LIVING BEYOND
BREAST CANCER®

Thriving Together

2025 CONFERENCE ON METASTATIC BREAST CANCER

Personalized Medicine in MBC: What it means for you

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Leader, Breast Oncology Program

Disclosures

Virginia Kaklamani

Research: EISAI

Speaker's Bureau: Astrazeneca, Gilead

Advisory Panel/Consultant: Lilly, Menarini, Astrazeneca, Tersera, Genentech

Stock/Shareholder: None

Employee: none

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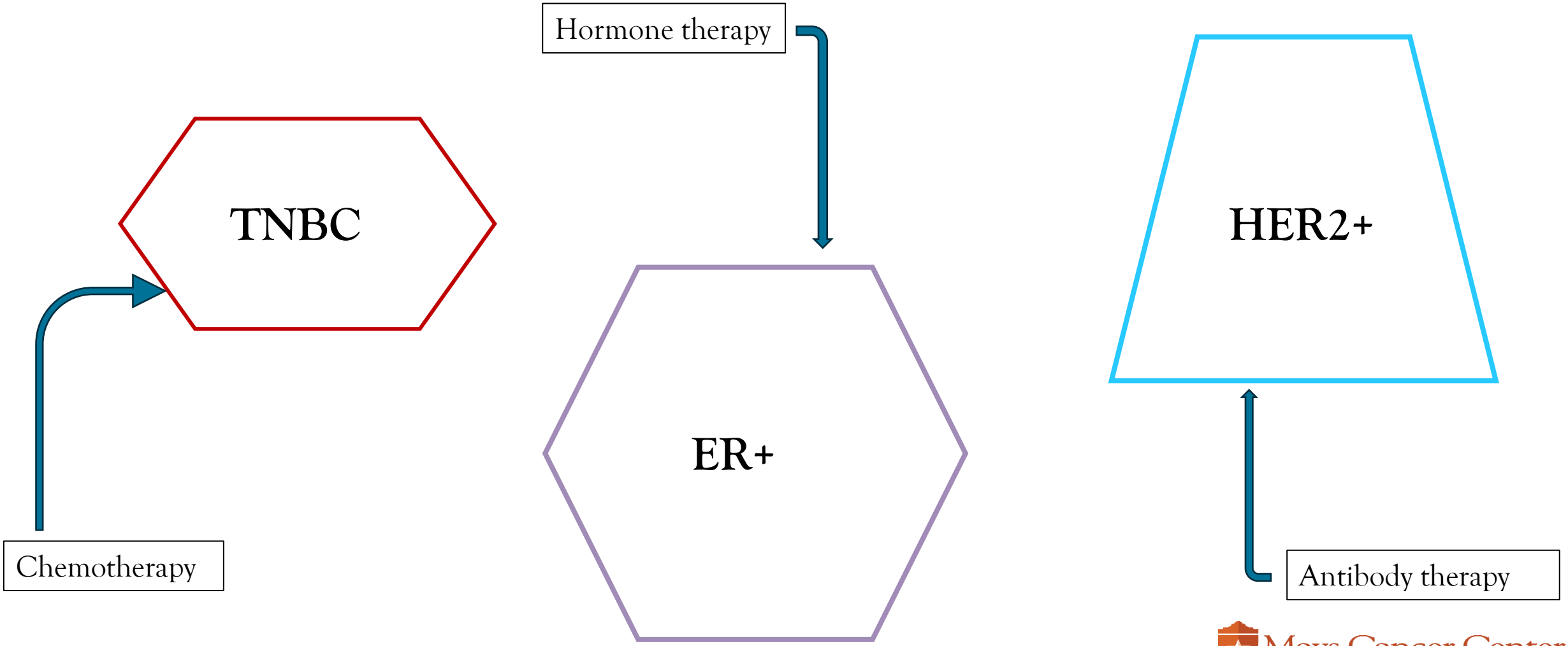
UT Health San Antonio MD Anderson Cancer Center

What was our past



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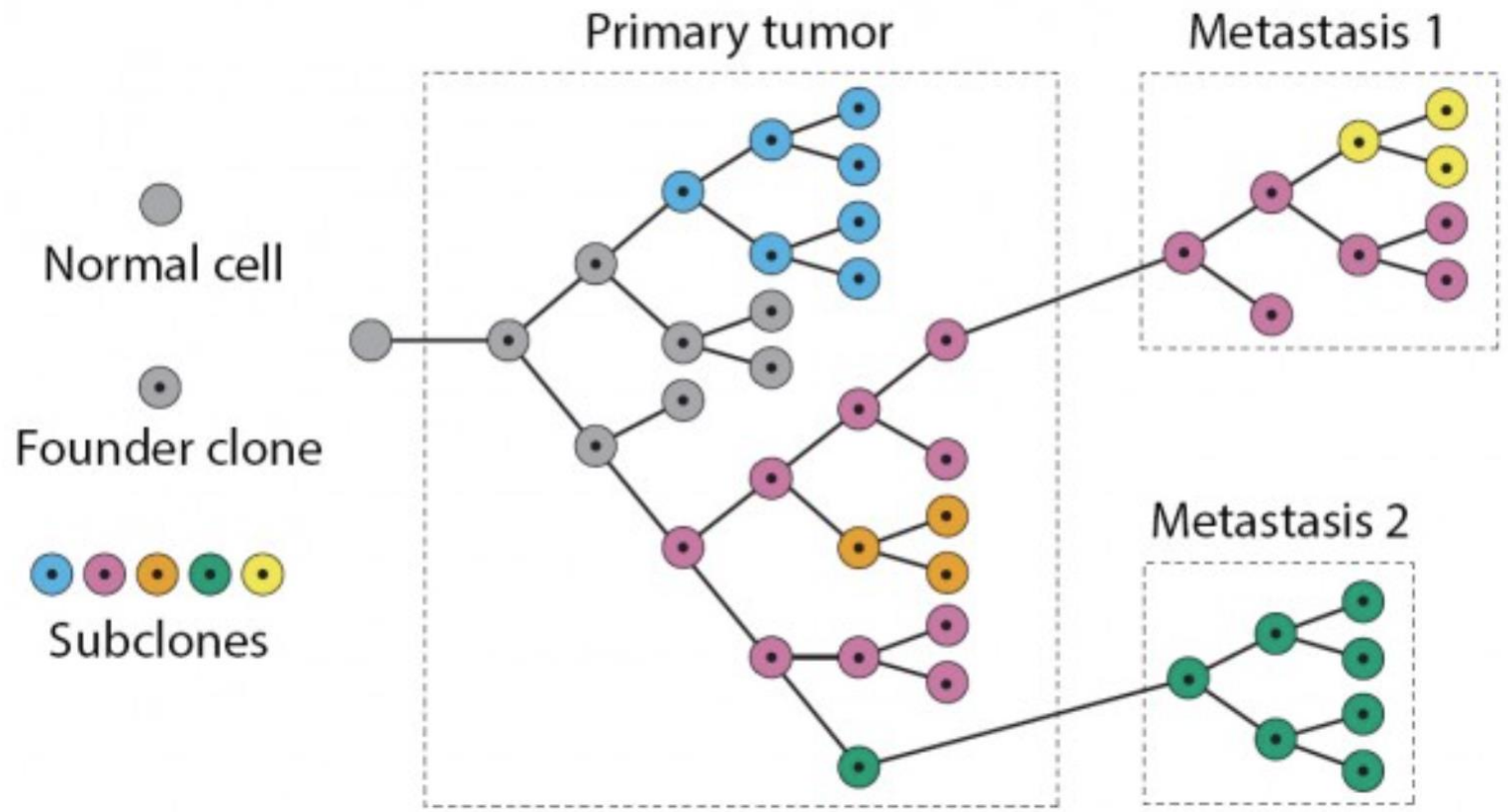
What have we realized?

- Breast cancer is much more complicated that these three subsets
- Breast cancer evolves over time
- The original breast lump is comprised of different cells that may behave differently
- When breast cancer spreads, each site behaves independently
- Breast cancer evolves and changes based on what therapies it is exposed to

Why is it so hard to cure metastatic breast cancer?



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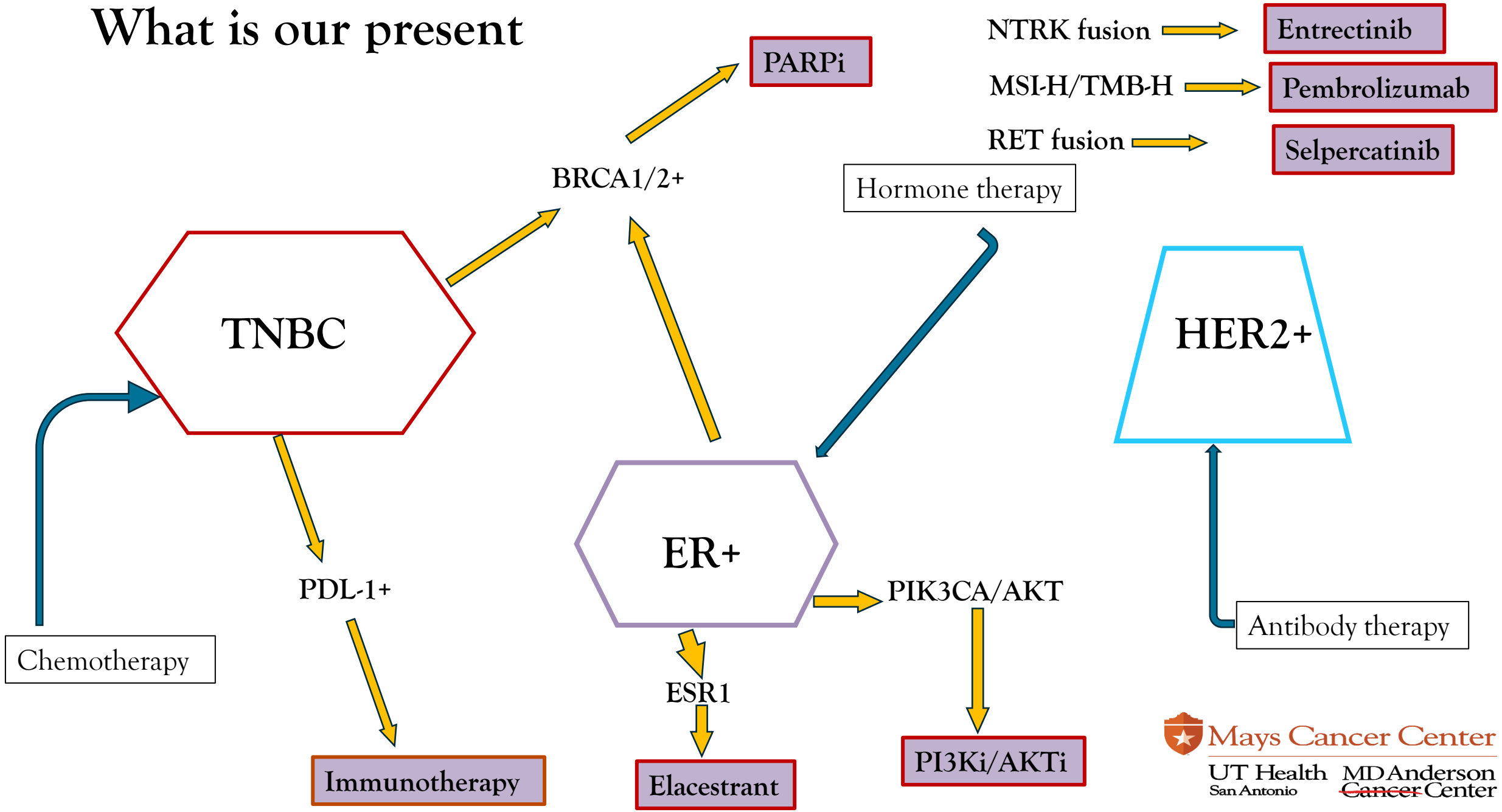
What is our present



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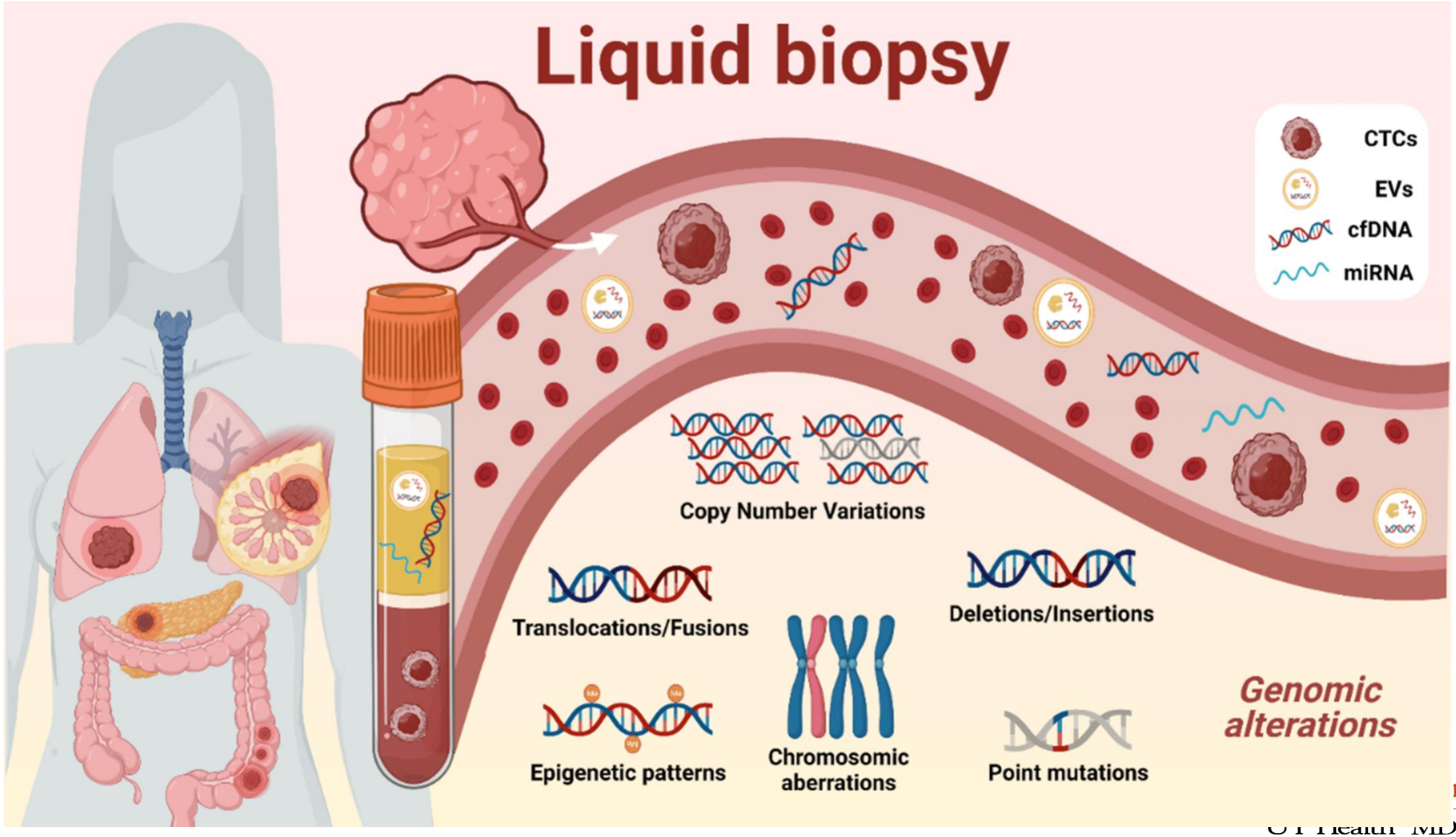
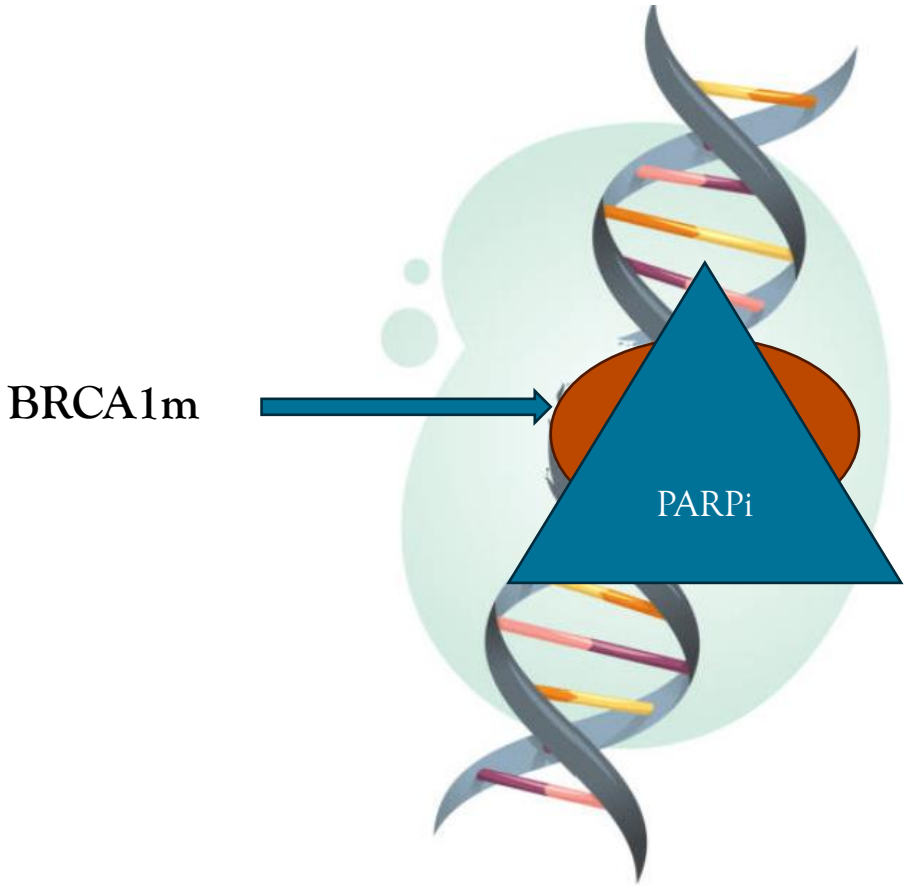

Liquid biopsy
CTCs
EVs
cfDNA
miRNA
Copy Number Variations
Translocations/Fusions
Deletions/Insertions
Epigenetic patterns
Chromosomic aberrations
Point mutations
Genomic alterations

BRCA1/2 mutations



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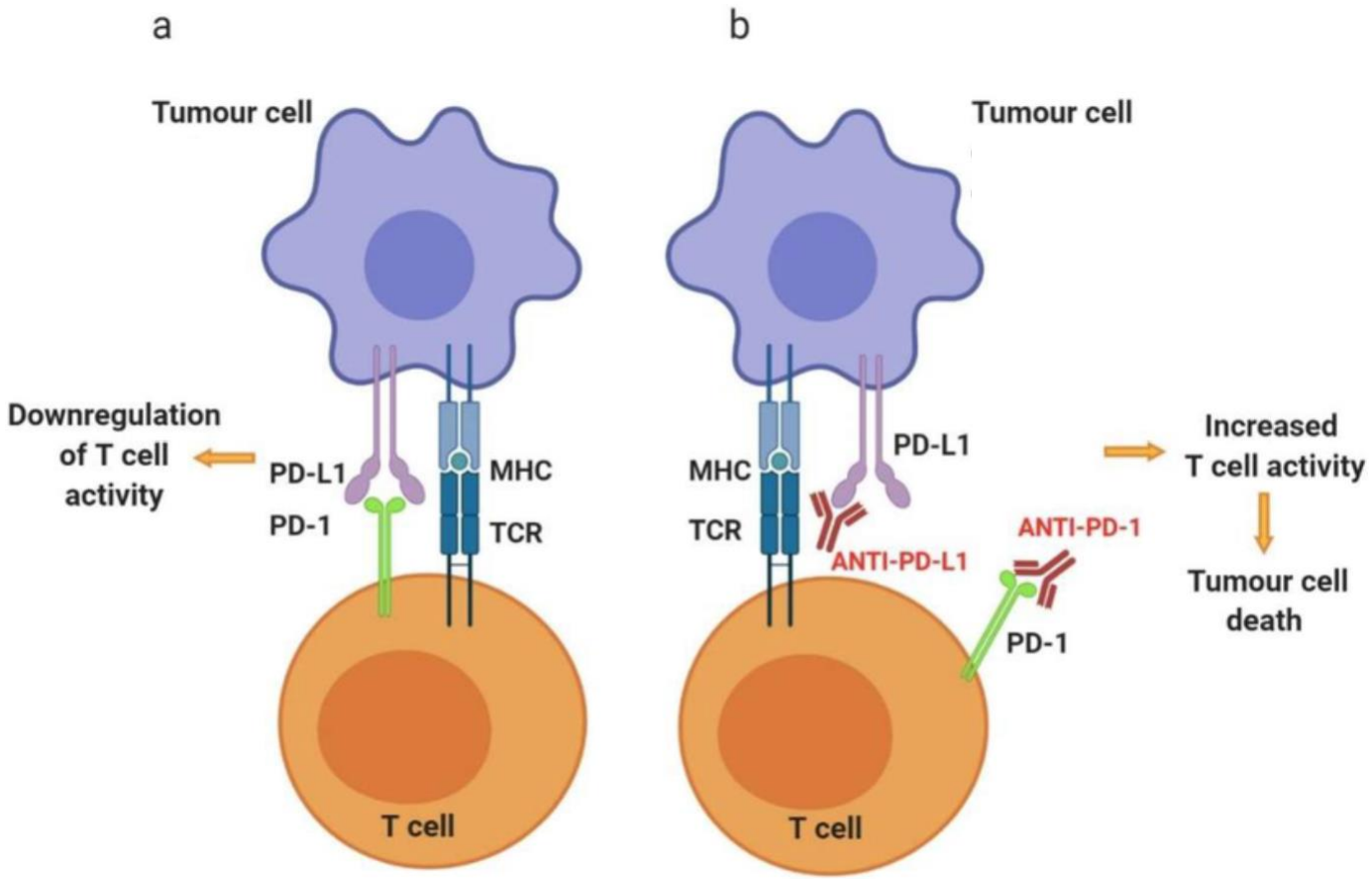
Immunotherapy



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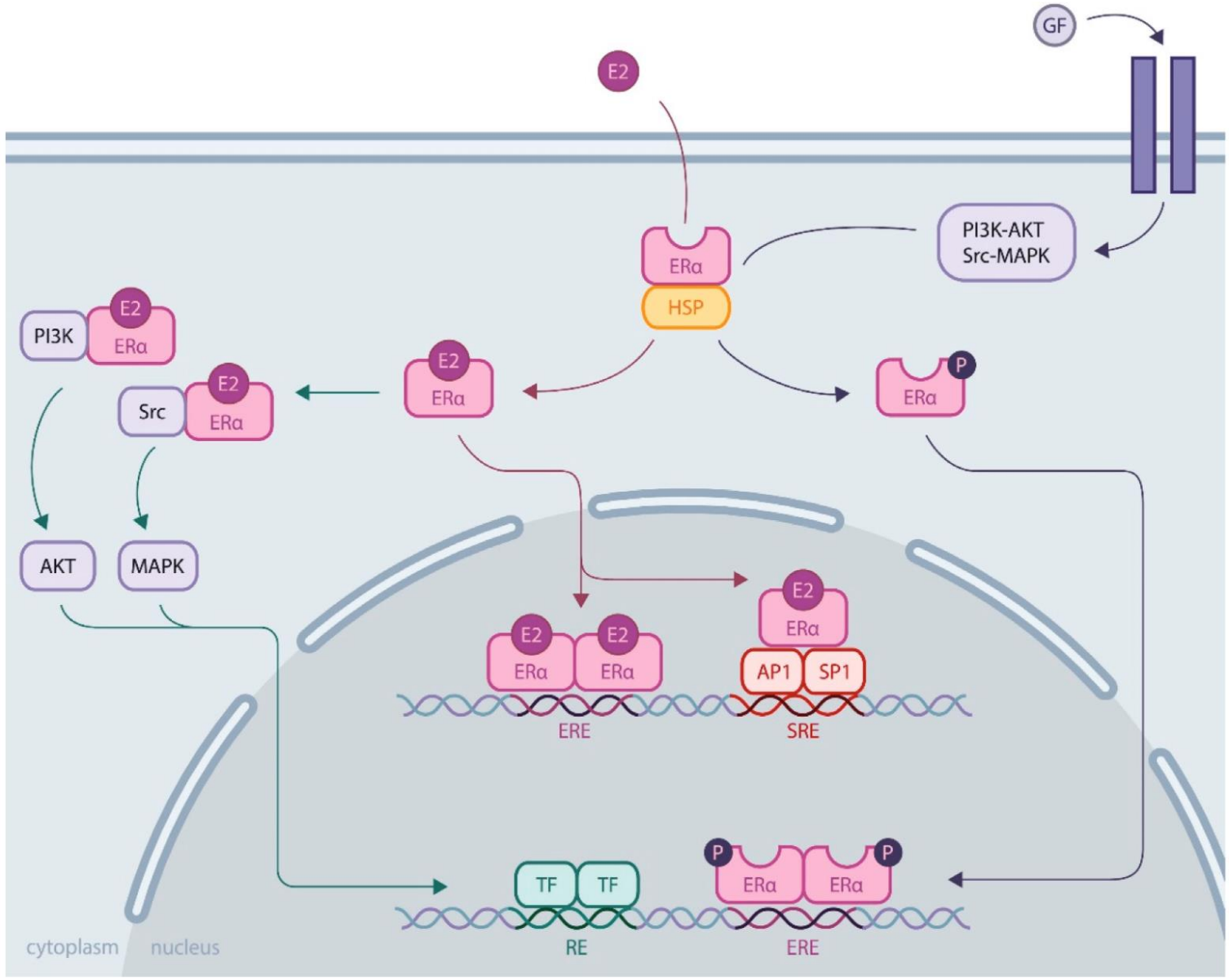
ESR1 mutations



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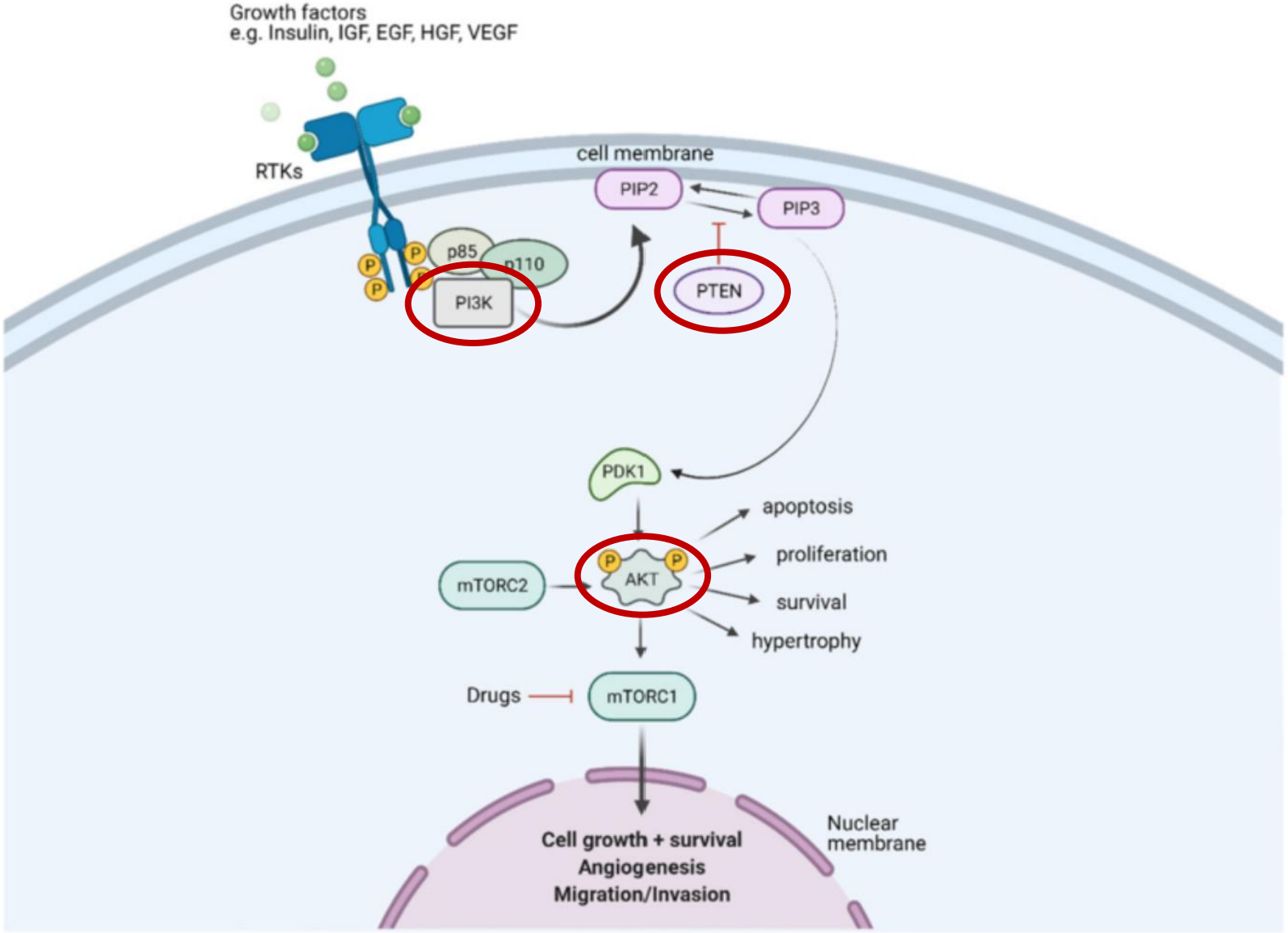
PIK3/AKT pathway



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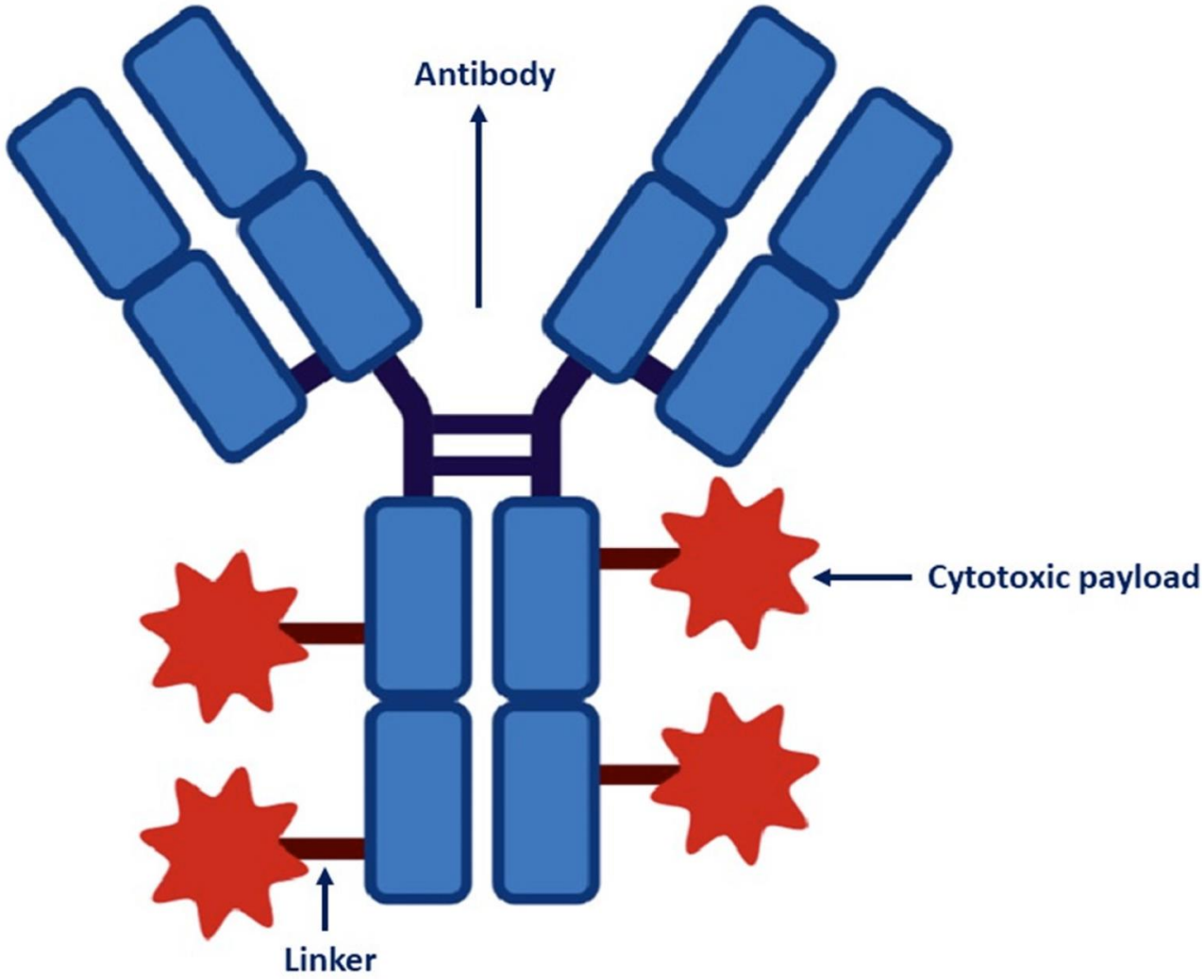
Antibody Drug Conjugate (ADC)



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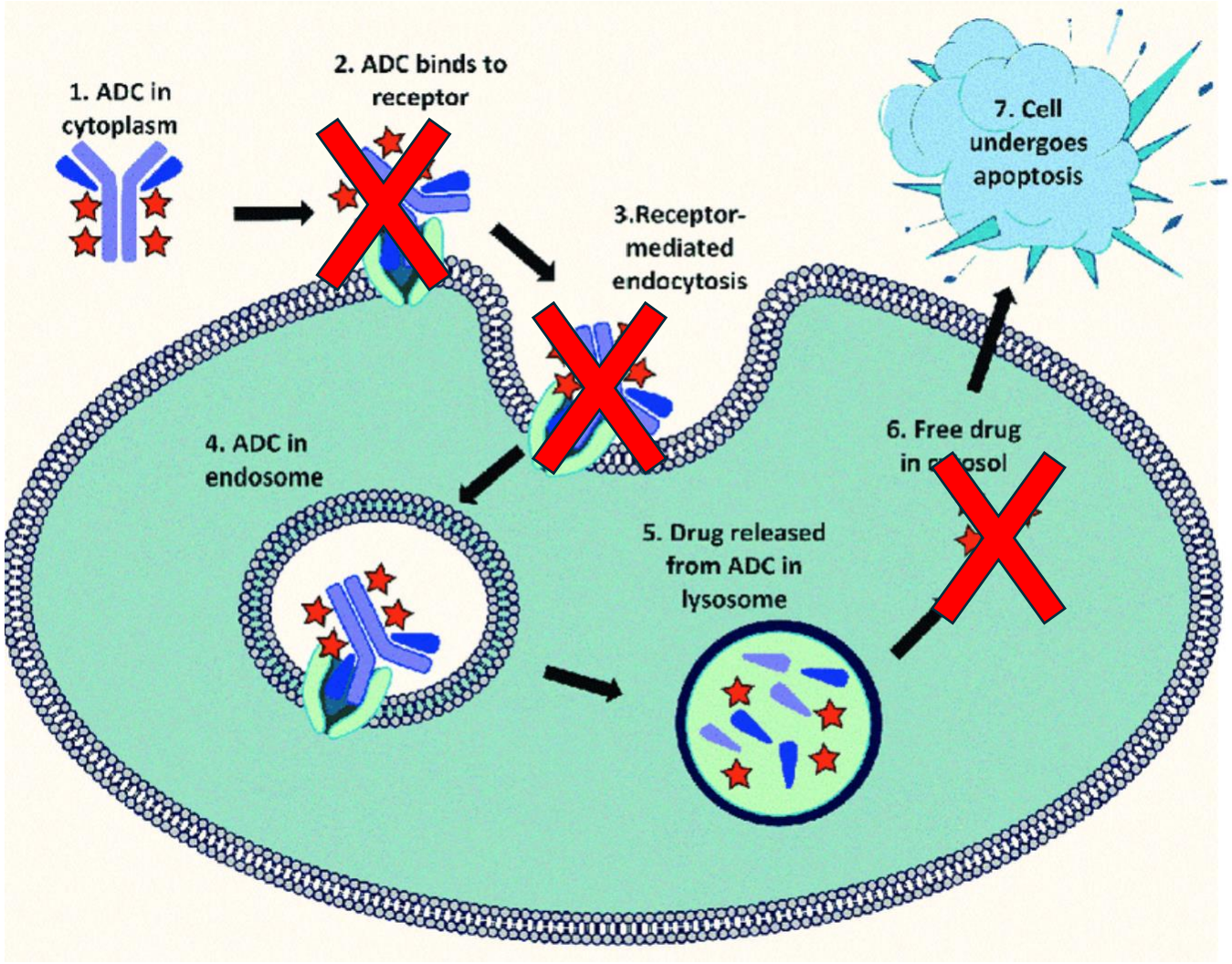
How ADCs work and how do the cancer cells adapt



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How can we individualize care

Limited Tissue, Final Report | CARIS LIFE SCIENCES

Patient

Specimen Information

Primary Tumor Site: Breast, NOS
Specimen Site: Vertebra
Specimen ID: S24-12447-A1
Specimen Collected: 07-Jun-2024
Test Report Date: 04-Jul-2024

Ordered By

Virginia G. Kaklamani, MD
UT Health - Mays Cancer Center - Breast Center
7979 Wurzbach Road, Suite Z500
San Antonio, TX 78229 USA
(210) 450-1000

Results with Therapy Associations

BIOMARKER	METHOD	ANALYTE	RESULT	THERAPY ASSOCIATION	BIOMARKER LEVEL*
PIK3CA	Seq	DNA-Tumor	Pathogenic Variant Exon 5 | p.N345K	capivasertib + fulvestrant The AKT inhibitor capivasertib in combination with fulvestrant, is FDA-approved for hormone receptor positive, HER2-negative/low breast cancer patients following progression on an endocrine-based regimen(s) and with an alteration(s) in the PIK3CA/AKT1/PTEN pathway. This patient's sample harbors at least one qualifying alteration, however, therapy associations are not interpreted in the context of ER/PR/HER2 results produced by the local laboratory if those exist. Therefore, the utility of capivasertib + fulvestrant is unknown for this patient.	

* Biomarker reporting classification: Level 1 – Companion diagnostic (CDx); Level 2 – Strong evidence of clinical significance or is endorsed by standard clinical guidelines; Level 3 – Potential clinical significance. Bolded benefit therapies, if present, highlight the most clinically significant findings.

Important Note

There is an insufficient amount of tumor in the submitted specimen to perform Immunohistochemical stains. Whole Exome Sequencing and Whole Transcriptome Sequencing were performed.

Cancer-Type Relevant Biomarkers

Biomarker	Method	Analyte	Result
BRAF	Seq	DNA-Tumor	Mutation Not Detected
MSI	Seq	DNA-Tumor	Stable
NTRK1/2/3	Seq	RNA-Tumor	Fusion Not Detected
RET	Seq	RNA-Tumor	Fusion Not Detected
Genomic LOH	Seq	DNA-Tumor	Low
Tumor Mutational Burden	Seq	DNA-Tumor	Low, 3 mut/Mb
AKT1	Seq	DNA-Tumor	Mutation Not Detected
BRCA1	Seq	DNA-Tumor	Mutation Not Detected
	CNA-Seq	DNA-Tumor	Deletion Not Detected

Biomarker	Method	Analyte	Result
BRCA2	Seq	DNA-Tumor	Mutation Not Detected
	CNA-Seq	DNA-Tumor	Deletion Not Detected
ERBB2 (Her2/Neu)	Seq	DNA-Tumor	Mutation Not Detected
	CNA-Seq	DNA-Tumor	Amplification Not Detected
ESR1	Seq	RNA-Tumor	Fusion Not Detected
		DNA-Tumor	Mutation Not Detected
MTAP	CNA-Seq	DNA-Tumor	Deletion Not Detected
NF1	Seq	DNA-Tumor	Mutation Not Detected
	CNA-Seq	DNA-Tumor	Deletion Not Detected

Molecular testing of blood or tissue

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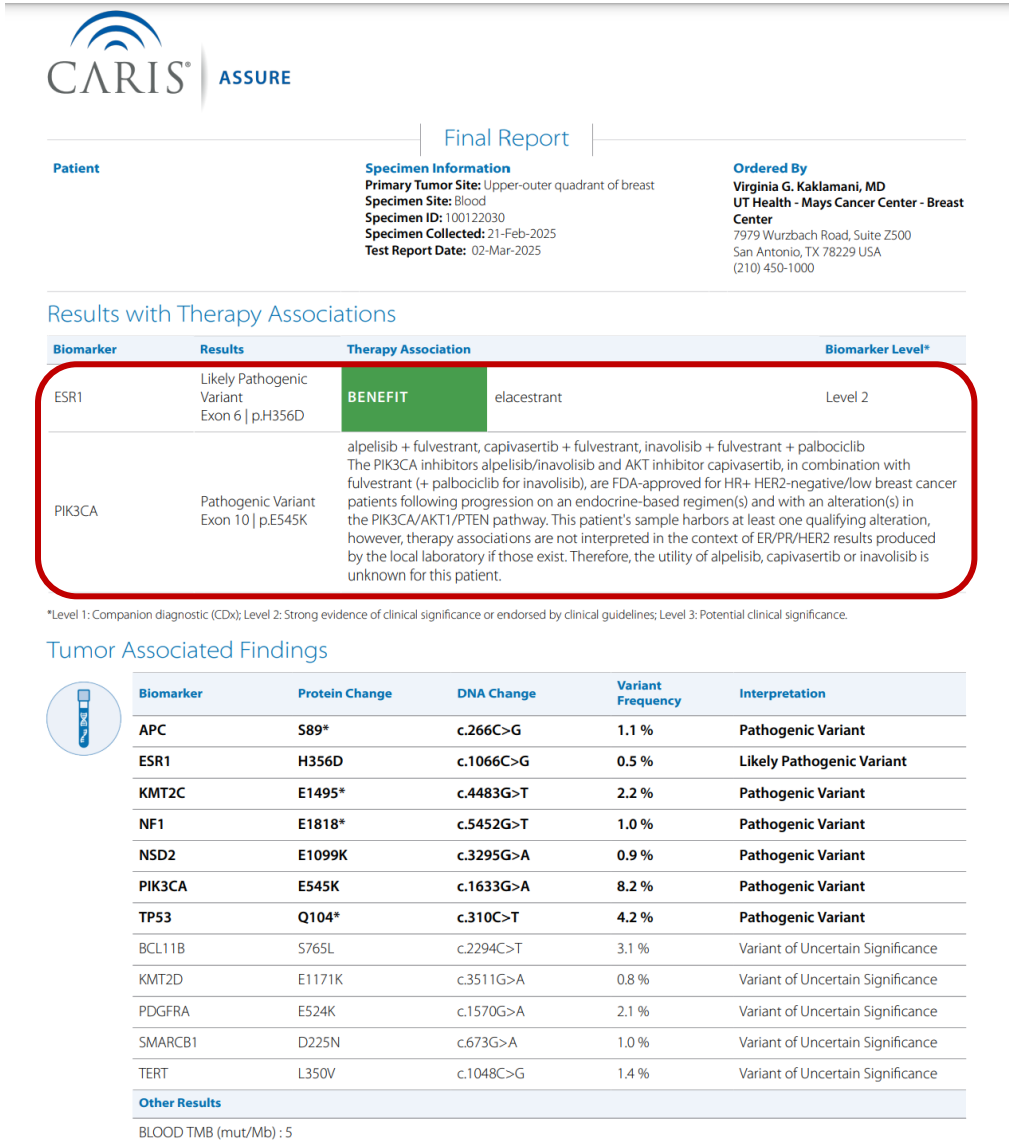
How can we individualize care?



CARIS® ASSURE

Final Report

Patient

Specimen Information
Primary Tumor Site: Upper-outer quadrant of breast
Specimen Site: Blood
Specimen ID: 100122030
Specimen Collected: 21-Feb-2025
Test Report Date: 02-Mar-2025

Ordered By
Virginia G. Kaklamani, MD
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Results with Therapy Associations

Biomarker	Results	Therapy Association		Biomarker Level*
ESR1	Likely Pathogenic Variant Exon 6 | p.H356D	BENEFIT	elacestrant	Level 2
PIK3CA	Pathogenic Variant Exon 10 | p.E545K	alpelisib + fulvestrant, capivasertib + fulvestrant, inavolisib + fulvestrant + palbociclib The PIK3CA inhibitors alpelisib/inavolisib and AKT inhibitor capivasertib, in combination with fulvestrant (+ palbociclib for inavolisib), are FDA-approved for HR+ HER2-negative/low breast cancer patients following progression on an endocrine-based regimen(s) and with an alteration(s) in the PIK3CA/AKT1/PTEN pathway. This patient's sample harbors at least one qualifying alteration, however, therapy associations are not interpreted in the context of ER/PR/HER2 results produced by the local laboratory if those exist. Therefore, the utility of alpelisib, capivasertib or inavolisib is unknown for this patient.		

*Level 1: Companion diagnostic (CDx); Level 2: Strong evidence of clinical significance or endorsed by clinical guidelines; Level 3: Potential clinical significance.

Tumor Associated Findings

Biomarker	Protein Change	DNA Change	Variant Frequency	Interpretation
APC	**S89***	**c.266C>G**	**1.1 %**	**Pathogenic Variant**
ESR1	**H356D**	**c.1066C>G**	**0.5 %**	**Likely Pathogenic Variant**
KMT2C	**E1495***	**c.4483G>T**	**2.2 %**	**Pathogenic Variant**
NF1	**E1818***	**c.5452G>T**	**1.0 %**	**Pathogenic Variant**
NSD2	**E1099K**	**c.3295G>A**	**0.9 %**	**Pathogenic Variant**
PIK3CA	**E545K**	**c.1633G>A**	**8.2 %**	**Pathogenic Variant**
TP53	**Q104***	**c.310C>T**	**4.2 %**	**Pathogenic Variant**
BCL11B	S765L	c.2294C>T	3.1 %	Variant of Uncertain Significance
KMT2D	E1171K	c.3511G>A	0.8 %	Variant of Uncertain Significance
PDGFRA	E524K	c.1570G>A	2.1 %	Variant of Uncertain Significance
SMARCB1	D225N	c.673G>A	1.0 %	Variant of Uncertain Significance
TERT	L350V	c.1048C>G	1.4 %	Variant of Uncertain Significance

Other Results

BLOOD TMB (mut/Mb) : 5

Other mutations help characterize the tumor

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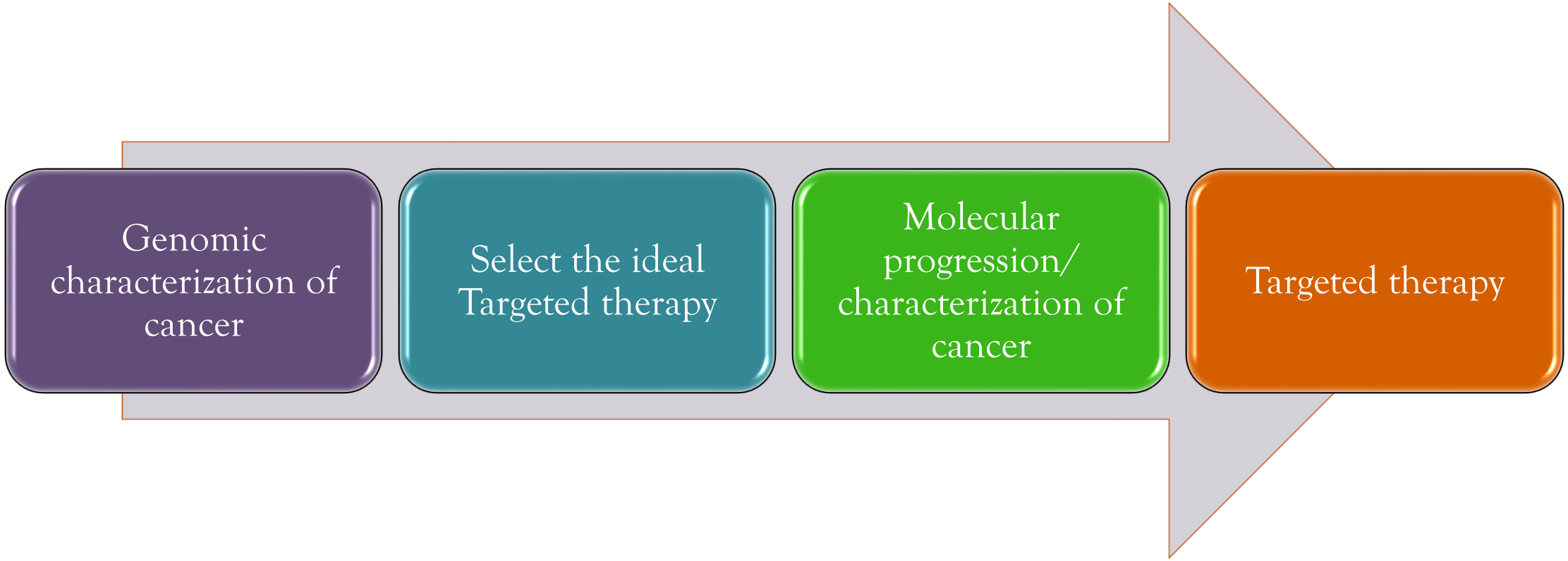
What is our future?



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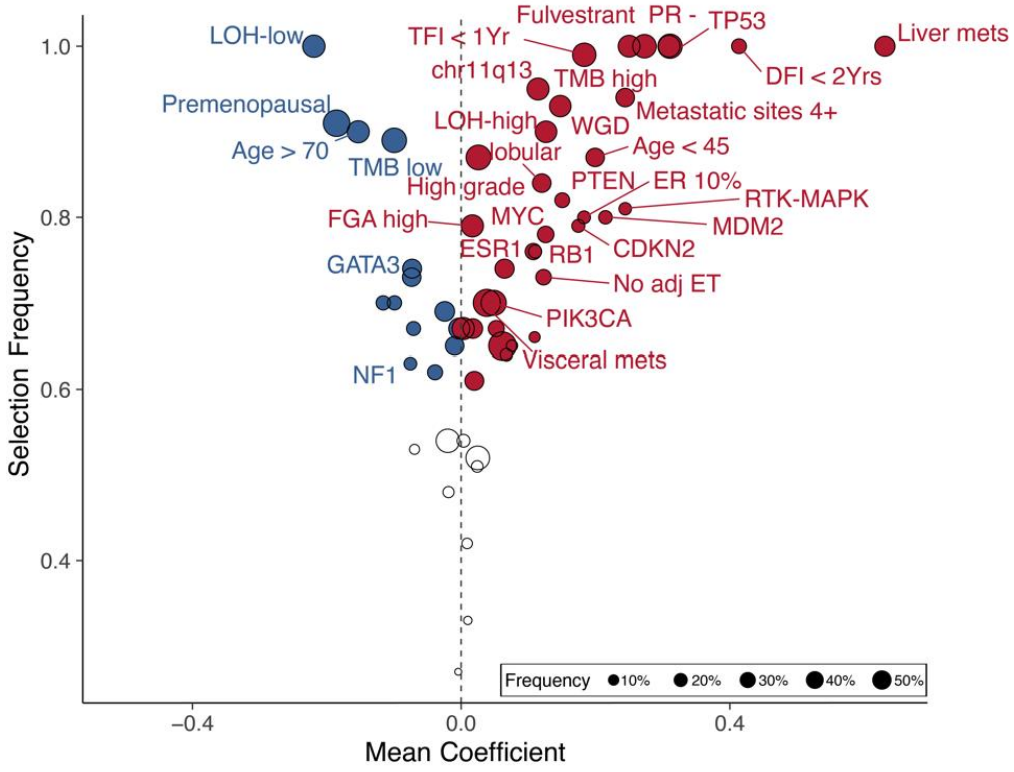
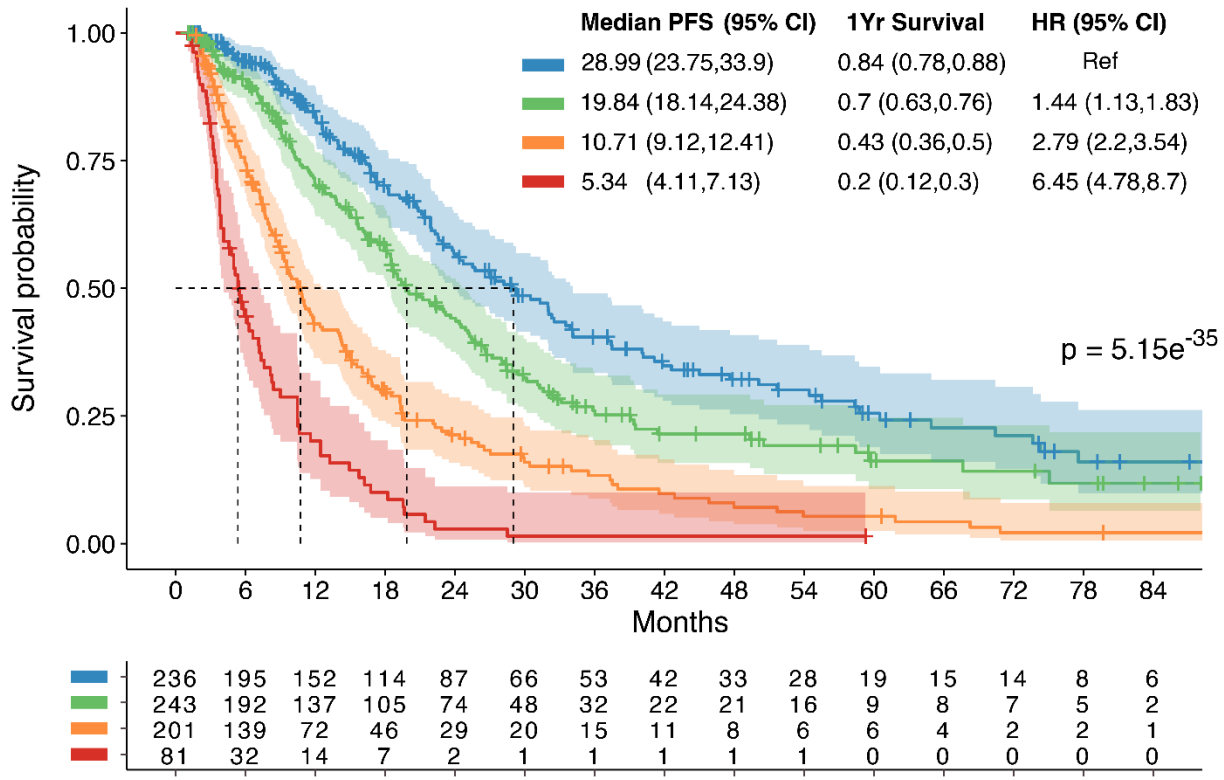
Predicting PFS on 1st line CDK4/6i+ET
Mixed clinico-genomic model



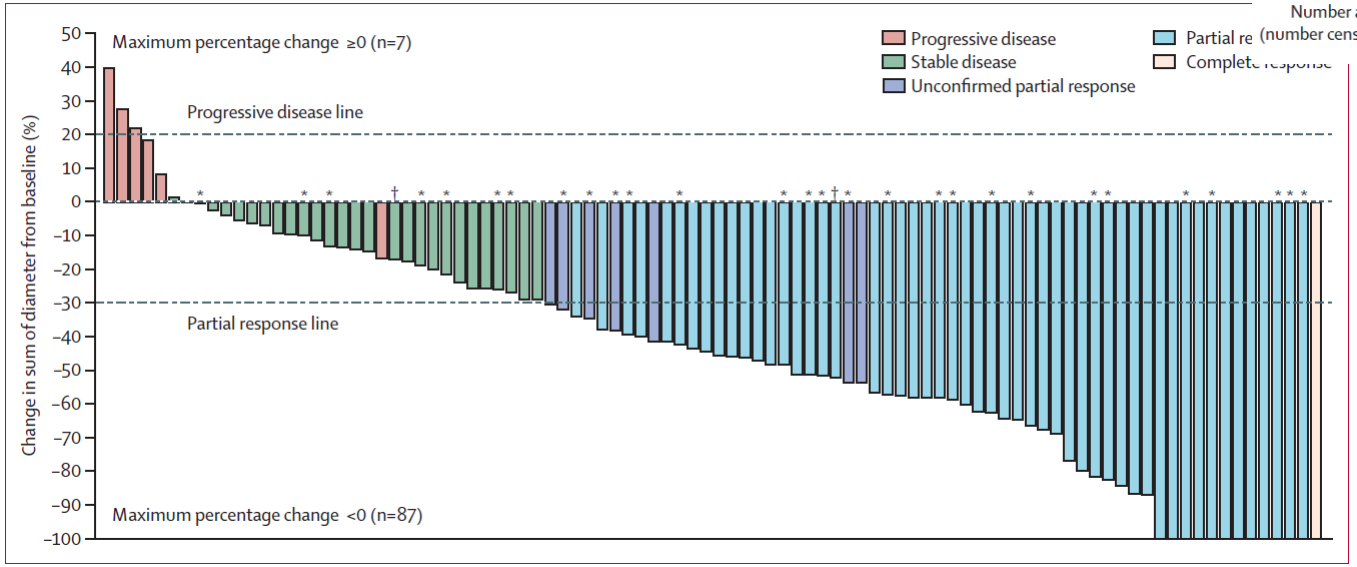


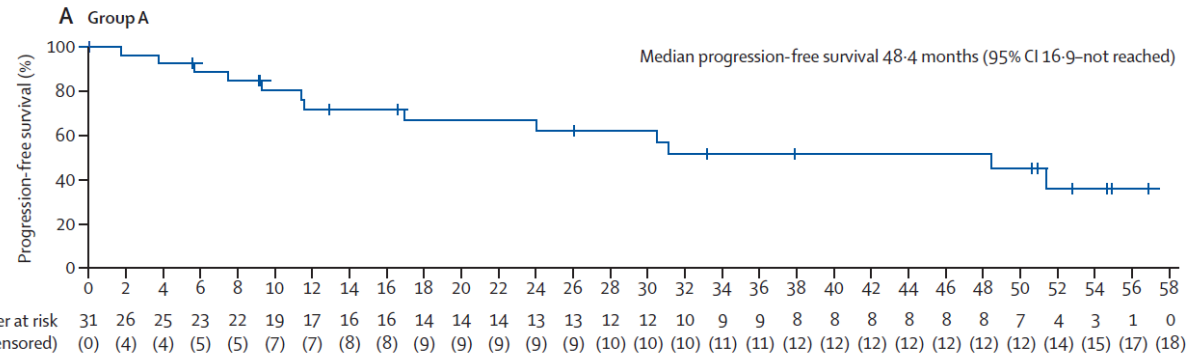
Razavi et al SABCS 2024

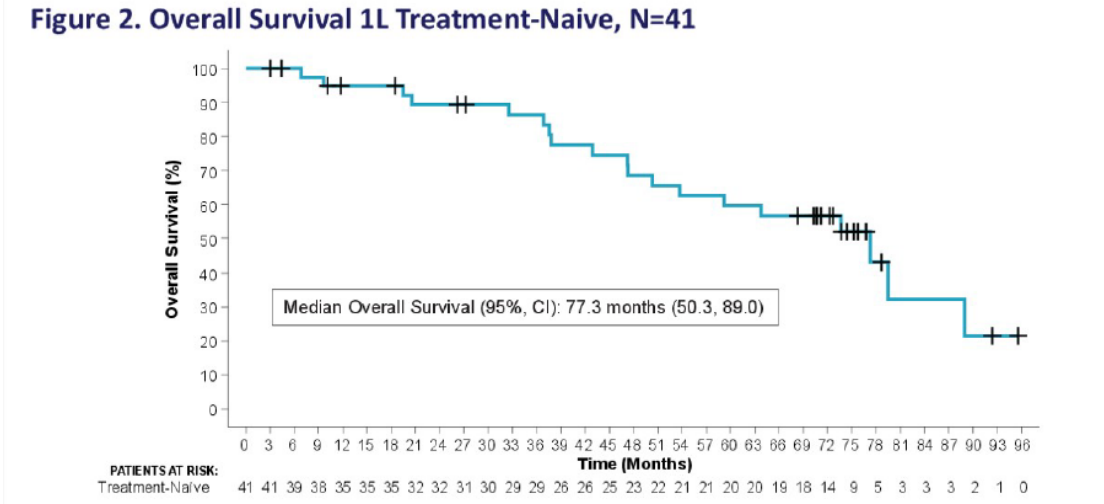
Novel PI3Ki

Gedatolisib in combination with palbociclib and endocrine therapy in women with hormone receptor-positive, HER2-negative advanced breast cancer: results from the dose expansion groups of an open-label, phase 1b study

Rachel M Layman, Hyo S Han, Hope S Rugo, Erica M Stringer-Reasor, Jennifer M Specht, E Claire Dees, Peter Kabos, Samuel Suzuki, Sarah C Mutka, Brian F Sullivan, Igor Gorbatchevsky, Robert Wesolowski







- Pan PI3K and mTOR1/2 inh
- IV
- Activity regardless of PI3K mutation
- Evaluated in 2 phase III trials VICTORIA-1 and VICTORIA-2

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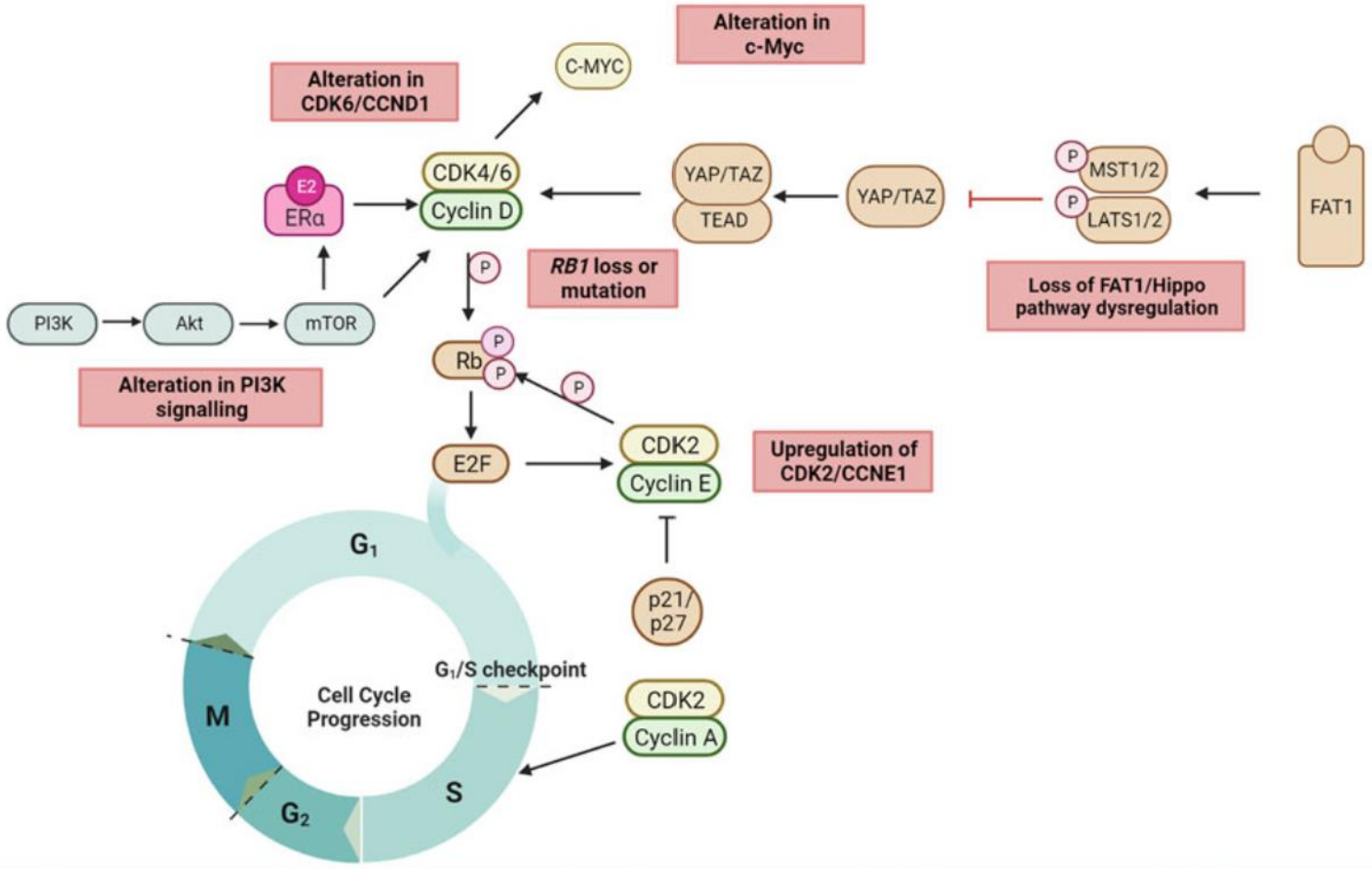
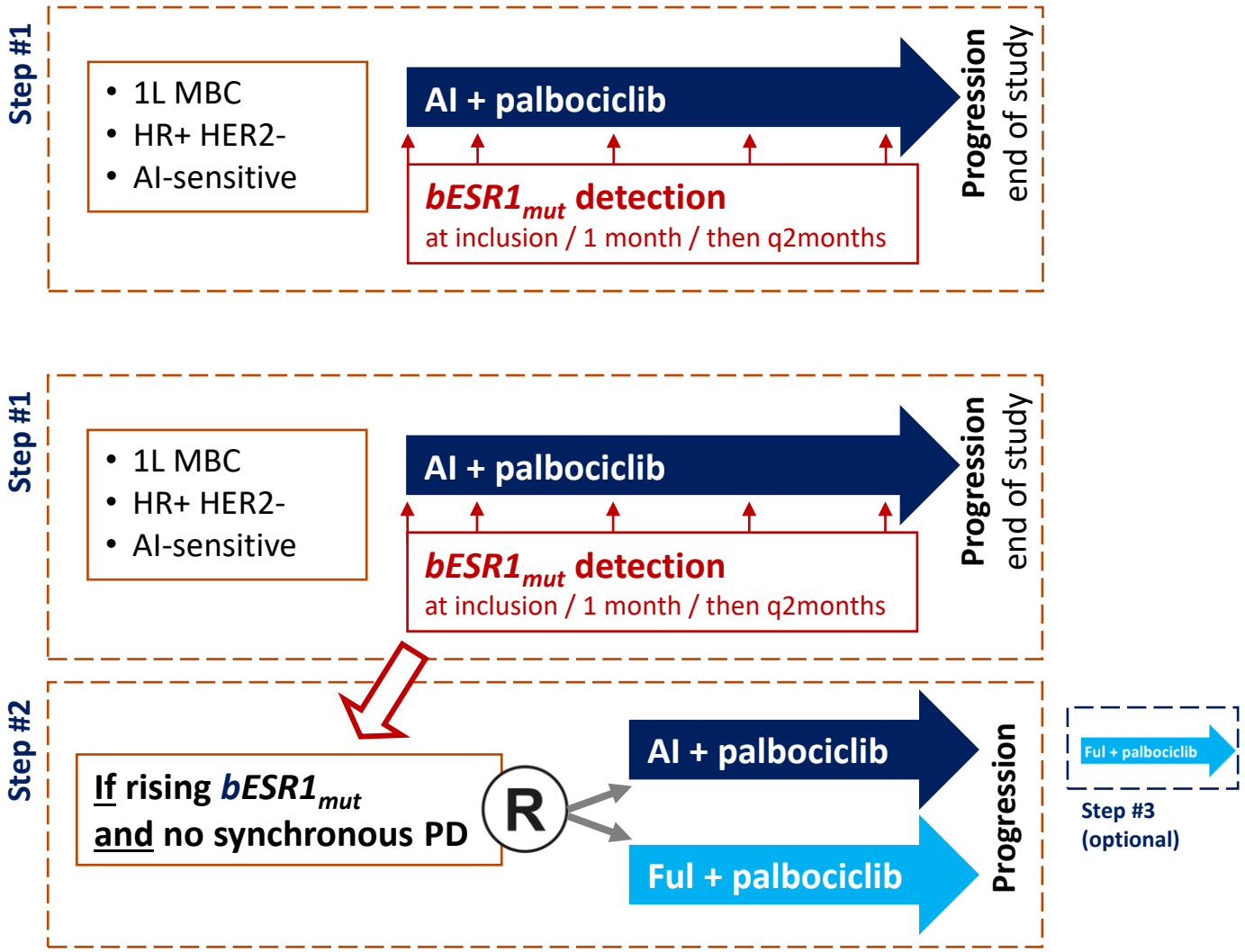
SABCS 2024

Mechanisms of resistance to CDK4/6i



PADA-1 Trial



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What have we learned?

- The same way we are all unique, all our breast cancers are unique.
- When we meet someone we want to get to know them. We need to get to know our cancers better too.
- The same way we evolve as people, our cancers evolve too.
- Instead of always being one step behind we need to strive to be one step ahead.

Thank you !

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