Breakout session

LIVING BEYOND
BREAST CANCER®

Understanding the role of personalized medicine in your cancer journey

Speaker: Elena Michaels, MD

Mass General Brigham
Cancer Institute

Understanding the Role of Personalized Medicine in Your Cancer Journey

Diagnostic Tools to Deliver Precision-Based Care

Living Beyond Breast Cancer: 2026 Conference on Metastatic Breast Cancer
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Disclosures

No disclosures to report.

Diagnostic Tools for Precision Medicine in Metastatic Breast Cancer

- Estrogen, Progesterone, HER2, and PD-L1 Status

- Methods to test for important biomarkers in metastatic breast cancer
  - Germline genetic testing
  - Next-generation sequencing (NGS)
    - Solid biopsy
    - Liquid biopsy

- Molecular residual disease (MRD)

- Non-genomic tools to personalize cancer care

- Summary, key questions, future directions

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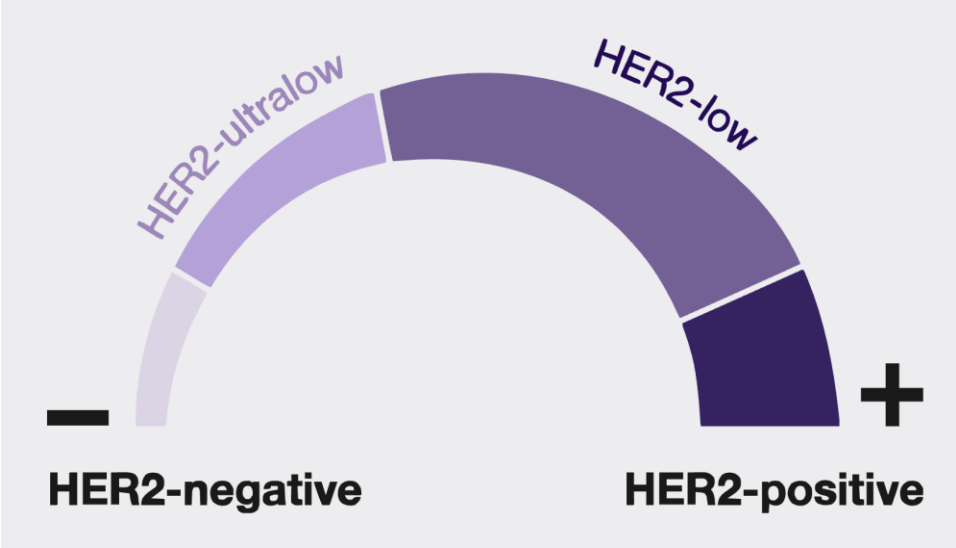
Breast Cancer Treatment Categories

HR+, HER2-	HR+, HER2+	HR-, HER2+	Triple-negative (HR-, HER2-)
HR+, HER2- cancer cells **have hormone receptors** and make small, or no, amounts of HER2 protein.	HR+, HER2+ cancer cells **have hormone receptors and make high levels of the HER2 protein.** This type of breast cancer is also called triple-positive because it is positive for estrogen receptors, progesterone receptors, and high levels of the HER2 protein.	HR-, HER2+ cancer cells don't have hormone receptors but do **make high levels of HER2 protein.**	Triple-negative cancer cells **don't have hormone receptors** for estrogen or progesterone. They also **make low to no amounts of the HER2 protein.** This type of cancer grows without the help of estrogen, progesterone, or the HER2 protein, and scientists are working to learn what fuels its growth.
~75% of cases	**~15% of cases**		**~10% of cases**

https://us.kisqali.com/early-breast-cancer/about-ebc/understanding-ebc
https://seer.cancer.gov/statfacts/html/breast-subtypes.html

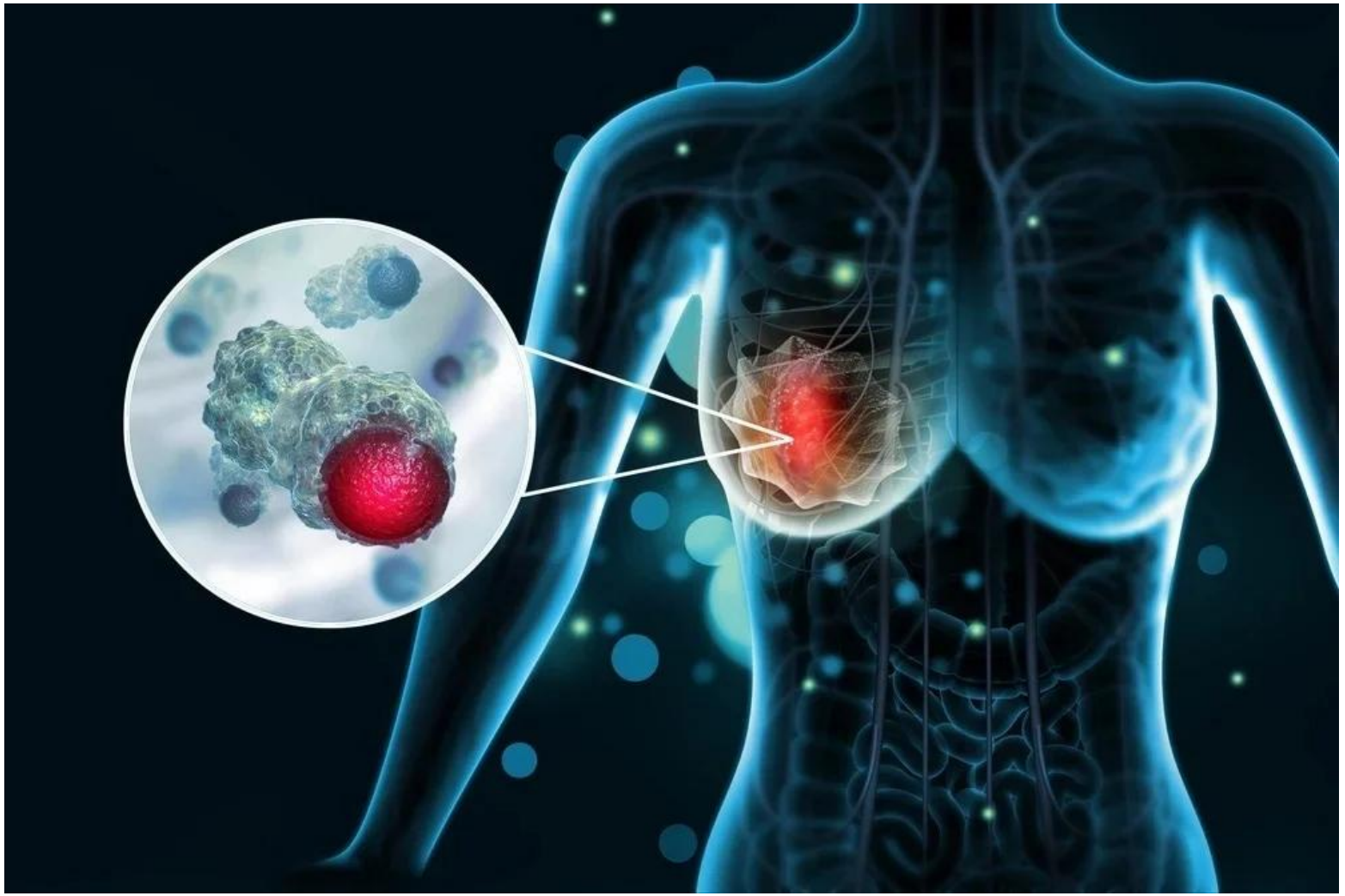
HER2-Low and -Ultralow Disease in Metastatic Breast Cancer

- Terminology used for HER2 negative metastatic breast cancer, assesses candidacy for trastuzumab deruxtecan AKA T-DXd (**Enhertu**)
  - **HER2-low:** low but detectable levels of HER2 (IHC 1-2+)
  - **HER2-ultralow:** very low levels of HER2 (IHC 0 but faint HER2 staining on cell membrane in a some cells)



https://www.komen.org/breast-cancer/diagnosis/factors-that-affect-prognosis/tumor-characteristics/
https://www.enhertu.com/en/her2-low-breast/understanding-her2-low-mBC

PD-L1 in Triple-Negative Breast Cancer



https://www.moffitt.org/endeavor/archive/why-is-triple-negative-breast-cancer-hard-to-treat/

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What is a biomarker?

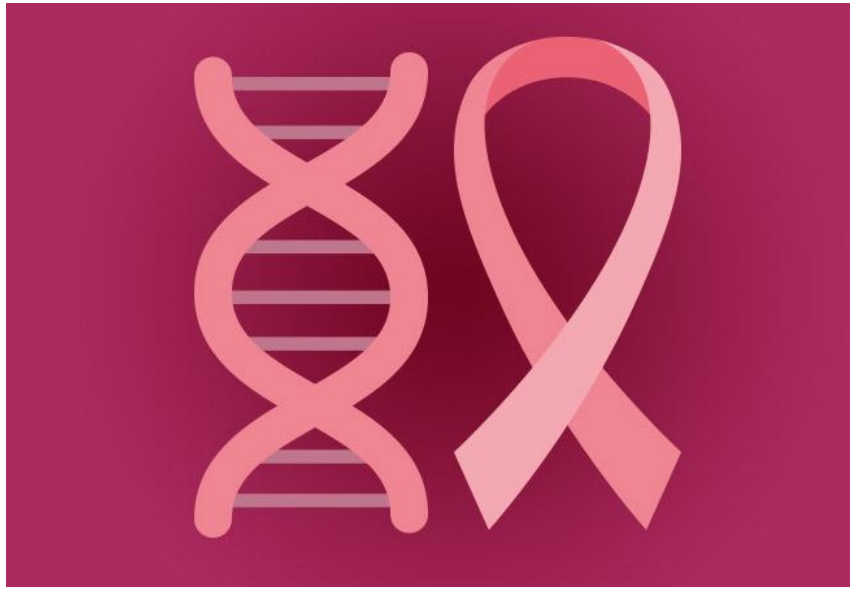
Protein, hormone, gene, genetic mutation, or molecule that provides information about a disease.

Biomarkers are used in breast cancer to: estimate prognosis, understand cancer biology, determine breast cancer subtype (estrogen, progesterone, HER2), consider candidacy for certain treatments and clinical trials (PD-L1), monitor response to treatment

https://www.breastcancer.org/screening-testing/tumor-marker-tests

Germline Genetic Testing

- Assesses for mutations in a panel of **inherited** cancer-related genes
- Certain mutations are associated with an increased risk of breast cancer
- Treatments are available for patients with metastatic breast cancer who have specific germline mutations
- Who should be tested?
  - Breast cancer <50
  - Male breast cancer
  - Triple-negative breast cancer
  - Family history
  - Ashkenazi Jewish ancestry



https://www.nccn.org/professionals/physician_gls/pdf/genetics_bopp.pdf

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Next-Generation Sequencing (NGS)

- Technology that analyzes the DNA/RNA of cancer cells to identify genetic mutations that drive cancer growth
- Medications and/or clinical trials may be available for certain mutations, allows oncologists to tailor treatment to a tumor's unique genetic profile
- Testing can be performed on tumor tissue (*solid biopsy*) or a blood sample (*liquid biopsy*), often repeated over the course of treatment

https://www.carislifesciences.com/what-is-next-generation-sequencing-and-how-does-it-work/

Solid Biopsy

- **Benefits**
  - Comprehensive analysis of tumor biology, allows for simultaneous estrogen, progesterone, HER2, PD-L1 testing
  - Can test older samples
  - Preferred for *PTEN* loss, assessing tumor mutational burden (TMB)
- **Limitations**
  - Invasive
  - Cost/time constraints
  - Anatomical limitations
  - Insufficient samples
  - Limited insight into tumor heterogeneity

https://www.nccn.org/professionals/physician_gls/pdf/breast.pdf

Turner et al, Lancet Oncol 2020.

Vasan et al, JCO 2024.

Liquid Biopsy

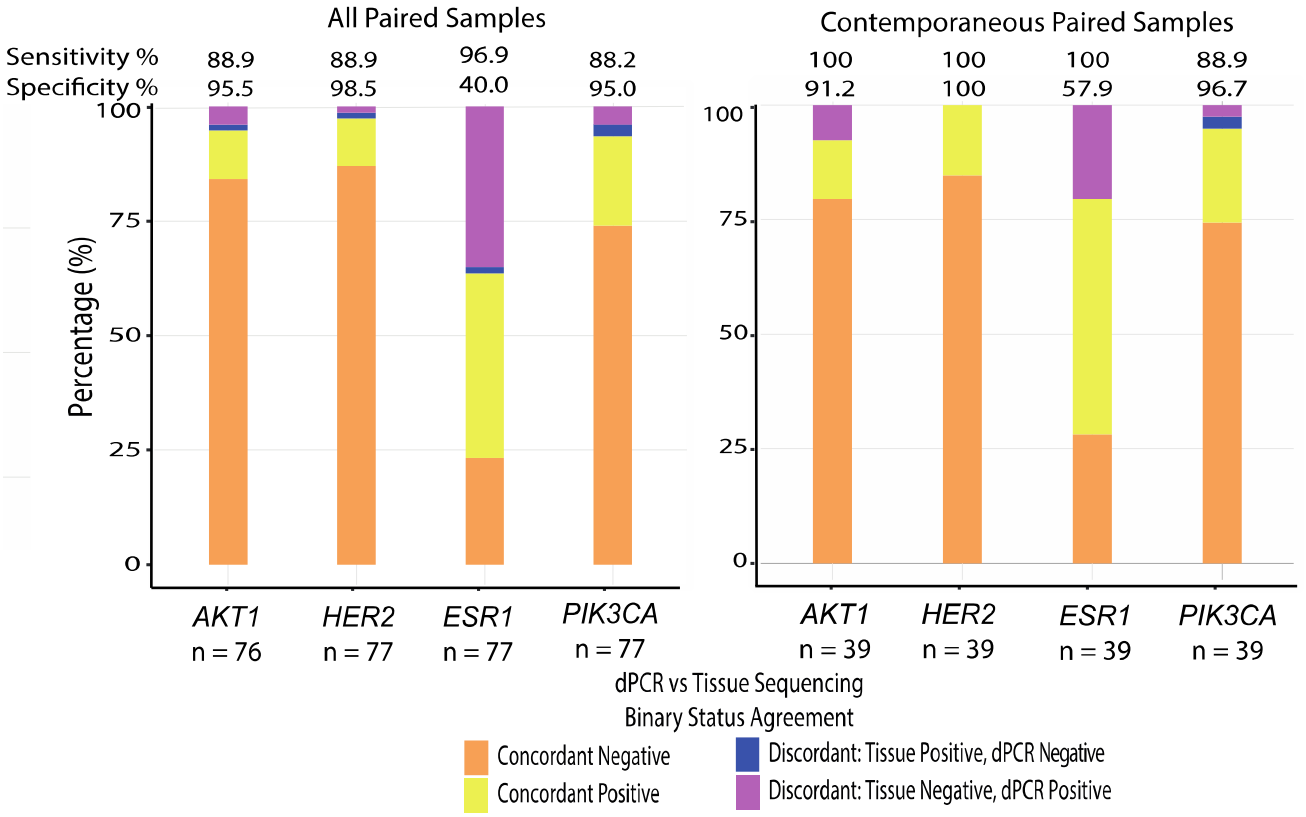
- **Benefits**
  - Minimally invasive
  - Reflects tumor heterogeneity
  - Serial monitoring of treatment response, detection of new resistance mutations
  - Preferred for *ESR1* mutations
- **Limitations**
  - Unable to assess estrogen, progesterone, HER2, PD-L1 (for now)
  - May not be able to detect mutations in tumors with low circulating tumor cells

https://www.nccn.org/professionals/physician_gls/pdf/breast.pdf

Turner et al, Lancet Oncol 2020.

Vasan et al, JCO 2024.

Solid vs Liquid Biopsy Concordance (plasmaMATCH)



plasmaMATCH Study Samples:

- Generally high concordance between solid and liquid NGS samples
  - ~75-100% in contemporaneous samples

- Differences noted by gene
  - *ESR1* with highest divergence
  - More often discordant ctDNA (+) and tissue (-)

Turner et al, Lancet Oncol 2020.

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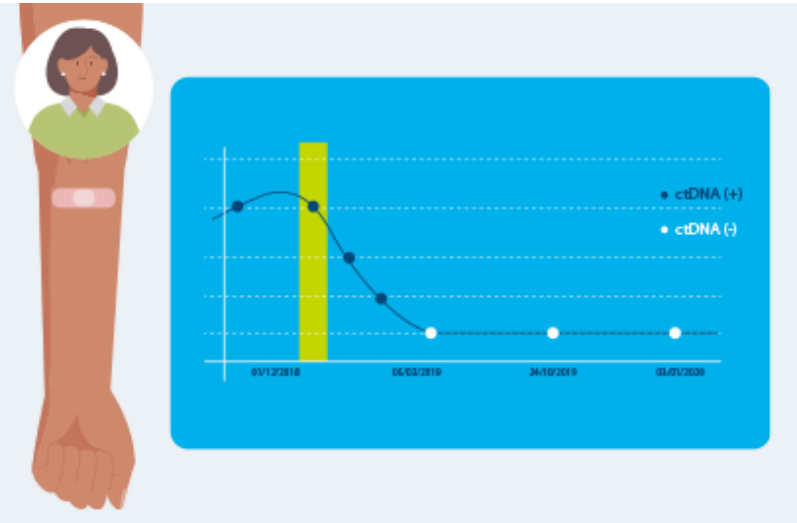
Molecular/Minimum Residual Disease (MRD)

- Blood test to detect cancer circulating in the blood (circulating tumor DNA)
- May be used in metastatic breast cancer to monitor treatment response
- Types of MRD tests:
  - **Tumor-informed**: personalized blood test created using the genetic signature from a patient's tumor i.e. Signatera, Personalis NeXT Dx
  - **Tumor-agnostic:** assesses for alterations in a panel of common breast cancer genes in the blood i.e. Guardant Reveal



https://www.natera.com/oncology/signatera-advanced-cancer-detection/
https://www.personalis.com/next-dx-patients/j
https://www.guardantcomplete.com/hcp/solutions/guardant-reveal
Medford et al, CCR 2023.

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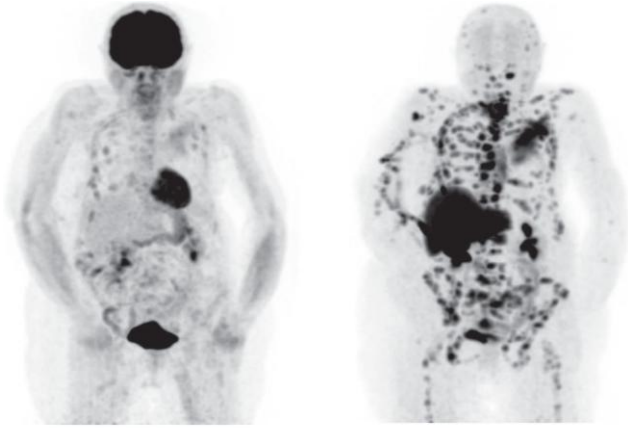
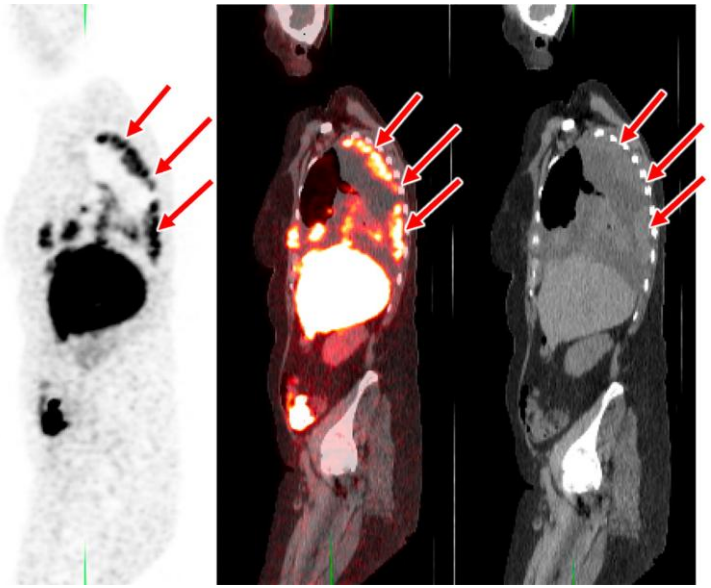
Precision Imaging: FES-PET for ER+ Breast Cancer



^{18}F-FDG PET/CT

^{18}F-FES PET/CT 1 day after ^{18}F-FDG PET/CT



- **Benefits**:
  - Useful when: biopsy is not feasible/safe, mixed biopsy results (ER+ and ER- disease), lobular breast cancers, inconclusive imaging
  - Can predict response to antiestrogen therapy
- **Limitations**:
  - Certain medications require washout periods prior to imaging
    - Tamoxifen – 8-week washout
    - Fulvestrant – 28-week washout
  - Cannot reliably assess liver lesions
  - Not widely available, long wait times

https://www.onclive.com/view/fes-pet-ct-expands-precision-imaging-potential-in-er-positive-breast-cancer
https://www.nccn.org/professionals/physician_gls/pdf/breast.pdf
Grabher BJ, Journal of Nuclear Medicine Technology 2023
O'Brien et al, Nuclear Medicine 2023.

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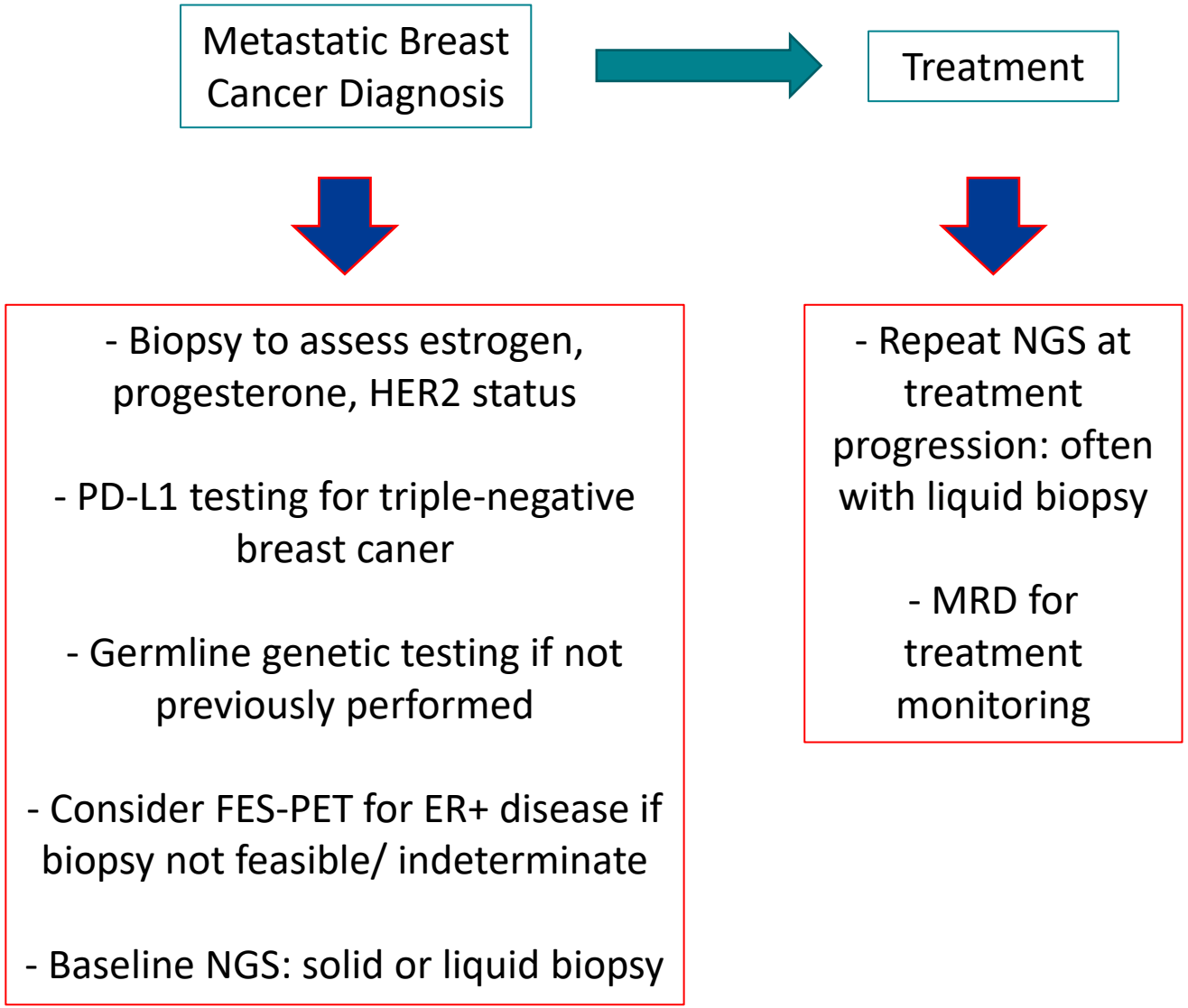
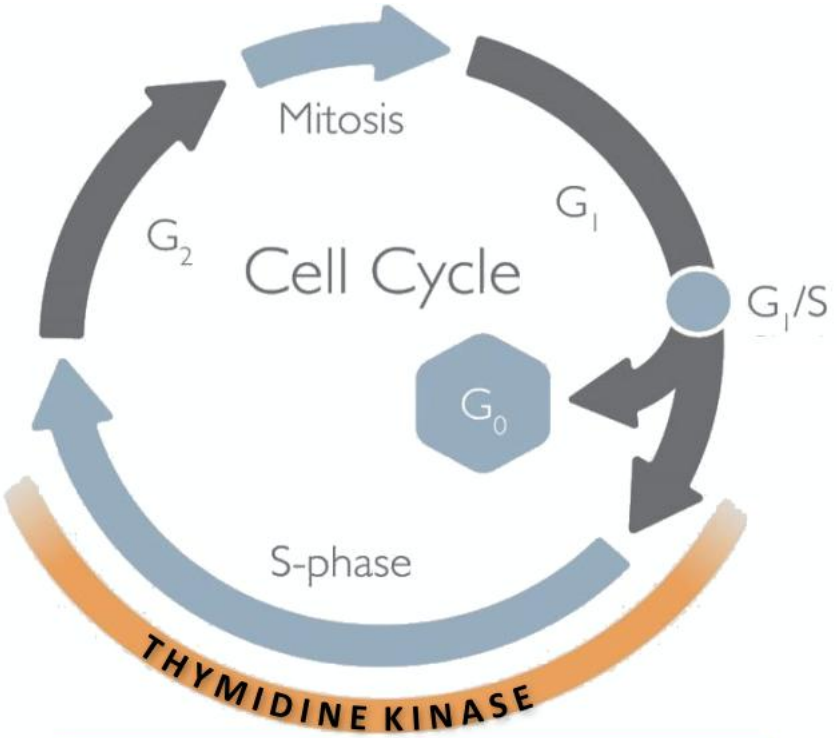
Tools to Consider in Your Breast Cancer Journey



DiviTum TKa

- FDA-approved test that measures thymidine kinase activity (TKa) in the blood, an enzyme that plays a key role in cell growth and proliferation
- TKa is often elevated in blood samples from patients with metastatic breast cancer and declines when started on effective cancer treatment
- Can be used in combination with scans and tumor markers (CEA, CA15-3) to monitor treatment response
- Rising TKa can suggest the development of treatment resistance weeks to months prior to imaging

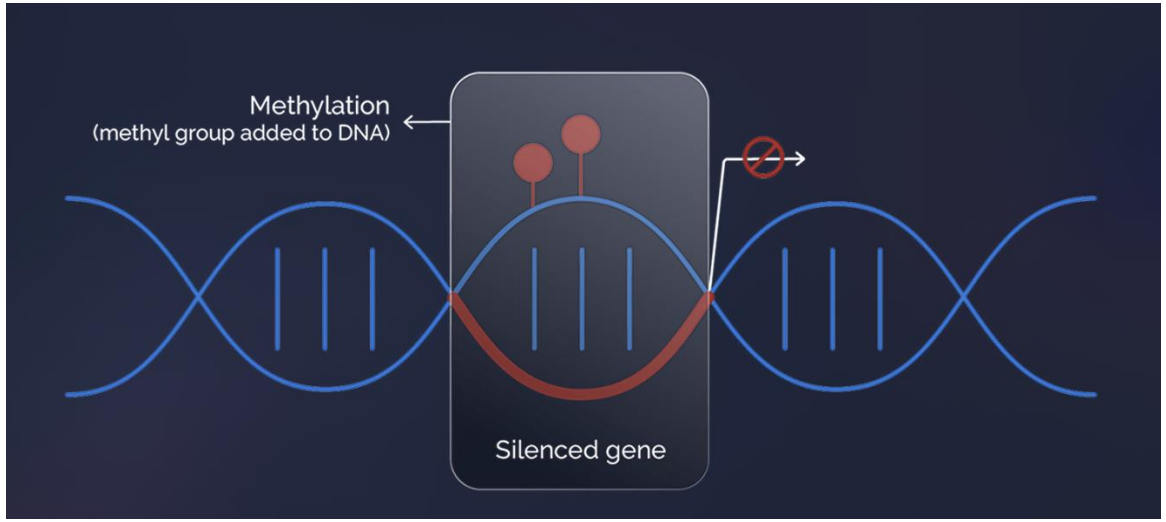


- Thymidine Kinase (TK) is a key enzyme required for cell division
- TK is synthesized ONLY during S-phase and then is degraded in M.
- Proliferating cells release TK into circulation

https://divitum.com/health-care-providers/the-science-behind-tka/

Methylation-Based Sequencing

- New form of blood test that provides a comprehensive, multidimensional understanding of a tumor
- Performs **genomic profiling** to look for mutations in tumor DNA, combines this information with **epigenomic profiling** to look for *methylation* - chemical tags on DNA that alter gene activation
- Multiple potential uses: guides treatment selection, assesses MRD, provides longitudinal treatment monitoring



https://guardanthealth.com/guardant-infinity/
https://www.precede.bio/#science

Thank You!