PIK3CA Analysis in Breast Cancer

Overview

Breast cancer is the most common cancer in the UK. Each year, about 55,000 women and 370 men in the UK are diagnosed with breast cancer, 15% of all newly diagnosed cancers are breast cancer, and 1 in 7 women will develop the disease during their lifetime. Depending on the type and stage of breast cancer, treatment can include surgery, chemotherapy, endocrine therapy, and targeted therapies[1].

Breast cancer is not a single disease, it is comprised of different subtypes that have different prognostic and therapeutic implications. Subtypes can be classified based on the presence or absence of hormone receptors on the surface of the cancer cells. The breast cancer subtype hormone receptor-positive, human epidermal growth factor receptor 2-negative (HR+/HER2) is the most common subtype, accounting for ~64% of metastatic breast cancers in women in the UK[2].

Genetic testing of breast cancers focuses on DNA changes linked to targeted therapy with phosphatidylinositol-3-kinase (PI3K) inhibitors. PI3K inhibitors slow or stop the cancer growth by blocking chemical messengers that cause cancer cells to grow and multiply.

PIK3CA (OMIM 171834): Genetic changes in the PIK3CA gene can drive cancer cell growth. PIK3CA gene variants have been identified in 30-40% of patients with HR+/HER2- breast cancer. NICE recommends the use of Apelisib (a PI3K inhibitor) plus Fulvestrant as an option for treating HR+, HER2-, PIK3CA-variant, locally advanced or metastatic breast cancer in adults, if the cancer has progressed after a CDK4/6 inhibitor plus an aromatase inhibitor[2].

Test Information

The All Wales Genomics Laboratory utilises the Illumina TruSight Oncology 500 High Throughput DNA/RNA assay for next generation sequencing using the Illumina NovaSeq 6000TM to identify nucleotide variants and gene rearrangements (fusions) in patients with solid tumours. More information on this service is available here.

Table 1. PIK3CA DNA Gene Regions

Breast	Hotspots	**PIK3CA exons 8, 10 & 21** Covers the eleven PIK3CA variants included in the BYLieve[3] and SOLAR-1[4] studies: Cys420Arg; Glu542Lys; Glu545Ala, Glu545Asp [1635G>T only], Glu545Gly, Glu545Lys, Gln546Glu, Gln546Arg; His1047Leu, His1047Arg, His 1047Tyr

A fully interpretative report will be issued.

Please be aware that variants of uncertain significance (VUS) may be identified with this test, these will be further investigated if they are in clinically relevant gene regions and reported as appropriate.

This test is performed to evaluate somatic variants within tumour samples and is not designed to assess for germline variants within the targeted genes.

Specimen Requirements

For information on sending FFPE samples refer to the CYSGODI service information sheet. Please use the PIK3CA analysis in breast request form and complete all fields (available at *http://www.medicalgenomicswales.co.uk*)

Links for further information

EDDNAL www.eddnal.com

OMIM https://www.omim.org/

Genetic Test Registry www.ncbi.nlm.nih.gov/gtr

CancerResearchUK www.cancerresearchuk.org

NICE: https://www.nice.org.uk/

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References

1. Breast cancer | Cancer Research UK
2. Overview | Alpelisib with fulvestrant for treating hormone receptor-positive, HER2-negative, PIK3CA-mutated advanced breast cancer | Guidance | NICE
3. André, et al. (2019). The New England journal of medicine, 380 (20), 1929–1940
4. Rugo, et al. (2021). The Lancet. Oncology, 22(4), 489–498

Consent for genetic testing and DNA storage is assumed when a test request and samples are received