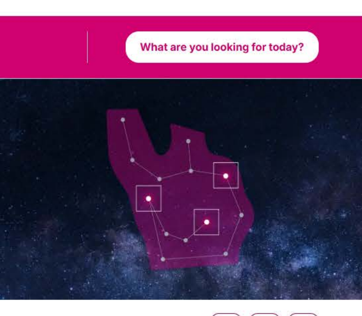
ESR1 Mutations in Breast Cancer



What is the significance of *ESR1*m in breast cancer?

Explore detailed information, guideline recommendations, and actionable best practices for *ESR1*m in breast cancer, an early and critical predictor of tumor progression.[1,2]

ESR1, estrogen receptor 1.

Reading time: **10 min**

Jump to: Role of *ESR1* | Prevalence | Testing Recommendations | ctDNA-Mediated Testing to Detect *ESR1*m | Considerations for

Role of *ESR1*

ESR1 is the gene encoding estrogen receptor alpha (ERα), a key driver of hormone-dependent cancers[1]

This is particularly evident in estrogen receptor-positive (ER+) breast cancer, including HR+/HER2-, where *ESR1* promotes tumor growth.

ESR1, estrogen receptor 1; HR+, Hormone Receptor-Positive; HER2-, human epidermal growth factor receptor-negative.

ESR1 mutations may promote breast cancer tumor growth through estrogen-mediated transcriptional regulation[3]

Acquired resistance

*ESR1*m is an acquired mutation that evolves frequently through resistance to endocrine therapy (ET).[4-7]

Proactive identification and *ESR1*m interpretation

Identify *ESR1*m as quickly as possible, as these mutations may lead to disease progression and poorer patient outcomes.[4]

ESR1, estrogen receptor 1; *ESR1*m, estrogen receptor 1 mutation.

ESR1 Mutation Prevalence: *ESR1* Mutations Are Not Commonly Present at Diagnosis of Metastatic Breast Cancer (mBC) in Patients Who Are Endocrine Therapy (ET) Naive[3-8]

~6%

of patients who are ET naive carry an *ESR1* mutation, which is detected when tested at mBC diagnosis[3,8]

Exposure to aromatase inhibitors (AIs) during 1L treatment leads to the emergence of endocrine resistance[8,9]

Among patients who typically receive AIs in the metastatic setting

nearly

40%

acquire *ESR1* mutations[4,9]

1L, first-line; AI, aromatase inhibitor.

Testing Recommendations for *ESR1*m[7,9-13]

ESR1 mutations may signal development of endocrine resistance[9]

Early and routine testing for *ESR1*m in addition to *ESR1*m analysis provides a pivotal opportunity to impact patient outcomes in breast cancer because its emergence precedes radiographic or clinical evidence of disease progression.[7]

NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) recommend evaluating *ESR1*m status through NGS or PCR[10]

NCCN Guidelines recommend testing *ESR1*m through liquid biopsy (blood samples).[10]

ctDNA is a validated method for identifying *ESR1*m.[11-13]

NCCN, National Comprehensive Cancer Network; NGS, next-generation sequencing; PCR, polymerase chain reaction.

*ESR1*m Testing Options Overview[14-32]

Laboratory	Assay name/platform	Technology	Sensitivity (VAF)	Sample type	Turnaround time	FDA-approved test
Guardant Health	Guardant360® Transpose CDx	NGS (Large panel CGP)	0.3–1.0%	Plasma (ctDNA)	7 days	✓
Foundation Medicine	FoundationOne® Liquid CDx	NGS (Large panel CGP)	0.33–0.5%	Plasma (ctDNA)	<10 days	✓
Thermo Fisher Scientific	Oncomine Precision Assay	NGS (Small panel)	0.25%	Plasma (ctDNA)	1 day	✓
Caris Life Sciences	Caris Assure® Liquid Biopsy*	NGS (Large panel CGP)	0.05–0.45%	Plasma (ctDNA)	7–10 days	RUO
Labcorp	Labcorp Plasma Complete Portfolio	NGS (Large panel CGP)	0.1–0.5%	Plasma (ctDNA)	8 days	RUO
NeoGenomics	NEO PanTracer LBx Assay	NGS (Large panel CGP)	0.17–0.31%	Plasma (ctDNA)	7 days	RUO
Roche	AVENIO ctDNA Expanded Kit V2	NGS (Large panel CGP)	0.5%	Plasma (ctDNA)	5 days	RUO
Thermo Fisher Scientific	Oncomine Pan-Cancer Cell-Free Assay	NGS (Large panel CGP)	0.1%	Plasma (ctDNA)	2 days	RUO
Tempus	Tempus® xF/xF+ Liquid Biopsy	NGS (Large panel CGP)	0.25%	Plasma (ctDNA)	7 days	RUO
Pillar Biosciences	OncoReveal™ Essential LBx	NGS (Small panel)	0.1%	Plasma (ctDNA)	~3 days	RUO
Thermo Fisher Scientific	Oncomine™ Breast cfDNA Assay	qPCR/dPCR	0.1%	Plasma (ctDNA)	2 days	RUO
BioRad Laboratories	ddPLEX *ESR1* Mutation Detection Kit	dPCR	0.010–0.025%	Plasma (ctDNA)	<8 hours	RUO
APIS Assay Technologies	*ESR1* Mutations qPCR Kit	qPCR	0.500%	Plasma (ctDNA)	2 hours	RUO
Asuragen (Bio-Techne)	Quantidex® qPCR *ESR1* exoMutation Panel	qPCR	0.120–0.150%	Plasma (ctDNA)	5–6 hours	RUO
QIAGEN	QIAcuity® Digital PCR	dPCR	NR	Plasma (ctDNA)	~8 hours	RUO
Stilla Technologies	Stilla *ESR1* (17 mutations) Crystal Digital PCR® Assay	dPCR	0.120–0.150%	Plasma (ctDNA)	Not specified	RUO
APIS Assay Technologies	APIS *ESR1* dPCR Kit	dPCR	0.100%	Plasma (ctDNA)	4 hours	RUO

Footnotes

CDx, companion diagnostic; CGP, comprehensive genomic profiling; ctDNA, circulating tumor DNA; ddPCR, droplet digital polymerase chain reaction; dPCR, digital polymerase chain reaction; FDA, US Food and Drug Administration; LBx, liquid biopsy; NGS, next generation sequencing; qPCR, quantitative polymerase chain reaction; RUO, research use only; VAF, variant allele frequency.

Utilizing ctDNA-Mediated Testing to Detect *ESR1*m[11]

- ctDNA-mediated testing with liquid biopsy (blood samples) identifies tumor-specific genomic alterations in patients with metastatic breast cancer
- NGS panel tests should be performed on blood samples

NCCN Guidelines do not recommend testing with primary archived tissue given the acquired nature of *ESR1*m.[10]

Benefits of ctDNA assays to detect mutations[11]

Less invasive

Analytically validated

Assesses multiple tumor locations in breast cancer

ctDNA testing options overview[24,30,32-34]

Method	Turnaround time	Results	Potential impact
NGS	7–14 days	Comprehensive genomic data	More informed decision-making
PCR	1 day	Efficient *ESR1* results only(single-gene test)	Faster decision-making

Detailed PCR testing overview[35]

PCR method	Detection timing	Quantification type	Assay type
qPCR	Real-time	Relative	Quantitative with standard curves
dPCR	End-point	Absolute	Qualitative
ddPCR	End-point	Absolute	Qualitative

When determining which method is appropriate for your patient and practice, consider the functional differences between timing, cost, and reporting characteristics.

Considerations for Your Practice

Collaboration between pathologists, medical oncologists, or tumor boards on *ESR1*m testing may help improve patient care.[7,36]

- Integrating ctDNA-mediated *ESR1*m testing into pathology workflows may help to identify the emergence of endocrine resistance, a valuable insight for your care team
- Evaluating your lab's capacity for ctDNA-mediated *ESR1*m testing, especially as demand increases with guideline-based adoption of liquid biopsy testing, enables preparedness
- Choosing a digital form of ordering vs manual forms improves your ordering experience

View educational resources that can help facilitate testing conversations between you and your patients with breast cancer in the **Resource Library**.

Helpful Resources

Check out these featured resources on *ESR1*m biomarker testing in metastatic breast cancer.

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FOR HCPS

Be an advocate for detection of emergent *ESR1* mutations in...

This Leave Behind highlights the clinical value of detecting emergent *ESR1* mutation in HR+/HER2– metastatic breast cancer. This guide features the what, why, whom, how, and where of *ESR1* testing for...

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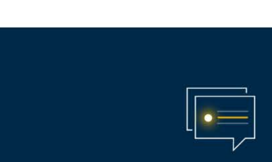

FOR PATIENTS

ctDNA-mediated testing for *ESR1* mutations in patients with...

Download this mini deck to elevate your awareness of the prevalence of *ESR1* mutations and the impact of predictive ctDNA-mediated noninvasive testing in HR+/HER2- advanced breast cancer.

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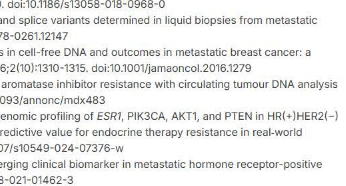

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