NHS England
Wellington House
133-155 Waterloo Road
London
SE1 8UG

17 January 2025

Dear Colleagues

Re: Implementation of genomic testing for ESR1 variants following the publication of NICE Technology Appraisal Final Draft Guidance: Elacestrant for treating oestrogen receptor-positive HER2-negative advanced breast cancer with an ESR1 mutation after endocrine treatment

Interim ESR1 genomic sample routing pathway 20th January 2025-31st March 2025.

NICE in their Final Draft Guidance (FDG) published on 19th December 2024 has stated that:

> Elacestrant is recommended as an option for treating oestrogen receptor (ER)-positive HER2-negative locally advanced or metastatic breast cancer with an activating ESR1 mutation that has progressed after at least 1 line of endocrine therapy plus a cyclin-dependent kinase (CDK) 4 and 6 inhibitor if the cancer has progressed after at least 12 months of endocrine treatment plus a CDK 4 and 6 inhibitor.

Elacestrant became available via the Cancer Drugs Fund (CDF) from 19th December 2024 in line with these recommendations and according to a set of treatment criteria which translates the NICE recommendation into a clinical guide as to use in practice.

The license for elacestrant requires identification of ESR1 variants from plasma only. Tumour tissue testing is not included in the current license. Testing for ESR1 variants in breast cancer therefore requires the genomic test to be performed on circulating tumour DNA (ctDNA) derived from a blood sample rather than a tissue sample.

ESR1 genomic test information

Testing will be available through the NHS Genomic Medicine Service (NHS GMS) and the National Genomic Test Directory will be updated on the 20th January 2025 to include ctDNA testing for ESR1. The unique test code is M3.13.

Testing for ESR1 variants will initially be available through the North Thames Genomic

Laboratory Hub (GLH) and the North West GLH as the designated genomic laboratory providers within the NHS GMS. This is an interim arrangement until 31st March 2025 and the Providers that will provide the service from 1st April 2025will be confirmed in due course.

Rather than sending to the local GLH where clinicians normally send patient samples for genetic testing, referrals for ESR1 ctDNA testing must be sent directly to the designated GLH provider for their area.

Clinicians in the following GMS geographies are required to refer samples to the North Thames GLH:

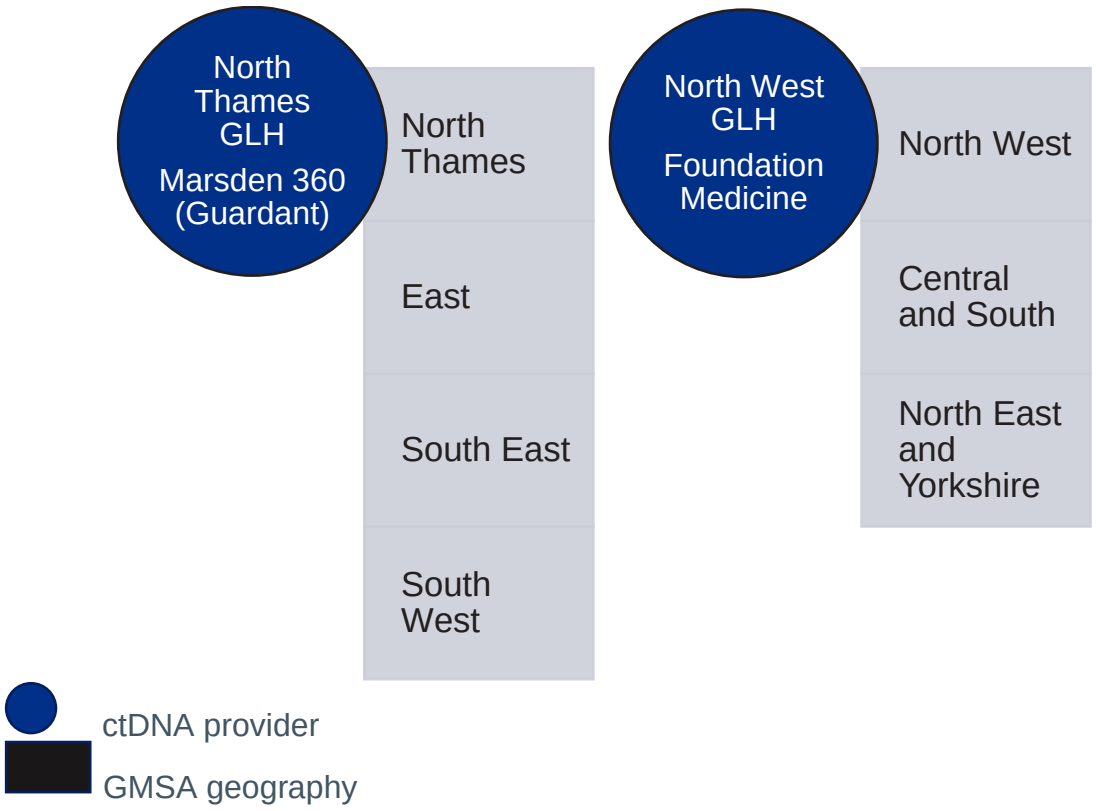
- North Thames, East, South East, and South West.

Clinicians in the following GMS geographies are required to refer samples to the North West GLH:

- North West, Central and South and North East and Yorkshire

The blood kits available from each GLH are specific to the testing method employed by the two designated GLHs, therefore it is paramount that the correct blood kit is used for the test routing.

Figure 1: Samples routing flowchart for ctDNA testing for ESR1



Resources

To support this new testing pathway, education and training webinars have been delivered and the recordings are available on the NW GLH and NT GMS websites. Please make sure your local teams review the available documents and the webinar for the correct GLH to understand the requirements as per the technology being used by that laboratory.

To access blood kits, documentation, and for any other information about ESR1 ctDNA testing please use the contact email for your designated GLH from the table below (also available on the websites).

GLH	North Thames GLH	North West GLH
Contact	Marsden360@rmh.nhs.uk	mft.northwest.ctdna@nhs.net
Website: GLH GMS	Marsden360 | The Royal Marsden https://norththamesgenomics.nhs.uk/	https://mft.nhs.uk/nwglh/test-information/cancer/ctDNA/
Address	Clinical Genomics The Centre for Molecular Pathology The Royal Marsden NHS Foundation Trust Cotswold Road Sutton Surrey SM2 5PT	NWGLH ctDNA service, 5th Floor, St Mary's Hospital, Manchester University Foundation Trust, Oxford Road, Manchester M13 9WL

We would be grateful if you could cascade this information to relevant clinical teams within your organisation to support the consistent adoption of ESR1 ctDNA testing for patients that meet the eligibility criteria for elacestrant.

Yours sincerely,

Professor Dame Sue Hill DBE FMedSci FRSB FRCP (Hon) FRCPath (Hon)
Chief Scientific Officer for England
Senior Responsible Officer for Genomics in the NHS