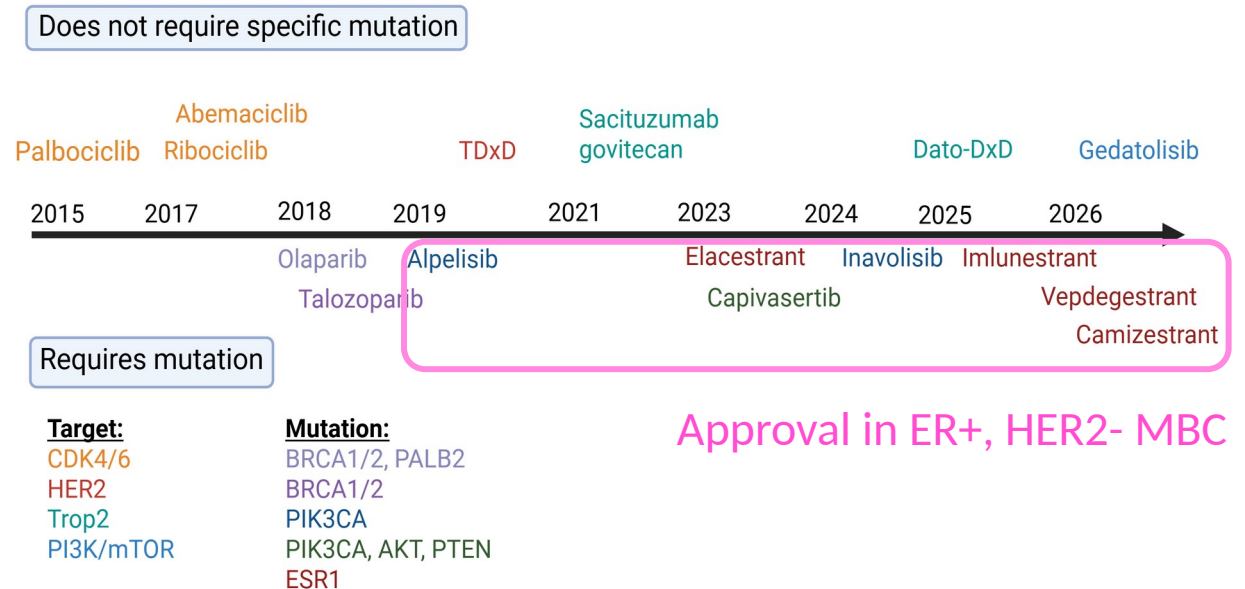
Timeline of Recent Approvals:



Somatic NGS Testing – When to test?

- Most of the approvals for targeted therapy are in ER+, HER2- MBC
 - ER+, HER2- MBC will acquire resistance mutations in response to treatment (ESR1) and so should have testing done multiple times
- All MBC should have comprehensive genomic profiling at least once
- Many clinical trials are based on genetic targets

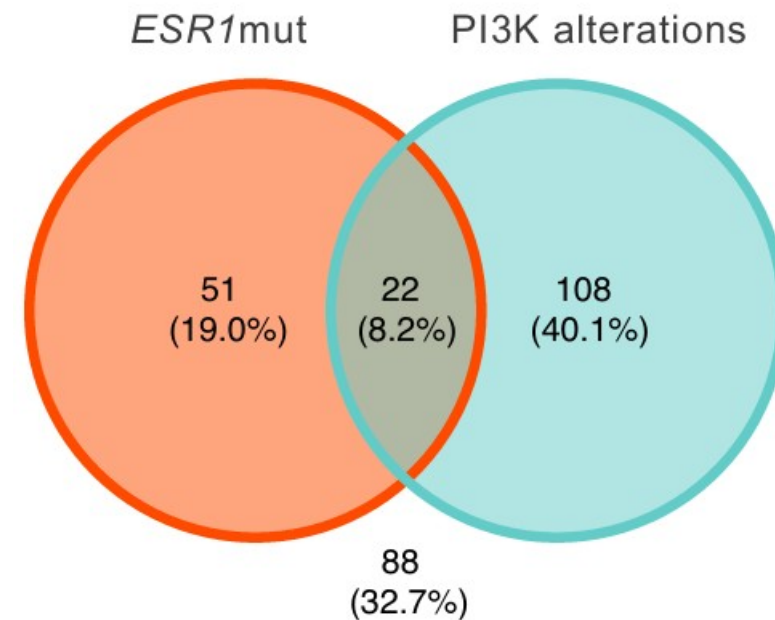
Timeline of Recent Approvals:



What to do if multiple targets?

- This happens – most commonly with ESR1 and PIK3CA which are both targetable
- Currently, we don't really know the best way to handle this
 - Try to target both at the same time? May not be possible
 - Target one, then the other?
 - Focus just on one? What criteria should we use to choose which is more important?

(B) *ESR1*mut and PI3K/AKT pathway alterations co-occurrence in 2nd line (n=269)



Bhave M et al. Breast Cancer Research and Treatment, 2024.

Take Home Message:



**Molecular
Tumor Board**

- This is a **RAPIDLY EVOLVING** field!
- Don't be afraid to ask your doctor if you should be getting genetic testing and what your testing results mean.
 - Genetic testing results are complicated. Molecular Tumor Boards exist to help providers make sense of it all.



Megan O'Neil

Diagnosed early stage age 30 and MBC age 36

Once told she was “too young” to have cancer, she’s now passionate about educating and empowering young people to know their bodies, recognize the signs of breast cancer, and advocate for themselves in healthcare settings.

Megan’s biomarker story includes tumors that are both HEr2+ and HER2-, as well as PIK3CA and ESR1 mutations.



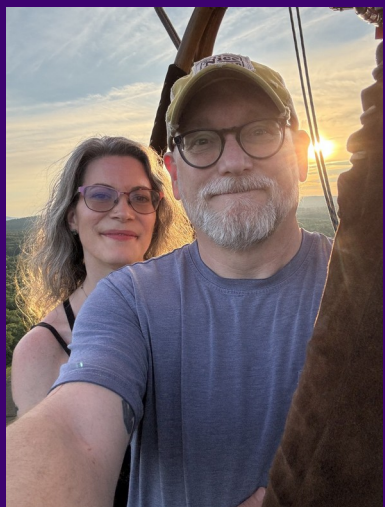


Jake Messier

Diagnosed Stage 2: 2023/Stage 4: 2025

@theguywithstage4breastcancer on TikTok and IG

Jake Messier is a marketing strategist and Stage IV breast cancer advocate living with ER-positive disease. His biomarker story includes a POLD1 variant of uncertain significance, unsuccessful tumor genomic testing, and an unknown somatic mutation profile, highlighting both the promise of precision medicine and the gaps that remain for patients today.



Questions?



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